SOUVENIR AND ABSTRACTS

45th Annual Meeting of
The Indian Association for Cancer Research (IACR)
and International Conference on

ADVANCEMENTS IN CANCER RESEARCH

DISCOVERIES, THERAPEUTICS AND CHALLENGES

10TH - 13TH APRIL 2026

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Prof. Nilofar Khan
Vice Chancellor
University of Kashmir
Hazratbal Srinagar-190006
Jammu and Kashmir

MESSAGE

I am pleased to know that the Department of Biochemistry, University of Kashmir, in collaboration with the Indian Association for Cancer Research (IACR), is organizing the 4sth Annual Meeting of the IACR and International Conference on Advancements in Cancer Research: Discoveries, Therapeutics and Challenges from April 10-13, 2026, at our university campus

The conference will bring together eminent scientists, clinicians, scholars, and young researchers to deliberate on the latest developments in cancer biology, diagnostics, therapeutics, and emerging interdisciplinary approaches. Such platforms are vital for promoting scientific dialogue, exchanging innovative ideas, and fostering collaborations that can accelerate progress in addressing one of the most pressing health challenges of our time. I am confident that the deliberations during this conference will stimulate meaningful discussions, encourage new partnerships, and inspire young researchers to pursue impactful work in cancer research.

The University of Kashmir has long been committed to nurturing excellence in teaching, research, and innovation. The Department of Biochemistry, one of the University's distinguished departments, has consistently contributed to advancements in biomedical sciences and has produced scholars who have made notable contributions in academia and research worldwide. Hosting this prestigious international gathering reflects the department's academic strength and its continued engagement with cutting-edge scientific inquiry. I trust that the tranquil surroundings of the University of Kashmir, nestled between the Dal Lake and the Zabarwan mountains, will provide an inspiring setting for intellectual exchange and collaboration.

I extend a hearty welcome to all the participants in this scientific event. I complement and congratulate the Department of Biochemistry University of Kashmir, Indian Association for Cancer Research (IACR) for this collaborative initiative. I also wish the organizers of this conference a great success.

Prof. Nilofer Khan

Prof. Subrata Sinha
MD PhD FNA, FASc, FNASc, FAMS
President IACR & National Science Chair (SERB/ANRF)
Department of Biochemistry,
AIIMS, New Delhi 110029

MESSAGE

It gives me great pleasure to welcome everyone to the 45th Annual Meeting of the Indian Association for Cancer Research (IACR) and International Conference: Advancements in Cancer Research: Discoveries, Therapeutics and Challenges held at the University of Kashmir. The annual academic feast of the IACR holds a special place in the minds and hearts of the cancer research community in India. A number of speakers and delegates from all over India and abroad, and most importantly an array of young scientists and students, are all set on the spring board to reach the next level of scientific achievement. They will inform us about and showcase their work, and the resulting discussion and interaction will fertilize our thoughts towards a sprouttng of new knowledge.

The cancer research community in India has made great strides over the years. Many of the fruits of our results are being translated in the clinics. We are at the threshold for moving from being critical and relevant to the growth of knowledge and technology, to being making a visible impact to the wellbeing of our society. As a very well established forum for interdisciplinary research, the IACR is at the forefront of integration of different levels of science, clinical medicine and technology. Long before 'interdisciplinary science' became a buzz word, the IACR was steadily and surely combining the different elements that go into cancer research into a meaningful and effective whole.

The wonderful environment of Srinagar is an ideal setting for the conference. There is no substitute for personal interactions for advancing scientific research and collaborations. The University of Kashmir, especially the Department of Biochemistry and the Organising Committee, ably steered by the Organizing Secretary, Prof Shaida Andrabi, have worked tirelessly to ensure the success of the conference. I once again welcome everyone to the conference and hope that you take back memories of wonderful scientific, academic and personal interactions.

Subrata Sinha

Prof. Subrata Sinha

Prof. Naseer Iqbal
Registrar
University of Kashmir
Hazratbal Srinagar-190006
Jammu and Kashmir

MESSAGE

It gives me immense pleasui e to learn that the Department of Biochemistry, University of Kashmir, is organizing the 45th Annual Meeting of the Indian Association for Cancer Research (IACR) along with an International Conference on “Advancements in Cancer Research: Discoveries, Therapeutics and Challenges” from 10th to 13th April 2026.

This prestigious gathering of eminent scientists, clinicians, researchers, and academicians front across the globe provides a valuable platform for sharing cutting-edge know ledge and fostering meaningful collaborations in the field of cancer research. Such initiatives are vital in addressing one of the most pressing health challenges of oui' time and contribute significantly to scientific advancement and societal well-being.

The University of Kashmir has always been committed to promoting excellence in research and innovation. Hosting an event of this magnitude reflects the growing academic stature of the University and the dedication of the Department of Biochemistry towards advancing biomedical research.

I am confident that the deliberations and interactions during the conference will lead to fruitful outcomes, inspire young researchers, and strengthen interdisciplinary approaches in cancer' research.

I congratulate the organizing committee for their efforts and extend my best wishes for the grand success of the conference.

Prof. Naseer Iqbal

Prof. Shariefuddin Pirzada
Dean Academic Affairs
University of Kashmir
Hazratbal Srinagar-190006
Jammu and Kashmir

MESSAGE

I am pleased to know that the Department of Biochemistry, University of Kashmir, is organizing the 45th Annual Meeting of the Indian Association for Cancer Research (IACR) and the International Conference on "Advancements in Cancer Research: Discoveries, Therapeutics, and Challenges". This gathering of intellectuals and scientists from across the globe and different parts of the country will provide a great opportunity to deliberate upon critical challenges and develop recommendations and strategies to combat the global burden of cancer.

Research in cancer biology has contributed immensely to our understanding of disease mechanisms and developing efficient diagnostic and treatment strategies to improve the global health. I am confident that this conference will provide our students and scholars with a platform to share knowledge and ideas, and enhance their understanding of the rapidly evolving Fealms of canCer biology and therapeutics.

On behalf of the organizing committee, I extend a warm welcome to all the scientists, delegates, and participants. I hope they enjoy their stay in the valley and find this conference academically stimulating and intellectually productive.

I congratulate the organizing committee for their dedicated efforts and wish them all the best for a successful event.

Prof. Shariefuddin Pirzada

Prof. M Sultan Bhat
Dean Research
University of Kashmir
Hazratbal Srinagar-190006
Jammu and Kashmir

MESSAGE

It is a profound honor for the University of Kashmir to host the 45th Annual Meeting of the Indian Association for Cancer Research (IACR) and International Conferehce on "Advancements in Cancer Research: Discoveries, Therapeutics and Challenges". As we gather at the Convocation Complex from April 10th to 13th, 2026, we reaffirm our commitment to fostering a robust research ecosystem that addresses some of the most pressing health challenges of our time.

Cancer remains a formidable global adversary, and the pursuit of scientific breakthroughs requires the kind of high-level, multi-disciplinary collaboration that this conference exemplifies. The scientific program, featuring sessions on Cell Cycle Regulation, Immunotherapy, CAR T Cell Therapy, and Signal Transduction Pathways, highlights the cutting-edge nature of the research being discussed here. We are particularly privileged to welcome an esteemed gallery of speakers from world-class institutions, including Emory University, Harvard University, AIIMS, IISc, and various IITs, whose presence elevates the academic stature of this event.

At the University of Kashmir, we believe that research is not a solitary endeavor but a collective journey toward discovery. This meeting provides an invaluable platform for our faculty and students to interact with global leaders in oncology, share their findings during the Oral and Poster sessions, and forge partnerships that will lead to future therapeutic innovations. The focus on Modern Trends in Diagnosis and Predictive Precision through AI platforms reflects the necessary evolution of our field toward more personalized and effective patient care.
I would like to extend my heartfelt appreciation to the Department of Biochemistry and the organizing committee, led by Prof. Shajrul Amin, for their dedication in hosting this prestigious meeting at the University.

I wish all the delegates a highly productive and intellectually enriching experience. May the deliberations in this four day event spark new ideas that bring us closer to a future free from the burden of cancer

Prof. M Sultan Bhat

Prof. Fayaz Ahmad
Dean, School of Biological Sciences
University of Kashmir

MESSAGE

I am pleased to know that about 400 delegates have register ed for presentations during the 45th Annual Meeting of the Indian Association for Cancer Research (IACR) and International Conference on "Advancements in Cancer Research: Discoveries, Therapeutics and Challenges". We are humbled as well as encouraged by this overwhelming response from the scientific fraternity and thank each participant for their valuable contribution.

We hope that the deliberations during this conference. to be held from April 10-13, 2026, will be highly fruitful. We anticipate that new ideas and approaches will emerge for a better understanding of cancer at the cellular and molecular levels. By exploring cutting-edge themes such as Immunotherapy, CAR T Cell therapy, and Signal transduction pathways, we aim to understand and pave the way for more effective management of this complex disease.

We also expect that this conference will provide a vital platform for transforming the fragmented research landscape into a collaborative and co-operative venture. This synergy is urgently needed to realize the ambitious goals of advancing healthcare outcomes through predictive precision and innovative therapeutics.

We are grateful to the Indian Association for Cancer Research (IACR) for entrusting the responsibility of hosting this 45th edition to the Department of B iocliemistry, University of Kashmir, Srinagar. I am glad that the organizers of the conference are working coherently to make this international event a success.

I hope that the participants attending this conference physically at our Convocation Complex wit 1 have a productive time in Kashmir and wil I visit us again in the near future for similar scientific endeavors.

Prof. Fayaz Ahmad

Prof. Shajrul Amin
Head, Department of Biochemistry
University of Kashmir

MESSAGE

I am excited to welcome distinguished scientists, clinicians, researchers, scholars, and students from India and across the globe to the "45th Annual Meeting of the Indian Association for Cancer Research (IACR) and the International Conference on "Advancements in Cancer Research: Discoveries, Therapeutics and Challenges." It is indeed a matter of pride for the Department of Biochemistry, University of Kashmir, to host this prestigious scientific gathering.

Cancer research continues to evolve rapidly, driven by advances in molecular biology, genomics, diagnostics, and targeted therapeutics. This conference will provide an important platform for bringing together leading experts, early-career researchers, and students to share knowledge, present cutting-edge findings, and engage in meaningful scientific dialogue. I am confident that the discussions and interactions during the conference will stimulate new ideas, strengthen collaborations, and contribute to addressing the global challenges posed by cancer.

The Department of Biochemistry has always remained committed to promoting excellence in teaching and research in the biomedical sciences. Hosting this conference reflects our continued dedication to fostering scientific exchange and encouraging young scholars to pursue impactful research in areas of critical societal relevance.

I express my gratitude to the Indian Association for Cancer Research, invited speakers, collaborators, and all participating delegates for their enthusiastic support and participation. I would like to place on record my sincere appreciation for the organizing committee, whose dedication, teamwork, and tireless efforts have made this event possible.
The program has already shaped up to be excellent and the networking opportunities will be indeed outstanding. The backdrop of the beautiful and historic city of Srinagar will add to the pleasure of the conference and provide lasting memories beyond the science.

I add my best wishes for a successful and fruitful conference and my thanks to all organizers.

Prof. Shajrul Amin

Dr. Shaida Andrabi
Department of Biochemistry
Organizing Secretary-IACR 2026

MESSAGE

It is a matter of great pleasure for the Department of Biochemistry and the University of Kashmir to host the 45'h meeting of the Indian Association for Cancer Research and International Conference at the University of Kashmir between April I 0-13, 2026. We hope that it will be an outstanding conference given that very reputed scientists from India and abroad have kindly agreed to come to this event and share their cutting-edge research with the audience. Cancer, we all know, has become one of the most lethal chronic diseases around the world. While there have been tremendous advancements in the field of cancer diagnosis and treatment, yet cancer biologists and oncologists are still struggling to overcome the problem of chemoresistance. Development of non-invasive, affordable, fast and advanced molecular techniques for an early diagnosis Of cancer are gaining popularity, and hold a lot of promise to substantially reduce the mortality. The emergence of liquid biopsy approaches and artificial intelligence are the latest additions to this field that will substantially help to address many of these issues and find efficient, targeted and long-lasting treatments against this disease. In this conference, we have invited renowned scientists from diverse backgrounds who have carried out outstanding work and will discuss their findings during this event. This meeting will therefore help scientists and students to share their ideas/ resources, collaborate, network and hence contribute to the advancement of research at a much faster pace than would be otherwise possible. Many of these findings will certainly have translational value and hence help directly or indirectly in the treatment of this deadly disease.

I also want to take this opportunity to offer my profound gratitude to various stakeholders who have played an enormously significant role in helping us to organize this prestigious conference successfully. These include the past and the present IACR executives who accepted our request and trusted our ability to be able to organize this grand event. I also thank our University administration to allow us to hold this conference and offer us an unwavering support. This includes the Vice Chancellor, Dean Academics, Dean Research, Registrar, Dean Biological Sciences and the Director, Convocation Complex. I am also highly thankful to Prof. Shajrul Amin, Head Department of Biochemistry, Prof. Nazir A Dar, Dr M Ashraf Dar, Dr Gulzar Ahmad, Dr Shabbir Ahmad Mir, all members in the office of the Department, research scholars, and all members of the organizing committee, within and outside the Department, who have offered all sorts of support that is needed to organize this event. I also want to specially mention the names of Prof. M Ayub Qadri, Prof. V Radha and many other colleagues who offered invaluable support during this journey. I also want to thank all the funding agencies namely DBT, ANRF, JKSTIC and all the sponsoring companies

who offered financial support which helped us to conduct this event successfully. I also want to acknowledge the support of Mr Aasim Banday from IT&SS of Kashmir University who took keen interest to design and constantly update/improve the website. I also want to thank Mr Sajjad Ahmad from Maxus Solutions for elegantly designing all the electronic and printed material contents that added a lot of value to this conference. I appreciate his patience during this long process as we used to constantly bother him to make multiple changes for each document.

I sincerely hope that this conference will be able to meet its objectives and goals, foster a collaborative scientific temperament at our University and among the participants, and play a pivotal role in promoting cutting edge research in the field of cancer biology, both at the regional as well as the national level.

Finally, I must express my profound thanks to all the outstanding speakers who, despite their extremely busy schedule, accepted our request to come to this event and share their invaluable findings and knowledge. I must also thank other notable participants who accepted our invitation to be chairs of the sessions, judges in the oral and poster presentations or play a role in other proceedings of the conference. And finally, thanks to all the participants who showed their keen interest to come to this conference and add grace to this grand event.

I also hope that all the participants will have a great time during this memorable event. We had carefully chosen the timings to convene this meeting in the spring season, so that the participants would have a truly memorable time in Kashmir. We hope to have an exciting conference, which would encourage us to conduct even more prestigious events in the coming years.
Thank you

Dr. Shaida Andrabi

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S. No.	Abstract Code	Author/s	
Abstracts of Invited Speakers (Alphabetical order)			
1.	I-1	Prof. Ambarish Ghosh	Nanobots for cancer therapeutics
2.	I-2	Prof. Amit Dutt	Genomic drivers of endocrine therapy resistance in breast cancer
3.	I-3	Dr. Abhijit Majumder	Microfluidics-Based New Approach Methodologies (NAMs) in Cancer Research
4.	I-4	Dr. Arnab Mukhopadhyay	TORC2-mediated Metabolic Rewiring in Colorectal Cancer
5.	I-5	Dr. Arvind Panday	Chromatin Remodeling Regulates Repair Pathway Choices at the Stalled Replication Forks
6.	I-6	Dr. Ashraf Dar	Beyond p53: Mdm2 regulates cell cycle by targeting $CRL4^{Cdt2}$ E3 ubiquitin ligase
7.	I-7	Dr. Asim Rizvi	Robotics in Oncology: Redefining Precision in Cancer Surgery
8.	I-8	Prof. Chandi C Mandal	Breast cancer cells exploit unexplored dysregulated metabolic regulators to augment cell plasticity for favouring their progress
9.	I-9	Prof. Fazl Q Parray	Rectal Cancer: Lessons from 25 years of Surgical Practice
10.	I-10	Prof. G.P. Talwar	Development of an Immunotoxin that kills World-wide available Drugs Resistant Cancers Expressing Ectopically hCG
11.	I-11	Prof. Gaurav Prakash	Emerging Role of Low-dose Venetoclax in Management of Acute Myeloid Leukemia-comparing Efficacy and Pharmacokinetics of Venetoclax 50 mg with 400mg in Induction therapy
12.	I-12	Prof. Geetanjali Sachdeva	GPER-1 (G Protein-Coupled Estrogen Receptor-1) Activation: A Potential Strategy for Chemoprevention of Prostate Cancer
13.	I-13	Dr. Gowhar Shafi	OncoPredikt - An AI Platform: Revolutionizing Cancer Care Economics through Predictive Precision and Cost-Effective Solutions
14.	I-14	Dr. Hifzur R. Siddique	Chemoresistance of Cancer Stem Cells: Is Chemosensitization an Ideal Approach for Reversing Therapy Resistance?
15.	I-15	Prof. Javeed Iqbal	Peripheral T-Cell Lymphomas: Genomic classification, diagnostic refinement and disease pathobiology

16.	I-16	Prof. Jonathan Pines **(Plenary Lecture)**	Do nucleosomes hold the key to genomic stability?
17.	I-17	Prof. Lalit Kumar	Evolving Paradigms in Myeloma: Stem Cell Transplant and Emerging Immunotherapies
18.	I-18	Dr. M. Shafi Kuchay	When and Where Proteins Are Destroyed: Mechanisms of Spatiotemporal Control of Membrane Proteostasis and Disease
19.	I-19	Dr. Maddika Subba Reddy	Beyond Catalysis: Non-Canonical Functions of Phosphatases
20.	I-20	Dr. Manas Kumar Santra	From Genome Protection to Cancer Treatment: The Impact of Dynamic Ubiquitin Signaling
21.	I-21	Dr. Mayurika Lahiri	The Making of a Renegade: Coordinating DNA Damage Response and Apoptotic Evasion in Breast Cancer Origins
22.	I-22	Dr. Mir Mohmad Hussain	Immune checkpoint Inhibitors in Hodgkin's Lymphoma: Transforming the therapeutic Landscape
23.	I-23	Dr. Mohd Jamal Dar	Discovery of Novel Therapeutic Agents Using Structure Based Drug Design
24.	I-24	Prof. Nazir Ahmad Dar	Releasing the Brake on RhoA: Phosphorylation-Dependent Sequestration of RhoGDIα by 14-3-3ε Drives Cancer Cell Migration
25.	I-25	Prof. Rafi Ahmed ***(Keynote Lecture)***	What is T Cell Exhaustion?
26.	I-26	Dr. Riyaz Ahmad Mir	R2TP-Bridging peptides: A Novel Therapeutic strategy to restore tumor suppressor networks in cervical cancer
27.	I-27	Prof. Rizwan Romee	Novel CAR T cell approaches to overcome immune escape in solid tumors
28.	I-28	Dr. Sachin Kotak	Material Property of Spindle Poles Determines the 3-Dimensional Nuclear Architecture
29.	I-29	Dr. Sagar Sengupta **(IACR Oration Lecture)**	A Personal Journey How Discovery Science Can Co-Exist With Translational Biology
30.	I-30	Prof. Sameer Bakhshi	Cancer Immunotherapy and Gut Microbiome: Is there a Relationship?
31.	I-31	Prof. Sathees C. Raghavan	Targeting Nonhomologous End Joining: Potentiating Cancer Therapy through DNA Repair Disruption
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33.	I-33	Prof. Sharmila Mande	Gut Microbiome and Cancer
34.	I-34	Prof. Shilpee Dutt	Unveiling GBM's Survival Blueprint: From Senescence Escape to DNA Repair Modulation
35.	I-35	Dr. Shiva Bamezia	R-Loop Homeostasis as a Selective Vulnerability in Cancer Stem Cells
36.	I-36	Dr. Sutapa Mukherjee	Cholesterol metabolic reprogramming and PI3K/Akt/mTOR hyperactivation are predictive of carboplatin resistance in High-Grade Serous Ovarian Carcinoma
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1.	IACR-635	Dr. Nazia Chaudhary ***(Kamat/Jaju Award)***	Targetable Metabolic Dependencies Drive Therapy Resistance in Treatment-Refractory Colorectal Cancer
2.	IACR-799	Dr. Anshika Chauhan ***(Kamat/Jaju Award)***	Transcriptomic profiling identifies metastasis-competent subtypes of circulating tumour cells, driven by microbial signatures in oral squamous cell carcinoma: development of a predictive gene panel for early relapse
3.	IACR-666	Dr. Showkat Yahya ***(Post-doc Travel Award)***	Proteomic Identification of 14-3-3γ Glutathionylation Reveals an LCN2-Mediated Redox Axis in Colorectal cancer
Abstracts Selected for Oral Presentation (Ph.D students)			
1.	IACR-601	Aijaz Ahmad Rather, Ritika Sachdeva, T R Santhosh Kumar	Mechanistic and Quantitative Dissection of Car T Cell-Induced Cytotoxicity Using A Dual Live-Cell Biosensor Platform
2.	IACR-610	Samya Dey, Rumpa Mahata, Koushik Saha, Sourav Pal, Soumi Basu, Debmalya Bhattacharyya, Deepam Pushpam, Rajib De, Arindam Talukdar, Manas K Santra, Somsubhra Nath	Beyond Kinase Domain Mutations In BCR-ABL1: A Preclinical Insight Into A Novel Mutation Pair Of SH3-SH2 Domain Underlying Imatinib Resistance In Chronic Myeloid Leukemia
3.	IACR-622	Akshay Subodh Paradkar, Sanjeev K Waghmare	Dab2 Loss Delays Tumour Initiation and Prevents Disease Progression in Murine Squamous Cell Carcinoma
4.	IACR-627	Sanchari Chatterjee, Barun Mahata, Abhisek Sarkar, Debarati Paul, Subhra Ghosh Dastidar And Kaushik Biswas	Dissecting The Molecular Events Involved In GM2 Mediated Modulation Of Tumor Suppressor Hippo-Yap/Taz Signaling Axis

5.	IACR-634	Muqtada Ali Khan, Saumya Ranjan Satrusal, Deepakash Das, Abhipsa Sinha, Biswajit Mandal, Arihant Dey, Priyanka Rai, Akash Singh, Vineeta Rai, Tanweer Hussain, And Dipak Datta	When A GPCR Meets the Ribosome: An Intracellular CXCR4-RPL35A Axis Governs Translational Control and Metastasis In TNBC
6.	IACR-637	Bushra K. Khan, Prerana D. Uttankar, Bhagya Shree Choudhary, Nazia Chaudhary, Rinki Doloi, Sorab N. Dalal	Identification of Mechanisms by Which Lcn2 Promotes Autophagy and Tumour Progression in Colorectal Cancer
7.	IACR-647	Geeta S Boora , A Chauhan, Jaimati Bakshi, Arindam Maitra, Arnab Pal	Spatial Transcriptional Profile Reveals Aggressive Circulating Tumour Cell Dissemination Driving Early Recurrence In Oral Squamous Cell Carcinoma
8.	IACR-651	Smriti Suri, S Ghoshal, S Mitra, J Bakshi, A Pal	Diagnostic and Prognostic Significance of LCN2, MMP9, and the LCN2/MMP9 Complex in Oral Squamous Cell Carcinoma
9.	IACR-662	Shivani Bansal, Lokendra Kumar Sharma, Chandi C. Mandal	A Specific Sub-Population Derived from Breast Cancer Cells Augments Oncogenic Activity by Exploring a Calcium-Associated Scaffold Protein
10.	IACR-681	Omkar Dhurat, Kunal Nandgaonkar, Vaibhavi Bagade, Ananya, Sharathchandra Arandkar	Targeting Tumor-CAF Alliance: Decoding TMEs Role in Drug Resistance
11.	IACR-706	Suhail Ahmad, Ashwin Butle, Akshay Karn, Roma Sunder, Rohit Mishra, *et al.*	CDKN1B inactivation Impacts ER Signaling and Drives Resistance to Endocrine Therapy in Breast Cancer
12.	IACR-730	Sommya Sinha, Nirlipta Khandai, Adesh Shrivastava, Sanjeev Shukla	Hypoxia-Induced RBM47 Regulates the Alternative Splicing of FN1 in Glioblastoma via Intracellular and Exosome-Mediated Mechanisms
Abstracts Selected for Oral Presentation (Mid-level faculty/Postdocs)			
1.	IACR-603	Abdul Wasai & Adhiraj Roy	Synthesis and Biological Evaluation of a Novel Zinc (II) Trinuclear Complex with Tetradentate Schiff Base Ligand and Azido Ion as a Potent PI3K/AKT and Ras/MAPK/ERK Signalling Dual Inhibitor in Prostate Adenocarcinoma

2.	IACR-621	Dr. Zeeza Hussain Shah, Dr. Shashwat Lohia, Dr. Sheikh Muzamil, Dr. Jaskaran Vir Singh, Dr. Mohmad Hussain Mir, Dr. Syed Nisar Ahmad, Dr. Ulfat Ara Wani, Dr. Faisal Rashid Guru	Familial Clustering of Cancers: 2 Families and 2 Cancers in 1st Degree Relatives: CML In A Mother-Daughter Duo and Multiple Myeloma in a Father-Son Pair
3.	IACR-636	Swathi K A, Soumitri Santra, R Srivatsan, Prathibha Ranganathan	Drug Specific Gene Expression Signatures of Cancer Chemoresistance
4.	IACR-644	Qaiser Farooq Dar , Gulbadin Farooq Dar, Ashiq Hussain Bhat	Artificial Intelligence based Visualization of Cancer-Related Viral Infections for Surveillance and Risk Stratification
5.	IACR-656	Ashiq Hussain Bhat, Krishna Pandey, Qaiser Farooq Dar	Cancer Screening Uptake Among Women in Jammu & Kashmir: District-Wise Analysis from the Fifth Round of the NFHS-5 (2019-2021)
6.	IACR-703	Udita Jindal, Astha Soni, Deepak Kumar, Neeraj Jain	Oncogenic Signaling and Synthetic Vulnerabilities to Overcome Immune Escape in Chemo-Immunotherapy Resistant B-Cell Lymphoma
7.	IACR-707	Leena Chandrasekhar, Babu T D, Vaka Harideep, Arjth PP, T R Santhosh Kumar	Parkin-Driven Mitophagy promotes Stress Adaptive Lung Metastasis in Melanoma
8.	IACR-722	Nazia Nazam, Sorina N. Shirley, Joel C. Opara, Shamza Manzoor, Maryam Shaikh Jianmei W. Leavenworth, Michael Ohlmeyer, Elizabeth A. Beierle	Targeting Therapy Induced Senescence via PP2A Activation In Neuroblastoma
9.	IACR-733	Zubair Ahmad Najar, Mohammad Hussain Mir, Ajaz Nabi Koul	Paraneoplastic Syndromes as the Initial Manifestation of Occult Malignancies: A Seven-Year Observational Study from a Tertiary Care Center in Kashmir
10.	IACR-749	P.K.Singh, M.L.B.Bhatt	Evaluation of Whole Genome Expression Data of Indian Urinary Bladder Cancer Patients
11.	IACR-750	Nathiya Muthalagu	Myc Dependent Mouse Model of Pancreatic Neuroendocrine Tumours: A Preclinical Model for Aggressive Proliferative Subtype
12.	IACR-755	P Kakani, A Bansal, B Jithin, R Maria, A Brahma, A Panda, Sa Mutnuru, S Shukla	Metabolism Associated Epigenome Mediates Differential Alternative Splicing In Breast Cancer And Its Implication In Therapy Resistance

13.	IACR-756	Naveen Soni, Bhawana Bissa	Synergistic Targeting of Autophagy and Exosome Biogenesis: The GABARAPL2-Alix Regulatory Axis in Breast Cancer
14.	IACR-797	Dr Sahila Nabi, Seema Mushtaq, Iqra Nisar	Barriers for early detection of cancer amongst women in a rural setting in kashmir- A cross sectional sectional Study
15.	IACR-798	Dr Darakshan	Awareness Regarding Breast Cancer Screening Among ASHA Workers in the Field Practice Area of Government Medical College: A Cross-Sectional Study
16.	IACR-799	Kavitha Premkumar, Soundharya Ramu, Mohit Kumar Jolly and Bhavani S. Shankar	Increased production of TGF-β^{+} tumor evoked B regulatory cells by tumorderived PGE2 is associated with poor survival in PTGS2^{hi} cancers.
17.	IACR-800	Vipul K. Pandey, Kavitha Premkumar, Priya Kundu, Bhavani S. Shankar	PGE2–EP4–miR-365 axis drives IL-6/STAT3-dependent dendritic cell dysfunction and tumor progression
18.	IACR-804	Dr Seema Mushtaq	Strengthening Cancer Screening Programs in India: Public Health Challenges and Opportunities – A Community-Based Study from a Rural Field Practice Area of North Kashmir
19.	IACR-805	Vidisha Tripathi	LncRNAs as orchestrators of genome maintenance
20.	IACR-806	Puneet Bhardwaj, Vinita Suri, Nalini Gupta, Indu Sharma	Therapeutic efficacy of co-administered Cisplatin and Vincristine in RL95-2 endometrial cancer cell line
21.	IACR-807	Vishnu Priy Muralia, Shamjith S, Kaustabh Kumar Maiti	Design and Optimization of a Sandwich Magnetic Capture System for Serum Pancreatic Cancer Biomarker Detection via SERS Immunoassay
22.	IACR-808	Shubhraneel Saha, Kavita Kundal, Saloni Sainger, Himanshu Shekhar, Samiksha Kukal, Anjali Bhat, Shilpi Minocha, Manoj Phalak, Rahul Kumar, Santosh Mathapati, Saran Kumar	Perfusion-Driven Spatial Methylome Heterogeneity in Glioblastoma
Abstracts selected for Poster Presentation			
1.	IACR-602	Roy A	A Pathophysiological Affair Between Protein Kinase D and Epithelial Ovarian Cancer: Promising Roadmap Towards Translating the Mechanism From Bench To Bedside

2.	IACR-604	Snehal Bhatia, Dr. Mayurika Lahiri	From Survival to Stemness: Api5 Reprograms Breast Epithelial Cells via Wnt/ÃŸ-Catenin
3.	IACR-605	Zubair Ahmad Mir, Amrutha Mohan, Snijesh, Dr Tessy Thomas Maliekal	Tif1γ As a Double-Edged Sword in Oral Cancer
4.	IACR-606	Manav Goenka, Bismita Nayak	Development of Bio-Compatible Curcumin-Loaded BSA Nanoparticles with Enhanced Anti-Cancer and Anti-Bacterial Potential
5.	IACR-607	Anurupa Mistry	Exploring the Antitumor Effects of Berberine On Migration And Proliferation Against U87mg Glioblastoma Cell Line
6.	IACR-608	Chitrakshi Chopra, Chandra Prakash Prasad and Manish Kumar	Balancing Efficacy and Safety: Advances In Understanding And Mitigating Doxorubicin-Associated Cardiotoxicity
7.	IACR-609	Nawneet K Kurrey, Pankaj Singh Chouhan, Mahak Bhandari, Kavita Madipalli	Chemopreventive Effects of Bioactive Compounds From Tulsi *(Ocimum Sanctum)* Against Ovarian Cancer: In Vitro And Animal Model Investigations
8.	IACR-611	Nandani Dharwal, Dr. Heena V. Dave	Subtype-Specific Metastasis-Associated Gene Signatures in Breast Cancer: An Integrative TCGA-Based Bioinformatics and In vitro Experimental Study
9.	IACR-612	Sanjana Sarkar, Jimlee Saikia, Murali Dharan Bashyam	A Tale Of Two ARID2s: Truncating Mutations Flip A Chromatin Remodeler Into An Oncogenic Driver
10.	IACR-613	Deepshikha Rathore, Heena V. Dave	MicroRNAs As Metastatic Markers For Prognosis And Therapeutics In Triple-Negative Breast Cancer: A Bioinformatics, Preclinical, And Clinical Study
11.	IACR-614	Ajay J Malik, Mayurika Lahiri	Investigating the Role of Api5 during Replication Stress
12.	IACR-615	Aditi Singh & Adhiraj Roy	Elucidating the Prognostic and Pro-Tumorigenic Potential of Protein Kinase D2 (PKD2)/ Laminin Subunit A5 (LAMA5) Signalling Axis In High Grade Serous Epithelial Ovarian Cancer
13.	IACR-616	Hetal Bhadricha, Abhijit Sarma, Bhalchandra J. Kulkarni *et al.*	PSP94/PSA Ratio As A Cost-Effective Adjunct Biomarker For Enhancing Prostate Cancer Risk Stratification
14.	IACR-617	Himanshi Goyal, Veena Puri, Jyotdeep Kaur	The Linc00657â€“mir-17 Axis Drives Upr Activation In Alcohol-Associated Hepatocellular Carcinoma
15.	IACR-618	Supriya Halder, Salona Kar, Swayambara Mishra,	Investigating Microbial Intervention against Peritoneal Metastasis Of Gastrointestinal

		Ritwik Biswas, Shantibhusan Senapati	Cancers
16.	IACR-619	Ritwik Biswas, Amlan Priyadarshee Mohapatra, Supriya Halder, Salona Kar, Sneha Swain, Shantibhusan Senapati	High-Throughput Screening of FDA-Approved Drugs Identifies Potential Inhibitors of TGF- β-induced Activation of Cancer-Associated Fibroblasts in Pancreatic Cancer
17.	IACR-620	Preeti, Alo Nag	Hpv16 E7 Hijacks Plk1 To Collapse Cell-Cycle Control In Cervical Cancer
18.	IACR-623	Devaunshi Sadanand Mudodi, Dhanshree Janwade, Murali Dharan Bashyam	Tumor-Specific Cytoplasm-Localized ARID1B Regulates RNA Metabolism
19.	IACR-624	Bhanu Teja Korra, Rahul Kumar	Onco-eQTM: An Interactive Platform For Pan-Cancer Epigenetic Regulation
20.	IACR-625	Salona Kar, Amlan Priyadarshee Mohapatra, Deepti Parida, Swayambara Mishra,Supriya Halder, Ritwik Biswas, Sneha Swain	Isolation and Characterization of Novel Mouse Pancreatic Cancer Cell Lines From Kc (Krasg12d, Pdx1-Cre) Model of Pancreatic Adenocarcinoma
21.	IACR-626	Jimlee Saikia, Sanjana Sarkar, Murali Dharan Bashyam	Inactivation of ARID2 Disrupts PBAF Assembly and Promotes Colorectal Tumorigenesis
22.	IACR-628	Aishwarya Ray, Debojyoti De, Kaushik Biswas	Decoding Extracellular Matrix Stiffness Related Gene Signatures and Its Modulation by Plant Derived Flavonoid Eriodictyol in Inhibiting Metastasis
23.	IACR-629	Sumaiya Moiz, Barsha Saha, Varsha Mondal[a], Debarati Bishnu, Biswajit Das, et. al.	Differential Expression of miRNAs between Young-Onset and Late-Onset Indian Colorectal Carcinoma Patients
24.	IACR-630	Supti Das, Sumaiya Moiz, Rubi Das , Biswajit Das, Soumen Das, Rahul Agarwal, Indranil Dey, Amitava *et al.*	Stratification of CRC Tumours into Consensus Molecular Subtypes Using an Immunohistochemical Protein Marker Panel: An Eastern India Cohort Study
25.	IACR-631	Madanmohan Mishra	Antiproliferative and Anti-Metastatic effects of ethanolic Leaf Extract of *Cascabela Thevetia* against Cholangiocarcinoma Cells
26.	IACR-632	Saumya Ranjan Satrusal, Indranil Chatterjee, Arpon Biswas, Gaurav Srivastava, Arpita Banerjee, Muqtada Ali Khan, Biswajit Mandal, *et al.*	Breaking The BRCAness Barrier: Discovery of a First-In-Class PARP/mTOR Dual Inhibitor As Triple-Negative Breast Cancer Therapy
27.	IACR-	Swastik Arya, Bismita	Development and Characterization of

	633	Nayak	Pegylated Chitosan Nanoparticles Co-Loaded With Curcumin and Thymoquinone for Glioblastoma Therapy
28.	IACR-638	Benchamin Abraham, Dhananjay Virkar, Ayushi Upadhyay, Mayurika Lahiri	Api5 Regulates Genomic Integrity by Modulating DNA Damage Response and Repair
29.	IACR-639	Dr Farah Sameem	Skin as a Window to Hidden Malignancy: A Three-Year Study of Paraneoplastic Dermatoses in a Tertiary Care Centre
31.	IACR-640	Avi Pandey, Amol Lonare, Sorab Nariman Dalal	Role of 14-3-3s in Regulating Therapy Resistance and Tumour Progression in Breast Cancer
32.	IACR-641	Apoorva Abikar, Mohammad Mehaboob Subhani Mustafa, *et al.*	Comparative Transcriptome of Normal and Cancer-Associated Fibroblasts
33.	IACR-642	Dr Pandit Abrar Ahmad	Beyond Clinical Mimics: Histopathological Unveiling of Atypical Skin Malignancies
34.	IACR-643	Kainat, Prateekshya Das, Amere Subbarao Sreedhar	Understanding the Crosstalk Between Iron and Cellular Energy Metabolism in Human Breast Cancer Cells
35.	IACR-645	Ab Nasir Sheikh, Gulzar A Bhat , Sukhdeep Kumar, Farooq Ahmad Ganie, Syed Mudassar Jan	Decoding the Transcriptomic Landscape of Esophageal Squamous Cell Carcinoma in Kashmir: Insights from a High-Risk Population
36.	IACR-646	Prerana Uttankar , Bushra Khan , Bhagya Shree Choudhary , Rinki Doloi , Sorab Nariman Dalal	Turning The Tables on KRAS: How LCN2 Rewires EGFR Sensitivity In Colorectal Cancer
37.	IACR-648	Sumaiya Sabnam, Dr Murali Dharan Bashyam	Context-Dependent Roles of Arid1b: Evaluating A Possible Non-Canonical Oncogenic Behaviour of ARID1B in Specific Cancer Types
38.	IACR-649	Sneha G. Patil, Monika A. Jaiswal, Sorab N. Dalal	Comparative Proteomic Analysis of 14-3-3 Ligand Association and Their Specific Function
39.	IACR-650	Sakshi, S Thakur, B Rai, R Srinivasan, A Pal	KMT2C Mutation (C>A; chr7:151882672) Predicts Treatment Response in Indian Cervical Cancer Patients
40.	IACR-652	Sushree Sangita Kar, Rahul Kumar	An Ml-Based Integrative Prognostic Model for Triple-Negative Breast Cancer using Single-Cell and Bulk Transcriptomics
41.	IACR-653	Mrinmoyee Mondal, Souradeep Biswas, Priya Samanta, Shampa Pakhira, Jhinuk Basu, Rituparna Ghosh, Subhadip Hajra, Prosenjit Saha	Modulation of LAT1 Expression in Triple-Negative Breast Cancer by Natural Compound Rutin through HIF1/MTOR Pathway

42.	IACR-654	Souradeep Biswas, Jhinuk Basu, Mrinmoyee Mondal, Priya Samanta, Shampa Pakhira, Rituparna Ghose, Subhadip Hajra, Prosenjit Saha	Rutin Synergizes with Paclitaxel to Elicit Immunogenic Tumor Cell Death and Re-Programmed the Tumor Microenvironment in TNBC
43.	IACR-655	Zahoor, F., Shafi, H., & Mustafa, S. A.	Sexuality as a Determinant In Quality Of Life Among Post-Mastectomy Breast Cancer Patients
44.	IACR-657	Sayak Banerjee, Priyanka Adhikary, Sankalan Mitra, Nisha Bhat, Soumen Das, Subhadeep Karanjai, Alangkar Saha, Zulkarnan Neguive *et al.*	Clinical Implications of Circulating Cell-Free MALAT1 in Plasma as Liquid Biopsy Biomarker for Risk Stratification to Predict Prognosis in Oral Squamous Cell Carcinoma Patients
45.	IACR-658	Afiya Dalwai, Eeshrita Jog, Ashwin Kumar Jainarayanan, Alessandro La Ferlita *et al.*	Exploiting Lipid Metabolism Dependencies to overcome Therapy Resistance in Colorectal Cancer
46.	IACR-659	Shampa Pakhira, Souradeep Biswas, Priya Samanta, Rituparna Ghosh, Mrinmoyee Mondal, Jhinuk Basu, Prosenjit Saha, Subhadip Hajra	Revealing the Potential Role of 3, 3'-Diindolylmethane to Enhance the Efficacy of 5-Fluorouracil Therapy in Colorectal Cancer through Modulation of Mitochondrial Apoptosis Pathway
47.	IACR-660	Christy Moncy A, Gaurav Gade B, Afiya Dalwai A, Mufaddal Kazi C, D, Avanish Saklani *et al.*	Role of ACSL 4-Mediated Lipid Metabolism in Colorectal Cancer Drug Resistance and Metastasis
48.	IACR-661	R S Valdar, M A Hussain, M Kulkarni1, S Laha	Fractionated Radiation Alters Epigenetic Signatures, Instrumental in Regulating DNA Repair in Breast Cancer Cells
49.	IACR-663	Pankaj Kumar Mahato, Saikishore Ramanathan, *et al.*	Role of Transforming Growth Factor Beta-Induced (TGFβI) in Cancer-Associated Fibroblast and its Influence on TME
50.	IACR-664	Manisha Mohapatra , Subarno Paul , Chinmay Das, Aakash Goswami, Aashi Thakur, Tithi Parija	Study of the Anti-Cancer Effects of Quinacrine & Resveratrol Drug Combination against Breast Cancer
51.	IACR-665	Jyoti Poswal, Vidya RS, And Chandi C Mandal	Gossypin Suppresses Mutant KRAS G12d Driven Oncogenic Activity by Considering NFκB Mediated Lipid Dysregulation in Pancreatic Cancer
52.	IACR-667	Aakash Goswami, Subarno Paul, Chinmay Das, Subhasmita Bhal, *et al.*	Quinacrine Suppresses Metastasis and Angiogenesis of Oral Squamous Cell Carcinoma by Inhibiting Tumor-Associated Macrophage-Derived Inflammatory Cytokines

53.	IACR-668	Nandini Sahani, Deeptashree Nandi, Pradeep Singh Cheema, Alo Nag	Hepatitis B Virus X Protein Upregulates Foxm1, A Tumor Promoter in Hepatocellular Carcinoma
54.	IACR-669	Ankit Dekate, Jaya Ghosh, Pritha Ray	PI3K Inhibition by Alpelisib Augments Cisplatin Induced Cell Death in Epithelial Ovarian Cancer Cells
55.	IACR-670	Riyaz, M., Dar, I. A., Shafi, H	Care-Giving Burden and Suicidal Ideation among Caregivers of Cancer Patients: Moderating Role of Resilience and Socioeconomic Status
56.	IACR-671	Md Fazlur Rahman, Ozair Alam, Asif Husain	Click-Enabled Design and Synthesis of Nitrogen-Containing Hybrid EGFR Inhibitors with in Silico Insights and Anticancer Evaluation
57.	IACR-672	Dr. Sheikh Muzamil, Dr. Zeeza Hussain Shah, Dr. Jaskaran Vir Singh, Dr. Shashwat Lohia, *et al.*	Triple Jeopardy: Three Primary Synchronous Cancers and One Journey; A Single Woman and Surviving
58.	IACR-673	Shaheen Ali, Ozair Alam, Sonam Grover	Design, Synthesis, and Computational Evaluation of Novel Triazole Derivatives as EGFR-Targeted Anticancer Agents
59.	IACR-674	Aashi Thakur, Chinmay Das, Subarno Paul, Aakash Goswami, Manisha Mohapatra and Tithi Parija	To Study the Role of D-Limonene in Combination with Tamoxifen on DNA Damage Repair in Breast Cancer Cells
60.	IACR-675	Subarno Paul, Chinmay Das, Subhasmita Bhal, Saptarshi Sinha, Somya Ranjan Dash *et al.*	5-FU in Combination with PARP Inhibitor ABT-888 Deregulates MGMT-Dependent Mismatch Repair (MMR) Pathway in MMR-Proficient Colorectal Cancer Stem Cells by Modulating MGMT/PARP1/MSH6 Complex
61.	IACR-676	Sweta H. Makwana and Chandi C. Mandal	PHKA1 Orchestrated Glucose Metabolic Shift: A Novel Link between Diabetes and Breast Cancer
62.	IACR-677	Rishabh Kulkarni, Rahul Kumar	Integrated Radiogenomic Framework for Prognosis and Biological Characterisation of Lung Adenocarcinoma
63.	IACR-678	Monika Kumari, Kalla Mani Chandana, Chandi C. Mandal	Modulation of ZNF726 Oncogene Reveals Metabolic Shift and Concurrent Regulation of Various Unexplored Gene Expressions
64.	IACR-679	Chinmay Das, Subarno Paul, Subhasmita Bhal, Sushree Subhadra Acharya, *et al.*	Talazoparib Enhances the Anti-Angiogenic Potential of Quinacrine through the Deregulation of P300 And GCN5 Chromatin Remodelers in Patient-Derived Oral Cancer Stem Cells
65.	IACR-680	Ghanapriya Devi Yengkhom, Kunal	Reshaping the Stromal Landscape-IGFBPS as Critical Mediators of CAF-Driven Tumour

		Nandgaonkar, Meng Dong, Rahul Thorat, *et al.*	Progression
66.	IACR-682	Dr. Jyotika Rajawat, Dr. Geeta Singh and Dr. Madhu Kumar	Poly (ADP-Ribose) Polymerase 1 (PARP1) as a Diagnostic Biomarker in Oral Cancer and Cervical Cancer: A Comparative Expression Analysis
67.	IACR-683	Priyanka Adhikary, Sayak Banerjee, Nisha Bhat, Sankalan Mitra, Subhadeep Karanjai, Alangkar Saha, *et al.*	Revealing the Potential of Mir-154-5p in Blood Plasma as a Groundbreaking, Non-Invasive Tool in Liquid Biopsy for Predicting Patient Outcomes in Oral Squamous Cell Carcinoma
68.	IACR-684	Arijit Bhowmik, Souvik Das, Biswarup Basu	Evaluation of Bacopa Monnieri Derived Saponins for Anti-Glioblastoma Activity, Brain Biodistribution, and Neuroprotective Potential
69.	IACR-685	Rupali Sarkar, Souradeep Biswas, Subhadip Hajra	A Novel Exosome-Based Nanotherapeutic Strategy to Inhibit Cancer Stem Cell "driven EMT in Triple-Negative Breast Cancer
70.	IACR-686	Koppala Pratibha Bhavani, Tanvi Sawant, Anbarasan Sekar, Amar Deshpande, Sejal Patwardhan	Circulating Exosomal Thrombospondin-1 as a Minimally Invasive Biomarker for Breast Cancer Aggressiveness and Metastatic Potential
71.	IACR-687	Rehman S, Ahmed S, Khan I	Uptake and Accumulation of Antibiotics in Leafy Vegetables - A Comprehensive Review
72.	IACR-688	Haider J	Targeting Cell Cycle Checkpoints: Emerging Strategies to Overcome Cancer Proliferation
73.	IACR-689	Dr. Sadish Kumar, Dr. Nafees Ahmad Khan, Dr. Nabeela, Professor Mohammad Shameem	Spirometry as Response Assessment Criteria in Non-Small Cell Lung Cancer Patients Treated with Chemotherapy
74.	IACR-690	Vijaylaxmi Saxena, Dasari Abhilash, Anshul Budhraja, Pawan Tiwari, Anant Mohan, Ishaan Gupta, Sachin Kumar	Molecular Characterization of circRNA Expression in Human Small-Cell Lung Cancer
75.	IACR-691	Priyadarshini Singh, Harshavardhan Jana J, Nitesh Kumar Gupta, Karishma Raulo, Akhil Kotwal and Amere Subbarao Sreedhar	Hsp90 Isoforms Modulate Cellular Heterogeneity and Disease Aggression in Cancer
76.	IACR-692	Prateekshya Das, Kainat Fatima, Dhanush Pulluri, Vivek Chaudhary, Shrikant P Dharaskar And Amere Subbarao Sreedhar	TRAP1 Modulates Iron Metabolism in Cancer Cells
77.	IACR-693	Vivek Chaudhary, Anit Antony, Amere Subbarao	Hsp90 Chaperone Modulates the Epigenetic Landscape of MDR1 (Multidrug Resistance 1)

		Sreedhar	Promoter in Drug-Adapted Cancer Cells
78.	IACR-694	Baseerat Mashqoor, Devyani Bhatkar, Dhanashree Bomle, Mahima Bansode, Sachin C Sarode, Nilesh Kumar Sharma[1]	Modifications of Free Tyrosine, a Form of Metabolic Reprogramming in Cancer Cells and Mimetic of Tyrosine as an Inhibitor of PI3K Enzyme
79.	IACR-695	Swapna M Nair, Harsha K, Sandhya Mohan, Divya Lakshmanan M	SIN3A Mediated Estrogen Receptor a Repression by Cyanidin-3-Rutinoside Sensitizes Hormone Positive Breast Cancer to Chemo/ Radiotherapy
80.	IACR-696	Sandhya Mohan, Divya Lakshmanan M	Vitamin D VDR Signaling as an Adjuvant Strategy to Limit Estrogen-Driven EMT and Invasiveness in ER-Positive Breast Cancer
81.	IACR-697	Harsha K, Swapna M Nair, Sandhya Mohan, Divya Lakshmanan M	Butylated Hydroxyanisole Alleviates Radiation Induced DNA Damage While Amplifies DNA Damage Response and Repair in Breast Cancer Leading to Cell Survival and Radioresistance
82.	IACR-698	Mehwish Nafiz, Aditya Ramdas Iyer, Sivaprakash Ramalingam	Targeting Antigen Heterogeneous B Cell Malignancies with Multi-Specific Car Molecules
83.	IACR-699	Amisha Joshi, Girish Panigrahi, Khushboo Gandhi, Vikram Gota	Investigating the Effect of Mitocurcumin on Metastatic Potential of Non-Small Cell Lung Cancer (NSCLC)
84.	IACR-700	Sindhu R	Association between Oral and Gut Microbiome Dysbiosis in Various Types of Cancer: An Umbrella Review of Systematic Reviews and Meta-Analysis
85.	IACR-701	Gayathiri R	Natures Shield: Phytochemicals as Guardians against Cancer
86.	IACR-702	Jyothilakshmi Sajimon, Radhika Nair	Hybrid Epithelial/ Mesenchymal States Contribute to Endocrine Resistance in ER+ Breast Cancer
87.	IACR-704	Pratik Kumar Rath, Prof. (Dr.) Kangjam Rekha Devi	Comprehensive Genomic Profiling of Gastric Cancer in Patients from North East India
88.	IACR-705	Anam Ilyas, Ozair Alam	Design and Biological Evaluation of a Pyrazole-Thiazolidinedione-Based EGFR Tyrosine Kinase Inhibitor for Breast Cancer Therapy
89.	IACR-708	Vaka Harideep, Arjith P.P., Jayalakshmi J., K.M. Lucy, A.R. Sreeranjini, Radhika G., Ajith K.S., Leena Chandrasekhar	Nutrient Stress Drives Dual Metabolic-Structural Evolution in Tumours: Insights from a Calorie-Restriction Model
90.	IACR-709	Arjth P.P., Vaka Harideep, Tijina Rachel Thomas, Sreelaksmi N.S,	The Role of OAS-ISG-GBP Antiviral Axis in Spontaneously Regressing 4T1 Tumours

		Jayalakshmi J, Babu T. D., Pramod Darwin and Leena Chandrasekhar[1]	
91.	IACR-710	D Raksan	In Silico Induction of Immunogenic Cell Death in TNBC by Phytochemicals from *Gloriosa Superba* and *Artocarpus Heterophyllus*
92.	IACR-711	Safiya Mehraj, Shazia Ali, Chetan Kumar, Asif Ali and Zahoor Ahmad	Host-Directed Therapy using Dehydrozingerone Diaryl Ethers and Repurposed Drugs Suppresses Macrophage Mycobacterial Growth Via Nf-κB Inhibition
93.	IACR-712	Rituparna Chaudhuri, Debanjana Ghosh, Subhankar Bose, Amit Kumar Dixit, Amit Kumar Srivastava	Kanchanar Guggulu Promotes P-ERK-dependent Apoptosis and Inhibits Tumor Growth in Ovcar-3 Xenografts
94.	IACR-713	Bhawna Singh, Archana Jaiswal, Swati Gogoi, Karan Kumar, Suhail Ahmad, Amit Dutt	Replication Stress Adaptation and Genome Instability Drive Endocrine Therapy Resistance in Breast Cancer
95.	IACR-714	Balasubramaniyan Vairappan, Manoj Kumar Nagar	Nimbolide Suppresses Lung Metastasis and Inflammatory Signaling in Experimental Hepatocarcinogenesis
96.	IACR-715	Riddhiman Bhattacharyya, Chandra Biswas, Soumya Basu, Supriya Kheur, B. M. Rudagi, Samir Gupta, Jayanta K. Pal, Subhayan Sur	Multi-Level Transcriptomic Profiling Reveals Dysregulation of LncRNA Fal1 with Prognostic and Therapeutic Significance in Indian Oral Squamous Cell Carcinomas
97.	IACR-716	Pratheeksha Hebbar, Alfa Florence Rodrigues, Shama Prasada Kabekkodu, Padmalatha S Rai, Samatha Bhat	Investigating the Role of the miR-127/136 Cluster in Regulating Tumour Behaviour and Stemness in Cervical Cancer
98.	IACR-717	Neeha Sinai Borker, Rifat Aara, Radhika Nair	Targeting Chemoresistant Heterogenous Tumor Populations in Metastatic Breast Cancer using Combination Therapy
99.	IACR-718	Prianka Kumari, Shirley James , Aparna J S, Harikumar KB	Antitumor Efficacy of Graveoline, A Quinoline Alkaloid from *Ruta Graveolens*, in Solid Tumor Systems
100.	IACR-719	Priyanka Kashid, Shubham Jha, Sejal Patwardhan	ECM Stiffness Dictates Radio-Resistance in TNBC via Translational Reprogramming
101.	IACR-720	Rifat Aara, Neila Firzan, Radhika Nair	Engineered Mirror-Image Peptide Nanopores Induce Selective Cytotoxicity via Membrane Disruption in Breast Cancer
102.	IACR-721	Anwesha Manasingh, Vinay Bulusu	The Goldilocks Relationship of Nutrient and Wnt Signalling Pathway
103.	IACR-	Mariya Reji, Shamima	Identification of Synthetic Lethal Interactions

	723	Azma Ansari, Rupesh Dash, Nathiya Muthalagu	of *MEN1* In Pancreatic Neuroendocrine Tumors
104.	IACR-724	Bilal Ahmed, Seema Kashyap, Seema Sen, Rachna Seth, Bhavna Chawla, Neiwete Lomi, Lata Singh	Prognostic Significance of Mitochondrial Ferroptosis Signalling in the Pathogenesis of Retinoblastoma
105.	IACR-725	Lata Singh, Bilal Ahmed, Seema Kashyap, Bhavna Chawla, Rachna Seth, Neiwete Lomi	Identification of Prognostic Genes Associated with Mitochondrial Biogenesis in Pediatric Ocular Malignancy
106.	IACR-726	Kumar N, Singh L, Singh Mk, Lomi N, Meel R, Sen S, Kashyap S	Dysregulated Hippo-Yap Signaling Drives Tumor Progression in Uveal Melanoma
107.	IACR-727	P Samal, Dr S A Ansari, Dr B Ravindran, Dr R Dash	Disruption of the NOSIP-INOS Axis Sensitizes Colorectal Cancer to 5-Fluorouracil via Nitrosative Stress Signalling
108.	IACR-728	Aswathy Chankaramkandath Vasu, Sheeja T Tharakan Suraj Kadunganattil	Anticancer Potential of *Indigofera Longiracemosa* Stem Ether Extract
109.	IACR-729	Monika A. Jaiswal, Akshay Karn1, Aparna Das, Anisha Kumari, Shilu Tiwari, And Sorab N. Dalal	When to Let Go: 14-3-3e as a Gatekeeper of Centriole Disengagement
110.	IACR-731	Mubashraa, Sameer Srivastava	Comprehensive Expression and Prognostic Analysis of COMMD10 in Pan Cancer
111.	IACR-732	Siva Kumar Raju Rathnakaram, Nathiya Muthalagu	Epithelial to Neuroendocrine Transition in PDAC: Neuroendocrine Plasticity as a Driver of Aggressive Pancreatic Cancer
112.	IACR-734	K. B. Jyothi, Sajitha I.S., Prasanna K. S., Krithiga K., Devi S S, Divya C., Soumya R	Immunohistochemical Evaluation of MTA1 Expression in Canine Mammary Tumours: Correlation with Tumour Type and Grade
113.	IACR-735	Aubaidah Akhtar, Farheen Showket, Dr. Mohd Jamal Dar	Identification of Insulin-Like Growth Factor-1 Receptor (IGF1R) Specific Small Molecule Allosteric Inhibitors as Novel Anti-Cancer Agents
114.	IACR-736	Sumbul Fatima, Sana Parveen, Mariyam Fatma, Laiba Misbah, Kashim Ibrahim Muhammad, Snober Shabnam Mir	Emerging Frontiers in Organoid Modeling of Epithelial-Mesenchymal Transition (EMT)
115.	IACR-737	Sumit Mallick, Akhila Balakrishna Rai, Vanya Kadla Narayana, Thottethodi Subrahmanya	Powers of hematopoietic Stem Cells - Conditioned Media to Modulate Cellular Energetics via Mitochondrial Dysfunction and Dynamics to Eliminate Colorectal Cancer Cells

		Keshava Prasad, Sudheer Shenoy P, Anirban Chakraborty, Siddhartha Biswas and Bipasha Bose	
116.	IACR-738	Laiba Misbah, Sana Parveen, Mariyam Fatma, Sumbul Fatima, Kashim Ibrahim Muhammad, Snober Shabnam Mir	The Molecular Glue an Innovative Approach Better than Inhibitors against Cancer and Neurological Disorders
117.	IACR-739	Aishath Shaheeda and Shama Prasada Kabekkodu	C14MC-Driven Metabolic Reprogramming Modulates Cisplatin Sensitivity in Cervical Cancer
118.	IACR-740	Rubiada Wani, Mohd I. Dar, Shivam Maurya, Gauri Shankar, Yusuf Akhtar, Atul Kumar, Mohd Idris, Irba Ayani, Iqra Mushtaqa, Sajad Hussain Syed	Sam-Competitive Inhibition of EHMT2, SUV39H1, and EZH2 Reveals a Shared Epigenetic Vulnerability in Cancer and Sickle Cell Disease
119.	IACR-741	Beenish Khursheed, Neetu Badesra, Dr. Mohd Jamal Dar	Understanding Cross-Talk Between β-Catenin, GSK-3β and JNK3 Signaling to Develop Therapeutic Strategies for the Treatment of Neurodegenerative Disorders
120.	IACR-742	Sabra Parveen, Faisal Irshad, Mohammad Saleem Dar, Mohd Jamal Dar	Elucidating the Role Of Mj04 as Janus Kinase (JAK) Inhibitor, Regulating Pro-Inflammatory Cytokines against the Pathogenesis of *Alopecia Areata*
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124.	IACR-746	Sushmita Kundu, Promit Ganguly, Lalnunfela Varte, Shifali Mahajan, E.N. Prabhakaran, Bushra Ateeq	Targeting TMPRSS2-ERG Fusion-Driven Prostate Cancer Using Novel HBS-α-Helicomimics
125.	IACR-747	Deeksha Pal, Ashutosh Rai, Sunil K Arora, Amanjit Bal	Differential Telomere Repeat Binding Factor-1 Expression in Breast Cancer Molecular Subtypes: A Possible ER Mediated Telomere Regulation

126.	IACR-748	P. K. Singh, Sonia Thapa, Sagar Arya, M. L. B. Bhat[2], D. Dalela, M. M. Goel	Expression of the *Forkhead Box M1* (FOXM1) in Human Urinary Bladder Transitional Cell Carcinoma
127.	IACR-751	Jhumpa Chatterjee, Dr. Soumya Ranjan Mohapatra	Targeting Downstream of Tryptophan Catabolism to Overcome Immune Checkpoint Blockade (ICB) Resistance in Oral Squamous Cell Carcinomas
128.	IACR-752	Mellvan Prakash, F Annie Evangaline, Nathiya Muthalagu	Characterization of FRG1 Mutation in Pancreatic Cancer
129.	IACR-753	Malati Tudu, Dr. Soumya Ranjan Mohapatra	Targeting Aromatic Amino Acid Metabolism via Synthetic Biology-Based Gene Silencing Methods in Glioma
130.	IACR-754	Sohidul Islam , Satish Kumar Mungamuri, Harish Chander	A DNA Topology encoded P53-TERF2 Axis Enforces G-Quadruplex Directed Transcriptional Repression and Proteostatic Control
131.	IACR-757	Mukesh V, Gopalakrishna Thamil Selvan	Reciprocal Cooperation of Type A Procyanidin and Nitrofurantoin against Multi-Drug Resistant (MDR) UPEC: A pH-Dependent Study
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133.	IACR-759	Haran Williams .D	Triggering the Anti-Tumor Immune Response: A Review of ICD-Inducing Phytochemicals from South Indian Flora
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	765		Subcutaneous Fat Necrosis
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166.	IACR-792	Medha Bairy, Sanjiban Chakrabarty, Shama Prasada Kabekkodu	MicroRNA Cluster–Mediated Control of PDK3 Drives Metabolic Plasticity and EMT in Cervical Cancer
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170.	IACR-796	Afiya Dalwai, Eeshrita Jog, Ashwin Kumar Jainarayanan, Alessandro La Ferlita *et. al.*	Exploiting Lipid Metabolism Dependencies to Overcome Therapy Resistance in Colorectal Cancer
171.	IACR-801	Gajenthiran Eswaran , Naveen Kumar Perumal	In silico Screening and Molecular Dynamic Simulation Approach: A Drug Repurposing Strategy targeting a novel oncogene RPP25 against Triple-Negative Breast Cancer
172.	IACR-802	Prayag J. Amin and Bhavani S. Shankar	PGE2–Galectin-9 axis driven three-way crosstalk between tumor- APC- NK Cell in the microenvironment
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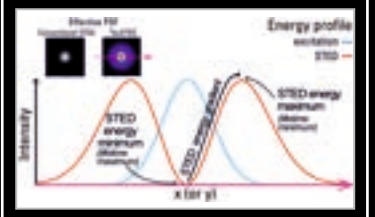
TauSTED: Pushing STED beyond its Limits with Lifetime

TauSTED combines the optical signals from STED and the physical information from fluorescence lifetime at confocal speeds. This approach delivers outstanding STED resolution and image quality due to background removal, at gentle imaging conditions for extended STED acquisitions in time and space.

What is TauSTED?

TauSTED exploits the physical lifetime readout of fluorescence to describe the STED process, probe the energy gradient experienced by fluorophores, and identify signals coming from uncorrelated background noise. It operates simultaneously with the typical scanning STED acquisition.



This information is inaccessible to conventional STED approaches that must compromise on speed, performing multiple rounds of STED imaging and setting intensity thresholds to improve resolution or quality.

How does it work?

TauSTED measures the fluorescence lifetime-based information acquired in every STED experiment and captures the STED response of the fluorophores in real time. It does this in an automated way, so you can get the results with the resolution and level of detail your application demands.

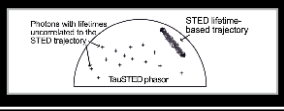
From automated acquisition...

Collect the lifetime-derived information at confocal speed in each scanning point

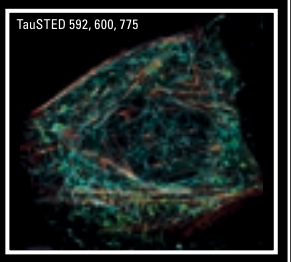
photon-counting acquisition

scanhead signal handling

Generate TauSTED phasor



...to result

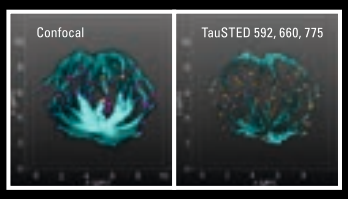


TauSTED on live cells labeled with SiR-actin (glow), SPY555-tubulin (cyan), and CF488A-WGA (green). Scale bar: 2 µm. SiR-actin from Spirochrome and CF488A-WGA from Biotium.

What are the benefits of TauSTED?

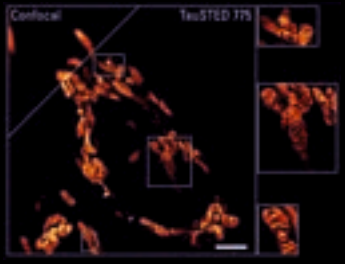
Outstanding image quality and resolution

By identifying the lifetime fingerprint of photons coming from background noise, you can selectively remove them and keep just the relevant photon counts. This ability translates into images with excellent signal-to-noise ratio.



Mitotic cells stained for tubulin (cyan), CENP-C (yellow) and BUB1 (magenta).
Sample courtesy: Carlos Sacristan Lopez, Hubrecht Institute, Utrecht, the Netherlands.

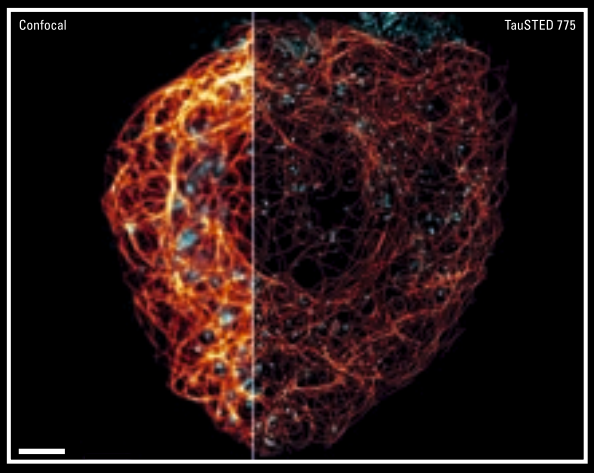
At the same time, you can push the resolution beyond the limits of intensity-based STED at any excitation and STED line you use.



HeLa cells stably expressing COX8A-SNAP labeled with SiR-BG. Scale bar, 2 µm.
Sample courtesy T. Dellmann and A. Garcia, CECAD, Köln, Germany. Cell line originally from S. Jakobs.

Gentle live-cell imaging

Your specimen is protected during long time-lapse STED experiments at lower excitation and STED light doses thanks to access to lifetime information at confocal speed.



Live cell labeled with SiR-tubulin (glow) and CF594-WGA (cyan). Scale bar: 5 µm.
SiR-tubulin is from Spirochrome and CF594-WGA is from Biotium.

Reference
Alvarez et al., Nature Methods 2021. TauSTED: pushing STED beyond its limits with lifetime.
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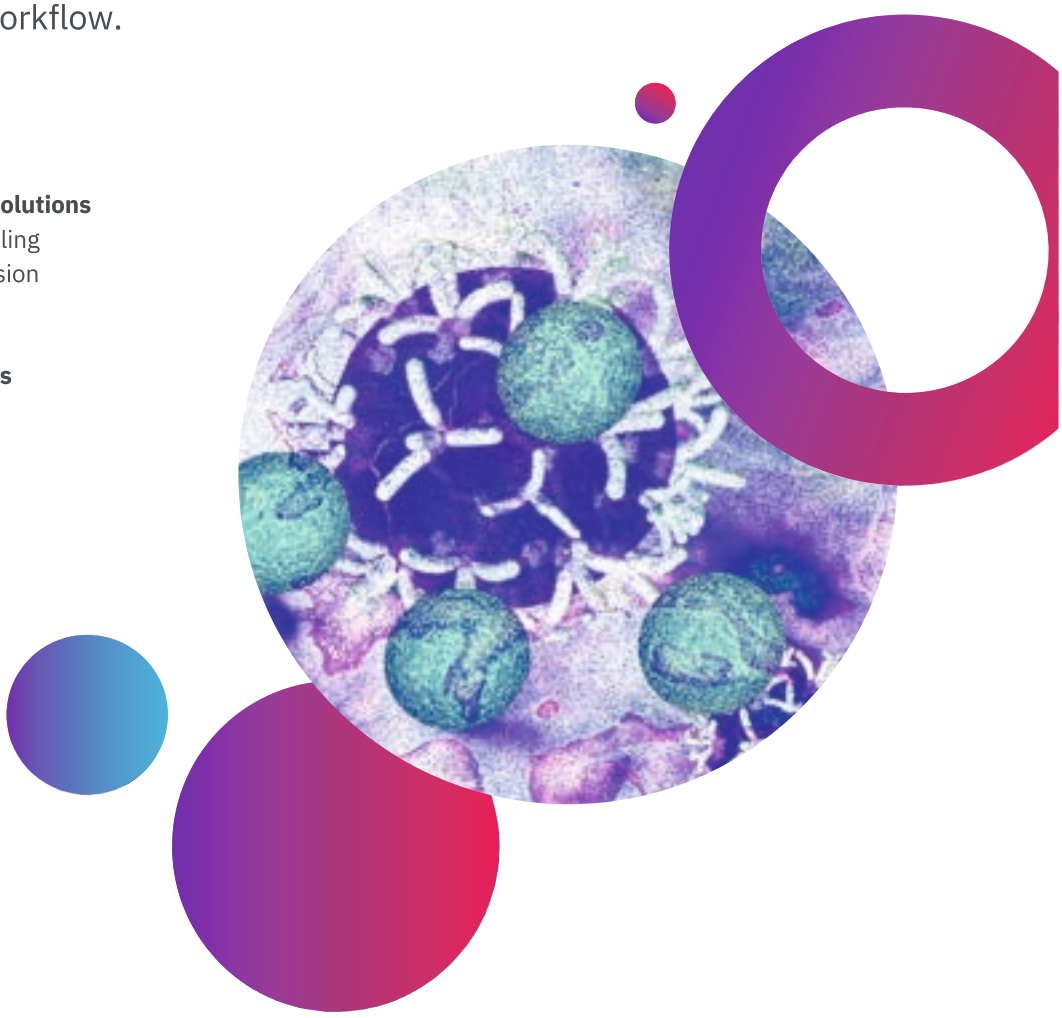

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Nanobots For Cancer Therapeutics

Prof. Ambarish Ghosh
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The idea of "fantastic voyagers" carrying out medical tasks within the human body has existed as part of popular culture for many decades. The concept revolved around a miniaturized robot that can travel inside the human body and perform complicated functions such as surgery, navigation of otherwise inaccessible biological environments, and delivery of therapeutics. With current advances in nanotechnology, there have been several strategies to realize this dream of a "nano-voyager," which is of great fundamental and technological importance.

We will talk about a specific approach toward this problem using magnetic manipulation and show examples in which this system can impact diverse applications in biology and medicine.

Genomic Drivers Of Endocrine Therapy Resistance In Breast Cancer

Prof. Amit Dutt

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Hormone receptor–positive, HER2–negative breast cancer frequently relapses on endocrine therapy, and key resistance drivers remain undefined for many patients, especially in non-Western populations. We performed integrated whole-exome, transcriptomic, and clinicopathological profiling of 86 Indian HR+/HER2– tumors (44 endocrine-sensitive, 42 endocrine-resistant), complemented by in-vitro and orthotopic xenograft models. We identified recurrent CDKN1B (p27) loss-of-function mutations and copy-number deletions significantly enriched in resistant tumors, associated with reduced CDKN1B mRNA/protein, proliferative gene signatures, early relapse, and poor survival in both in-house and TCGA/METABRIC cohorts. Functionally, CDKN1B silencing in ER+ cell lines conferred tamoxifen and fulvestrant resistance, whereas ectopic p27 restoration re-sensitized acquired-resistant derivatives and partially rescued ER and Rb signaling. Notably, CDKN1B-deficient cells and xenografts retained dependence on CDK4/6 and remained responsive to palbociclib monotherapy and to palbociclib–endocrine combinations that overcame endocrine resistance in vivo. These data establish CDKN1B loss as a recurrent, clinically actionable driver of endocrine resistance and support p27 status as a prognostic and predictive biomarker to guide CDK4/6-targeted strategies in HR+/HER2– breast cancer.

Microfluidics-Based New Approach Methodologies (NAMs) in Cancer Research

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Cancer cells do not exist in isolation; their behavior is shaped by the mechanical and spatial context of the surrounding microenvironment. However, many commonly used in vitro systems simplify this context, often overlooking tissue stiffness, three-dimensional organization, and gradient-driven transport. In this talk, I will describe how our laboratory integrates mechanobiology with microfabrication and microfluidic engineering to incorporate selected features of the tumor microenvironment into experimentally tractable models. We examine how transitioning from conventional 2D culture to controlled 3D spheroid systems alters phenotypic outcomes such as motility and drug response. I will further present our microfabricated, high-throughput platforms for uniform spheroid generation and gradient-based drug testing, designed for quantitative and reproducible interrogation of tumor behavior. These approaches aim to complement conventional petri dish cultures by enabling controlled hypothesis testing under physiologically relevant mechanical and transport constraints. Such microengineered New Approach Methodologies provide scalable and accessible tools for probing tumor biology with improved contextual fidelity.

TORC2-mediated Metabolic Rewiring in Colorectal Cancer

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RICTOR, a core component of the mTORC2 complex, is frequently overexpressed in cancer, where it supports tumour growth. Although traditionally associated with cytoskeletal organisation and AKT signalling, we identify a previously unknown role for RICTOR in regulating the folate and methionine cycles, a central metabolic hub supporting nucleotide synthesis, methylation reactions, and redox homeostasis. We show that RICTOR enables cancer cells to meet increased metabolic demands by coordinating the one-carbon metabolism and mitochondrial dynamics. We further show that perturbation of dietary inputs into one-carbon metabolism modulates RICTOR-dependent metabolic outputs, revealing a nutrient-sensitive layer of regulation. These findings identify RICTOR-regulated metabolic pathways as a potential therapeutic vulnerability in cancer.

Chromatin Remodeling Regulates Repair Pathway Choices at the Stalled Replication Forks

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Genomic instability is a hallmark of cancer cells and a potential source of tumorigenesis. A major cause of genomic instability is replication fork stalling at sites of DNA damage or abnormal DNA structure. We adapted the Escherichia coli Tus/Ter replication fork barrier (RFB) to induce site-specific replication fork stalling on a mammalian chromosome.
Tandem duplications (TDs) in primary cells lacking BRCA1 are induced specifically by a Tus/Ter block but not by a conventional double strand break (DSB), indicating specificity for the stalled fork response. Intriguingly, breast and ovarian cancers lacking BRCA1 similarly acquire large numbers of small (~10 kb) TDs. We found that the stalled fork motor protein-FANCM acts synergistically with BRCA1 to suppress Tus/Ter-induced TDs. We discovered a novel synthetic lethal interaction between Brca1 and Fancm loss in mouse embryonic stem (ES) cells and in breast and ovarian cancer cells. Further, we discovered that a Fancm mutant defective only for the ATPase function is defective in all repair functions and, unexpectedly, is synthetic lethal with Brca1 mutation. My data using CUT&RUN revealed a nucleosome-free zone (NFZ) at Tus/Ter. Further, we found that the INO80 chromatin remodeler regulates the formation of NFZ.

We are exploring the novel FANCM-BRCA1 synthetic lethal interaction in cancer cells to determine the mechanism of synthetic lethality. Further, we are delineating the chromatin environment and protein dynamics at the stalled fork. This holistic approach will provide a full picture of the mechanism of FANCM-BRCA1 synthetic lethal interactions and will encourage me, in the future, to develop high throughput screens for specific small molecule inhibitors targeting the key players involved in this pathway, as novel therapeutics in BRCA1-linked cancer.

Beyond p53: Mdm2 regulates cell cycle by targeting CRL4Cdt2 E3 ubiquitin ligase

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The canonical function of the Mdm2 oncoprotein is widely recognized as the negative regulation of the p53 tumor suppressor. However, growing evidence indicates that its physiological activities extend far beyond p53. Here, we show that Mdm2 promotes cell cycle progression at the G2/M phase through the ubiquitin-mediated degradation of the substrate recognition adaptor Cdt2 of the CRL4Cdt2 E3 ubiquitin ligase complex, independently of p53. The attenuation of CRL4Cdt2 activity by Mdm2 stabilizes its cell cycle-specific substrates including p21, Set8, and Cdt1, at the G2/M phase following their proteasomal degradation in the S phase. Furthermore, the delay in cell cycle progression at the G2/M phase and the decreased cell proliferation observed in the absence of Mdm2 are largely caused by an increase in Cdt2 and a subsequent decrease in p21. Collectively, our data illustrate a previously unexplored mechanism by which Mdm2 regulates the cell cycle and promotes cellular proliferation by neutralising the CRL4Cdt2 E3 ubiquitin ligase activity, thereby stabilizing p21 at G2/M.

Robotics in Oncology: Redefining Precision in Cancer Surgery

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Robotic surgery has emerged as a transformative advancement in oncologic care, redefining precision, ergonomics, and minimally invasive cancer management across multiple specialties. With enhanced three-dimensional visualization, tremor filtration, articulated instruments, and superior dexterity, robotic platforms such as the da Vinci Surgical System enable surgeons to perform complex oncologic resections with improved accuracy while preserving critical structures. In urologic, gynecologic, thoracic, and gastrointestinal malignancies—including prostate, colorectal, cervical, endometrial, and pancreatic cancers—robotic-assisted procedures have demonstrated reduced blood loss, shorter hospital stay, decreased postoperative pain, and faster functional recovery without compromising oncologic outcomes. Emerging evidence from randomized trials and large cohort studies suggests comparable margin negativity and lymph node yield when contrasted with conventional laparoscopy and open surgery, with potential advantages in technically demanding pelvic and retroperitoneal dissections. Robotics also enhances surgeon ergonomics and may reduce fatigue during prolonged procedures, thereby contributing to consistency in performance. The integration of fluorescence imaging, real-time navigation, and artificial intelligence further expands the scope of precision oncology surgery. However, challenges including cost, learning curve, access disparities, and the need for structured training programs remain significant considerations, particularly in resource-limited settings. As technology evolves and long-term oncologic data mature, robotic surgery is poised to become an integral component of multidisciplinary cancer care, aligning surgical innovation with the overarching goals of improved patient safety, oncologic efficacy, and quality of life.

Breast cancer cells exploit unexplored dysregulated metabolic regulators to augment cell plasticity for favouring their progress

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Metabolic reprogramming, particularly coordinated dysregulation of glucose and lipid metabolism drives cancer progression. Cancer cells adopt distinct glycolytic, mitochondrial, and lipid metabolic states to sustain growth and also to foster cell plasticity. This study demonstrates that glucose and lipid metabolism dysregulation function as coordinated rather than independent oncogenic drivers. Cancer tissue analysis revealed a concurrent upregulation of a key lipid metabolic genes alongside two previously unexplored metabolic regulator PLPP4 and PHKA1, whose expression correlated with poor survivability in breast cancer patients. Functional studies revealed that knockdown of PHKA1 drives a dual metabolic program by simultaneously reducing glycolytic flux through downregulating hexokinase and GLUT expression, and decreasing mitochondrial oxidative capacity, thereby manipulating energy and biosynthetic demands of rapidly proliferating cancer cells. PLPP4, conversely, functions as a critical regulator of lipid metabolic changes which enabling cancer cells to acquire adipocyte-like phenotypes. Experimental evidences revealed that these adipocyte-like cancer cell population enhances cancer growth and metastatic potential in breast cancer. Thus, the poorly explored genes PLPP4 and PHKA1 represent critical regulators of this metabolic coordination and cellular plasticity.

Keywords: Breast cancer, metabolic rewiring, glucose metabolism, lipid metabolism, PHKA1, PLPP4, cellular plasticity, and adipogenic differentiation

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Rectal Cancer: Lessons from 25 years of Surgical Practice

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This presentation will be mainly focused on the evolution of diagnostics, multimodal management and surgical techniques used to address the rectal carcinoma in last 25 years. Just 25 years back, only diagnostic modalities to diagnose and stage the disease were a colonoscopy, biopsy of the lesion and a USG abdomen and pelvis. Rarely some patients would opt for adjuvant treatment because of the reasons of affordability and fear of toxic complications. The introduction of CECT abdomen, pelvis, HRCT Chest gave a new concept of stage specific management. The addition of MRI pelvis introduced the concept of downstaging with neoadjuvant in a big way. The introduction of staplers made technically demanding procedures to be performed with ease. Now a days now the armamentarium is assisted further with molecular diagnostics, tumor board discussions, neo-adjuvant, adjuvant, complete conservative /wait and watch protocols, stage specific disease management by advanced laparoscopic/robotic gadgets, energy sources, chemoradiation, immunotherapy has made ca rectum in most of the cases with favourable histology, a completely treatable disease. As a surgeon what fascinates me to discuss would be with a focus on the evolution of surgical techniques in these 25 years of which I became a part by working and rendering my services as a colorectal surgeon in this era.

Development of an Immunotoxin that kills World-wide available Drugs Resistant Cancers Expressing Ectopically hCG

Prof. G.P. Talwar

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We made an Immunotoxin linking Single Chain of our high affinity anti-hCG monoclonal antibody PiPP with α-Sarcin, a non-immunogenic fungal origin toxin. This immunotoxin was expressed as a 45 kDa size protein in E. coli. The purified immunotoxin retains binding to hCG expressed by the cancer cells, and Sarcin kills the cancer cells. In vivo experiments conducted in Nude Mice also demonstrated significant reduction of hCG expressing tumors. We plan to conduct preclinical Toxicology studies followed by Therapeutic Clinical trial in patients doomed to die, as such cancers are resistant to available drugs round the World.

Emerging Role of Low-dose Venetoclax in Management of Acute Myeloid Leukemia- comparing Efficacy and Pharmacokinetics of Venetoclax 50 mg with 400mg in Induction therapy

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Venetoclax is a bcl2 inhibitor and as a result it has demonstrated a strong pro-apoptotic activity in many hematological cancers like chronic lymphocytic leukemia(CLL), Acute myeloid leukemia (AML) and multiple myeloma.

The biggest challenge faced in treating AML patients with venetoclax is co-administration of Azole antifungal agents for antifungal prophylaxis during AML induction therapy.

All azole antifungal agents like, posaconazole and voriconazole are strong inhibitors of CYP3A enzyme pathway. As a result, venetoclax when co-administered with an azole antifungal agent can lead to very high toxicity and detrimental outcome.

We studied drug levels, pharmacokinetics and clinical efficacy of low-dose venetoclax therapy in combination with posaconazole in newly diagnosed AML patients. We found that C0, Cmax and AUC achieved with VeN50 were significantly lower than the VeN400 cohorts. The average CL/F was 2.82 ml/hr in VeN50 cohort and 9.39 ml/hr in VeN400 cohort ($p < 0.001$). Venetoclax CL/F rate was reduced by 70% when combined with posaconazole. Despite decreased apparent clearance of venetoclax when combined with posaconazole, the AUC0-24 was significantly lower with VeN50 compared to VeN400 [48.0 µg·h/mL (19.96-94.79) vs 17.885 µg·h/mL (8.09-81.47) $p = 0.002$]. Our study highlights significant inter-population differences in venetoclax pharmacokinetics, with Indian patients exhibiting lower clearance of venetoclax and higher drug exposure. Despite differences, clinical response rates and MRD negativity were comparable between VeN50 and VeN400, indicating a weak exposure-response relationship. the faster neutrophil recovery with VeN50 and posaconazole suggests that lower venetoclax doses may optimize efficacy while minimizing myelosuppression. The outcome of this research paves the way for reducing cost and toxicity of treatment while retaining its efficacy.

GPER-1 (G Protein-Coupled Estrogen Receptor-1) Activation: A Potential Strategy for Chemoprevention of Prostate Cancer

Prof. Geetanjali Sachdeva

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Adenocarcinoma of the prostate is the second leading cause of cancer in men characterized by a prolonged latency period, thus providing a critical window for chemopreventive intervention. However, clinical studies evaluating chemopreventive agents for prostate cancer have failed to demonstrate positive outcomes, highlighting the need to identify novel and effective molecular targets. G Protein-Coupled Estrogen Receptor-1 (GPER1) signalling is reported to play a context-dependent role in tumorigenesis and disease progression of multiple cancers. In prostate cancer (PCa), activation of GPER1 has been shown to inhibit tumor cell proliferation both in- vitro and in-vivo, and is currently being explored as a therapeutic target in uveal melanoma. Accumulating evidence also indicates that GPER1 modulates the tumor microenvironment through regulation of immune cell infiltration in lung and hepatocellular carcinomas, and by maintaining stemness in breast cancer stem cells. These findings highlight the importance of not only understanding the direct effect of GPER-1 activation on tumor cells but also understanding the crosstalk between GPER1 signalling and the tumor microenvironment. The present study was undertaken to evaluate the potential of GPER1 as a chemopreventive target in prostate cancer and to delineate the mechanisms through which GPER1 activation or expression affects the tumor and its microenvironment.

Towards this, we initially assessed the GPER1 expression and percent GPER1-positive prostatic cells in human and TRAMP (Transgenic Adenocarcinoma of Mouse Prostate) prostates. The percent GPER1 positive cells in the epithelial compartment as well as GPER1 expression were found to be reduced in high-grade cancer compared to non-cancerous tissues. This observation was corroborated by our reanalysis of the existing human prostate cancer GEO datasets. GPER1 silencing in LNCaP, PC3 and RWPE-1 did not alter the proliferation of cells, however it led to increased migration and invasion. Further GPER1-regulated epithelial to mesenchymal transition was found to be mediated through the miR200a-ZEB2-E-Cadherin loop and other metastasis-associated genes. Consistent with these findings, activation of GPER1 using G1 (agonist) in prostate epithelial cell lines led to decreased proliferation and invasion. Thus, GPER1 expression was found to be protective in PCa. Pharmacological activation of GPER1 using G1 in TRAMP mice prevented disease progression from high-grade prostatic intraepithelial neoplasia to poorly-differentiated carcinoma. This effect was abrogated on co-administration of G15, an antagonist of GPER1. To further delineate the mechanisms underlying GPER1-mediated tumor inhibition, studies

GPER-1 (G Protein-Coupled Estrogen Receptor-1) Activation: A Potential Strategy for Chemoprevention of Prostate Cancer

were undertaken to characterize immune cell populations in the prostates of G1-treated TRAMP mice. Flow cytometric analysis revealed a significant increase in the frequency of circulating macrophages especially in M1 macrophages and a decrease in that of M2 macrophages and polymorphonuclear myeloid-derived suppressor cells in G1-treated group compared to vehicle-treated group. Thus, overall, our data suggest that GPER1 is a promising target for chemoprevention of prostate cancer and its activation alters the immune milieu of the tumor.

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OncoPredikt - An AI Platform: Revolutionizing Cancer Care Economics through Predictive Precision and Cost-Effective Solutions

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Background: For the last decade, precision oncology has been celebrated as a scientific breakthrough but in much of the world, it has quietly become an economic paradox. Growth of molecular technologies have enabled effective stratification of early-stage breast cancer to avoid unnecessary chemotherapy. But commercial genomic assays that enable this are expensive, slow, and infrastructure heavy. In countries like India, where 70–80% of cancer care is paid out-of-pocket, precision medicine has unintentionally become a driver of financial toxicity rather than relief. In addition, these techniques are inaccessible by majority of people in developing countries like India. Thus, patients either forgo testing, or they undergo testing at devastating financial cost. This is the economic problem OncoPredikt was designed to solve. OncoPredikt reframes precision oncology not as a sequencing problem, but as an information problem. The focus was to deliver genomics grade clinical insight without genomics-grade cost by integrating routinely generated histopathology, clinicopathologic features, and AI-inferred transcriptomic signals.

Methods: The model functions by generating a BreastRS score (0-100) that provides, "Virtual genomics-grade" recurrence stratification, and treatment de-escalation decisions.

Results: The model showed an overall specificity of 92.24%, sensitivity of 65.31%, NPV and PPV of 91.46% and 68.09% respectively. The Kaplan–Meier, C-index, and HR analyses show BreastRS provides prognostic information for DRFI beyond standard clinicopathologic and genomic markers. In addition, a positive correlation (r = 0.66) between BreastRS and Oncotype DX scores were achieved upon validation.

Conclusions: OncoPredikt's high negative predictive value allows clinicians to confidently identify patients who can safely avoid chemotherapy since chemotherapy is not just clinically toxic; it is financially catastrophic. This is not incremental efficiency, but a structural cost reduction. From a health economics perspective, the highest value intervention in cancer care is not adding another expensive test but avoiding unnecessary treatment. Thus, using this AI approach, we move from centralized, high-cost precision oncology to distributed, scalable, and affordable decision making.

Chemoresistance of Cancer Stem Cells: Is Chemosensitization an Ideal Approach for Reversing Therapy Resistance?

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The paucity of knowledge about the mechanism of chemoresistance and the lack of appropriate therapeutic molecules against Cancer Stem Cells (CSCs) are major stumbling blocks in managing and treating therapy-resistant cancers. Symmetric division of CSCs is thought to sustain self-renewal and recurrence of cancer after therapy. We recently discovered a common mechanism regulated by the RNA-binding protein MSI2 that enhances translation of multiple cancer-causing proteins and HCV RNA. Disruption of the interaction between MSI2 and oncogenes/HCV RNA significantly inhibited CSC self-renewal, reduced viral RNA translation, and reduced tumor volume. Next, we attempted to chemosensitize CSCs to the FDA-approved drug- a well-known multikinase inhibitor, Sorafenib, using the triterpene Lupeol. We analyzed the highly expressed molecules in CSCs, such as AKT, β-Catenin, c-MYC, and c-FLIPL. We performed in silico, in vitro, and animal studies to prove our hypothesis. Docking and MD simulation data show the interactions between Lupeol and Sorafenib with the examined proteins. By MTT assay, Flow cytometry, and gene expression analysis, we observed that Lupeol significantly inhibits the growth of CSCs, sparing normal cells, chemosensitize the CSCs to the drug Sorafenib, and substantially ameliorates Sorafenib-induced toxicity in an animal model. We conclude that multiple proteins play a crucial role in the self-renewal and chemoresistance of CSCs. Lupeol alone or as an adjuvant to Sorafenib could be developed to chemosensitize the therapy-resistant CSCs and ameliorate the drug-induced toxicity.

Peripheral T-Cell Lymphomas: Genomic classification, diagnostic refinement and disease pathobiology

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Peripheral T-cell lymphoma (PTCL) representing ~15-20% of non-Hodgkin lymphomas (NHLs) is a complex group of post-thymic T-cell lymphomas. PTCL encompasses more than 30 distinct entities associated with enormous heterogeneity in morphology, immunophenotype and clinical features. PTCL classification has evolved through continuous refinements integrating immunophenotypic, molecular and clinical data. The rarity and morphological variability of PTCLs continue to complicate the definition of biologically and clinically meaningful entities, as well as the application of current diagnoses in daily practice. Genome-wide investigations have revealed the mutational landscape and transcriptomic profiles of PTCL entities, defined the cell-of-origin as a major determinant of T-cell lymphoma biology, and allowed for the refinement of biological and clinical meaningful entities for precision therapy. These advances in molecular diagnostics and functional genomics have improved our understanding and markedly accelerated the discovery of molecular or genetic signatures and some of the discoveries have been included in the revised WHO or ICC classification-2024. The overall survival of the major PTCL entities is dismal and has not improved for decades, thus there is an urgent unmet clinical need to improve clinical outcomes. CHOP-based treatment regimens are the backbone of current treatment protocols for nodal PTCLs, but primarily fail to respond or relapse within two years. While some targeted therapies have shown promising results, including ALK inhibitors for ALK+ ALCL, brentuximab-vedotin (BV) for ALCL, PDL1/PD1 blockade in extranodal NK/T-cell lymphoma (ENKTCL), mogamulizumab in adult T-cell leukemia/lymphoma (ATLL), and epigenetic therapy in PTCLs with follicular helper T-cells (TFH) features, most PTCLs lack effective, evidence-based targeted treatment options. Precise molecular and functional characterization facilitate more effective treatment strategies This presentation explores the challenges in diagnosing or classification of PTCLs, focusing on the intricate biology of the more common nodal PTCL entities. It will facilitate a better biological understanding of the different PTCL entities, and their stratification for additional studies and target-directed clinical trials.

PLENARY LECTURE:
Do Nucleosomes Hold The Key To Genomic Stability?

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To maintain the stability of the genome it is essential that all chromosomes attach to the mitotic spindle before sister chromatids separate. The Spindle Assembly Checkpoint ensures this by inhibiting the Anaphase Promoting Complex/Cyclosome (APC/C) ubiquitin ligase in the presence of any unattached chromosomes. Even one unattached chromosome is sufficient to keep the APC/C inactive, but once the last chromosome attaches, we can measure the disappearance of its key substrate, Cyclin B1, within one minute. We are searching for the mechanism responsible for reactivating the APC/C so rapidly. Using Fluorescence Cross Correlation Spectroscopy, we found that the APC/C is not uniformly reactivated throughout the cell: chromosome bound APC/C recognises Cyclin B1 before the APC/C in the cytoplasm. Our experiments indicate that this requires both the APC/C and Cyclin B1 to bind to nucleosomes, and I will propose a mechanism to explain this.

Contribution: *Luca Cirillo, Saptha Veerapithiran, Catherine Coates, Annalisa Roberti, Iulia-Teodora Vermesan, Rose Young, Claudio Alfieri, Hiro Yamano*, and Jonathon Pines*

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Evolving Paradigms in Myeloma: Stem Cell Transplant and Emerging Immunotherapies

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The therapeutic landscape of newly diagnosed multiple myeloma (NDMM) has transformed with the introduction of novel agents, autologous stem cell transplantation (ASCT), and maintenance strategies. These advances, coupled with deeper biological insights, have significantly improved survival outcomes. Induction with bortezomib, lenalidomide, and dexamethasone (VRd) remains the standard backbone. The addition of anti-CD38 monoclonal antibody daratumumab (Dara-VRd/VTd) has enhanced depth of response. Consolidation with ASCT in eligible patients, followed by lenalidomide maintenance for three years, is associated with superior progression-free survival (PFS) and overall survival (OS). Median OS for transplant recipients is 8.5–10 years, with 15–20% surviving beyond 15 years.

Despite these gains, relapse—particularly in high-risk disease—remains the major cause of treatment failure. Recent advances in immunotherapy, including CAR-T cell therapy and bispecific antibodies targeting BCMA and GPRC5D (e.g., teclistamab), have revolutionized management of relapsed/refractory myeloma. Both modalities demonstrate impressive efficacy with manageable toxicity. Initial Indian experience with teclistamab is encouraging, while CAR-T availability remains limited. The choice between these approaches depends on patient profile, institutional capacity, and evolving long-term data.

Measurable residual disease (MRD) has emerged as an important prognostic marker, with bone marrow MRD negativity correlating with superior PFS in both transplant and non-transplant settings. Next-generation flow cytometry and sequencing are increasingly employed for MRD assessment, guiding post-transplant strategies in MRD-positive patients. Together, these evolving paradigms—quadruplet induction, ASCT consolidation, maintenance therapy, and novel immunotherapies—are reshaping the future of myeloma care.

When and Where Proteins Are Destroyed: Mechanisms of Spatiotemporal Control of Membrane Proteostasis and Disease

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Spatial organization of protein turnover is essential for cellular homeostasis, yet how the ubiquitin–proteasome system (UPS) achieves compartment-specific regulation remains poorly understood. Although the UPS is classically viewed as a predominantly cytosolic system, we have uncovered a previously unrecognized lipidation-dependent mechanism that directs the dynamic trafficking of UPS components to cellular membranes. Integration of multi-omics datasets across normal and disease states further reveals widespread deregulation of membrane-associated UPS components in cancer, neurodegenerative disorders, and rare genetic diseases.

In this seminar, I will present our recent findings on UPS components that establish lipidation as a previously unappreciated organizing principle of the UPS. This mechanism integrates spatial organization with environmentally responsive control of protein degradation, providing a new conceptual framework for understanding how membrane- associated proteostasis is dynamically coordinated in health and how its disruption contributes to diseases such as cancer.

Beyond Catalysis: Non-Canonical Functions of Phosphatases

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Phosphatases are essential to maintain phospho-protein homeostasis in cells. They play a crucial role in biological functions and control nearly every cellular process. However, the functional map of all human phosphatases and their interactome is not fully available. By using a biochemical and proteomic analysis our lab has established the interaction network of nearly every human protein phosphatase in the cell. Among several functional protein interactions, we found many phosphatases associated with the components of mTOR kinase complex.

mTOR (mechanistic Target Of Rapamycin) is a key protein kinase that coordinates cell growth and metabolic signaling and is implicated in a number of pathologies, including cancer, obesity, type 2 diabetes, and neurodegeneration. mTOR exists in two functionally distinct multiprotein complexes: mTORC1 and mTORC2. However, the molecular details of the assembly of multiprotein mTOR complex are not fully understood. Our work demonstrating the requirement of distinct phosphatases in the assembly of mTOR complexes and their functional role will be discussed.

From Genome Protection to Cancer Treatment: The Impact of Dynamic Ubiquitin Signaling

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Ubiquitin proteasome system (UPS) is a key player in maintaining cellular homeostasis. SCF (SKP1-cullin1-F-box protein) E3 ubiquitin ligases are the integral component of UPS. FBXO31 is a substrate-recognizing subunit of SCF E3 ubiquitin ligase and acts as a dedicated DNA damage checkpoint protein. It helps to arrest the cells at the G1 and M phases of the cell cycle under genotoxic stresses. Following genotoxic stresses, FBXO31 is activated and physically interacts with and mediates the proteasomal degradation of MDM2 to activate p53. In addition, FBXO31 degrades cyclin D1 to arrest the cells at the G1 phase. Further, we found that FBXO31 depleted cells are more sensitive to ionizing radiation as well as anti-cancer chemotherapeutic drugs, indicating that FBXO31 is a critical player in anti-cancer therapy efficacy. Interestingly, our study showed that ablation of FBXO31 enhances the potency of chemotherapeutic drug to suppress the tumor growth in vivo mice model due to inefficient DNA damage repair. Mechanistically, our study demonstrates that FBXO31 controls the potency of anti-cancer drugs through controlling DNA damage response signaling and repair processes. Thus, FBXO31 could be a potential biomarker to determine the efficacy of the cancer chemotherapeutic drugs. Details will be discussed in the meeting.

The Making of a Renegade: Coordinating DNA Damage Response and Apoptotic Evasion in Breast Cancer Origins

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Breast cancer initiation involves a complex interplay between external genotoxic stress and the deregulation of endogenous survival pathways. Our studies elucidate how the coordination of DNA damage response (DDR) and apoptotic evasion drives the transformation of healthy breast epithelial cells into a malignant "renegade" phenotype. We identified DNA-dependent protein kinase (DNA-PK) as a central mediator in response to alkylation damage induced by N-methyl-N-nitrosourea (MNU). While DNA-PK is a critical component of the DDR, its chronic activation following methylating stress triggers structural collapse, specifically Golgi dispersal and impaired intracellular tra fficking. This disruption facilitates the loss of apico-basal polarity and the induction of an epithelial-tomesenchymal transition (EMT)-like state, providing a mechanistic link between chemical DNA damage and cellular transformation. Complementing this, we demonstrated how apoptotic evasion, mediated by the upregulation of Apoptosis Inhibitor 5 (Api5), reinforces this oncogenic progression. Api5, frequently overexpressed in breast cancer patients, functions as a molecular switch that promotes survival and proliferation. By activating FGF2 signaling and subsequently the PDK1-Akt/cMYC and Ras-ERK pathways, Api5 enables cells to bypass programmed cell death and sustain growth under stress. Together, these findings suggest that breast tumorigenesis is orchestrated through a dual mechanism: the DNA-PK-mediated structural remodeling following DNA damage and the Api5-dependent evasion of apoptosis. This synergy transforms stable epithelia into invasive, proliferative entities, identifying both DNA-PK and Api5 as critical therapeutic targets for intercepting breast cancer at its origins.

Immune checkpoint Inhibitors in Hodgkin's Lymphoma: Transforming the therapeutic Landscape

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Background: Hodgkin's Lymphoma constitutes 10% of all Lymphomas and 1% of all Cancers. It arises from the germinal centre B lymphocytes. It is among the cancers with very high cure rates in early stage and satisfactory outcomes even in advanced stage disease. Conventional chemotherapy with or without radiation induces high cure rates but these treatments can have relevant long-term toxic side effects. Besides 15-25% patients can have primary refractory disease to chemotherapy. As a result, there remains a lot of debate about the optimal management of these patients. Classical Hodgkin's lymphoma (cHL) represents a unique model of immune evasion, characterized by scarce malignant Reed–Sternberg cells embedded within an extensive but functionally suppressed immune microenvironment. A defining biological hallmark of cHL is the frequent amplification of chromosome 9p24.1, leading to overexpression of PD-L1 and PD-L2 and constitutive activation of the JAK–STAT pathway. This molecular vulnerability renders Hodgkin's lymphoma exquisitely sensitive to immune checkpoint inhibition targeting the PD-1 axis. The advent of PD-1 inhibitors, including Nivolumab and Pembrolizumab, has dramatically altered the management of relapsed or refractory cHL. In heavily pretreated patients, these agents have demonstrated high overall response rates, durable remissions, and a favorable safety profile compared with conventional salvage chemotherapy. Beyond salvage therapy, immune checkpoint inhibitors are increasingly being integrated into earlier lines of treatment. Clinical trials evaluating combinations of PD-1 blockade with chemotherapy or with targeted agents such as Brentuximab vedotin have demonstrated promising response rates with manageable toxicity. Emerging strategies include chemo-free regimens, response-adapted approaches, and novel combinations aimed at enhancing depth and durability of response while minimizing long-term treatment-related morbidity.

Conclusion: Immunotherapy has shifted Hodgkin's lymphoma from a chemotherapy-dominated paradigm to an immune-driven precision treatment model. With continued research, the goal is durable remission with minimal toxicity, potentially redefining cure strategies in this highly immunogenic malignancy.

Discovery of Novel Therapeutic Agents Using Structure Based Drug Design

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Structure based drug design is a powerful and cost-efficient method for discovering novel therapeutic agents, compared to traditional method of high-throughput drug screening. We employed structure-based drug design to identify novel scaffolds targeting Glycogen Synthase Kinase-3 Beta (GSK-3β). Dysregulation of GSK3β is associated with several pathological conditions such as bipolar disorder, depression, sleep disorders, and Alzheimer's disease, thus making it a potential drug target to counter these abnormalities. Overexpression of GSK3β has been reported in various cancers, including pancreatic and breast cancer; leading to tumor progression, metastasis, and therapy resistance. This study focused on the identification of MJ34 as a highly potent anticancer agent tartgeting GSK3β. MJ34 was seen to significantly reduce growth and survival of human mutant KRas dependent pancreatic tumors. MJ34 mediated GSK3β inhibition was seen to induce apoptosis in a β-catenin dependent manner and downregulate NF-kB activity in MiaPaCa-2 as well as in MCF-7 cells thereby impeding cell survival and anti-apoptotic processes in these cells as well as in the xenograft model of pancreatic cancer. In vivo acute toxicity and in vitro cardiotoxicity studies indicate that MJ34 is well tolerated without any adverse effects. Taken together, we report the discovery of MJ34 as a potential drug candidate targeting GSK3β mediated cancer growth and survival.

Releasing the Brake on RhoA: Phosphorylation-Dependent Sequestration of RhoGDIα by 14-3-3ε Drives Cancer Cell Migration

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Metastasis is responsible for the majority of cancer-related deaths and is critically dependent on the ability of tumour cells to acquire a migratory phenotype. The small GTPase RhoA is a central regulator of cytoskeletal remodelling and actomyosin contractility during cell migration, yet the mechanisms enabling sustained RhoA activation in cancer cells remain incompletely understood.

Here, we identify a previously unrecognised regulatory mechanism controlling RhoA activation during cancer cell migration. Protein interaction analyses revealed that the stress-inducible chaperone HSPA1A associates with RhoA and promotes a migratory phenotype characterised by cytoskeletal remodelling and enhanced cell motility. Interactome analysis of this complex uncovered members of the 14-3-3 protein family, with 14-3-3ε emerging as a critical regulator of this signalling axis. Functional studies demonstrate that 14-3-3ε enhances RhoA activation and stimulates downstream ROCK signalling, thereby promoting cytoskeletal reorganisation and cell migration. Mechanistically, we show that 14-3-3ε interacts with the negative regulator RhoGDIα in a phosphorylation-dependent manner. Site-directed mutagenesis identified serine-81 of RhoGDIα as essential for this interaction, and disruption of this site abolishes RhoA activation.

Together, our findings reveal a regulatory mechanism in which 14-3-3ε sequesters RhoGDIα, releasing the inhibitory constraint on RhoA and driving cytoskeletal remodelling and cancer cell migration. This HSPA1A–14-3-3ε–RhoGDIα–RhoA axis provides new insight into the molecular regulation of metastasis and highlights potential targets for therapeutic intervention.

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KEYNOTE LECTURE:
What is T Cell Exhaustion?

Prof. Rafi Ahmad
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R2TP-Bridging peptides: A Novel Therapeutic strategy to restore tumor suppressor networks in cervical cancer

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Cervical cancer remains a major global health burden, predominantly driven by persistent infection with high-risk human papillomavirus (HPV) types 16 and 18. A hallmark of HPV-mediated oncogenesis is the functional inactivation of the key tumor suppressors p53 and pRB by the viral oncoproteins E6 and E7, respectively. These proteins subvert host cellular machinery, promoting uncontrolled proliferation and malignant transformation. In this study, we uncover a previously uncharacterized mechanism by which E6 and E7 hijack a novel host chaperone complex to facilitate the degradation and inactivation of p53 and pRB. Building on this insight, we identified a peptide derived from host proteins that interact with the R2TP chaperone complex. Remarkably, this peptide exhibits a dual mode of action: it scavenges E6, thereby preventing p53 degradation, and simultaneously competes with E7 for binding to pRB, restoring its tumor-suppressive function. This coordinated reactivation of both p53 and pRB highlights a promising therapeutic strategy targeting the core drivers of HPV-induced carcinogenesis.

Our findings not only provide new mechanistic insights into viral-host interactions in cervical cancer but also introduce a novel peptide-based intervention with significant therapeutic potential. This approach may pave the way for the development of targeted treatments for HP Vassociated malignancies, addressing a critical unmet need in cancer therapy.

Novel Car T Cell Approaches to Overcome Immune Escape in Solid Tumors

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Solid tumors remain largely resistant to cellular immunotherapy due to immune exclusion, antigen heterogeneity, and immunosuppressive tumor microenvironments (TME). To address these barriers, we are developing novel platforms that combine targeted cellular therapy with localized immune reprogramming. First, we have armored chimeric antigen receptor (CAR) NK cells with interleukin-12 (IL-12) to enhance effector function, promote epitope spreading, and remodel the TME. By restricting IL-12 activity to the tumor site through the inclusion of a collagen binding A3 domain, we aim to amplify cytotoxicity while minimizing systemic toxicity. Second, we leverage tumor-targeting, non-pathogenic bacterial strains as programmable delivery systems for immunomodulatory payloads. These engineered microbes selectively accumulate within tumors and can be designed to secrete cytokines, present neoantigens, or locally modulate suppressive pathways. Together, these approaches enable spatially controlled immune activation, converting immunologically “cold” tumors into inflamed, therapy-responsive sites. Our integrated strategy seeks to overcome antigen escape, enhance endogenous T and NK cell recruitment, and establish durable anti-tumor immunity. By combining cell engineering with microbial synthetic biology, we aim to create modular, scalable platforms capable of reshaping the immune landscape of solid tumors and advancing next-generation cancer immunotherapy.

Material Property of Spindle Poles Determines the 3-Dimensional Nuclear Architecture

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Animal cells dismantle and reconstruct their nuclear envelope (NE) in coordination with spindle pole organization. While the purpose of this coordination is unclear, we found that Aurora A kinase maintains the spindle pole protein NuMA in a dynamic state during anaphase. Without Aurora A, NuMA shifts from a dynamic to a solid phase, abnormally accumulating at the spindle poles, leading to chromosome bending and misshapen nuclei formation around the poles. NuMA's localization relies on interactions with dynein/dynactin, its coiled-coil domain, and intrinsically disordered region (IDR). Mutations analysis revealed that cation-π interactions within IDR are key for NuMA's accumulation, while glutamine residues trigger its solid-state transition upon Aurora A inhibition. This work, which I will present, emphasizes the role of material properties of spindle poles in organizing the nucleus and genome post-mitosis.

IACR-2026 ORATION LECTURE: A Personal Journey How Discovery Science Can Co-Exist With Translational Biology

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It has often been observed that researchers tend to put unseen barriers between cancer biologists who do blue sky research and who practise clinical and translational biology. This often causes an impediment not allowing meaningful expansion of the horizon of research. A personal journey will be recounted where a basic biologist tried to overcome this mental block and consciously took some steps trying to do answer questions in basic biology with a societal outcome. As a test case two recent advances will be briefly recounted – where (a) a peptide based DNA Damage Response (DDR) agonist has been discovered which may have an implication in breast cancer; (b) three FDA approved small molecules which can revert chemoresistance in colon cancer.

Cancer Immunotherapy and Gut Microbiome: Is there a Relationship?

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There is a significant, evidence-based relationship between the gut microbiome and cancer immunotherapy efficacy. A diverse gut microbiome influences systemic immunity, directly impacting how patients respond to immune checkpoint inhibitors (ICIs); side effects could be reduced but also accentuated with this manipulation. Specific bacterial compositions are associated with better anti-tumor responses.

Key Findings on the Microbiome-Immunotherapy Link

- **Response Predictor:** The composition and diversity of the gut microbiota can determine whether a patient responds to immunotherapy
- **Responders vs. Non-responders:** Patients with a higher abundance of specific bacteria (e.g., Faecalibacterium, Akkermansia) tend to have better outcomes, showing higher immune cell activation and tumor infiltration.
- **Antibiotic Interference:** Using broad-spectrum antibiotics before or during immunotherapy can disrupt the gut microbiota, leading to poorer survival rates.
- **Therapeutic Modulation:** Fecal microbiota transplantation (FMT) and probiotics may shift the microbiota toward a profile that improves therapeutic success.

How the Microbiome Affects Immunotherapy

The gut bacteria work with the immune system by:

- **Metabolite Production:** The production of short-chain fatty acids (SCFAs) is linked to improved immunotherapy outcomes.
- **Immune Regulation:** Modulating the balance between anti-tumor immune activity and immunosuppression.
- **Reducing Toxicity:** A healthy microbiota can potentially reduce adverse events from immunotherapy.

Ongoing research is looking into manipulating the microbiota through diet, FMT and radiotherapy (low dose) and see as to how this may improve immunotherapy responses.

Targeting Nonhomologous End Joining: Potentiating Cancer Therapy through DNA Repair Disruption

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Small-molecule inhibitors of nonhomologous end joining (NHEJ), a major DNA double-strand break repair pathway, can enhance cancer therapy by increasing unrepaired damage in tumour cells. SCR7, a first-in-class DNA Ligase IV inhibitor, induces persistent DSBs and tumour regression but is limited by relatively high IC50 values, and formulation improvements have not markedly lowered this in cell-based systems. Derivatization of this scaffold has therefore been a priority to improve potency and translational potential.

Two newer inhibitors, SCR116 and SCR132, target the DNA-binding domain of Ligase IV and achieve nanomolar IC50 values, representing over 100-fold improvement compared with SCR7. They selectively inhibit Ligase IV–dependent NHEJ without significantly affecting Ligases I and III and show reduced activity in Ligase IV–null cells, confirming target specificity. Functionally, these compounds potentiate radiation and chemotherapeutic agents, increase DSB accumulation, and induce G2–M arrest and apoptosis. In vivo, SCR116 and SCR132 reduce tumour growth in mouse allograft models as monotherapy and in combination with radiation, and oral dosing in xenografts decreases tumour burden and improves survival with no major toxicity in dose-escalation studies.

Decoding the Cancer-Associated Fibroblasts Role in Cancer Progression and Drug Resistance

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The tumour ecosystem constitutes a dynamic interaction between the cancer cells and its microenvironment, comprising mainly cancer-associated fibroblast (CAF), immune cells, endothelial cells and extracellular matrix. CAFs are one of the abundant stromal cells in the tumour microenvironment (TME) in many cancers. Understanding the molecular mechanisms to maintain the CAF phenotype is important to control disease outcomes. In the present work, we have identified Insulin-like Growth Factor Binding Proteins (IGFBPs) are differentially expressed in CAFs compared to Normal Fibroblasts (NFs) derived from NSCLC patients. In this study, we investigated the role of IGFBPs in CAFs and their impact on tumour cells. Our study highlights the importance of individual IGFBPs' role in shaping distinct CAF subpopulations and extrinsically enhancing tumour cell properties. Targeting the underlying mechanisms by which these different CAF subpopulations influence tumour cell properties could support the available conventional therapies. Also, we demonstrated that CAFs support tumour cell drug resistance. Further, we have identified CAF secreted proteins that contributes to drug resistance in lung cancer.

Gut Microbiome and Cancer

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It is now well established that the human body harbours a vast and dynamic microbial population that profoundly influences host metabolism, immune function, and overall health. Perturbations in this finely balanced ecosystem, commonly referred to as dysbiosis, have been implicated in a wide spectrum of diseases and metabolic disorders affecting multiple organs. Recent advances in highthroughput technologies, systems biology, and computational approaches have revolutionised our ability to characterise these previously inaccessible microbial ecosystems and to decipher their functional impact on the host.

The gut microbiome plays a central role in maintaining metabolic and immune homeostasis and is increasingly recognised as one of the key determinants of cancer initiation, progression, and therapeutic response. This talk will examine the contribution of the gut microbiome to cancer through the framework of Gut–Organ axes, illustrating how microbial signals originating in the intestine influence tumour biology in distant organs. Particular emphasis will be placed on gut microbiome derived metabolites, including short-chain fatty acids, bile acid derivatives, indoles, polyamines, microbial toxins, etc., and their context-dependent roles in preserving epithelial integrity, modulating inflammation, activating oncogenic pathways, and shaping the tumour microenvironment. Building on these insights, the talk will further discuss potential strategies for monitoring gut health and outline next-generation microbiome-targeted therapeutic approaches, highlighting the how gut microbiome can be utilized both as a biomarker and a modifiable target in cancer prevention and treatment.

Unveiling GBM's Survival Blueprint: From Senescence Escape to DNA Repair Modulation

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GBM treatment is an arduous task due to its location, resistance to therapy, and high rate of recurrence. We established a GBM residual disease survival and recurrence cellular and in vivo model using clinically relevant patient samples and observed that radiation Therapy-Induced Senescence (TIS) in GBM reverses, generating a recurrent population. In this presentation, I will present data from two of our recent studies, 1) in which we identify that ER stress led the PERK-mediated UPR pathway to act as a switch for senescence reversal in residual senescent cells of GBM. CHOP, a transcription factor downstream of PERK, likely steers TIS towards survival. Accordingly, we demonstrate that PERK inhibition/knockdown in combination with radiation has a senostatic effect, thus increasing disease-free survival in vivo. Remarkably, when PERK inhibitor is administered in the residual senescent stage, it acts as a senolytic drug, completely abrogating residual senescent disease in vivo. This data provides evidence for a new seno-therapeutic option for eliminating residual GBM and preventing recurrence. 2) In this study, we identified an untraversed DSB repair function of GCN5, a histone acetyltransferase, and provided detailed mechanistic insights into both transcriptional and post-translational regulation of HR-NHEJ master regulators, DNA-PKcs and ATM. Alongside, we also highlight the translational importance of the PARP1-GCN5 axis in mediating GBM radio-resistance.

R-Loop Homeostasis as a Selective Vulnerability in Cancer Stem Cells

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Hypertranscription is a hallmark of cancer and correlates with poor clinical outcomes. R-loops, three-stranded DNA:RNA hybrid structures, arise naturally as a consequence of elevated transcriptional activity. Cancer stem cells (CSCs) engage in a delicate R-loop balancing act. CSCs exploit regulatory R-loops to sustain oncogenic transcriptional programs while preventing excessive R-loop accumulation that would otherwise trigger transcription–replication conflicts and genome instability. To maintain this balance, CSCs depend on specialized proteins that tightly modulate R-loop dynamics, representing a compelling yet largely untapped class of therapeutic targets. Here, we identify the germline-associated protein PIWIL4 as a critical R-loop-resolving factor that is aberrantly upregulated in acute myeloid leukemia (AML). PIWIL4 prevents pathological R-loop accumulation and transcription–replication conflicts in AML stem cells, sustaining CSC self-renewal while being dispensable for normal human hematopoietic stem cell function in vivo. Proximity-dependent proteomics revealed that PIWIL4 interacts with a network enriched for proteins involved in R-loop regulation. A targeted CRISPR–Cas9 dropout screen uncovered N-acetyltransferase 10 (NAT10) as a key mediator of regulatory R-loops. Loss of NAT10 markedly diminished regulatory R-loop formation. Mechanistically, NAT10's RNA helicase domain, but not its acetyltransferase activity, is required for R-loop stabilization. NAT10 preferentially occupies promoter-proximal regions, maintaining R-loops at MYC-driven loci and modulating MYC chromatin engagement. Together, these findings delineate distinct mechanisms of R-loop regulation essential for CSC maintenance and highlight PIWIL4 and NAT10 helicases as eraser and writer of R-loops, respectively, and potential therapeutic targets in AML.

Cholesterol metabolic reprogramming and PI3K/Akt/mTOR hyperactivation are predictive of carboplatin resistance in High-Grade Serous Ovarian Carcinoma

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Clinical challenges with carboplatin in High-Grade Serous Ovarian Cancer (HGSOC) are often mediated by alterations within the PI3K/Akt/mTOR prosurvival axis and consequent reprogramming of cholesterol metabolism. To evaluate the clinical relevance of these alterations in predicting carboplatin response among HGSOC patients, we conducted a pilot study. Thirty-one (31) non-NACT HGSOC patients were classified into normal, borderline, and high groups based on quantified blood and tumor cholesterol levels. We integrated TCGA data and in silico modelling with Western blotting, co-immunoprecipitation, and immunohistochemistry to characterize PI3K/Akt/mTOR and cholesterol-regulatory markers. Carboplatin sensitivity was assessed in ex vivo primary cultures along with membrane rigidification measurements. Findings were validated in vitro and confirmed by statistical analysis. Marked dysregulation of PI3K/Akt/mTOR signalling and cholesterol regulators (SREBP1/2, SR-B1, HMGCR), along with prosurvival effectors (Akt, mTOR, p70S6K, p38 MAPK, HIF-1α, COX-2, VEGF), was predominant in the high-cholesterol HGSOC cohort. Elevated HMGCR-driven cholesterol turnover correlated with aggressive histology and carboplatin resistance, characterized by poor DNA adduct retention and minimal induction of DNA damage, ROS, and mitochondrial depolarization. The borderline cohort showed similar but attenuated trends. Consequently, high and borderline groups were classified as non-responders and intermediate responders, respectively, while the normal group was identified as carboplatin responders. This proof-of-concept study demonstrate that monitoring cholesterol-regulatory and PI3K/Akt/mTOR pathways may offer a promising strategy for personalizing HGSOC therapy, specifically by stratifying patients based on their predicted responsiveness to carboplatin.

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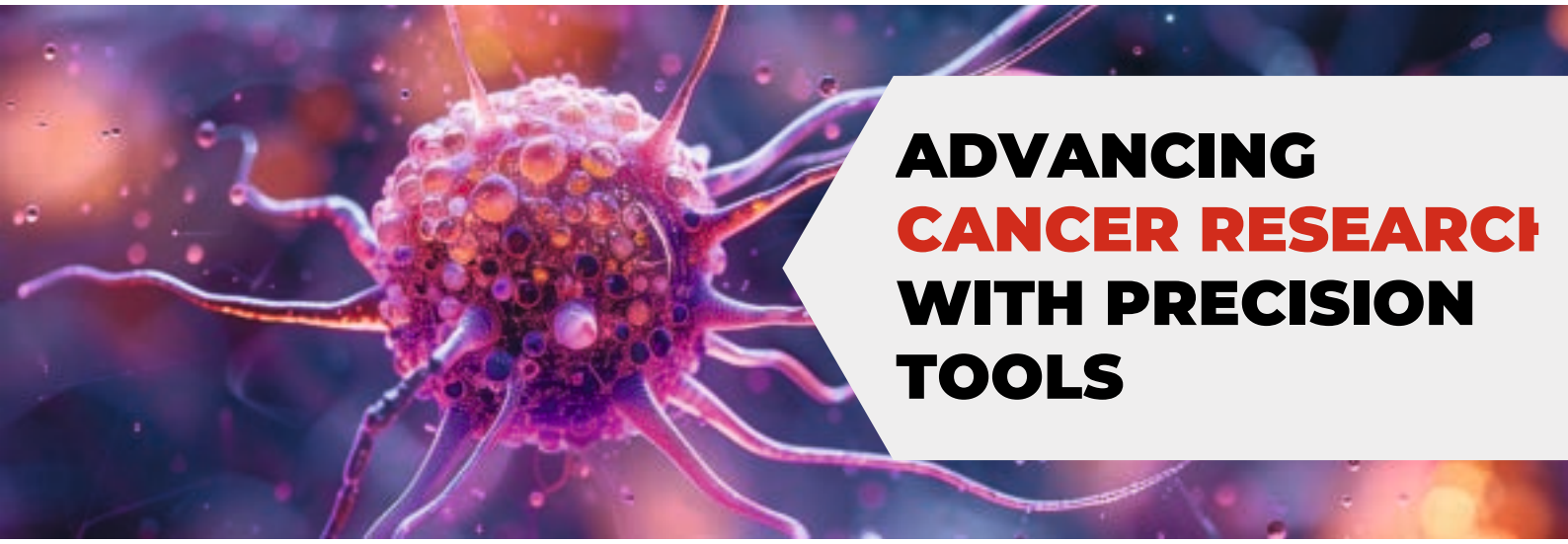

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IACR 2026 - Dr Virendra Balkrishna Kamat Award and Mr Ram Nath Hiralal Jaju Award for Young / Mid-level scientists

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Targetable Metabolic Dependencies Drive Therapy Resistance in Treatment-Refractory Colorectal Cancer

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Therapy resistance remains a major clinical challenge in colorectal cancer (CRC), driving disease relapse and poor patient outcomes. Resistant tumour cells survive therapeutic stress by activating adaptive metabolic and stress-response programs; however, the molecular determinants of these adaptations remain poorly understood. Elucidating these mechanisms is critical for identifying targetable vulnerabilities in refractory disease.

In this study, we investigated metabolic adaptations underlying therapy resistance in colorectal cancer using patient-derived organoid (PDO), xenograft (PDX), and persister cell models. Using integrated transcriptomic, biochemical, lipidomic, and ultrastructural analyses, we identify lipid metabolic reprogramming as a central survival mechanism in therapy-resistant CRC models. These cells upregulate de novo lipogenesis and sequester lipids in droplets via an ETS1–PTPN1–c-Src–CEBPβ–Lipin1 axis. Pharmacological disruption of lipid droplet biogenesis using Lipin1 inhibitors or clinically approved statins restores lipid toxicity, induces ferroptotic cell death, and re-sensitizes DTPs and PDOs. In parallel, studies using aggressive signet ring cell carcinoma (SRCC) derived systems demonstrated that increased autophagic flux represents a dominant compensatory survival mechanism

following chemotherapy. Combination treatment with microtubule-targeting agents and standard FOLFIRI chemotherapy or pharmacologic inhibition attenuated autophagy, significantly reducing tumour growth and peritoneal metastasis.

Collectively, our findings delineate lipid metabolism and autophagy as key survival pathways driving therapy resistance in colorectal cancer, with LPIN1-driven lipid droplet formation representing a critical metabolic vulnerability. This work highlights patient-derived models as a bridge to clinical translation and supporting repurposing of tractable agents to improve outcomes in refractory CRC.

Key words: Drug Tolerant Persister Cells, De Novo Lipogenesis, Non-Responder, Ferroptosis, Autophagy, SRCC, PDX, PDO.

IACR 2026 - Dr Virendra Balkrishna Kamat Award and Mr Ram Nath Hiralal Jaju Award for Young / Mid-level scientists

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Transcriptomic profiling identifies metastasis-competent subtypes of circulating tumour cells, driven by microbial signatures in oral squamous cell carcinoma: development of a predictive gene panel for early relapse

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Background: Metastasis is the primary cause of cancer mortality, yet the traits enabling tumour cells to spread remain poorly defied. Circulating tumour cells (CTCs) are rare cells shed from primary tumours that survive in the bloodstream and drive tumour spread. Understanding their molecular programs is essential for improving risk stratifiation and preventing relapse. We examined CTC biology in Oral Squamous Cell Carcinoma (OSCC), a major public health burden in the Indian subcontinent, where nearly one-third of patients relapse within a year despite achieving clinical remission.

Methods and results: We conducted whole transcriptome analysis of paired CTCs (using ultra-low cell input RNAseq) and primary tumours collected from 24 patients. Unsupervised hierarchical clustering revealed that all CTC-samples and primary tumour samples form distinct clusters, indicating intrinsic differences in their gene expression. Importantly, CTC transcriptome data alone stratified patients into two molecular subgroups with significant differences in lymph node metastasis (p=0.008), recurrence rates (p=0.0305), and overall survival (p=0.0306), independent of conventional primary tumour characteristics. We next performed pathway enrichment followed by Weighted gene co-expression network analysis (WGCNA) and identified various pathways, including inflammation and ECM receptor interaction, in CTCs, which are crucial for metastasis to loco-regional lymph nodes and poor disease outcome. Analysis of the matched primary tumours corresponding to high-risk CTC profiles showed enrichment of epithelial-to-mesenchymal transition (EMT)-related pathways and stem-cell like transcriptional programs, indicating that a distinct subset of CTCs, characterized by specific molecular features represents the biologically aggressive population responsible for disease progression.

To facilitate clinical translation, we derived a minimal gene signature from the aggressive CTC transcriptome. The top candidate genes were subjected to absolute quantification using multiplex digital PCR and machine learning algorithms were utilized to develop a clinically feasible recurrence-prediction panel. Feature selection integrating pointbiserial correlation, gene–gene correlation, and recursive feature elimination identified a non-redundant four-gene panel TNFAIP2, NFKBIZ, NFKBIA, and PTGS2. Comparative machine learning models with SMOTE balancing and 5-fold cross-validation demonstrated superior performance of XGBoost (AUC 0.84), outperforming Random Forest, Stacking, and Logistic Regression. Regularised XGBoost maintained robust performance (AUC 0.80) with reduced overfitting. Collectively, these findings demonstrate that baseline CTC gene expression profiling enables accurate relapse prediction in OSCC.

In addition to tumour-intrinsic programs, we identified microbial signatures within CTCs. Analysis of unmapped RNA sequencing reads demonstrated enrichment of Fusobacterium nucleatum within CTC samples and primary tumours, which shed CTCs. These findings were independently validated using quantitative RT-PCR and RNA in situ hybridisation. We have also shown internalisation of Fusobacterium nucleatum by oral cancer cells in vitro using confocal microscopy. The presence of microbial transcripts within circulating tumour cells suggests a potential role for oral commensal bacteria in facilitating tumour dissemination or modulating metastatic behaviour. Conclusion: Our study provides molecular evidence that metastasis in OSCC may be driven by a selectively adapted subpopulation of CTCs characterised by convergent transcriptional programs and distinct microbial associations. We also propose a clinically actionable framework for identifying patients at high risk of relapse through CTC-based molecular profiling. This work advances the understanding of metastatic biology and supports the implementation of precision surveillance strategies to intercept cancer progression before clinically overt relapse occurs.

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IACR 2026 - Postdoctoral Fellow Travel Award

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Proteomic Identification of 14-3-3γ Glutathionylation Reveals an LCN2-Mediated Redox Axis in Colorectal cancer

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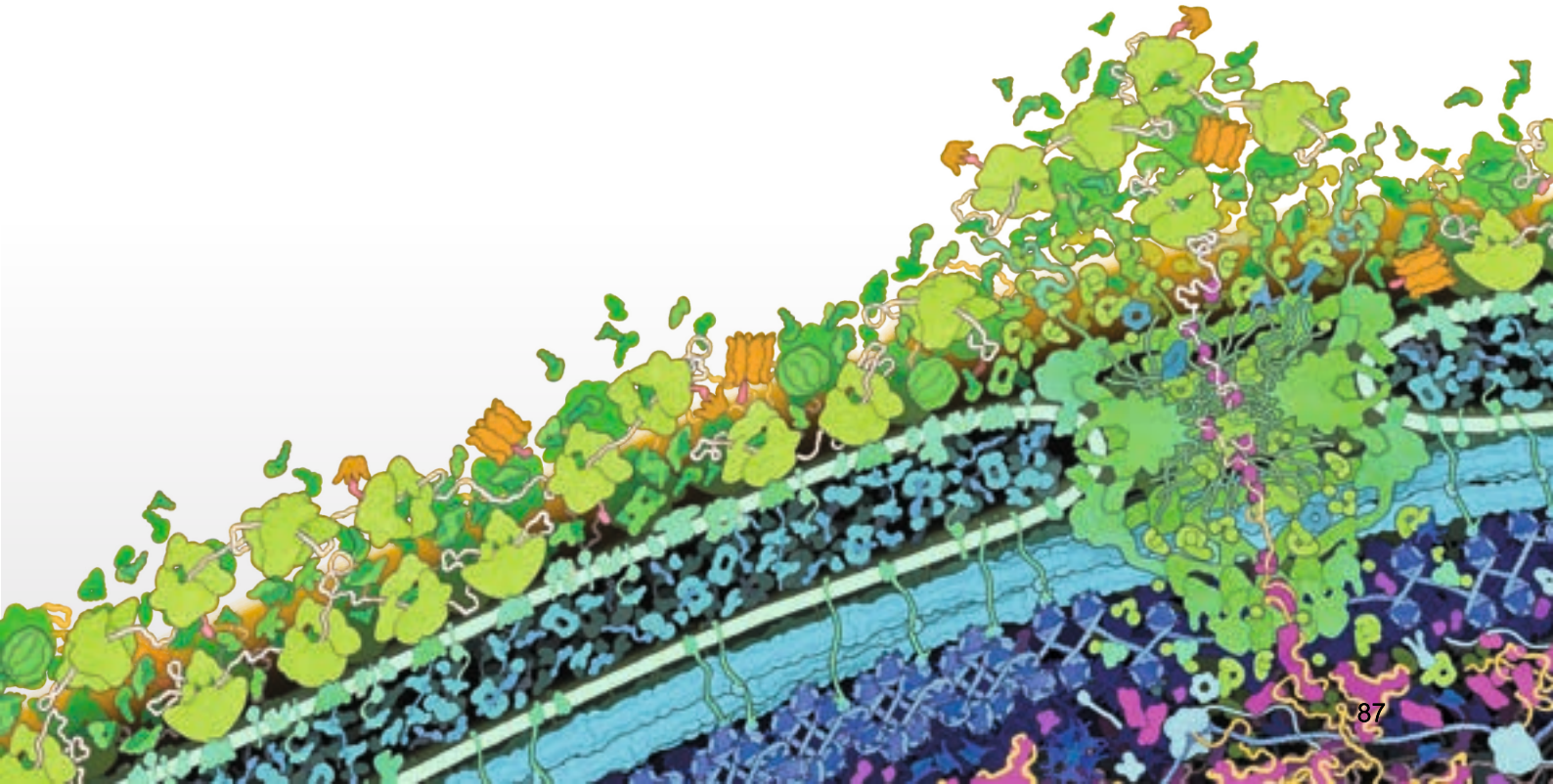
Chemotherapy induced oxidative stress alters cytoskeletal dynamics and cell–cell adhesion, yet the molecular nodes that couple redox signaling to junctional protein assembly remain incompletely defined. We earlier reported LCN2 prevents actin glutathionylation. Here, we examined how glutathionylation affects 14-3-3γ structure and desmosome assembly. A label free proteomic screen combined with GST–pulldown assays were used to identify glutathionylated targets in human colorectal cancer cells. We focused on 14-3-3γ and generated cysteine-to-serine mutants at C97S, C112S and C194S. Glutathionylation was assessed biochemically, desmosome formation, desmosomal protein expression, and actin organization were analyzed under basal and 5-FU treatment conditions. Proteomic screen identified 14-3-3γ and 18 other proteins to be enriched. Site-directed mutagenesis revealed that C97 and C112 are required for 14-3-3γ glutathionylation. The change in the Cysteine residue at these sites exacerbated desmosomal protein overexpression concomitant with altered 14-3-3γ modification, consistent with a coordinated redox dependent shift in junctional and microtubule polymerization. These data identify glutathionylation of 14-3-3γ at C97 and C112 as a redox-sensitive switch that links actin dynamics to desmosome assembly, and show that LCN2 overexpression reprograms this axis under 5-FU stress. Targeting the 14-3-3γ glutathionylation may modulate chemotherapy associated junctional remodelling and influence therapeutic response.

Keywords: 14-3-3γ, Colorectal Cancer, Desmosomes, Glutathionylation

Complete Workflow Automation

Extraction | Pre-processing | Quantitation | Post-processing | Analysis



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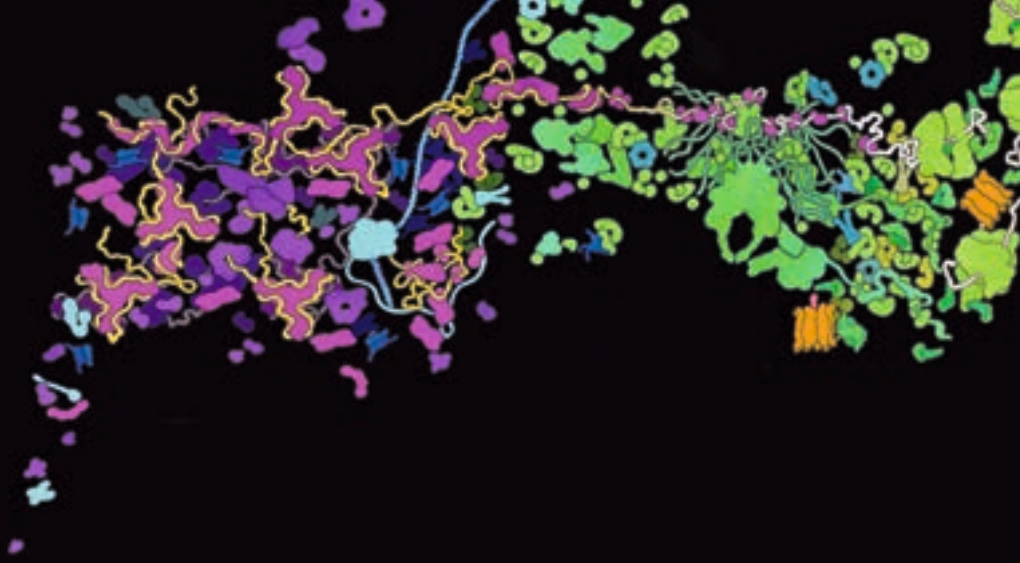

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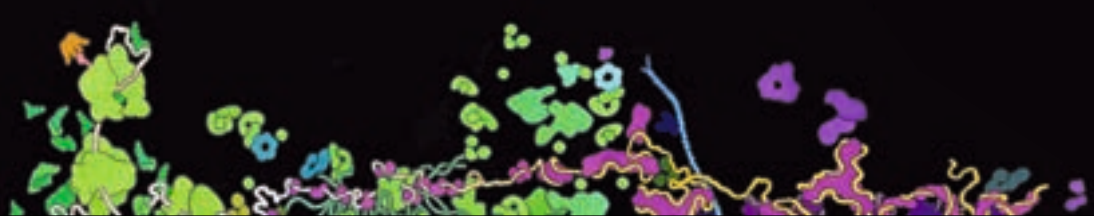

ASTRACTS SELECTED FOR ORAL PRESENTATION

(Ph.D students)

IACR – 601 **ORAL**

Mechanistic and Quantitative Dissection of Car T Cell-Induced Cytotoxicity Using A Dual Live-Cell Biosensor Platform

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A mechanistically resolved and quantitative understanding of CAR T-cell induced cytotoxicity is essential for engineering safer and more effective cellular immunotherapies. Current assays largely treat tumor killing as a binary endpoint and lack the spatial–temporal resolution needed to discriminate regulated cell-death (RCD) programs. Consequently, the field lacks a quantitative framework for defining how CAR T cells engage in apoptosis versus primary or secondary necrosis, trajectories that differ markedly in kinetics, inflammatory potential, and therapeutic consequences.

Here, we present an integrated live-cell imaging and flow cytometry platform that combines a FRET-based caspase-3/7 biosensor with a mitochondrial reporter to decode apoptosis and primary/secondary necrosis in real-time during CAR T-cell engagement. Using EGFR? MDAMB-231 and SiHa tumour models across varying effector-to-target ratios, we quantify death-pathway engagement at single-cell resolution and reconstruct the temporal sequence of cytotoxic events. CAR T cells initiate a rapid, caspase-dependent apoptotic program in the majority of tumour cells, whereas a distinct subset progresses to late primary necrosis or transitions into secondary necrosis—modes of death that are routinely missed by conventional CAR T evaluation assays. These trajectories exhibit unique kinetics, correlate with CAR T target synapse stability, and are associated with divergent inflammatory signatures.

This dual-sensor framework establishes a mechanistic and quantitative benchmark for dissecting CAR T-mediated cytotoxicity, providing a platform for evaluating of next-generation CAR constructs, dosing strategies, and combination therapies. By resolving death-pathway heterogeneity in real time, our approach enables the rational optimisation of CAR T-cell therapies with improved efficacy and reduced toxicity.

Key words: Car T-Cell Therapy, Immunotherapy, Apoptosis, Necrosis, Fret Biosensor, Cytotoxicity Mechanisms, Single-Cell Resolution

IACR – 610 **ORAL**

Beyond Kinase Domain Mutations in BCR-ABL1: A Preclinical Insight into a Novel Mutation Pair of SH3-SH2 Domain Underlying Imatinib Resistance in Chronic Myeloid Leukemia

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Chronic Myeloid Leukemia (CML) is a type of hematological malignancy characterized by presence of Philadelphia chromosome. BCR-ABL1 translocation, in Philadelphia chromosome, is the main genetic driver of this myeloid neoplasia. Targeted CML treatment was made possible by the discovery of Imatinib, a Tyrosine Kinase Inhibitor (TKI). This competitive ATP inhibitor binds at the kinase domain of BCR-ABL1 oncoprotein, thus abrogating leukemic blasts proliferation. Despite this, Imatinib resistance is a major concern in CML management, globally. Imatinib failure affects 30% of CML patients, 50% of whom had Kinase Domain (KD) mutations. These mutations induce conformational alterations in BCR-ABL1 that obstruct Imatinib accessibility to the binding site, leading to Imatinib resistance. However, the remaining ~50% patients with imatinib resistance lack any KD mutations. We performed targeted deep sequencing and identified two *de novo* SH3-SH2 domain mutations in 30% of Imatinib-resistant CML cases. *In silico* molecular dynamics (MD) simulation analyses predicted modification between the SH3 and SH2 domain upon presence of this mutation pair. Performing *in vitro* viability and clonogenicity assays we observed imatinib-resistance due to presence of these mutations. Further, xenograft studies with NOD-SCID mice corroborated the same. While searching for potential next generation TKIs to overcome this resistance, MD simulation analyses suggested that Dasatinib is the best next generation TKI to overcome Imatinib resistance. Dasatinib efficacy was confirmed *in vitro,* followed by *in vivo* preclinical studies. Together, this study comprehensively expands current understanding of CML pathophysiology upon Imatinib resistance and emphasizes routine SH3-SH2 domain mutation screening for CML management.

Key words: Chronic Myeloid Leukemia, Tyrosine Kinase Inhibitor, BCR-ABL, Targeted Therapy, Drug Resistance

IACR – 622 **ORAL**

Dab2 Loss Delays Tumour Initiation and Prevents Disease Progression in Murine Squamous Cell Carcinoma

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Dab2 is an endocytic adapter protein involved in endocytosis of the receptors of key signalling pathways. Dab2 loss has been reported in multiple cancers; however, its role in tumour initiation and CSCs regulation is still obscure. We used a DMBA/TPA murine skin SCC model with a conditional knockout of Dab2 in the skin. Further, we isolated CSCs from WT and Dab2 cKO mouse skin at various time points between 5 and 52 weeks post the initiation of TPA treatment. Transcriptomic analysis of CSCs harvested at 10- and 20-weeks post TPA treatment

Revealed enrichment of proliferative and metabolic pathways in WT CSCs. Interestingly, enrichment of epigenetic and DNA damage repair pathways was observed in the Dab2 cKO CSCs. Markers associated with stemness such as CD34, SOX4 & NFATC1, and TGF-beta signalling such as TFGB2, TGFB3 were differentially expressed in Dab2 cKO CSCs as compared to WT. These findings were validated using immunofluorescence analysis of markers associated with stemness, quiescence, proliferation and DDR such as SOX9, NFATc1, Ki-67 and γH2AX. Our data revealed lower incidence and delayed tumour initiation in Dab2 cKO mice compared to WT mice. Hitherto, our data showed that Dab2 loss delays tumour initiation and progression in mouse SCC.

Key words: Disabled-2, Squamous Cell Carcinoma, Cancer Stem Cells, Tumorigenesis, Gene Set Enrichment Analysis

IACR – 627 **ORAL**

Dissecting the Molecular Events Involved in GM2 Mediated Modulation of Tumor Suppressor Hippo-YAP/TAZ Signaling Axis

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Ganglioside (GM2) is reported to be extensively overexpressed in several types of cancer and are shed from tumor cell surface promoting cancer cell migration, invasion and anchorage independent growth (AIG). Global transcriptomic data suggests ganglioside GM2-mediated upregulation of YAP/TAZ target genes. However, the precise signaling events leading activation of YAP/TAZ is still unclear. This study aims to address the mechanism of GM2 mediated cancer progression via modulation of Hippo-YAP/TAZ signaling axis. Exogenous administration of GM2 in HeLa cells promotes time dependent modulation of several components of Hippo-YAP/TAZ signaling axis along with target gene expression namely ctgf, cyr61. Perturbation of actin polymerization significantly reduces GM2 mediated YAP/TAZ activation suggesting modulation of F-actin cytoskeletal dynamics in GM2-mediated YAP/TAZ activation. Abrogation of YAP-TEAD interaction via Verteporfin blocks GM2 mediated downstream gene expression both at the transcriptional as well as translational level, indicating functional association of YAP-TEAD in GM2 dependent target gene expression. To investigate whether GM2 exerts its downstream effects through membrane bound receptors, especially GPCRs, an inverse Docking Screening was performed. The study reveals GNRHR (7BR3), S1PR1 (7TD4), CHRM5 (6OL9), GRM2 (8JCY), CHRM2 (6ZFZ) and BDKRB1 (7EIB) receptors as potential targets of GM2, which needs further in-vitro validation.

Key words: Ganglioside GM2, Hippo, YAP/TAZ, Cancer

When A GPCR Meets the Ribosome: An Intracellular CXCR4-RPL35A Axis Governs Translational Control and Metastasis in TNBC

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Triple-negative breast cancer (TNBC) is the most aggressive breast cancer subtype, with limited therapies and early metastasis causing >90% deaths. Multi-cohort analyses show that chemokine receptor CXCR4 is uniquely upregulated in TNBC, with higher expression in metastases than primary tumours. While CXCR4 has been extensively studied as a cell-surface GPCR, the role of intracellular-CXCR4 (non-canonical) has remained undefined despite its predominant intracellular localization in TNBC. Here, we uncover a previously unrecognized intracellular receptor–ribosome coupling mechanism in TNBC, wherein intracellular-CXCR4 directly associates with ribosomal protein RPL35A to drive metastasis. Using intracellular-retaining deletion-mutants, surface-restricted constructs, and CXCR4 knockdown TNBC cell lines, we demonstrate that intracellular, but not surface-localized, CXCR4 promotes metastatic phenotypes in-vitro and in-vivo. Integrated proteomic and transcriptomic analyses show post-transcriptional enrichment of translation-associated signatures in intracellular-CXCR4 overexpressing cells. Co-IP mass-spectrometry identifies RPL35A as the key CXCR4-interactor, with translation-related pathways again overrepresented. Mechanistically, co-IP, cycloheximide chase, and RNA-immunoprecipitation assays show that intracellular CXCR4 stabilizes RPL35A and enhances its ribosomal RNA associations. Functional assays, including HPG-incorporation, puromycin labelling, and polysome profiling, confirm that CXCR4 loss suppresses global translation, whereas intracellular-CXCR4 enhances translational efficiency relative to surface-localized CXCR4. Domain mapping studies identify CXCR4 residues 66–71 as critical for RPL35A binding; disruption of this motif impairs translation and metastasis in-vivo. Clinically, IHC reveal that CXCR4 and RPL35A are elevated in metastatic TNBC tissues and associate with poor patient survival. Together, these findings reveal a novel intracellular receptor–ribosome axis sustaining translational capacity and metastatic competence, establishing the CXCR4–RPL35A axis as a targetable vulnerability in TNBC.

Key words: CXCR4, RPL35A, Protein Translation, TNBC, Metastasis

Identification of Mechanisms by which LCN2 Promotes Autophagy and Tumour Progression in Colorectal Cancer

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Previous studies from our laboratory have demonstrated that LCN2 (an iron-binding secretory glycoprotein) inhibition using monoclonal antibody led to colorectal cancer (CRC) tumor regression and increased sensitivity towards 5-fluorouracil(5-FU), a first line-chemotherapy drug. Additionally, increased LCN2 and autophagy contribute to radio-resistance. Thus, we aim to study the LCN2-autophagy association as a potential CRC therapeutic target. The cellular autophagy was evaluated in LCN2-overexpressing and knockdown celllines using techniques – Western blotting, immunofluorescence, and SEM. In tamoxifen-inducible transgenic KPC:APC mice, levels of LCN2 and autophagic-proteins were strikingly higher in colon adenocarcinoma and rectal squamous cell carcinoma tissue than their respective adjacent normal tissues. In the DLD1 xenograft NOD/SCID model, the combination of 5-FU with an autophagy-inhibitor chloroquine (CQ) results in significantly greater reduction in tumour volume compared to the control and monotherapy-groups. CQ treatment results in reduced cell-migration, invasion, and survival of CRC cells. LCN2 is reported to inhibit ferroptosis by regulating cellular-iron and ROS levels and promotes focal adhesion assembly (FA), assisting in cell migration. Autophagy is found to be essential for LCN2-dependent Lipid-ROS clearance and formation of FA. The study reveals a novel interaction between LCN2-p62 and the interaction of LCN2 with ATG4B, indicating a coupled function of LCN2 and autophagy aiding in CRC progression.

Key words: CRC Progression, Lipicalin2 (LCN2), Autophagy, Focal Adhesion Assembly, Ferroptosis, and Therapy Resistance

IACR – 647 **ORAL**

Spatial Transcriptional Profile Reveals Aggressive Circulating Tumour Cell Dissemination Driving Early Recurrence in Oral Squamous Cell Carcinoma

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Oral squamous cell carcinoma (OSCC) is a major disease burden in India and is associated with high incidences of early relapse. Here, we have explored the spatial and temporal heterogeneity of primary tumour and circulating tumour cells (CTCs) to understand the molecular mechanisms driving early relapse and treatment failure. Three spatially different regions of the tumour, the invasive front (T1) and two deeper regions (T2, T3), along with matched tumour-free margins (TFM), in each group, early recurrence (EarlyR) and no recurrence (NoR) (N=5 per group; n=40 samples) of OSCC patients, proceeded for RNAseq. Ultra-low input RNA sequencing of CTCs was performed at two time points (baseline and post-therapy/recurrence) for temporal analysis. Integrated analysis was performed to identify the spatio-temporal signatures associated with early relapse. EarlyR tumours exhibited significantly greater transcriptional divergence from their adjacent TFMs compared to NoR. The invasive front of EarlyR tumours was enriched for epithelial– mesenchymal transition, TNFα–NFκB signalling, and extracellular matrix remodelling, suggesting a site of

dissemination of aggressive CTCs. Temporal analysis revealed marked transcriptomic evolution in post-therapy CTCs from EarlyR patients, suggesting therapydriven selection of aggressive clones. Immune evasion and cell-death resistance genes like VMP1, RIN3, GBP5, ITGAX and IRF1 genes are commonly upregulated in CTCs and primary-tumours of EarlyR patients. A cytoskeletal regulator, FNBP1L, was consistently overexpressed in the pre and post therapy CTCs EarlyR patients. Our Spatial-temporal transcriptional reprogramming of primary tumours and CTCs drive aggressive dissemination and early relapse in OSCC, suggesting the potential biomarker and therapeutic role.

Key words: Oral Squamous Cell Carcinoma, circulating Tumour Cells, early Recurrence tumour, Heterogeneity

IACR – 651 **ORAL**

Diagnostic and Prognostic Significance of LCN2, MMP9, and the LCN2/MMP9 Complex in Oral Squamous Cell Carcinoma

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135 differentially regulated candidate proteins identified in previous study using LC/MS-based shotgun proteomics in the saliva of OSCC patients. Lipocalin 2(LCN2) and Matrix Metalloproteinase 9(MMP9) were significantly upregulated. In this study, we evaluated their probable biomarker potential in oral squamous cell carcinoma (OSCC) patients. This study recruited 356 OSCC patients, 26 oral premalignant disorders (OPMDs) and 118 healthy controls. Saliva and blood samples were collected at baseline and follow-ups. Protein levels were measured by ELISA, IHC and mRNA expression analysed using RT-qPCR compared between tumour and tumor-free margins(TFM), then correlated with therapy response and disease outcomes. Levels of LCN2, MMP9, and their complex were significantly higher ($p \leq 0.0001$) in both saliva and serum of patients compared to OPMD and control groups. These increased protein levels correlated with disease staging and locoregional lymph node involvement. ROC analysis showed significant AUCs for LCN2 in saliva and serum (0.7446, 0.6802), serum MMP9 (0.9326), and the LCN2/MMP9 complex in both saliva and serum (0.7415, 0.7266), demonstrating good sensitivity and specificity. A combined risk prediction model using multiple logistic regression achieved an improved AUC (0.8025 & 0.9369). Furthermore, pretreatment salivary LCN2 and MMP9 were identified as predictive markers for overall survival (HR 1.915) and disease-free survival (HR 2.823) respectively. Significantly higher gene expression of LCN2 and MMP9 in tumour compared to TFM and presence in tumour tissue found associated with poor differentiation status. Baseline LCN2,MMP9 and LCN2/MMP9 complex can serve as a potential biomarker for the diagnosis and prognosis of patients with OSCC.

Key words: Oral Squamous Cell Carcinoma, Proteomic Biomarkers, Elisa, Lipocalin 2(LCN2), Matrix Metalloproteinase 9 (MMP9)

IACR – 662 **ORAL**

A Specific Sub-Population Derived from Breast Cancer Cells Augments Oncogenic Activity by Exploring a Calcium-Associated Scaffold Protein

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Cellular plasticity, along with the infiltration of various stromal/non-cancerous cells, contributes to the heterogeneity within a tumor. This plasticity potential presence within cancer cells often drives to make various cell lineages, especially during the scarcity of growth factors, fuels, and other essential factors within a tumor microenvironment. In this context, this current study has identified and isolated a specific breast osteoblast-like cell subpopulation (BOCS) from epithelial breast cancer 4T1 cells upon induction with osteogenic inducer. Cell culture and mouse model study have revealed an augmented oncogenic potential in BOCS. Transcriptomic analysis coupled with gene ontology pointed out the involvement of various crucial signaling pathways, including pluripotent stem cells, PI3-AKT, and cancer. Through our experimental analysis, it was found that this population exhibited an elevated stemness potential with increment of Oct4, KlF4, cMYC, and Nanog stemness factors, and epithelial to mesenchymal transition (EMT). Notably, a set of underexplored/unexplored genes (e.g., EIF4E2, MMP10, ARPC1A, etc.) shows elevated expression in BOCS compared to the rest of the cell populations, and also BMP-2 treatment showed upregulation of these genes. Finally, in-depth analysis along with literature survey pointed that a calcium-associated scaffold protein might play a crucial role in augmentation of oncogenic and osteoblast-like potential of BOCS. Further clinical sample analysis will ascertain the diagnostic/prognostic potential of these unexplored genes. Future study confirms the presence of BOCS in tumor tissue or blood circulation as early metastatic marker. Thus, targeting this scaffold protein might be a new therapeutic strategy for treatment of breast cancer

Key words: Breast Cancer Cell, Breast Osteoblast-Like Cell Subpopulation (BOCS), Transcriptomic Analysis, Calcium-Associated Scaffold Protein, Mice Model

IACR – 681 **ORAL**

Targeting Tumor-CAF Alliance: Decoding TMEs Role in Drug Resistance

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KRAS mutations account for 35 % of the total NSCLC cases, and are associated with poor overall survival. Recently FDA-approved mutant specific KRAS inhibitors, Sotorasib and Adagrasib, showed resistance and progressive disease. Half of the NSCLC resistant patients did not harbour any secondary alterations, implying the possibility of cell non-autonomous resistance mechanisms, such as the role of the Tumor microenvironment (TME). Through in-silico cytometry, we found Cancer-associated fibroblast (CAFs) are abundant in KRAS mutant NSCLC patients. The mechanism of CAF-induced KRAS inhibitor resistance is yet to be investigated. In this study, we explore CAF's role in driving resistance to KRAS inhibiton. Using indirect and direct co-culture systems, we observe that CAF secreted factors confer resistance to sotorasib, through PI3K-AKT and ERK pathways. We speculate that the CAF-mediated KRAS resistance bypasses the oncogenic signalling through upstream receptor tyrosine kinase activation. We identified the MET activation in tumor cells upon co-culture with Cancer-associated fibroblasts. The genetic or pharmacological inhibition of MET in tumor cells, under the influence of CAF, makes tumor cells sensitive to KRAS inhibition. We believe that targeting tumour-CAF interactions through targets like MET may improve the efficacy of KRAS inhibitors in NSCLC patients, giving rise to new combinatorial therapies.

Key words: KRAS, Tumor Microenvironment, Cancer Associated Fibroblast, KRAS Inhibitor Resistance

IACR – 706 **ORAL**

CDKN1B inactivation Impacts ER Signaling and Drives Resistance to Endocrine Therapy in Breast Cancer

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Hormone receptor–positive (HR^+), HER2-negative breast cancer accounts for ~70% of all breast cancers and is primarily treated with endocrine therapies, including tamoxifen, aromatase inhibitors, fulvestrant, and CDK4/6 inhibitors. However, resistance develops in ~40% of patients, limiting therapeutic benefit. To identify molecular drivers of resistance, we performed integrated genomic, transcriptomic, and functional analyses of 181 HR+/HER2− tumors (87 sensitive and 94 resistant). Resistant tumors exhibited a significantly higher mutational burden and were enriched for alterations in *ESR1, NF1,* and *CDKN1B*, whereas *AKT1* and *DNMT3A* mutations were more frequent in sensitive tumors. Mutations in *PIK3CA, TP53,* and *GATA3* were common in both groups. we identify frequent *CDKN1B* (p27) loss-of-function mutations or deletions as a key and clinically actionable driver of endocrine resistance. *CDKN1B* knockdown induced resistance to tamoxifen and fulvestrant, whereas its restoration re-sensitized resistant cells by reactivating estrogen signaling. Importantly, *CDKN1B*-deficient tumors remain responsive to CDK4/6 inhibition, *in vitro* and *in vivo*. Immunohistochemistry and transcriptomic analysis of clinical cohorts (n=107) and TCGA-METABRIC data (n=1398) identify low p27 as an independent predictor of early relapse and poor survival. Together, our results highlight *CDKN1B* as a prognostic biomarker to guide CDK4/6-targeted therapy and a predictor of endocrine resistance in HR+/HER2− breast cancer.

Key words: Breast Cancer, CDKN1B, Endocrine Resistance, Hormone Receptor-Positive, P27, ESR1, CDK4/6 Inhibitors, Palbociclib, Genomics

IACR – 730 **ORAL**

Hypoxia-Induced RBM47 Regulates the Alternative Splicing of FN1 in Glioblastoma via Intracellular and Exosome-Mediated Mechanisms

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Glioblastoma multiforme is the most common primary tumor found in CNS, with a median survival of only 15 months. It contains intratumoral regions of hypoxia, which are major drivers of invasiveness and therapeutic resistance. Hypoxia induces widespread changes in the alternative splicing landscape and facilitates tumor growth by favouring the generation of protein isoforms that support cellular adaptation and survival. Within the tumor microenvironment, exosomes (small extracellular vesicles) play a crucial role in intercellular communication, as they contain a variety of bioactive molecules. While hypoxia is known to induce exosome biogenesis as well as affect its cargo, the effect of hypoxia-derived exosomes on alternative splicing remains largely unexplored.

In this study, we observed that under hypoxia, RBM47, an RNA-binding protein, is upregulated via HIF1A-mediated transcriptional activation. Under hypoxic conditions, RBM47 is also packaged within exosomes and, upon uptake by normoxic cells, increases RBM47 abundance. We performed bulk RNA-seq under RBM47 knockdown and in cells treated with normoxia or hypoxia-derived exosomes. Our RNA-seq analysis revealed that RBM47 mediates the alternative splicing of FN1, an ECM protein, favouring the inclusion of exon 25, thus generating pro-tumorigenic isoform FN1-EDB. We further utilized the dCasRx system to validate the splicing using gRNAs targeting the RBM47-binding region within the FN1 pre-mRNA. Thus, we demonstrate the interplay between hypoxia-derived exosomes and alternative splicing in mediating tumor progression.

Key words: Glioblastoma, Hypoxia, Exosomes, Alternative Splicing, RNA-Binding Proteins

ASTRACTS SELECTED FOR ORAL PRESENTATION

(Mid-level faculty/Postdocs)

IACR – 603 **ORAL**

Synthesis and Biological Evaluation of a Novel Zinc (II) Trinuclear Complex with Tetradentate Schiff Base Ligand and Azido Ion as a Potent PI3K/AKT and Ras/MAPK/ERK Signalling Dual Inhibitor in Prostate Adenocarcinoma

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Prostate adenocarcinoma (PAC) ranks second in cancer-related deaths in men worldwide. Although surgical debulking of visible tumour following androgen deprivation therapy (ADT) using androgen receptor antagonists, including enzalutamide, initially improves patient outcome, castration-resistant, metastatic PAC emerges with a high relapse rate. There is an unmet need to develop improved therapeutic interventions against this deadly pathology. Novel azido trinuclear zinc (II) Schiff base complex [{ZnL(N_3)}$_2$ Zn]. H_2O (1) (ComAR1) was synthesized using NaN_3, methanolic solution of $Zn(CH_3COO)_2.2H_2O$ and Schiff base ligand H_2L. Schiff base H_2L was derived from the condensation of 1,4-butadiamine and 3-methoxy salicylaldehyde (O-valine) at a 1:2 ratio and was characterised. Validation of drug-like property done by In-silico, molecular docking and ADMET analysis, followed by in-vitro evaluation of anti-cancer activity of ComAR1 for PAC. ComAR1 inhibited PAC cell proliferation, EMT, migration and induced G0/G1 cell cycle arrest following apoptosis. Molecular docking, simulation and ADMET analyses revealed that ComAR1interacted with key components of signalling circuits associated with tumorigenesis, including AKT, ERK1/2 and exhibited excellent pharmacokinetic and drug-like features. Mechanistically, ComAR1 dampened PI3K/AKT and Ras/MAPK/ERK signalling activation, stabilised pro-apoptotic BAD by suppressing its AKT- and ERK-mediated phosphorylation in PAC cells. Conclusively and taken together, our results indicate that azido trinuclear zinc (II) Schiff base ComAR1 could emerge as a novel, dual inhibitor of PI3K/AKR and MAPK/ERK pathways and an excellent therapeutic choice for improved outcomes of PAC patients.

Key Words: Prostate adenocarcinoma, Androgen deprivation therapy, Enzalutamide, Zinc (II) Trinuclear Complex, In-silico

IACR – 621 **ORAL**

Familial Clustering of Cancers: 2 Families and 2 Cancers in 1st Degree Relatives: CML in a Mother-Daughter Duo and Multiple Myeloma in a Father-Son Pair

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Background: Familial clustering of hematologic malignancies is uncommon and suggests a possible interplay between genetic susceptibility and shared environmental exposures.
Family 1: Familial Chronic Myeloid Leukemia (CML)
Case 1 (Daughter): 40-year-old woman was diagnosed with CML-CP after being evaluated for chronic fatigue. RT-qPCR detected BCR–ABL1 p210 transcript with an international scale of 21.19%. She was started on Imatinib and achieved complete hematologic remission at 3 months. **Case 2 (Mother)**: 65-year-old woman, mother of aforementioned, incidentally found to have massive splenomegaly, was diagnosed with CML-CP. RT-qPCR detected identical BCR–ABL1 p210 transcripts with IS 25.02%. She also was started on Imatinib and achieved complete hematologic remission at 3 months.
Family 2: Familial Multiple Myeloma (MM)
Case 3 (Father): 60-year-old male evaluated for chronic back pain was diagnosed with Multiple myeloma- IgG-κ. FISH analysis demonstrated deletion 13q. He was started on Bortezomib, Lenalidomide, and Dexamethasone(VRd) and achieved complete response after eight weeks of treatment. **Case 4(Son)**: 40-year-old male, son of aforementioned, admitted for evaluation of nephrotic-range proteinuria and renal failure was diagnosed with light chain Multiple myeloma. Renal biopsy confirmed light-chain cast nephropathy. FISH showed deletion 13q and 1p. He has been initiated on Cyclophosphamide, Bortezomib, and Dexamethasone (CyBorD).
Discussion: Familial aggregation of CML and MM is exceedingly rare with scarce literature and emphasize the importance of encouraging further research into genetic predisposition, and highlight the need for evidence-based screening recommendations.

Key words: Familial Chronic Myeloid Leukemia, Familial Multiple Myeloma, Hereditary CML, Hereditary MM.

IACR – 636 **ORAL**

Drug Specific Gene Expression Signatures of Cancer Chemoresistance

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Cancer remains a major global health burden, with over 20 million new cases and 9.7 million deaths reported in 2022. Despite advances in cancer therapy, the effectiveness of chemotherapy is frequently limited by intrinsic and acquired chemoresistance, leading to treatment failure and disease relapse. Current strategies such as combination and adjuvanta chemotherapy are further constrained by toxicity and the eventual development of resistance, underscoring the need for molecular signatures that can reliably predict treatment response. In this study, we performed an integrative analysis of gene expression datasets derived from chemoresistant cancer cell lines resistant to multiple classes of drugs and across different cancers. Differentially expressed genes were identified to define both common and tissue-specific chemoresistance signatures. The clinical relevance of these signatures was assessed through survival analysis using independent patient cohorts using data from TCGA. Our analysis revealed distinct gene expression patterns associated with chemoresistance, with several gene signatures showing significant associations with patient survival outcomes. These findings highlight the potential of gene expression profiling to predict chemotherapy response and patient prognosis. This study provides a foundation for understanding chemoresistance, drug-specific mechanisms of

resistance and with further validation aid in the development of therapeutic strategies which can improve patient outcome both in terms of efficacy and quality of life.

Key words: Chemoresistance, Transcriptomics, Molecular Signatures, Prognostic Gene Signatures

IACR - 644 **ORAL**

Artificial Intelligence-Based Visualization of Cancer-Related Viral Infections for Surveillance and Risk Stratification

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Cancer-related viral infections, particularly those caused by oncogenic viruses such as Human Papillomavirus (HPV) and Hepatitis B and C viruses (HBV/HCV), contribute significantly to the global cancer burden. Effective surveillance and early risk stratification are critical for prevention and control; however, the complexity and volume of epidemiological and clinical data pose challenges for conventional analytical approaches. Artificial intelligence (AI)–based visualization offers novel opportunities to enhance data interpretation and decision-making. This study aims to develop and demonstrate AI-based visualization frameworks for improved surveillance and risk stratification of cancer-related viral infections using secondary data sources. Secondary data from cancer registries, surveillance systems, and publicly available health databases were analyzed using a combination of machine learning techniques and biostatistical methods. Key variables included viral infection status, demographic characteristics, clinical indicators, and cancer outcomes. AI-driven dimensionality reduction, clustering, and visual analytics techniques were applied to generate intuitive and interpretable visual representations of disease patterns and risk profiles.
AI-based visualizations effectively revealed hidden patterns, spatial–temporal trends, and high-risk population clusters associated with cancer-related viral infections. Compared to traditional summary statistics, these approaches enabled enhanced identification of risk stratification groups and improved interpretability for surveillance and public health planning. Artificial intelligence–based visualization represents a powerful and scalable tool for surveillance and risk stratification of cancer-related viral infections. Integrating AI-driven visual analytics with biostatistical modeling can support evidence-based decision-making, strengthen cancer control programs, and facilitate targeted prevention strategies, particularly in resource-limited settings.

Key words: HPV; HBV; HCV; Artificial Intelligence; Visualization; Surveillance; Cancer

IACR - 656 **ORAL**

Cancer Screening Uptake Among Women in Jammu & Kashmir: District-Wise Analysis from the Fifth Round of the NFHS-5 (2019-2021)

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Cancer mortality among women can be significantly reduced through early detection. However, participation in screening programs for cervical, breast, and oral cancers remains uneven across India.

This study examines the prevalence and socio-demographic determinants of cancer screening uptake among women in the Union Territory of Jammu & Kashmir. We analysed unit-level data from the NFHS-5 (2019–2021), focusing on ever-married women aged 15–49 years. The outcome variable was defined as having undergone screening for cervical, breast, or oral cavity cancer. We employed descriptive statistics to estimate prevalence and performed district-level mapping to visualize regional disparities. Multivariate logistic regression was used to assess associations between screening uptake and factors such as age, education, caste, and wealth quintile.

Analysis reveals a critically low screening prevalence, with less than 2% of women in J&K undergoing screening for any of the three cancers. District-wise analysis highlights significant heterogeneity; certain districts exhibited marginally higher uptake compared to other districts. Regression results indicate a strong socio-economic gradient: women in the highest wealth quintile and those with higher educational attainment had significantly higher odds of being screened compared to their counterparts.

Overall, cancer screening uptake in J&K is both inadequate and inequitable. The findings suggest an urgent need for targeted public health interventions that focus on low screening uptake districts and socio-economically vulnerable populations to enhance awareness and accessibility of screening services.

Key words: Cancer Screening, Jammu & Kashmir, NFHS-5, Womens Health, Public Health

IACR - 703 **ORAL**

Oncogenic Signaling and Synthetic Vulnerabilities to Overcome Immune Escape in Chemo-Immunotherapy Resistant B-Cell Lymphoma

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B-cell lymphoma is highly heterogeneous, and in India, it manifests approximately a decade earlier than in Western countries like the United States. Despite similar chemoimmunotherapy regimens, the mortality rate among Indian patients, particularly those with diffuse large B-cell lymphoma (DLBCL), is significantly higher at 69% compared to 30% in the United States. Several factors contribute to this high mortality, including lost follow-up and the prohibitive cost of advanced therapies like CAR T-cell and targeted treatments. However, the molecular mechanisms underlying tumor resistance in Indian cohorts remain largely unexplored. Our primary goal is to investigate the molecular signatures involved in the development of chemo-immunotherapy resistance in B-cell lymphoma, particularly in relation to changes within the tumor immune microenvironment. Utilizing multiple drug screening models, including patient-derived tumor cell co-cultured with stromal cells, we have begun to uncover key molecular drivers of resistance.

Through our clinical collaborations with five hospitals across India and our international partnerships, we have identified resistance-associated molecular signatures, including both

coding and non-coding RNA and proteins, in two major areas: (1) Tumor-Initiating Cells and (2) Alterations in Tumor Cell Surface Receptors Proteins such as CD36, FGFR1, CD44, CD24, PDL1, and nucleolin, many of which are direct targets of current chemotherapy regimens, are prominently involved. By integrating clinical tumor-derived data, in vitro assays, and animal studies, we have identified molecular mechanisms and therapeutic targets that are uniquely expressed in small tumor subsets. These subsets, which contribute to the heterogeneity of B-cell lymphoma, are believed to play an essential role in the development of chemo-immunotherapy resistance, leading to disease relapse.

Key words: Chemoimmunotherapy, Resistance, Signatures tumour Immune Microenvironment, tumor-Cell-Surface, Signatures drug, Screening, Development B-Cell Lymphoma

IACR - 707 **ORAL**

Parkin-Driven Mitophagy promotes Stress Adaptive Lung Metastasis in Melanoma

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Mitophagy a specialized form of autophagy maintains mitochondrial quality by removing damaged mitochondria for cellular health and energy balance. In cancer, it enables tumour cells to survive stress and promotes metastasis. Parkin, PINK1-activated E3 ubiquitin ligase, regulates this process. Although considered a tumour suppressor, Parkin shows context-dependent roles in supporting tumour survival and progression. To investigate how Parkin-driven mitophagy regulates metabolic adaptation, stress tolerance, and metastatic potential in cancer cells. B16F10 melanoma cells were genetically engineered to overexpress Parkin. Metastasis was evaluated using a murine lung metastasis model. Survival and metastatic burden of mice were evaluated. Dual proteomic profiling of primary tumour cells and matched lung metastases was conducted using mass spectrometry-based analysis. Activation of mitophagy triggered metabolic reprogramming is marked by collapse of the TCA cycle and near-complete suppression of oxidative phosphorylation. Instead of undergoing metabolic attrition, these impaired melanoma cells mounted a compensatory glycolytic rescue response, enabling survival despite profound bioenergetic dysfunction. Unexpectedly, Parkin-overexpressing cells showed enhanced lung metastasis, forming aggressive, inflammation-rich lesions supported by neutrophil activation, complement signalling, IDO1-mediated immunosuppression, and VEGFR1-driven niche conditioning. Contrary to classical expectations that mitophagy would restrain malignant progression, Parkin-overexpressing cells acquired a stress-adapted, metastasis-competent phenotype that disseminated aggressively once exposed to the permissive lung niche. Metastatic lesions arising from these metabolically compromised cells did not exhibit a weakened phenotype. Instead, they formed highly destructive, inflammation-driven metastatic foci enriched in neutrophil activation, complement cascade components, and IDO1-mediated immunosuppression, indicating that metastatic success can be achieved by exploiting host inflammatory circuitry rather than intrinsic proliferative fitness. The lung microenvironment appeared to compensate for tumour metabolic deficiencies through VEGFR1-associated angiogenic signalling, immunological reframing,

and niche conditioning that supported the outgrowth of these stress-tolerant metastatic seeds. Together, these findings establish an important conceptual shift that metastasis can be driven not by the most metabolically robust tumour cells but by those most capable of withstanding metabolic collapse and leveraging host inflammatory responses. Parkin-driven mitophagy forces melanoma cells into a persister-like, stress-adapted state that becomes highly metastatic within an inflammation-primed lung microenvironment, revealing a previously underappreciated axis of tumour–host metabolic cooperation.

Key words: Mitophagy, Metastasis, Melanoma, Parkin

IACR - 722 **ORAL**

Targeting Therapy Induced Senescence Via PP2A Activation In Neuroblastoma

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Therapy induced senescence (TIS), while initially growth suppressive, may promote tumor recurrence through the persistence of senescent cells and the senescence-associated secretory phenotype (SASP). Topotecan, a topoisomerase inhibitor and a key component in the treatment of neuroblastoma (NBL), is known to lead to TIS. Protein phosphatase 2A (PP2A) is a serine/threonine phosphatase that has been linked to cellular senescence. The current study investigates the novel PP2A activator, ATUX-1215, as a senotherapeutic strategy in NBL. We demonstrate that combining ATUX-1215 with topotecan leads to a synergistic reduction in senescent cell burden. Combination therapy suppressed PAI-1 and CCL2, key components of the SASP secretome, suppressed pro-survival AKT/NF-κB signaling and enhanced apoptosis. PP2A activation reduced DNA damage, stemness, and clonogenic survival post-TIS. The therapeutic response differed between senolytic and senomorphic depending upon the cell line investigated. SK-N-BE(2) cells showed a senolytic response with enhanced caspase-3/PARP cleavage. In contrast, the response in SK-N-AS cells shifted between senolytic and senomorphic, based on compound dosing. *In vivo*, the combination significantly delayed tumor growth and attenuated the pro-tumorigenic serum SASP. Our findings position PP2A activation as a senotherapeutic approach, transforming the tumor promoting TIS program into a therapeutic vulnerability, offering a promising avenue to mitigate therapy resistance and improve outcomes in NBL.

Key words: Therapy-Induced Senescence (TIS), PP2A, Topotecan, Senescence-Associated Secretory Phenotype (SASP), Neuroblastoma

IACR - 733 **ORAL**

Paraneoplastic Syndromes as the Initial Manifestation of Occult Malignancies: A Seven-Year Observational Study from a Tertiary Care Center in Kashmir

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Paraneoplastic syndromes (PNS) are rare, immune-mediated systemic manifestations of occult malignancies that are unrelated to direct tumor invasion or metastasis. They often precede the diagnosis of cancer, providing an important opportunity for early detection. This study aimed to characterize the clinical spectrum of PNS presenting as the initial manifestation of underlying malignancies at a tertiary care center in Kashmir. This observational study was conducted at Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar, over seven years (2018–2024). Fifty-three consecutive patients fulfilling clinical criteria for PNS underwent detailed evaluation including imaging, serological testing for onconeural antibodies, and histopathological confirmation of suspected malignancies. Syndromes were categorized into: (1) ectopic hormone production, (2) hematologic, and (3) neurological PNS. A total of 53 patients (27 males, 26 females) presented with paraneoplastic syndromes, of whom 31 (58.5%) had biopsy-confirmed malignancies. Ectopic hormone syndromes included SIADH secondary to small-cell lung carcinoma (n=8) and hypercalcemia associated with non-Hodgkin lymphoma (n=2). Hematologic manifestations comprised lower limb deep vein thrombosis (n=10) linked to pancreatic (n=4), lung (n=4), and prostate adenocarcinoma (n=2); pulmonary thromboembolism (n=2) in lung and prostate adenocarcinoma; polycythemia in renal cell carcinoma (n=2); and eosinophilia in non-Hodgkin lymphoma (n=2). Neurological PNS with confirmed malignancy (n=5) included limbic encephalitis (anti-LGI1) in small-cell lung cancer (n=2), cerebellar ataxia (anti-Yo) in ovarian carcinoma (n=1), myeloradiculopathy in male breast carcinoma (n=1), and myasthenia gravis associated with thymoma (n=1). Among 22 patients without detected malignancy, 5 had high-risk and 17 had moderate/low-risk paraneoplastic neurologic syndromes, all currently under surveillance. PNS may be the earliest manifestation of an underlying malignancy. Early recognition and systematic cancer screening are essential for timely diagnosis and improved outcomes.

Key words: Paraneoplastic Syndromes; Occult Malignancy; Onconeural Antibodies

IACR - 749 **ORAL**

Evaluation of Whole Genome Expression Data of Indian Urinary Bladder Cancer Patients

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Gene expression profiling has emerged as a powerful approach for identifying novel biomarkers in oncology, with significant potential for early diagnosis and prognostication of urinary bladder cancer (UBC) in clinical settings. To identify candidate biomarkers, whole genome expression profiling was performed using high-density oligonucleotide microarrays

(Affymetrix Human Gene 1.1 ST arrays). Tumor tissue specimens were obtained from seven patients with histopathologically confirmed non-muscle invasive (n = 2) and muscle-invasive UBC (n = 5) were analyzed. RNA was extracted by standardized protocols. Human Bladder Total RNA (Clontech, Palo Alto, CA, USA) was used as a reference for microarray analysis. Statistical analysis was conducted using the R programming language, and downstream biological interpretation was performed using Genowiz. A ≥4-fold change threshold (log2 fold change ≥ 2) was applied to identify differentially expressed genes. A total of 380 genes were upregulated and 725 were downregulated in UBC compared with normal bladder tissue. Among the upregulated genes, five cancer-testis (CT) genes ZNF165**,** CEP55, PBK/TOPK, TTK, and CASC5 were identified. These CT genes were further validated at the mRNA level using quantitative real-time PCR (qRT-PCR). The study demonstrated frequent expression of CT genes in UBC, with significantly higher expression observed in muscle-invasive tumors. In contrast, their expression was restricted in normal tissues. Overall, high-density oligonucleotide microarray analysis is a valuable tool for identifying novel molecular targets and potential biomarkers in urologic oncology, offering promise for improved diagnosis, prognostication, and therapeutic targeting in UBC.

Key words: Urinary Bladder Cancer, Oligonucleotide Microarray, Cancer-Testis, Real-Time PCR

IACR - 750 **ORAL**

Myc Dependent Mouse Model of Pancreatic Neuroendocrine Tumours: A Preclinical Model for Aggressive Proliferative Subtype

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Pancreatic cancer (PC) is a deadly disease, accounting for 4.5% of all global cancer related deaths. Despite the advancements in cancer detection and treatment strategies, the 5-year survival rate of pancreatic cancer patients still stands at dismal 9%. Pancreatic ductal adenocarcinoma (PDAC) and pancreatic neuroendocrine tumours (PanNET) are two distinct histological subtypes with different molecular and clinical features. Our recent work using genetically engineered mouse models (GEMM) of pancreatic cancer revealed that the oncogene MYC can drive PanNET tumours, whereas it drives PDAC when combined with mutant KRAS. Histological analysis of PanNET tumours revealed that these mice develop a mixture of functional tumours and aggressive, poorly differentiated tumours. Furthermore, RNA sequencing analysis of end stage PanNET tumours revealed that the pathways upregulated in human PanNET were represented in mouse tumours, particularly those of highly aggressive proliferative subtypes. These GEMM models with distinct tumours give the opportunity to unravel the molecular signatures of PanNET tumours, with the aim of identifying novel therapeutic targets for the same.

Key words: Myc, Mouse Model

IACR - 755 **ORAL**

Metabolism Associated Epigenome Mediates Differential Alternative Splicing In Breast Cancer and Its Implication In Therapy Resistance

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Cancer can be perceived not only as a genetic disease but also through the perspective of metabolism. Breast cancer subtypes are classified by the presence of estrogen receptor alpha (ERα). The comparative analysis between ERα-positive and ERα-negative breast cancer revealed that triple-negative breast cancer cells exhibiting increased glycolytic activity and more aggressive phenotype. The function of chromatin and the enzymes linked to it in transmitting metabolic information to the transcriptional network remains unexplored. In this study, we decoded that breast cancer subtype assimilate metabolic information differently leading to altered epigenome and CTCF occupancy, influencing alternative splicing that contribute to the more aggressive characteristics. We observed that difference in lactate production under hypoxia has subsequent effect on histone lactylation in different subtypes, plays a significant part in tumor progression through the regulation of oncogenic differential alternative splicing through splicing factor recruitment. Our study unveil that treatment of tamoxifen to ER-positive cells significantly altered the metabolism that mediates the switch in alternative splicing landscape in hypoxic condition that promotes proliferation and hence resistance in hypoxic cells. In conclusion, this study deciphered the metabolism mediated epigenetic changes and associated alternative splicing landscape in cancer progression and its therapeutic vulnerability to manage cancer perturbations.

Key words: Metabolism, Lactate, Hypoxia, Epigenome, Alternative Splicing, Therpay Resistance

IACR - 756 **ORAL**

Synergistic Targeting of Autophagy and Exosome Biogenesis: The GABARAPL2-Alix Regulatory Axis in Breast Cancer

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Cancer cell resilience is driven by a dynamic interplay between internal energy maintenance (autophagy) and intercellular communication (exosome biogenesis). This study investigates the reciprocal regulation of these pathways in MDA-MB-231 breast cancer cells, revealing a compensatory survival network. Findings demonstrate that independent inhibition of either pathway fails to restrict growth; notably, blocking exosome biogenesis alone increases proliferation, while inhibiting autophagy triggers a compensatory surge in exosome release despite reduced expression of biogenesis markers Alix and CD63. Conversely, exosome inhibition upregulates autophagy genes (ATG5, ATG16L1) while depleting GABARAPL2. Crucially, we identify GABARAPL2 as the molecular bridge in this crosstalk: its knockdown abrogates the decrease in Alix levels during autophagy inhibition, confirming its essential role in modulating exosome secretion via Alix. Given that current clinical strategies, such as the use of Hydroxychloroquine (HCQ), which offer only broad, non-specific inhibition of these pathways, our discovery of the GABARAPL2-Alix axis highlights a precise therapeutic vulnerability. We propose that transitioning from broad lysosomal inhibitors to targeted agents, such as GABARAP-specific stapled peptides or Alix-modulating repurposed drugs (e.g., Docetaxel), may provide the necessary dual-pathway disruption to effectively stifle breast cancer progression and overcome resistance.

Key words: Breast Cancer, Autophagy, Exosome, GABARAPL2

IACR – 797 **ORAL**

Barriers for early detection of cancer amongst women in a rural setting in Kashmir- A cross sectional sectional study

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Breast and cervical cancers are among the leading causes of cancer-related deaths among women globally, although both conditions are largely preventable and treatable when detected early. In many developing countries, healthcare professionals frequently encounter women presenting with advanced and incurable stages of these cancers. The health status of rural Indian women and their ability to access healthcare services are often limited by sociocultural, economic, and environmental barriers. To identify the factors and challenges related to the early detection of cancers among women residing in rural areas, a communitybased cross-sectional study conducted in a rural setting of RTHC Kalantra, Kashmir. The study included women aged 35 years and above. Women who were unwilling to participate were excluded. All eligible women from randomly selected villages were included in the study. The duration of the study was three months. Data were collected using a pretested questionnaire. Data analysis was performed using percentages, chi-square test, analysis of variance (ANOVA), and multivariate analysis.The study revealed low levels of awareness regarding cancer symptoms, the possibility of early detection, available screening tests, and the potential for cure. The most significant barrier to screening was a cognitive barrier, reflected by the high proportion of "don't know" responses: 83.99% for cervical cancer, 84.93% for breast cancer, and 67.26% for oral cancer. Awareness scores showed a significant association with age ($\chi^2 = 17.77$, $P = 0.001$), education ($\chi^2 = 34.62$, $P < 0.001$), and income ($\chi^2 = 16.72$, $P = 0.002$). Attitude scores were significantly related to age ($\chi^2 = 16.27$, $P = 0.012$) and education ($\chi^2 = 25.16$, $P = 0.003$). Practice scores were significantly associated with age ($\chi^2 = 11.28$, $P = 0.023$), education ($\chi^2 = 32.27$, $P = 0.003$), and occupation ($\chi^2 = 10.69$, $P = 0.03$). Women who reported a family history of cancer demonstrated significantly higher awareness, attitude, and practice scores compared to those without such a history. The findings indicate that lack of knowledge or cognitive barriers play a major role in preventing rural women from participating in cancer screening. Addressing these barriers through awareness and educational interventions is essential for improving early detection.

Keywords: Breast cancer, awareness, screening.

IACR – 798 **ORAL**

Awareness Regarding Breast Cancer Screening Among ASHA Workers in the Field Practice Area of Government Medical College: A Cross-Sectional Study

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Breast cancer is the most common cancer among women worldwide and a leading cause of cancer related mortality in India. Early detection through screening methods such as breast self-examination (BSE), clinical breast examination (CBE) and mammography can significantly improve survival. Accredited Social Health Activists (ASHAs) are frontline community health workers responsible for promoting health awareness in rural communities. Their knowledge regarding breast cancer screening is essential for early detection and timely management. A cross-sectional study was conducted among ASHA workers working in the field practice area of the Department of Community Medicine, GMC Baramulla. Data were collected using a pre-tested semi-structured questionnaire assessing knowledge of breast cancer risk factors, warning signs and screening methods including BSE, CBE, and mammography. Data were analyzed using descriptive statistics.A total of 85 ASHA workers participated in the study. Most of them (92%) had heard about breast cancer. Awareness regarding breast self-examination was reported by 68% participants, while 45% knew the correct frequency of BSE. Knowledge regarding clinical breast examination and mammography was reported by 41% and 36% participants respectively. Only 38% of ASHA workers demonstrated adequate awareness regarding breast cancer screening. Although most ASHA workers were aware of breast cancer, significant gaps exist in their knowledge regarding screening methods. Regular training and capacity-building programs for ASHA workers are essential to improve early detection of breast cancer at the community level.

Keywords: Breast cancer, Screening, ASHA workers, Awareness, Early detection

IACR – 799 **ORAL**

Increased production of TGF-β^{+} tumor evoked B regulatory cells by tumorderived PGE2 is associated with poor survival in PTGS2^{hi} cancers

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B cells have increasingly gained attention as a key regulator in the tumor microenvironment (TME). Although Regulatory B cells (Bregs) with immunosuppressive properties have been described in infection and autoimmunity, the specific molecular cues that define Bregs in cancers remain poorly elucidated. We have previously reported about the TGF-β secreting tumor-evoked Breg (tBreg)-Treg axis as key mediator of immunosuppression in mouse fibrosarcoma (WEHI- 164). In this study, we identified tumor-derived prostaglandin E2 (PGE2) as a major player of tBreg induction in WEHI-164. B cell depletion or COX-2 inhibition decreased tBreg generation and reduced tumor progression in mice. PGE2 induced tBregs through an EP2/EP4 receptor mediated non-canonical MAPK dependent STAT3 activation. Inhibition of JNK and NF-kB in tBregs completely abrogated tBreg mediated T cell suppression, confirming the importance of this pathway. Using murine and human single-cell RNA-seq datasets, we further demonstrate the presence of TGF-βhi B cells with transcriptional signatures consistent with tBregs in in PTGS2hi cancers. TCGA-Pancancer analysis revealed

that the proportion of patients with Breg signature was higher in the PTGS2 high cohorts, and are correlated with a poor survival rate. In summary, for the first time, we have identified that the tumor-derived PGE2 induces TGF-β secreting tBregs in murine fibrosarcoma and other cancers. Our studies add to the growing body of literature identifying immunosuppressive B cell subsets in human cancers. The significant correlation between Bregs and patient prognosis suggests that Breg-targeted therapy could provide a breakthrough immunotherapy for patients with PTGS2 high cancers.

Key Words: B cells, Tumor microenvironment, tBreg, TGF-β, Immunosuppression

IACR – 800 **ORAL**

PGE2–EP4–miR-365 axis drives IL-6/STAT3-dependent dendritic cell dysfunction and tumor progression

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Prostaglandin E2 (PGE2) is a major immunosuppressive mediator in cancer, but the dendritic cell (DC)-intrinsic signalling events that translate PGE2 exposure into systemic immune dysfunction remain incompletely defined. Using the 4T1 mammary tumor model, we combined in vivo tumor studies with mechanistic assays in bone marrow derived DCs and splenocytes. Cytokines were quantified by ELISA/ELISpot, and pathway readouts were assessed by RT-PCR and flow cytometry. Complementary in silico analyses of human mammary cancer datasets evaluated the association between PGE2 and IL-6. Across in silico, in vitro, and in vivo experiments, PGE2 promoted DC dysfunction by engaging EP4 and inducing an IL-6–phospho-STAT3 signalling program. Pharmacologic or antibody-mediated disruption of EP4 signalling, as well as inhibition of STAT3, reversed these suppressive effects. We identified miR-365 as an upstream regulator of PGE2-driven IL-6 production in DCs: a miR-365 mimic attenuated IL-6 induction, whereas miR-365 inhibition enhanced IL-6 levels. Human dataset analysis demonstrated a strong positive association between PGE2 and IL-6 expression (R = 0.94). In vivo, tumors with PTGS2 (COX-2) knockdown exhibited reduced tumor burden alongside diminished PGE2/EP4/IL-6/pSTAT3 signalling and improved DC and T-cell functional readouts. Therapeutically, COX-2 inhibition or EP4 antagonism reduced tumor burden; importantly, the anti-tumor efficacy of EP4 antagonism was lost upon CD11c+ cell depletion, indicating DC dependence. These findings position DCs as critical mediators of PGE2-driven immunosuppression and support targeting EP4/STAT3 or leveraging miR-365 modulation to restore DC immunogenicity and constrain tumor progression.

Keywords: PGE2; EP4; dendritic cells; IL-6; STAT3; miR-365; COX-2/PTGS2

IACR – 804 **ORAL**

Strengthening Cancer Screening Programs in India: Public Health Challenges and Opportunities – A Community-Based Study from a Rural Field Practice Area of North Kashmir

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Cancer is an emerging public health challenge in India with rising incidence and mortality. Early detection through screening significantly improves treatment outcomes and survival. However, awareness and utilisation of screening services remain low in rural communities despite national initiatives such as the National Programme for Prevention and Control of Non-Communicable Diseases (NP-NCD). To assess awareness and utilisation of cancer screening services and identify barriers to screening among adults in a rural field practice area. A community-based cross-sectional study was conducted among adults aged ≥30 years in RTHC Kalantra. The sample size was calculated using the single population proportion formula, assuming awareness of cancer screening to be 30% from previous studies, with 95% confidence level and 8% absolute precision. After adding 10% for non-response, the final sample size was 140 participants. Data were collected using a pre-tested structured questionnaire and analysed using descriptive statistics and the chi-square test.Among 140 participants, 40% were aware that certain cancers can be detected early through screening. Only 24% knew specific screening methods, and 17% had ever undergone any screening. Lack of awareness (42%) was the most common barrier. Awareness was significantly higher among participants with secondary education and above ($p < 0.05$).The study highlights low awareness and poor utilisation of cancer screening services in rural communities. Strengthening health education and improving accessibility to screening services may enhance early detection and reduce the burden of cancer.

Key Words: Cancer, Non-Communicable Diseases (NP-NCD), Rural communities

IACR – 805 **ORAL**

LncRNAs as orchestrators of genome maintenance

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DNA is constantly exposed to various types of extrinsic (chemicals or UV radiation) or intrinsic (replication errors and cellular metabolism) challenges. Prolonged or repetitive exposure to these factors may lead to the formation of DNA double-stranded breaks (DSBs), resulting in DNA damage response. DSB is the most lethal form of DNA damage in cells and is repaired by the NHEJ, HR, or MMEJ pathways. Although the molecular players of these repair pathways have been well characterized; recently there has been much discussion about the precise roles and molecular mechanisms by which lncRNAs regulate DNA damage response (DDR). Data from our laboratory demonstrate that depletion of several DDR-associated lncRNAs leads to increased DNA damage and altered DDR markers**,** indicating that these lncRNAs are important regulators of genome maintenance. In addition, perturbation of these lncRNAs affects RNA modification machinery and alters epitranscriptomic signatures. In our laboratory, we have discovered a nuclear-retained lncRNA *DRASTIC* [DNA Repair Associated Transcript In Cell] that plays important role in cellular proliferation. Depletion of *DRASTIC* leads to arrest of cells at G1/S and S phase with a concomitant decrease in G1 phase of the cell

cycle. Furthermore, *DRASTIC* depleted cells showed defective loading of pre-RC components onto chromatin and stalled replication forks in addition to DNA damage during S phase leading to intra-S checkpoint activation. Several components of the major repair pathways were underrepresented in *DRASTIC* depleted cells suggestive of severely defective DNA repair program, implicating its role in regulating DNA repair in cells. We further confirmed that *DRASTIC* RNA interacts with proteins involved in the DNA repair pathway including FUS, RBMX, NONO, SFPQ, PARP1. Interestingly, FUS is one of the upstream regulators of the DDR pathway as it recruits DDR factors onto DNA damage sites by promoting LLPS thereby physically contributing to the efficient recruitment of key DDR factors. *DRASTIC* depletion led to increased levels of FUS suggesting that FUS is stabilized upon *DRASTIC* depletion. Additionally, FUS protein was homogenously redistributed in the nucleus in *DRASTIC* depleted cells suggesting that interaction of *DRASTIC* with FUS helps it to form aggregates. To summarize, our results indicate that *DRASTIC* lncRNA interacts with FUS protein and promotes LLPS thereby might play a central role in guiding FUS to recruit at damage sites and initiate repair.

Keywords: LncRNA; DNA damage response; RBPs; *DRASTIC;* LLPS.

IACR – 806 **ORAL**

Therapeutic efficacy of co-administered Cisplatin and Vincristine in RL95-2 endometrial cancer cell line

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The combination therapy can unlock doors to chemotherapeutic advancement in endometrial cancer management by targeting hallmark processes such as angiogenesis, cell proliferation, hypoxia, and apoptosis. In this study, the evaluation of combination therapy of cisplatin and vincristine was performed on human endometrial cancer (RL95-2) cells on expression of selected genes (*COX-2*, *VEGF*, *TNF-α*, *HIF-1α*, *C-MYC* and *TP-53*) and related miRNAs (miR-16, miR-20A, miR-34B, miR-99B, miR-143B and miR-145B) in patient serum vs FBS exposed cells. The IC50 of cisplatin and vincristine was found to be 2 µM (53.62%) and 4 µM (53.84%) respectively and chosen for combinational therapy. SEM analysis of HS cells treated with cisplatin or vincristine alone demonstrated round or oval shape with reduced number of microvilli and combination of drugs resulted in holes and blebs in cells with distorted morphology. The combination resulted in significant ($P<0.05$) down regulation of *COX-2, TNF-α*, and *HIF-1α* in HS exposed cells than FBS while non-significant effect on *VEGF, cMYC*, and *TP-53*. The miRNA expression was significantly ($p<0.05$) upregulated in HS exposed cells with either of the drugs; however, combination resulted in higher level of statistically significant miRNAs in contrast to HS exposed cells. To confirm the effectiveness and safety of Cisplatin-Vincristine combination therapy in patients with various cancer types, clinical trials are required with large sample size to translate or support the present observations.

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IACR – 807 **ORAL**

Design and Optimization of a Sandwich Magnetic Capture System for Serum Pancreatic Cancer Biomarker Detection via SERS Immunoassay

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Pancreatic cancer (PC) forms one of the deadliest cancers with a 5 year survival rate of 5-8%, primarily due to inadequate early-stage detection. The development of a non-invasive screening platform for the timely detection of PC would be enormously advantageous. Here, a surface-enhanced Raman spectroscopy (SERS)-based immunoassay was developed to facilitate multiplex detection of clinically relevant PC biomarkers—CA19.9, GDF-15 (MIC-1), OPN-1, and CEACAM-1. The system employs antibody tethered PEGylated iron-core gold-shell nanoparticles (Fe@Au@PEG@mAb) as paramagnetic capture probes and Raman reporter–encoded gold nanopopcorns with antibody (AuNPop@RR@PEG@pAb) as detection probes. Upon incubation of serum samples with Fe@AuNP@mAb, the biomarkers presentin the serum will get bound to their respective antibody on it, leading to the sandwich formation with the detection probe (AuNPop@RR@PEG@pAb). Magnetic separation enables highly specific SERS fingerprint readout from this complex. Optimized SERS-Immune assay demonstrated femtogram-level sensitivity in spiked samples, with limits of detection of 500 fg/mL for CA19.9 and CEACAM-1, and 800 fg/mL for GDF-15 and OPN-1—well below their physiological serum ranges. Secretome analysis of PANC-1 cells validated differential biomarker expression, consistent with ELISA and Western blot findings. Further the study will be extended to the differential biomarker detection in pancreatic cancer and pancreatitis patients.

Key Words: Pancreatic cancer, Surface-enhanced Raman spectroscopy, PC biomarkers

IACR – 808 **ORAL**

Perfusion-Driven Spatial Methylome Heterogeneity in Glioblastoma

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Glioblastoma (GBM) exhibits profound intratumoral heterogeneity (ITH) driven by its dynamic tumor microenvironment (TME), posing significant therapeutic challenges. While metabolic niches and transcriptomic programs defined by perfusion are recognized, the epigenetic drivers underlying this spatial ITH remain poorly understood. To address this, we developed PFDLC-Methylome Sequencing (PFDLC-MeS), a novel technique enabling spatial epigenetic profiling of cancer cells based on perfusion gradients. Our study provides the first spatial methylome atlas for any cancer, revealing that differential perfusion profoundly shapes the GBM methylome, leading to distinct Differentially Methylated Regions (DMRs) in perivascular, intermediate, and hypoxic niches. Integrating spatial methylome and transcriptomic data, we identified 125 hypomethylated/upregulated and 42 hypermethylated/downregulated genes in the hypoxic fraction. Notably, GBE1 and CXCL14 emerged as key genes exhibiting hypoxia-induced promoter hypomethylation and subsequent transcriptional upregulation. These findings were robustly validated across in vitro, in vivo xenograft models, bulk GBM patient samples, and further confirmed by single-cell RNA sequencing and spatial transcriptomics datasets. GBE1 and CXCL14 expression correlated with aggressive GBM subtypes (mesenchymal, IDH-wildtype, Non-G-CIMP), pseudopalisading cells (a hallmark of hypoxia), and critically, with poor patient survival. Single-cell analysis further demonstrated distinct pathway associations for GBE1 (strong hypoxia, H1 subcluster) and CXCL14 (milder hypoxia, H3 subcluster). This study unveils differential methylation as a pivotal hierarchical driver of GBM's spatial ITH and provides a novel framework to identify therapeutic targets for overcoming treatment resistance.

ASTRACTS SELECTED FOR POSTER PRESENTATION

A Pathophysiological Affair Between Protein Kinase D and Epithelial Ovarian Cancer: Promising Roadmap Towards Translating the Mechanism From Bench To Bedside

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High grade serous epithelial ovarian cancer (HGSOC) is deadliest gynecological malignancy due to lack of specific early-detection biomarkers, late-stage diagnosis and chemoresistance. Despite several emerging therapeutic interventions including Olaparib, Mirvetuximab, Soravtansine-gynx and anti-PD-1 antibodies, HGSOC remains unmanageable and discovery of novel, druggable tumor-drivers and their pathophysiological roles in this lethal malady is highly warranted.

Protein kinase D2 (PKD2), a multifaceted, serine/threonine kinase of diacylglycerol-targeting, Ca^{++}-Calmodulin family emerged as a novel, targetable driver of HGSOC. Its genetic knockdown or pharmacological inhibition by highly selective small-molecule inhibitor CRT0066101 significantly suppressed SKOV3 and OVCAR8 cell proliferation, EMT/migration/invasion *in vitro*. Mechanistically, PKD2 modulated Runx2, stabilized Aurora kinase-A via MAPK/ERK1/2 pathway to promote tumor phenotypes, aberrant G2/M cell cycle transition and chemoresistant neuroendocrine transdifferentiation (NEtD). Furthermore, CRT0066101 reversed NEtD phenotype, resensitized HGSOC cell to cisplatin/carboplatin, followed by suppression of ATP-dependent efflux pump P-glycoprotein. Taken together, PKD2 emerged as novel mitotic regulator, modulator of ERK1/2/Runx2, Aurora kinase A/MAPK/ERK1/2 signalling axes and druggable onco-driver in HGSOC. Translationally, these studies open promising opportunities for developing improved PKD2 inhibitors, preclinical and clinical pipelines to assess their therapeutic efficacy in combination with other regimens and novel tumor cell-targeting nanotheranostics approaches to deliver PKD2-targeting nanoparticulate drugs/ASOs/siRNAs for improved patient outcomes.

Key words: High-Grade Serous Epithelial Ovarian Cancer; Tumor-Initiating Cell Phenotypes; Neuroendocrine Transdifferentiation; Protein Kinase D Signalling; Cancer Therapeutics

From Survival to Stemness: Api5 Reprograms Breast Epithelial Cells via Wnt/β-Catenin

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Apoptosis Inhibitor 5 (Api5) is recognised as an anti-apoptotic protein that plays a role in various cellular functions, such as cell cycle regulation, mRNA export, metastasis, and resistance to chemotherapy. Previously, we found that overexpression of Api5 in breast epithelial cells grown in three-dimensional (3D) cultures resulted in partial cell transformation. This study investigates whether increased Api5 expression enhances cancer stem cell-like characteristics in non-tumorigenic breast epithelial cells.

To assess the influence of Api5 on stemness, we cultured Api5-overexpressing cells to form mammospheres—3D structures arising from mammary stem or cancer stem cells under conditions that prevent adherence and differentiation. Unlike typical epithelial cells, which

undergo anoikis in non-adherent conditions, stem-like cells can self-renew in these cultures. Our results indicated that cells with elevated Api5 exhibited a greater capacity for mammosphere formation and self-renewal upon serial passaging. Furthermore, these mammospheres exhibited increased expression of pluripotency markers, including Oct4, Nanog, Bmi1, and Sox2.
Mechanistically, Api5 enhances canonical Wnt signalling, indicated by increased phosphorylation of β-catenin and elevated pathway activity. In conclusion, our findings suggest that Api5 promotes cancer stem cell-like characteristics in breast epithelial cells by modulating the Wnt/β-catenin signalling pathway, highlighting its potential as a therapeutic target in early tumorigenesis.

Key words: Api5, Cancer Stem Cells, Wnt Signaling

IACR – 605 **POSTER**

Tif1γ As a Double-Edged Sword in Oral Cancer

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Oral cancer remains a major health burden in India, with high recurrence despite advances in surgery, chemotherapy, and radiotherapy. Tumor recurrence is largely attributed to cancer stem cells (CSCs), which possess self-renewal capacity and resistance to therapy. Transcription intermediary factor1γ (TIF1γ), a downstream regulator of TGF-β signalling, has been reported to play important role in development, hematopoiesis and immune regulation. In cancer, TIF1γ was considered as a tumor suppressor as it blocks epithelial-to-mesenchymal transition (EMT), by its E3 ubiquitin ligase activity. However, our laboratory previously demonstrated that TIF1γ promotes self-renewal in oral cancer by acting as an acetylation reader of H2A.Z and ubiquitinating H2B, leading to transcriptional activation of self-renewal genes.
The present work aims to investigate the dual role of TIF1γ in tumor promotion and suppression, regulating CSC self-renewal and EMT, respectively. We also assess whether its bromodomain (acetylation reader domain) is specifically involved in self-renewal, and that can be targeted without affecting its EMT role. Knockdown of TIF1γ significantly reduced the ALDH1A1-positive CSC population and decreased stem cell frequency as determined by extreme limiting dilution assays (ELDA), confirming its role in CSC maintenance. Conversely, wound healing assays, qRT-PCR, western blotting, and RNA-seq analysis revealed that TIF1γ suppresses EMT. Currently, we are making Bromo domain deletion of TIF1γ. In parallel, optimization of a small-molecule inhibitor targeting the acetylation reader activity of TIF1γ has been initiated. Future work will focus on generating bromodomain-deleted cell lines and evaluating the therapeutic potential in oral cancer progression, both in vitro and in vivo.

Key words: Oral Cancer; TIF1γ (Transcription Intermediary Factor1γ); Cancer Stem Cells; Self-Renewal; Epithelial mesenchymal Transition (EMT); ALDH1A1; Extreme Limiting Dilution Assay (ELDA); H2a.Z Acetylation; Bromodomain (Acetylation Reader); Small Molecule Inhibitor

IACR – 606 **POSTER**

Development of Bio-Compatible Curcumin-Loaded BSA Nanoparticles with Enhanced Anti-Cancer and Anti-Bacterial Potential

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Glioblastoma multiforme (GBM), a highly aggressive and therapy-refractory brain tumor, with treatment efficacy severely limited by the blood–brain barrier, tumor heterogeneity, and systemic toxicity of conventional therapies. This study reports the development of a multifunctional and biocompatible nanoparticulate delivery system based on curcumin-loaded bovine serum albumin nanoparticles (CUR-BSA NPs) to address curcumin's poor solubility and bioavailability. Nanoparticles were synthesized using the desolvation method and optimized for size, zeta potential, and polydispersity index. Encapsulation efficiency, drug loading, and in vitro release studies demonstrated enhanced solubility and sustained release of curcumin. In vitro cytotoxicity assays using LN229 glioblastoma cells revealed significantly higher anticancer activity of CUR-BSA NPs compared to free curcumin. Hemolysis and hemagglutination tests confirmed blood compatibility, while antimicrobial evaluation against *Staphylococcus aureus* and *Escherichia coli* showed broad-spectrum antibacterial activity. Successful drug encapsulation and nanoparticle integrity were validated using FTIR and UV-Vis spectroscopy, while SEM, DLS, XRD, and DSC analyses confirmed suitable morphology, crystallinity, and thermal stability of the formulation. This study highlights CUR-BSA NPs as a potential nanocarrier system that can overcome curcumin's pharmacokinetic drawbacks and potentially enhance glioblastoma therapy through targeted and extended release.

Key words: Anti-bacterial, Anti-cancer, Bovine Serum Albumin, Curcumin, Glioblastoma Multiforme, Nanotherapy

IACR – 607 **POSTER**

Exploring the Antitumor Effects of Berberine on Migration and Proliferation against U87MG Glioblastoma Cell Line

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Cancer is a leading cause of mortality worldwide, with brain cancers accounting for approximately 3% of all reported cases. Glioblastoma is the most aggressive and treatment-resistant form of brain cancer, necessitating the development of novel therapeutic strategies. Berberine, a naturally occurring isoquinoline alkaloid derived from plants of the *Berberidaceae* family, has demonstrated significant anticancer potential due to its low toxicity and ability to cross the blood-brain barrier. In this study, we evaluated the cytotoxic and anti-invasive effects of berberine on U87MG glioblastoma cells. Berberine treatment significantly reduced cell viability and induced pronounced morphological changes indicative of cellular stress and apoptosis. Additionally, berberine effectively inhibited cell proliferation and migration. Molecular analysis revealed that berberine treatment increased expression of the epithelial marker E-cadherin while suppressing the expression of mesenchymal markers N-cadherin and vimentin, as well as the transcription factor NF-κB. These alterations suggest a reversal of the epithelial-mesenchymal transition (EMT), a critical process involved in tumour invasiveness and metastasis. Overall, our findings demonstrate that berberine exerts potent anticancer effects

in glioblastoma cells by modulating EMT-related pathways, highlighting its potential as a promising therapeutic agent for glioblastoma management.

Key words: Berberine, Glioblastoma, Cytotoxicity, Apoptosis, Cell Migration, Nf-kB, Blood-Brain Barrier (BBB), Epithelial-Mesenchymal Transition (EMT), E-Cadherin, N-Cadherin

IACR – 608 **POSTER**

Balancing Efficacy and Safety: Advances In Understanding And Mitigating Doxorubicin-Associated Cardiotoxicity

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A multifactorial pathophysiology involving oxidative stress, mitochondrial dysfunction, calcium dysregulation, inflammation, and various cell death pathways such as apoptosis, pyroptosis, and ferroptosis limits the effectiveness of doxorubicin, a key chemotherapeutic agent. Individual susceptibility is further modulated by pharmacogenomic variability and endothelial injury. Timely intervention depends on early detection using cardiac biomarkers (such as troponins, natriuretic peptides, and miRNAs), advanced imaging, and new genetic and molecular markers. The use of cardioprotective agents like dexrazoxane, antioxidants, β-blockers, RAS inhibitors, and natural compounds, as well as tumor-specific delivery systems to improve therapeutic precision, are strategies to reduce cardiotoxicity. In order to maximize the clinical utility of doxorubicin while maintaining cardiac health, this review summarizes the most recent findings regarding the mechanisms, monitoring, and mitigation of doxorubicin-induced cardiotoxicity.

Key words: Doxorubicin-Induced Cardiotoxicity, Cardiotoxicity Monitoring, Cardio-protective Strategies, Tumor-Specific Targeting

IACR – 609 **POSTER**

Chemopreventive Effects of Bioactive Compounds from Tulsi (*Ocimum Sanctum*) Against Ovarian Cancer: In Vitro and Animal Model Investigations

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Extraction and identification of bioactive molecules from natural sources with potential anticancer properties have become pivotal in cancer research. This study focuses on the chemopreventive effects of bioactive compounds derived from Tulsi (Ocimum sanctum) leaves against ovarian cancer, employing both in vitro cell lines and a natural animal model.
Tulsi leaves were extracted using standard protocols, and the resulting solution was assessed for cytotoxicity against ovarian cancer cells. The findings revealed a concentration-dependent reduction in cell viability, accompanied by altered cell morphology, DNA damage, and cell death. Anti-inflammatory activity was further investigated using a nitric oxide assay with mouse macrophage cells, demonstrating significant effects on cellular health.

In animal experiments, a laying hen model—a spontaneous model of ovarian cancer—was utilised. Laying hens, aged one-and-a-half years, were randomly divided into control and test groups. The test group received Tulsi extract in capsule form at varying doses (167, 334, and 667 mg/kg body weight) for 90 days. Surrogate endpoints were examined to identify the optimal dose for long-term studies. Results indicated a dose-dependent increase in antioxidant activity in ovarian and liver tissues, specifically in the Tulsi-treated groups. Prostaglandin E2 levels were notably reduced in ovarian tissue, suggesting a potential protective effect against inflammation.

Ovarian cancer remains a substantial cause of mortality, necessitating innovative approaches for prevention and treatment. This research proposes a nutritional intervention using Tulsi, a traditional herb, to prevent or delay ovarian cancer naturally. The utilisation of a laying hen model, mirroring the spontaneous development of ovarian cancer in humans, provides valuable insights into the potential health benefits of Tulsi. If successful, this intervention holds promise for enhancing women's overall well-being in society.

Key words: Chemoprevention, Ovarian Cancer, Tulsi, Cell Lines, Laying Hen Model

IACR – 611 **POSTER**

Subtype-Specific Metastasis-Associated Gene Signatures In Breast Cancer: An Integrative TCGA-Based Bioinformatics And *In vitro* Experimental Study

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Breast cancer (BC) is a biologically heterogeneous disease comprising multiple molecular subtypes with distinct clinical outcomes. Metastasis remains the leading cause of BC-related mortality; however, subtype-specific molecular drivers of metastasis are not fully elucidated. This study aimed to identify metastasis-associated gene signatures across defined BC subtypes using integrative bioinformatics approaches. BC RNA-sequencing data along with corresponding clinical information were retrieved from The Cancer Genome Atlas and stratified into 5 molecular subtypes: Luminal A (LA), Luminal B (LB), HER2+, triple-negative breast cancer (TNBC), and triple-positive breast cancer (TPBC) based on hormone receptor status, with each subtype further divided into metastatic and non-metastatic cohorts. To address the substantial class imbalance between metastatic and non-metastatic samples, a bootstrapping approach was implemented with defined iterations prior to downstream analysis. Differential gene expression analysis was then conducted using DESeq2 in R, comparing metastatic versus non-metastatic tumors within each subtype. The identified significantly differentially expressed genes (DEGs) were subsequently subjected to Gene Set Enrichment Analysis (GSEA) to evaluate their association with epithelial–mesenchymal transition (EMT). Additionally, functional enrichment analyses were carried out using Gene Ontology and KEGG pathway databases to elucidate cancer- and metastasis-related biological processes. Finally, the prognostic significance of key genes was assessed through Kaplan–Meier survival analysis. The integrative workflow identified distinct, subtype-specific metastasis-associated DEGs across BC subtypes. In total, 96 unique DEGs were identified, including 13 in LA, 12 in LB, 14 in HER2+, 44 in TPBC, and 13 in TNBC based on stringent thresholds criteria (adjusted pvalue < 0.05 and $\log_2$ fold change ± 1). Key regulatory genes were identified within each subtype, including DKK1, MMP1, and CXCL12 in LA; MMP3, COMP, IGFBP2, and CXCL1

in LB; SFRP1 and DPYSL3 in HER2+; FOXC2, SFRP4, ANPEP, and COL6A3 in TNBC, and TGFBR3, and BDNF in TPBC. These genes were predominantly enriched in pathways associated with cell migration, extracellular matrix remodelling, and oncogenic signalling, highlighting their potential roles in driving metastasis and serving as subtype-specific therapeutic targets.

Key words: Breast Cancer; Metastasis; TCGA; Molecular Subtypes; Differential Gene Expression; Network Analysis

IACR – 612 **POSTER**

A Tale of Two ARID2s: Truncating Mutations Flip a Chromatin Remodeler into an Oncogenic Driver

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The SWI/SNF chromatin remodeler regulates nuclear processes by using ATP hydrolysis to maintain an open chromatin state; this complex is essential for development and its constituents are frequently mutated in cancers. Through an analysis of TCGA and CCLE datasets, it was found that nearly one-third of tumor-specific ARID2 truncations cluster around amino acid 1010, including the p.Ser989fsArg21* variant found in colorectal cancer. Using cNLS Mapper to predict nuclear localization signals and immunofluorescence to evaluate subcellular localization, the study demonstrated that while full-length ARID2 localizes to the nucleus via its NLS (aa 1488–1518), truncated variants lacking this NLS but retaining the GLN domain localize to the cytoplasm. Tandem affinity purification-mass spectrometry, pull-down, and immunoblotting identified and validated ARID2 interactors, revealing that these truncated variants fail to bind SWI/SNF components but instead engage in a newly identified interaction with AKAP8L.Through functional assays to measure tumorigenic potential, it was shown that these cytoplasmic variants drive cancer progression through GLN domain mediated gain-of-function in both ARID2-proficient and -deficient cells by activating the AKAP8L–PKA–CREB axis. Finally, these effects were validated via immunohistochemistry in patient-derived tumors and nude mouse xenografts, revealing a Yin–Yang role for ARID2 and highlighting potential therapeutic targets in colorectal cancer.

Key words: ARID2, SWI/SNF, PBAF, Gain-of-Function, NLS

IACR – 613 **POSTER**

MicroRNAs as Metastatic Markers for Prognosis and Therapeutics in Triple-Negative Breast Cancer: A Bioinformatics, Preclinical, and Clinical Study

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Breast cancer metastasis is a major cause of patient mortality, especially in triple-negative breast cancer (TNBC). Metastatic tumors spread to different organs, making treatment difficult. Early detection of metastasis at the primary tumor stage is crucial. MicroRNAs (miRNAs) are one of the stable biomarkers found in both tissues and circulatory systems, regulating disease-related genes. This study aimed to identify miRNAs that can serve as biomarkers for metastatic TNBC. miRNA-sequencing data from TNBC patients were obtained from TCGA. Metastatic and nonmetastatic primary tumors were compared to identify differentially expressed miRNAs using RStudio. These were further shortlisted using their receiver's operating characteristics (ROC) curve analysis and their expression correlation with the overall survival (OS) of the patients. Their expression was also examined in metastatic TNBC cell lines. miRNA inhibitors were transfected into the cells to test their effect on cell proliferation, migration, and invasion. The expression of miRNAs was also evaluated in plasma samples from TNBC patients using RTqPCR. miRNA-Target genes were predicted using bioinformatics tools. All experiments were done in triplicate, and results were analyzed based on the level of significance ($p \leq 0.05$). Eleven miRNAs were initially identified as significantly differentially expressed (adj. p-value ≤ 0.05, Log2FC ± 2) in primary tumor tissues of metastatic TNBC patients from the TCGA database. Five miRNAs were shortlisted based on their expression in lymph node–positive, advanced-stage TNBC patients, as well as ROC and OS correlation analyses. Among the five miRNAs, only hsamiR-9-5p and hsa-miR-1-3p showed consistent patterns in metastatic TNBC cells, with hsa-miR- 9-5p downregulated and hsa-miR-1-3p upregulated. *In vitro*, Transfection-mediated reversal of their expression reduced cell proliferation by approximately 25% and significantly inhibited cell migration and invasion. > Consistently, these two miRNAs were also dysregulated in plasma samples from patients with metastatic TNBC. Target prediction analysis indicated that these miRNAs regulate genes involved in metastasis and tumor progression. hsa-miR-9-5p and hsamiR-1-3p are potential predicting biomarkers for metastatic TNBC patient samples. Alongside, metastatic activities of the metastatic TNBC cells were also suppressed by the transfection of miRNA substitutes, suggesting their additional potential as therapeutic targets.

Key words: Metastasis, TNBC, MicroRNAs

IACR – 614 **POSTER**

Investigating the Role of Api5 during Replication Stress

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Apoptosis inhibitor 5 (Api5) is a chromatin-associated protein implicated in cell survival and therapeutic resistance, notably in cisplatin-resistant cervical cancer. While known to regulate apoptosis and cell cycle progression, its function during DNA replication and replication stress remains unclear. Here, we demonstrate that Api5 expression increases under hydroxyurea-induced replication stress. Bioinformatic and immunoprecipitation analyses identify physical interactions between Api5 and core replisome components, including RPA subunits (RPA1, RPA2, RPA3), MCM5, and a novel binding partner, MCM2. Furthermore, Api5 co-localisation with RPA2 is enhanced under replication stress, and we report for the first time that Api5 localises to heterochromatin—a localisation that increases during stress. Preliminary data suggest that Api5 overexpression may impede replication fork restart following stress recovery.

Collectively, these findings reveal a previously unrecognised role for Api5 in DNA replication and the cellular response to replication stress.

Key words: Replication Stress, Replication Fork Stalling, Hydroxyurea

IACR – 615 **POSTER**

Elucidating the Prognostic And Pro-Tumorigenic Potential of Protein Kinase D2 (PKD2)/ Laminin Subunit A5 (LAMA5) Signalling Axis in High Grade Serous Epithelial Ovarian Cancer

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Epithelial ovarian cancer, especially high-grade serous subtype (HGSOC) is the most lethal gynaecological malignancy due to absence of reliable early diagnostic biomarkers, frequent late-stage detection, chemoresistance followed by high relapse rates; hence, identification of precise pathobiology and novel, druggable drivers are essential to improve patient outcome. Remodelling of Extracellular matrix (ECM) and its interaction with tumour microenvironment (TME) is critical in HGSOC, with laminins emerging as key regulatory components. Among all laminin family members, LAMA5 is the most significantly altered gene in HGSOC. Recently, protein kinase D2 (PKD2), a DAG-responsive, Ca^{2+}/calmodulindependent serine/threonine kinase was identified as a novel driver of HGSOC. Our results suggest that PKD2 might positively regulate LAMA5 in ECM remodelling, tumorigenesis of the ovary and PKD2/LAMA5 axis could emerge as novel druggable driver of this lethal pathology. Using patient datasets harbouring HGSOC clinical samples and OVCAR3/SKOV3 cell lines, LAMA5 expression and its clinical correlation with PKD2 were analysed using bioinformatic and biochemical analyses including GEPIA, TNMPlot tools, IHC, qRT-PCR and Western blotting. LAMA5 expression was significantly upregulated in HGSOC patient samples and cell lines with a strong positive correlation with clinical stages and grades. Its high expression was also associated with poor overall and progression-free survival. Expression of LAMA5 and PKD2 positively correlated and pharmacological inactivation of PKD2 significantly suppressed LAMA5 expression and cancer cell phenotypes *in vitro*. LAMA5 is a robust prognostic biomarker and driver of EMT and chemoresistance in HGSOC. PKD2 might positively regulate its activity to promote tumorigenesis and PKD2/LAMA5 axis could emerge as a novel, druggable target in HGSOC.

Key words: Gynaecological Cancer, HGSOC, PKD2/LAMA5, Diagnostic/Prognostic Biomarker, ECM Modelling

IACR – 616 **POSTER**

PSP94/PSA Ratio as a Cost-Effective Adjunct Biomarker for Enhancing Prostate Cancer Risk Stratification

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The Rising incidence of prostate cancer (PCa) and unregulated PSA testig in India have led to increase in unnecessary biopsies, highlightig the need for adjunct biomarkers. PSP94 has emerged as a promising biomarker for improving PSA specifiity. This study evaluates diagnosti performance of serum PSP94/PSA rati in diffrentitig PCa from non-cancer cases and compares its utiity with other biomarkers with focus on PSA <20 ng/ml. Following ethical approval from seven study sites, men aged ≥40 years suspected of PCa and scheduled for biopsy were recruited. Clinical data including prostate volume, MRI and biopsy outcomes were recorded. PSA, fPSA, p2PSA were measured using Beckman Coulter Access-2 Immunoanalyzer and PSP94 levels quantiid using an in-house ELISA. Diagnosti performance was evaluated through ROC curve analysis. Out of 173 partiipants, 106 were biopsy confimed PCa cases. Lower prostate volume and higher PSAD was observed in PCa group. Serum PSP94 levels and PSP94/PSA rati were signifiantly lower in PCa group compared to non-PCa group (P<0.01). ROC analysis revealed that PSP94/PSA rati (AUC 0.701) was comparable to PHI (AUC 0.720) and outperformed %fPSA (AUC 0.662), PSP94 (AUC 0.655) and PSA (AUC 0.509), while p2PSA showed no discriminatory value. In PSA 10– 20 ng/ml subgroup, diagnosti performance improved substantilly with PSP94/PSA rati achieving highest accuracy (AUC 0.801). PSP94/PSA rati demonstrates promising diagnosti performance partiularly in men with PSA 10–20ng/ml. Offring performance comparable to PHI, it can serve as a potentil cost-effctie adjunct biomarker to PSA to enhance diagnosti specifiity and reduce unnecessary prostate biopsies.

Key words: Prostate Secretory Protein 94, PSP94/PSA Ratio, Prostate Specific Antigen, Prostate Cancer, Biomarker

IACR – 617 **POSTER**

The Linc00657-miR-17 Axis Drives UPR Activation In Alcohol-Associated Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) is the fifth most common cancer worldwide and the second leading cause of cancer-related mortality. Alcohol is a major risk factor for HCC; however, the

mechanistic basis of alcohol-associated HCC (A-HCC) remains incompletely understood. Chronic ethanol exposure promotes oxidative and endoplasmic reticulum (ER) stress, resulting in sustained activation of the unfolded protein response (UPR). Our study investigated the role of lncRNAs in regulating the PERK/ATF4/LAMP3 arm of the UPR pathway in A-HCC. In silico analyses were performed to identify UPR-associated miRNAs and lncRNAs using IPA, TargetScan, TarBase, and lncBase v3. Selected lncRNA–miRNA pairs were validated by RT-qPCR. Functional validation was carried out by inducible shRNA-mediated knockdown of linc00657 in HepG2 cells, followed by assessment of downstream miRNA and target gene expression using RT-qPCR and western blot, respectively. Cancer hallmarks were evaluated using invasion, sphere-formation, and Annexin/PI assays. Bioinformatic analysis identified miR-17, miR-142, and miR-205 as key candidates and linc00657, MALAT-1, SNHG16, KCNQ1OT1, and SGMS-AS1were selected as upstream regulators. Linc00657 and MALAT-1 showed significant upregulation in ethanol-treated cells. RT-qPCR confirmed the downregulation of miR-17 and miR-142 and the upregulation of linc00657. Knockdown of linc00657 restored miR-17 expression, confirming its miRNA-sponging role, and resulted in decreased expression of eIF2α, ATF4, and LAMP3 under ethanol exposure. Collectively, these findings highlight linc00657 as a potential therapeutic target in A-HCC, although further in vivo validation is required.

Key words: HCC, LncRNAs, UPR, Invasion, Migration, Alcohol

IACR – 618 **POSTER**

Investigating Microbial Intervention against Peritoneal Metastasis of Gastrointestinal Cancers

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Peritoneal metastasis is a major concern in most gastrointestinal cancers including pancreatic cancer, colon cancer and gastric cancer. The pathophysiology of peritoneal metastasis consists of multiple stages including dissemination from primary sites, adherence to the peritoneal surface and establishment of tumor. During this process of metastasis immune cells may play a context dependent role on progression or inhibition of peritoneal metastasis. At the same time microbes/microbial products are known to have effects on peritoneal immune cells. Based on this rationale we made hypothesis that non-lethal dose of bacteria/bacterial components may inhibit peritoneal metastasis of cancer cells in vivo. To address this hypothesis, we established syngenic pancreatic and colon cancer model in C57BL/6 mice. Cancer cells were intraperitoneally injected with/without injection of bacteria (live/heat killed). At the end point the metastatic burden were quantified and histopathologically analysed. To understand the mechanism and evaluate immune regulatory gene expression, various molecular and immunological techniques were adapted. The findings of this study showed that intraperitoneal administration of non-pathogenic bacteria can inhibit peritoneal metastasis of gastrointestinal cancer. This protective effect may be due to systemic and/or immunomodulation.

Key words: Gastrointestinal Cancer, Peritoneal Metastasis, Microbe, Immunomodulation

High-Throughput Screening of FDA-Approved Drugs Identifies Potential Inhibitors of TGF-β-induced Activation of Cancer-Associated Fibroblasts in Pancreatic Cancer

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Transforming growth factor-β (TGF-β) is a key regulator of fibroblast-to-myofibroblast transition, driving fibrosis in diseases such as pulmonary and cancer-associated fibrosis. It promotes extracellular matrix deposition and tissue remodelling. Therefore, identifying novel or repurposed FDA-approved inhibitors of TGF-β–mediated fibroblast activation is of significant therapeutic interest. To identify FDA-approved drugs capable of inhibiting TGF-β–induced myofibroblast activation using high-throughput screening, and to validate top candidates in patient-derived cancer-associated fibroblasts through molecular and phenotypic assays. High-throughput screening of FDA-approved drugs in TGF-β–stimulated human lung fibroblasts identified candidate inhibitors of fibroblast activation. These compounds were validated in PDAC patient–derived CAFs, and the most effective drug was further assessed in CAF–tumor cell co-culture models, with gene expression analysis used to define its antifibrotic mechanisms. High-throughput screening in TGF-β–induced human lung fibroblasts identified several FDAapproved drugs that significantly reduced myofibroblastic features, including decreased α- SMA expression and altered fibroblast morphology. When tested in patient-derived CAFs, the top candidate compounds similarly suppressed TGF-β–driven activation. Molecular analyses further confirmed downregulation of key fibrotic genes, indicating a consistent antimyofibrotic effect across both fibroblast models.

Key words: High-Throughput Screening; TGF-β; Myofibroblast Activation; Cancer-Associated Fibroblasts (CAFs)

Hpv16 E7 Hijacks Plk1 to Collapse Cell-Cycle Control in Cervical Cancer

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Oncogenic viruses strategically hijack host kinases in concert with viral oncoplayers to override cellular fate. As a master regulator of mitotic progression, Polo like kinase1 (Plk1) represents a prime target for viral subversion of cell-cycle checkpoints. Cervical cancer, a silent, yet devastating malignancy in women, is predominantly instigated by persistent infection with high-risk human papillomavirus (HPV). Analysis of publicly available cohorts revealed significant overexpression of Plk1 in Cervical Squamous Cell Carcinoma (CESC) patients, strongly correlating with advanced disease stages and poor prognosis. The high-risk HPV16-E7 oncoprotein induces genomic instability to promote tumorigenic transformation. Here, we identify a reciprocal crosstalk between HPV16-E7 and Plk1, wherein each protein enhances the stability of the other. Mechanistically, we show that this mutual stabilisation is

mediated through attenuation of ubiquitin-dependent proteasomal turnover, independent of transcriptional regulation. Additionally, the interaction between HPV16-E7 and Plk1 promotes progressive nuclear translocation of Plk1, indicating coordinated spatiotemporal regulation. Notably, we also uncover a novel E7-Plk1-Rb axis, in which Rb is stabilised due to such interaction. These findings suggest that HPV16-E7 hijacks Plk1 to dismantle the normal temporal cell cycle phase boundaries, enabling uninterrupted proliferative programming. Consistent with this model, our gene set enrichment analysis in Plk1-high CESC patients revealed significant enrichment of DNA replication, mitosis, and nuclear division pathways. KEGG pathway analysis highlighted cell cycle, cell adhesion, viral infections, and immune-related signaling. Together, our study establishes Plk1 as a key driver of aggressive proliferation, apoptotic resistance, and immune evasion in HPV-mediated oncogenic reprogramming, supporting its therapeutic relevance.

Key words: Cervical Cancer, Plk1, Hpv16-E7, Oncogenic virus

IACR - 623 **POSTER**

Tumor-Specific Cytoplasm-Localized ARID1B Regulates RNA Metabolism

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ARID1B, a SWI/SNF chromatin remodeling complex component, is frequently inactivated in several cancer types. Previous studies from our laboratory have revealed a cytoplasmic oncogenic gain-of-function of mutant ARID1B form (cARID1B) in pancreatic and breast cancers. cARID1B induced the activation of ERK and Wnt/β-catenin signaling, resulting in potentiation of tumorigenic properties. Here, we report additional perturbations due to aberrant ARID1B cytoplasmic localisation. *In-silico* analysis of the cARID1B interactome identified RNA metabolism as an enriched pathway. We confirmed the interaction of cARID1B with UPF1, the master regulator of Nonsense-mediated mRNA decay (NMD) and a component of processing bodies (P Bodies). The potential activity of cARID1B in regulating NMD was validated using reporter assays, supporting cARID1B's predicted role in regulating mRNA stability. We further validated the interaction of cARID1B with additional P Body components, including EDC4 and DCP1A, using biochemical as well as intracellular fluorescence assays. Additional studies revealed perturbations in P-body size and number in the presence of elevated cARID1B levels. Given that both P bodies and NMD are critical regulators of RNA metabolism, our results suggest a possible functional role of cARID1B in regulating cytoplasmic RNA metabolism, revealing a new paradigm for aberrant tumor-specific SWI/SNF function.

Key words: SWI/SNF, ARID1B, RNA Metabolism, NMD, P Bodies.

IACR - 624 **POSTER**

Onco-eQTM: An Interactive Platform for Pan-Cancer Epigenetic Regulation

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Dysregulated DNA methylation is a key driver of tumorigenesis; however, most pan-cancer resources focus on SNP-based regulation, leaving methylation-driven control of gene expression and clinical phenotypes, such as drug response and the tumor immune microenvironment, underexplored. To address this, we developed Onco-eQTM (Expression Quantitative Trait Methylation), a resource mapping and functionally annotating high-confidence cis-eQTMs across 27 TCGA cancer types, comprising ~5.1 million CpG–gene pairs. Onco-eQTM integrates functional and therapeutic contexts by linking cis-eQTMs to drug response (8.52 million), immune infiltration (3.08 million), pathway activity (13.33 million), and miRNA regulatory networks (4.52 million). Users can query by cancer type, gene, CpG probe, miRNA, drug, pathway, or immune signature, and explore detailed association tables with genomic coordinates, regulatory annotations, effect sizes, statistical significance, and interactive visualizations rendered directly in the browser. Onco-eQTM captures both well-established and novel epigenetic regulatory relationships, such as promoter methylation–mediated silencing of MGMT in glioblastoma and methylation-driven repression of miR-21 leading to extracellular matrix gene derepression. Associations between PTPRCAP methylation and lymphocyte infiltration across 23 cancers further highlight immune-related regulatory mechanisms. Onco-eQTM enables mechanistic interpretation of epigenetic–phenotypic associations through an accessible web platform. https://project.iith.ac.in/cgntlab/OncoeQTM/index.html.

Key words: DNA Methylation, eQTM, Pancancer

IACR - 625 **POSTER**

Isolation and Characterization of Novel Mouse Pancreatic Cancer Cell Lines From KC (Krasg12d, Pdx1-Cre) Model of Pancreatic Adenocarcinoma

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Despite substantial advances in radiotherapy techniques, intrinsic and acquired radioresistance significantly contributes towards poor therapeutic response in majority of pancreatic cancer (PC) patients. A major impediment to advances in this field is the lack of suitable experimental model that could aptly recapitulate the dynamics of radiation response. While human xenografts have been invaluable, syngeneic mouse PC cell lines offer a critical advantage by allowing precise elucidation of radioresistance mechanisms in an immune competent background. In this study we aimed to establish and characterize a panel of syngeneic cell lines from KC mice challenged with pancreatitis inducing agent caerulein. Two cell lines with distinct response to radiation were selected for delineating the complex molecular mechanisms of radioresistance. The irradiated cell lines were characterized based on their distinctive response to radiation. Radiosensitivity, cell cycle and cell apoptosis of the irradiated cells were assessed Besides the differential DNA damage repair was evaluated by examining the expression status of γh2ax and other DNA damage repair proteins. Further, the varying radiosensitive properties of the cell lines were verified using mice syngeneic models. In future

the clones with distinct radiosensitive property could be used for effective screening of novel radiomodulators to improve radiotherapy-based interventions for PC.

Key words: Pancreatic Cancer, Syngeneic Cell Lines, Radiotherapy, Radioresistance, Kc Mice

IACR - 626 **POSTER**

Inactivation of ARID2 Disrupts PBAF Assembly and Promotes Colorectal Tumorigenesis

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BRG1-associated factor (BAF) chromatin-remodeling complexes exist in three biochemically distinct forms in humans: canonical (cBAF), polybromo (PBAF), and non-canonical (ncBAF). These complexes are defined by mutually exclusive ARID-domain–containing subunits, with ARID1A and ARID1B specifying cBAF and ARID2 defining PBAF. Although ARID2 has been proposed to contribute to PBAF stability, its role in maintaining PBAF integrity in colorectal cancer (CRC) remains incompletely understood. Here, we examine the functional significance of ARID2 in PBAF assembly and tumor suppression in CRC. Using ARID2 knockout HCT116 cells, we demonstrate a loss of tumor suppressive activity in vitro and in nude mouse xenograft models. ARID2 deficiency caused a marked reduction of PBAF-specific subunit protein levels, including BRD7, PHF10, and PBRM1, while core BAF and cBAF components remained unchanged. Pulldown-based interaction assays revealed an inability to isolate intact PBAF complexes in the absence of ARID2, indicating a critical requirement for ARID2 in complex assembly and stability. Re-expression of wild-type ARID2 restored PBAF integrity and reversed the tumorigenic phenotype. RNA-seq analysis revealed widespread transcriptional changes affecting signaling, cell cycle, and DNA damage response pathways, while transcript levels of PBAF subunits remained largely unchanged. qRT-PCR and TCGA analyses further confirmed that ARID2 regulates PBAF stability predominantly at the protein level. Collectively, these findings identify ARID2 as a structural stabilizer of the PBAF complex and a key mediator of tumor suppressive chromatin remodeling in colorectal cancer.

Key words: ARID2, Inactivation, Tumor Suppressor, CRC

IACR - 628 **POSTER**

Decoding Extracellular Matrix Stiffness Related Gene Signatures and its Modulation by Plant Derived Flavonoid Eriodictyol in Inhibiting Metastasis

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Chemotherapeutic drug resistance remains a significant issue leading to the relapse of several cancer cases. Determining possible anti-cancer substances, preferably derived from natural products, with unique mechanisms of action that can specifically target the tumour cells

without damaging normal cells is indeed essential. Previous work from our research group has shown that Eriodictyol, induces apoptosis in cancer cells by targeting the TNFR1/FADD/TRADD axis. In vivo experiments further showed that Eriodictyol treatment led to a dose-dependent reduction in tumor volume and significantly decreased the number of metastatic lung nodules in immunocompetent BALB/c mice. On integrating global transcriptomic and proteomic gene signatures upon Eriodictyol treatment, we found several extracellular matrix related genes were deregulated that are also associated with cancer metastasis. Extracellular matrix is a critical regulator of tumor progression, and increasing matrix stiffness has been shown to enhance the aggressive behaviour of several cancer types. Bioinformatic analysis of tissues of varying matrix stiffness revealed a potential oncogene that was upregulated on a stiffer tissue compared to a soft tissue and was markedly downregulated under Eriodictyol treatment. Further in vitro studies will reveal whether Eriodictyol remodels the extracellular matrix stiffness, thereby attenuating metastatic potential of the cancer cell.

Key words: Extracellular Matrix, Cancer, Metastasis, Eriodictyol

IACR - 629 **POSTER**

Differential Expression of miRNAs between Young-Onset and Late-Onset Indian Colorectal Carcinoma Patients

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Reports indicate a worldwide increase in the incidence of Early-Onset Colorectal Carcinoma (EOCRC; <50 years old). In an effort to understand the different mode of pathogenesis in early-onset CRC, colorectal tumours from EOCRC and Late-Onset CRC (LOCRC; ≥50 years) patients were screened to eliminate Microsatellite Instability (MSI), nuclear β-catenin and *APC* mutations as these are known canonical factors in CRC pathogenesis. Small RNA sequencing followed by comparative analysis revealed differential expression of 23 miRNAs specific to EOCRC and 11 miRNAs specific to LOCRC. We validated the top 10 EOCRC DEMs in TCGA-COAD and TCGA-READ cohorts followed by validation in additional EOCRC and LOCRC cohorts. Our integrated analysis revealed upregulation of hsa-miR-1247-3p and hsa-

miR-148a-3p and downregulation of hsa-miR-326 between the two subsets. Experimentally validated targets of the above miRNAs were compared with differentially expressed genes in the TCGA datasets to identify targets with physiological significance in EOCRC development. Downregulated targets were associated with metabolic reprogramming, downregulation of anoikis regulating pathways and changes in tissue morphogenesis, potentially leading to anchorage-independent growth and EMT progression. Upregulated targets include proteins present in the basal part of Intestinal Epithelial Cells and genes whose expression are known to correlate with tumour invasion and poor prognosis.

Key words: miRNA; Early-Onset Colorectal Cancer; Hsa-Mir-1247-3p; Hsa-Mir-326; Hsa-Mir-148a-3p

IACR - 630 **POSTER**

Stratification of CRC Tumours into Consensus Molecular Subtypes Using An Immunohistochemical Protein Marker Panel: An Eastern India Cohort Study

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Colorectal cancer exhibits heterogeneous clinical outcomes and treatment responses. Consensus Molecular Subtypes (CMS1 -4) offer prognostic and predictive value but require expensive transcriptomic profiling, limiting accessibility in resource-constrained settings. We aimed to stratify colorectal tumours into CMSs using a cost-effective immunohistochemistry (IHC)-based protein marker panel in an Eastern India cohort and validate findings through Sanger and whole-exome sequencing (WES). Microsatellite-instable (MSI) tumours were classified as CMS1. An IHC-CMS classifier was used to stratify CMS2/3 and CMS4 based on the staining intensity and distribution of CDX2, KER, FRMD6, HTR2B, and nuclear ZEB1 . Nuclear β-catenin positivity distinguished CMS2 from CMS3. Validation of IHC-detected molecular subtyping was performed by analysing *APC, TP53, KRAS, CTNNB1, PIK3CA,* and *BRAF* mutations using Sanger sequencing and WES. IHC-based evaluation of 88 tumours classified 26.14% as CMS1 , 38.64% as CMS2, 31.82% as CMS3, and 3.4% as CMS4. *BRAF* V600 mutations were detected in 3/12 (25%) CMS1 cases. WES of 22 tumours revealed *APC* mutations in 91%, *TP53* in 64%, *KRAS* in 41%, and *CTNNB1* and *PIK3CA* in 5% of tumours. KEGG pathway analysis of mutated genes showed enrichment of ECM–receptor interaction pathways across all CMSs, while CMS3 tumours showed enrichment of 'Metabolic Pathways' in concordance with previous literature. Our pilot study attempts to validate a cost-efficient IHC panel for classification of colorectal tumours into putative CMSs. The study needs to bemreplicated in wider settings and in a diverse patient pool before implementation in the clinic.

Key words: Colorectal Cancer, Consensus Molecular Subtypes, Immunohistochemistry, Molecular Subtyping, Microsatellite Instability, Whole-Exome Sequencing

IACR - 631 **POSTER**

Antiproliferative and Anti-Metastatic Effects of Ethanolic Leaf Extract of *Cascabela Thevetia* against Cholangiocarcinoma Cells

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NIT Rourkela

Cholangiocarcinoma is a highly aggressive malignancy often characterized by late diagnosis and resistance to conventional chemotherapies, necessitating the search for novel therapeutic agents from medicinal plants. This study investigated the anticancer potential of *Cascabela thevetia* (syn. *Thevetia peruviana*), a plant traditionally valued for its medicinal properties, specifically targeting cholangiocarcinoma cell lines.

Ethanolic and aqueous extracts of leaves (CtLEt, CtLAq) and flowers (CtFEt, CtFAq) were subjected to phytochemical profiling and biological evaluation. Phytochemical analysis identified significant variations in bioactive compounds; notably, the ethanolic leaf extract **(CtLEt)** exhibited high concentrations of flavonoids and proteins, while ethanolic fractions generally contained tannins and glycosides—compounds often associated with anticancer activity. Safety profiling demonstrated that all extracts possessed low hemolytic toxicity (<10% RBC lysis), suggesting biocompatibility.

In functional anticancer assays, **CtLEt** emerged as the most potent candidate. It significantly reduced cholangiocarcinoma cell viability and proliferation, indicating direct cytotoxicity. Furthermore, CtLEt demonstrated the ability to disrupt critical metastatic behaviors by **inhibiting cell migration** and **suppressing colony formation**. While the study also noted antibacterial efficacy against multidrug-resistant pathogens, the primary significance lies in the ability of *C. thevetia* leaf extracts to target key oncogenic processes. These findings position the ethanolic leaf extract of *C. thevetia* as a promising source of bioactive compounds for developing novel antiproliferative and anti-metastatic strategies against cholangiocarcinoma.

Key words: Cholangiocarcinoma, Anticancer, Phytochemical

IACR - 632 **POSTER**

Breaking The BRCAness Barrier: Discovery of a First-In-Class PARP/mTOR Dual Inhibitor as Triple-Negative Breast Cancer Therapy

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Triple-negative breast cancer (TNBC) remains a major clinical challenge due to aggressive metastasis and lack of targeted therapies. The "BRCAness" phenotype further worsens prognosis, limiting PARP inhibitor efficacy to BRCA-mutant tumor harbouring patients and leaving BRCA-wild-type cases unresponsive. PARP and mTORm are two well-known therapeutic vulnerabilities of TNBC. Additionally, previous studies report that mTOR inhibition sensitizes BRCA-proficient TNBC to PARP inhibition, providing a strong rationale for a bifunctional strategy to overcome the BRCAness barrier. We designed and synthesized 37 phthalazinone-based purine derivatives as dual PARP/mTOR inhibitors. Binding was confirmed by cell-free and cell-based assays, including CETSA and molecular dynamics simulations, with downstream pathway inhibition. Anticancer activity was evaluated in BRCA-wild-type and BRCA-KO cancer cells using SRB assays and an Indian TNBC patient-derived organoid model, and *in vivo* efficacy was validated in two TNBC mice models. The lead compound, S-023-1025, effectively disrupted DNA repair and mTOR-mediated survival signaling, leading to potent antiproliferative effects in both BRCA-deficient and BRCA-proficient TNBC cell lines (IC50 ? 2–4 μM), while sparing normal cells (IC50 >15 μM). S-023-1025 exhibited superior cytotoxicity in Indian TNBC PDO compared to parent drugs. With favourable pharmacokinetic parameters, S-023-1025 (100 mg/kg) significantly inhibited tumor growth and metastasis in BRCA1-mutant xenografts and BRCA-proficient allograft models, demonstrating superior efficacy to Olaparib as confirmed by bioluminescence imaging *in vivo*, without inducing systemic toxicity. Our findings identify S-023-1025 as a first-in-class PARP/mTOR dual inhibitor, offering a novel therapeutic avenue for TNBC, a malignancy where targeted therapy continues to be a critical vacuum.

Key words: TNBC, BRCA, PARP, mTOR, Dual Inhibitor

IACR - 633 **POSTER**

Development and Characterization of Pegylated Chitosan Nanoparticles Co-Loaded With Curcumin and Thymoquinone for Glioblastoma Therapy

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Glioblastoma multiforme (GBM) is an aggressive and therapy-resistant brain tumor, with treatment efficacy severely constrained by poor drug solubility, systemic toxicity, and the inability of conventional therapeutics to achieve sustained bioavailability. This study reports the development of a biocompatible PEGylated chitosan-based nanoparticle delivery system co-loaded with curcumin and thymoquinone, to address formulation and delivery barriers associated with these compounds. Nanoparticles were synthesized via ionotropic gelation and optimized for particle size, surface charge, and polydispersity index. PEGylation enhanced colloidal stability and reduced the zeta potential, thereby favoring systemic compatibility. High encapsulation efficiency and formulation yield confirmed effective incorporation of both drugs, while UV–Vis spectroscopy validated successful co-loading. Comprehensive physicochemical characterization, using FTIR, FESEM, DLS, XRD, DSC, and NMR, confirmed the integrity, amorphous dispersion, and thermal stability of the nanoparticles. The nanoparticle demonstrated excellent hemocompatibility, indicating suitability for systemic

administration. The dual-drug formulation exhibited enhanced antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* compared to single-drug nanoparticles, supporting synergistic bioactivity. In vitro cytotoxicity assays using LN229 glioblastoma cells revealed significantly higher anticancer activity of the dual-drug formulation relative to individual drug systems. Overall, this work highlights the potential of PEGylated chitosan nanoparticles co-delivering curcumin and thymoquinone for glioblastoma therapy.

Key words: Glioblastoma Multiforme, Pegylated Chitosan Nanoparticles, Curcumin, Thymoquinone, Drug Delivery, Anti-bacterial

IACR - 638 **POSTER**

Api5 Regulates Genomic Integrity by Modulating DNA Damage Response and Repair

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Api5 (Apoptosis Inhibitor 5) is a nuclear protein first characterized for its ability to block apoptosis and support cell survival, especially under conditions of growth factor withdrawal or cellular stress. It influences key processes such as cell cycle control, gene transcription, and pro-survival signaling, and its overexpression is frequently observed in various cancers, where it contributes to resistance against therapeutic interventions.

In this investigation, we present novel evidence demonstrating that Api5 is essential for preserving genomic integrity. Reducing Api5 expression through knockdown leads to pronounced genomic instability, manifested by abnormally small nuclei, aneuploidy, abnormalities during mitosis, heightened levels of DNA damage indicators (such as increased γH2AX foci and extended comet tail lengths in comet assays), and a rise in micronuclei formation.

Api5 protein levels are regulated in response to genotoxic insults, showing degradation following exposure to DNA-damaging agents. Cells lacking Api5 display greater vulnerability to DNA-damaging treatments like UV radiation and cisplatin, along with sustained Chk1 activation and defective DNA repair mechanisms. In contrast, forced overexpression of Api5 improves DNA repair capacity and diminishes checkpoint signaling.

Furthermore, Api5 depletion hinders colony-forming ability and anchorage-independent proliferation in vitro, while tumors deficient in Api5 exhibit improved responsiveness to cisplatin treatment in xenograft mouse models.

Analysis of TCGA datasets indicates a positive association between Api5 mRNA expression and measures of genomic instability specifically in breast cancer cases.

Collectively, these results identify Api5 as a previously unrecognized modulator of genome stability, offering important insights into cancer development and potential therapeutic strategies.

Key words: Api5, Genomic Stability, Genomic Instability, DNA Damage, DNA Repair, γH2AX, Micronuclei, Aneuploidy, Cisplatin Sensitivity, Checkpoint Activation

IACR - 639 **POSTER**

Skin as a Window to Hidden Malignancy: A Three-Year Study of Paraneoplastic Dermatoses in a Tertiary Care Centre

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Paraneoplastic dermatoses often provide the earliest clue to an occult internal malignancy, yet they remain under-recognized in routine practice. We conducted a three-year prospective observational study at a tertiary care centre to evaluate the spectrum of cutaneous manifestations associated with underlying cancers. Forty consecutive patients presenting with unexplained skin lesions—ranging from generalized pruritus and eczematous plaques to vesiculobullous eruptions—were included after detailed clinical assessment and appropriate oncological investigations. The objective was to correlate dermatological patterns with the type of malignancy and to highlight presentations that warrant active malignancy screening. Hematological cancers constituted the largest group, accounting for 56.4% of cases, followed by gastrointestinal malignancies in 15.4%. Bullous pemphigoid and paraneoplastic pemphigus were the most frequent specific dermatoses, each observed in 7.7% of patients. Other notable manifestations included dermatomyositis, acanthosis nigricans, exfoliative dermatitis, and nonspecific generalized itching. In several individuals, the skin disease preceded the diagnosis of cancer by weeks to months, emphasizing its sentinel role. Recognition of characteristic morphologies, supported by histopathology and immunological tests, facilitated early referral and oncologic management. The study underscores that diverse and sometimes subtle cutaneous findings may represent paraneoplastic phenomena. Awareness among clinicians can promote timely detection of hidden malignancy, improve interdisciplinary collaboration, and potentially influence overall prognosis.

Key words: Cancers, Dermatosis, Paraneoplastic, Pruritis

IACR - 640 **POSTER**

Role of 14-3-3δ in Regulating Therapy Resistance and Tumour Progression in Breast Cancer

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Therapy resistance is a major problem in most solid tumors and a major cause of disease progression. The 14-3-3 protein family regulates various cellular signaling pathways. Among the seven paralogs, 14-3-3σ exclusively forms homodimers and is expressed only in epithelial cells. 14-3-3σ loss in breast cancer (BC) correlates with poor prognosis, while better prognosis in colorectal cancer (CRC). 14-3-3σ loss leads to an EMT and decreased UPR pathway genes in HCT116 and MCF7 cells. However, the outcomes of 14-3-3σ loss are different in these two lines with respect to therapy resistance. Therefore, we wish to determine if the molecular mechanisms leading to EMT and decreased expression of UPR pathway genes are similar in these two cell lines. Further mechanistic studies also tell us how 14-3-3σ acts as a tumour suppressor in breast cancer. Based on our finding we hypothesize that the c-Jun-Slug axis might be the key contributor to EMT in breast cancer. We also wish to identify interacting partners of 14-3-3σ that might contribute to the tumour suppressive role of 14-3-3σ in BC. Hence, this

study aims to identify the mechanisms by which 14-3-3σ loss in BC shows therapy resistance, potentially aiding in the development of effective BC treatment.

Key words: 14-3-3δ, Therapy Resistance, UPR Pathway, EMT

IACR - 641 **POSTER**

Comparative Transcriptome of Normal and Cancer-Associated Fibroblasts

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The characteristics of a tumor are largely determined by its interaction with the surrounding micro-environment (TME). TME consists of both cellular and non-cellular components. Cancer-associated fibroblasts (CAFs) are a major component of the TME. They are a source of many secreted factors that influence the survival and progression of tumors as well as their response to drugs. Identification of markers either overexpressed in CAFs or unique to CAFs would pave the way for novel therapeutic strategies that in combination with conventional chemotherapy are likely to have better patient outcome.

This study has used fibroblasts have been derived from Benign Prostatic Hyperplasia (BPH) and prostate cancer. RNA from these has been used to perform a transcriptome analysis in order to get a comparative profile of normal and cancer-associated fibroblasts.

The study has identified 818 differentially expressed mRNAs and 17 lincRNAs between normal and cancer-associated fibroblasts. Also, 15 potential lincRNA-miRNA-mRNA combinations have been identified which may be potential biomarkers.

The differentially expressed markers between normal and cancer-associated fibroblasts, upon more experimental validation would help in strategizing therapy targeting TME factors, which could be used in combination with conventional therapy.

Key words: Tumor Microenvironment, Cancer-Associated Fibroblasts, Chemoresistance, Non-Coding RNA, LincRNA, Prostate Cancer

IACR - 642 **POSTER**

Beyond Clinical Mimics: Histopathological Unveiling of Atypical Skin Malignancies

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Introduction: Skin malignancies are a growing concern in dermatology due to rising incidence and diverse clinical presentations. Basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and malignant melanoma constitute the majority of cases. BCC typically occurs on sun-exposed sites with indolent growth, whereas SCC demonstrates greater invasive and metastatic potential. Malignant melanoma, though less common, is highly aggressive and may present in atypical forms, hindering early recognition. Rare tumors such as adnexal neoplasms, keratoacanthoma centrifugum, and desmoplastic melanoma further complicate clinical

diagnosis. **Methods:** This case series included patients presenting with atypical skin lesions initially considered benign. Subsequent histopathological evaluation established the presence of malignancy, highlighting the indispensable role of tissue diagnosis. **Discussion:** Five unusual malignancies were analyzed. An adnexal neoplasm mimicked a benign lesion, requiring histology for definitive identification. A melanoma arose in a non–sun-exposed site, delaying suspicion. Basi-squamous carcinoma exhibited aggressive behavior despite innocuous appearance. Keratoacanthoma centrifugum was misinterpreted as a cystic lesion due to rapid peripheral keratinization. Desmoplastic melanoma presented as a non-pigmented firm nodule, necessitating differentiation from fibrous tumors. **Conclusion:** Atypical morphology can mask skin cancers. Early biopsy and meticulous histopathological assessment are essential for accurate diagnosis and improved therapeutic outcomes.

Key words: Melanoma, Basi-Squamous, Keratoacanthoma, Desmoplastic Melanoma

IACR - 643 **POSTER**

Understanding the Crosstalk Between Iron and Cellular Energy Metabolism in Human Breast Cancer Cells

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Iron modulates rapid cell growth by regulating various cellular functions including energy metabolism. The iron metabolism involves absorption, transport, storage, utilization and recycling in different cellular compartments. Cytosolic iron is used directly or stored in the form of labile iron pool (LIP), while mitochondrial iron is utilized for heme and iron sulfur cluster (ISC) biosynthesis to regulate mitochondrial energy metabolism. Unlike, normal cells cancer cells exhibit increased iron metabolism and storage while avoiding iron induced cell death (ferroptosis). Therefore, it is intriguing to identify the molecular determinant(s) that favor, regulate, and protect cells from iron overload. The mitochondrial chaperone TRAP-1 functions as a molecular switch between glycolysis and oxidative phosphorylation (OXPHOS). Here, we explored whether or how TRAP-1 modulates iron metabolism. We establish that TRAP-1 favors iron import, storage, heme and ISC biosynthesis. This phenomenon was specific to cancer cells (MCF-7) while normal cells (MCF10A) failed to accumulate iron in the low TRAP-1 or no TRAP-1 background. Interfering with the TRAP-1 function leads to decreased heme and ISC biosynthesis, pointing to the fact that TRAP-1 regulate both upstream and downstream of iron metabolism in cancer cells. We demonstrate that TRAP-1 contributes to aerobic glycolysis (Warburg effect) by deregulating iron metabolism. We propose that interfering with TRAP-1 chaperone functions interferes with iron metabolism and sensitize cancer cells to either metabolic inhibitors or chemotherapeutic drugs.

Key words: TRAP-1, Iron Sulfur Cluster, Ferroptosis, OXPHOS, Labile Iron Pool

IACR - 645 **POSTER**

Decoding the Transcriptomic Landscape of Esophageal Squamous Cell Carcinoma in Kashmir: Insights from a High-Risk Population

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Background: Esophageal squamous cell carcinoma (ESCC) is a major public health concern in Kashmir, with incidence far exceeding national and global averages. The population exhibits reduced genetic diversity due to long-standing endogamy, which may contribute to population-specific disease mechanisms. Despite the high burden, existing studies from Kashmir are largely epidemiological, with limited comprehensive genetic-level research findings. **Methods:** We performed transcriptome sequencing on paired tumour and adjacent normal tissues from ESCC patients in Kashmir. Differential gene expression analysis was conducted to identify significantly dysregulated coding and non-coding transcripts. Pathway enrichment analyses were used to elucidate key biological processes and signalling pathways involved in ESCC pathogenesis. **Results:** Transcriptomic profiling revealed extensive molecular reprogramming, identifying 61,970 differentially expressed genes with prominent variations included activation of ECM-receptor interaction pathways and pro-tumorigenic JAK/STAT signalling, with significant upregulation of STAT3, CTSB, HCFC1, PDLIM7, and GPNMB. Conversely, metabolic and structural genes such as HNRNPA2B1, TAGLN, TPM1, and RPL15 were markedly downregulated, indicating disruption of epithelial integrity and translational control. Several lncRNAs, including H19 and SNHG29, also showed differential expression. **Conclusion:** This first transcriptome-level study of ESCC from Kashmir highlights distinct molecular signatures shaped by unique genetic and environmental factors, providing a foundation for population-specific biomarkers and targeted therapeutic strategies.

Key words: ESCC; Transcriptome Profiling; Differential Gene Expression; Kashmir Valley; High-Risk Region

IACR - 646 **POSTER**

Turning the Tables on KRAS: How LCN2 Rewires EGFR Sensitivity in Colorectal Cancer

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Therapy resistance is a major challenge in colorectal cancer (CRC) treatment. Around 40% of CRC patients harbor activating mutations in the *KRAS* gene and *KRAS*-mutant CRC exhibits resistance to anti-EGFR therapy. Hence, identifying new therapeutic targets for effective treatment of *KRAS*-mutant CRC is essential. Lipocalin 2 (LCN2) is a secreted glycoprotein, which regulates iron homeostasis by sequestering the iron-siderophore complex. LCN2 over-expressing CRC cells show an increase in colony formation and tumor growth upon 5-Fluorouracil (5-FU) treatment, indicating the role of LCN2 in 5-FU resistance. High LCN2

expression in *KRAS*-mutant CRC correlates with reduced overall survival following adjuvant chemotherapy. LCN2 over-expressing *KRAS*-mutant CRC cells exhibit increased EGFR activation and enhanced EGFR membrane localization upon 5-FU treatment. Moreover, inhibiting EGFR in LCN2 over-expressing *KRAS*-mutant CRC cells leads to a decrease in cell survival. Further, we aim to develop a genetic mouse model ($Kras^{LSL\text{-}G12D}$ $APC^{fl/fl}$ CDX2-Cre-ER^{T2+}) for *KRAS* mutant CRC expressing high LCN2 levels. The H&E sections of the colon & rectal tissues from these mice indicate tumor formation. LCN2 and activated EGFR levels were found to be elevated in the tumor tissues as compared to the normal. Hence, this study aims to understand how LCN2 rewires EGFR sensitivity in CRC.

Key words: LCN2, KRAS-Mutant CRC, Therapy Resistance, EGFR Recycling, Genetic Mouse Model of CRC

IACR - 648 **POSTER**

Context-Dependent Roles of Arid1b: Evaluating A Possible Non-Canonical Oncogenic Behaviour of ARID1B in Specific Cancer Types

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The mammalian BAF (SWI/SNF) complex is a central regulator of chromatin architecture and gene expression, frequently disrupted in human cancers. One of its subunits, ARID1B (AT-rich interactive domain 1B) has been traditionally characterized as a canonical tumor suppressor, particularly in pancreatic cancer where its loss or inactivation drives tumor progression. However, emerging evidence suggests its role may be highly context-dependent. In this study, we investigated the role of ARID1B in three distinct cancer models: HepG2 (hepatocellular carcinoma), U2-OS (osteosarcoma), and MCF7 (breast cancer). Utilizing CRISPR/Cas9-mediated gene editing, we successfully generated ARID1B-knockout (KO) cell lines to evaluate the consequences of loss-of-function on cellular fitness. Functional tumorigenic assays revealed that the absence of ARID1B significantly attenuates oncogenic potential. Specifically, ARID1B-KO resulted in a marked decrease in cell proliferation, viability and colony formation compared to wild-type (WT) controls. These data indicate that, unlike its role in pancreatic cancer, ARID1B is essential for the proliferation and survival of these specific cancer models, suggesting an oncogenic dependency.
To elucidate the molecular mechanisms driving this phenotype, we are currently performing comparative transcriptomic profiling of WT and KO cell lines. Our preliminary findings challenge the "one-size-fits-all" classification of ARID1B as a universal tumor suppressor and emphasizes the importance of considering tissue-specific configurations.

Key words: SWI/SNF, ARID1B, Oncogene

IACR - 649 **POSTER**

Comparative Proteomic Analysis of 14-3-3 Ligand Association and Their Specific Function

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The 14-3-3 protein family regulates diverse cellular pathways through interactions with phosphorylated ligands as homodimers or heterodimers. However, distinguishing paralog-specific binding remains challenging. Therefore, we designed a differential proteomic screen exploiting two conserved acidic residues (D129/E136 in 14-3-3γ; D127/E134 in 14-3-3ε) within the phosphopeptide-binding pocket. Mutations to alanine generate distinct binding profiles: Aspartate mutant increases ligand binding, whereas glutamate mutant reduces it, allowing the identification of paralog-specific associations in heterodimeric complexes. This study investigates 14-3-3γ and 14-3-3ε paralogs, focusing on their distinct roles in centrosome regulation and cell cycle progression. Our laboratory has previously demonstrated that 14-3-3ε prevents premature centriole disengagement by inhibiting the activity of Plk1 and separase at the centrosome. PLA assay revealed 14-3-3ε-Plk1 interactions localise to both centrosomes and cytoplasm, suggesting broader regulatory functions beyond centriole disengagement. Therefore, our current study examines how 14-3-3ε regulates Plk1-dependent pathways during cell cycle progression. Synchronisation studies showed interaction begins in the G2 phase and intensifies during mitosis, correlating with peak Plk1 activity. Since Plk1 orchestrates multiple mitotic events, we hypothesised that cytoplasmic 14-3-3ε-Plk1 binding might regulate additional Plk1-dependent pathways, consequently modulating downstream mitotic pathways and maintaining proper cell cycle timing.

Key words: 14-3-3e, Plk1, Cell Cycle Regulation

IACR - 650 **POSTER**

KMT2C Mutation (C>A; chr7:151882672) Predicts Treatment Response in Indian Cervical Cancer Patients

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Cervical cancer is the second most common cancer in India, with nearly one-third of patients experience relapses, primarily due to distant metastases. Reliable biomarkers to predict response to chemoradiation are lacking. In this study, we aimed to identify genomic predictors of treatment response and develop a machine-learning model incorporating a key mutation in KMT2C to predict treatment response in Indian cervical patients. A total of 416 biopsy-proven squamous cell carcinoma patients diagnosed between 2022–2025 were included. After six-month completion of chemoradiation followed by brachytherapy, patients were categorized as responders and nonresponders. Whole-exome sequencing (WES) was performed on treatment responders (n=11) and non-responders (n=5) to identify most frequent mutated genomic variants. Selected Variants were validated in a different cohort (n=400) using High Resolution

Melting analysis. Associations between genetic mutations and treatment response were measured using Fisher's exact test. Binary logistic regression and Cox regression were used to evaluate predictive and prognostic significance. Decision Tree, Random Forest, CART, and XGBoost were trained based on significant variables to develop a machine-learning model.WES identified KMT2C (C>A; chr7:151882672) ($p<0.002$) and PIK3CA (G>A; chr3:178936091) as frequently mutated in responders, while HLA-A (G>C; chr6:29910742) ($p<0.003$) was predominant in non-responders. Logistic regression showed a significant correlation between KMT2C mutation (C>A 151882,672) ($p < 0.02$), BSA ($p<0.019$), age($p<0.065$), FIGO stage (0.066) with treatment response. Cox regression shows prognostic relevance of KMT2C mutation ($p<0.011$). Among machine-learning models, XGBoost performed best (accuracy 86%; F1-score for responders 0.92). KMT2C mutation(C>A; chr7:151882672) is a promising genomic marker for predicting treatment outcome in addition to the clinical parameters.

Key words: Cervical Cancer, KMT2C, Genomic Alterations, Treatment Response, Machine Learning, Whole-Exome Sequencing, Biomarker Prediction

IACR - 652 **POSTER**

An Ml-Based Integrative Prognostic Model for Triple-Negative Breast Cancer using Single-Cell and Bulk Transcriptomics

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Breast cancer is known to have a significant degree of intratumoral heterogeneity, with triple-negative breast cancer (TNBC) exhibiting the most. Using single-cell RNA-sequencing (scRNA-seq), we identified an epithelial subpopulation with elevated activity of the ubiquitin proteasome system (UPS) and other related pathways. We intersected the marker genes of the these epithelial subpopulation with the differentially expressed genes derived from the bulk transcriptomes of TNBC to prioritize clinically relevant candidates.

Firstly, univariate Cox regression was performed on the intersected gene set to determine the survival-associated genes, and these were then used to form prognostic models via different machine-learning techniques, including single and combinatorial algorithms. Model performance was compared using the concordance index (C-index) and time-dependent receiver operating characteristic (ROC) curves. Among the evaluated models, we selected the model with the most prognostically relevant genes, exhibiting the highest C-index and demonstrating consistent prognostic performance, having favorable AUC values at 1, 3, and 5 years in the TCGA-TNBC cohort.

Patients stratified by the four-gene risk score into high- and low-risk groups demonstrated significantly different overall survival outcomes. The downstream functional analyses indicated that the prognostic signature was a reflection of the upper and lower bounds of malignant epithelial activity.

This study provides a single cell-supported four-gene prognostic signature for TNBC and demonstrates an integrative approach utilizing single cell and bulk transcriptomics, coupled with machine learning, for the discovery of novel biomarkers.

Key words: Single-Cell Rna Sequencing; Triple-Negative Breast Cancer; Prognostic Signature; Tumor-Microenvironment; Machine Learning; Survival Analysis

IACR – 653 **POSTER**

Modulation of LAT1 Expression in Triple-Negative Breast Cancer by Natural Compound Rutin through HIF1/MTOR Pathway

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L-type amino acid transporter-1 (LAT1/SLC7A5) is a heterodimeric transmembrane protein that mediates sodium-independent uptake of large neutral amino acids (leucine, phenylalanine, tryptophan) essential for cancer cell metabolism. LAT1 forms a disulfide-linked with CD98/4F2hc (SLC3A2), supporting mTORC1-dependent protein synthesis and metabolic reprogramming through L-tryptophan-driven NAD? synthesis and glycolytic amplification. LAT1 is selectively overexpressed in triple-negative breast cancer (TNBC) relative to other breast cancer subtypes, correlating with poor prognosis and chemotherapy resistance. In this study we evaluated inhibition of LAT1 in TNBC through activation of apoptotic pathways. Results of the present study showed that rutin treatment significantly ($P<0.05$) increased the expression of pro-apoptotic protein Bax whereas down-regulate the expression of Bcl2, leading to caspase mediated apoptosis in MDA-MB-231 cells. Additionally, we also showed that up-regulation of LAT1 correlated with upregulation of HIF1α through activation of mTORC1 pathway. Activation of these pathway acts as a feed-back loop within the cancer cells to maintains cancer cell viability under stress condition. *In vivo* results also validate our *in vitro* findings and showed that rutin significantly ($P<0.05$) downregulated LAT1 expression followed by expression of HIF1α in 4T1 cell line induced solid tumor in BALB/c mice. Additionally, rutin treatment did not alter hematological parameters or compromise any host organ functions. These findings establish that LAT1 inhibition by rutin represents a mechanistically novel, cancer-selective, non-toxic approach to restrict TNBC proliferation and growth in cancer patients.

Key words: Triple Negative Breast Cancer; LAT1; Rutin; Nutrient Transporters; Apoptosis

IACR – 654 **POSTER**

Rutin Synergizes with Paclitaxel to Elicit Immunogenic Tumor Cell Death and Re-Programmed the Tumor Microenvironment in TNBC

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Triple-negative breast cancer (TNBC) remains a formidable therapeutic challenge due to intrinsic and acquired chemoresistance, high metastatic propensity, and the paucity of clinically actionable targeted therapies. The present study investigates the mechanistic basis and immunological sequelae of combining rutin, a plant-derived flavonoid, with paclitaxel to

enhance antitumor efficacy while attenuating chemotherapy-associated toxicities. Network pharmacology analysis initially implicated apoptosis, proliferative signaling, and immune activation as major pathways modulated by the rutin–paclitaxel combination. These in silico predictions were subsequently validated in two TNBC cell lines (MDA-MB-231 and 4T1), demonstrating that co-treatment induces intrinsic (mitochondria-dependent) apoptosis, as evidenced by increased cytochrome c release, an elevated Bax/Bcl-2 ratio, and enhanced caspase activation.

In an in vivo TNBC model, combination therapy significantly ($P<0.05$) reduced tumor burden, prolonged host survival, preserved tissue architecture, and mitigated paclitaxel-induced oxidative injury, as indicated by normalization of ROS levels and restoration of antioxidant enzymes, including SOD and catalase. Mechanistically, rutin co-administration potentiated paclitaxel activity by suppressing PI3K–AKT–mTOR signaling both in vitro and in vivo. Furthermore, the combination elicited endoplasmic reticulum (ER) stress–associated immunogenic cell death (ICD), which was accompanied by downstream activation of NF-κB signaling. Paracrine interaction assays revealed that damage-associated molecular patterns (DAMPs) released from TNBC cells treated with rutin alone or in combination with paclitaxel robustly activated macrophage NF-κB signaling, promoted M1 polarization, and increased the secretion of pro-inflammatory cytokines. Pharmacological inhibition of AKT and NF-κB signaling reduced ICD-associated markers and attenuated macrophage activation, supporting a mechanistic dependence on these pathways. Consistent with these findings, in vivo analyses indicated enhanced systemic antitumor immunity, reflected by increased circulating CD3, CD4, and CD8 T-cell populations.

Collectively, these data demonstrate that rutin synergizes with paclitaxel to promote apoptosis, suppress proliferative signaling, reduce treatment-associated toxicity, and stimulate antitumor immune activation, underscoring its translational potential as an adjuvant strategy for TNBC management.

Key words: Triple Negative Breast Cancer; Rutin, Paclitaxel, PI3K-AKT-MTOR Pathway, Immunogenic Cell Death NF-κB Signaling, Immune Response

IACR - 655 **POSTER**

Sexuality as a Determinant in Quality of Life among Post-Mastectomy Breast Cancer Patients

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Breast cancer survivors frequently report persistent disturbances in Sexuality following mastectomy, which may substantially compromise their overall Quality of life. The present study aimed to examine the relationships among Sexuality and Quality of life in post-mastectomy breast cancer patients. A correlational research design was employed on a sample of 200 married premenopausal women who had undergone unilateral or bilateral mastectomy. Participants were recruited using a combination of availability and snowball sampling techniques from hospital and community settings in Kashmir division, J&K. Data were collected using standardized measures of Sexuality and Quality of life. Correlation analysis indicated that Sexuality showed a stronger association with Quality of life ($r = .682$, $p = .020$).

Regression analysis further revealed that Sexuality emerged as a robust predictor (β = .237, SE = .093, CR = 2.558, p = .011). These findings suggest that disturbances in Sexuality contribute meaningfully to variations in Quality of life among women following mastectomy. Ethical clearance for the study was obtained from the Institutional Ethical Committee of Government Medical College (GMC), Srinagar. Written informed consent was secured from all participants prior to data collection, ensuring confidentiality and voluntary participation. The results underscore the need for comprehensive psychosocial interventions addressing sexual health as integral component of breast cancer survivorship care, particularly for women adjusting to the long-term consequences of mastectomy.

Key words: Mastectomy, Sexuality, Quality of Life

IACR - 657 **POSTER**

Clinical Implications of Circulating Cell-Free MALAT1 in Plasma as Liquid Biopsy Biomarker for Risk Stratification to Predict Prognosis in Oral Squamous Cell Carcinoma Patients

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The current global pathological trend indicates a drastic rise in oral squamous cell carcinoma (OSCC), having a high rate of recurrence within the first two years of surgery and is associated with poor prognosis in OSCC patients. Till now, there is no blood-based molecular biomarker for risk stratification and to predict disease-free survival in OSCC patients. The present study aims to evaluate the circulation level of MALAT1 in the blood plasma as a potential biomarker for liquid biopsy for risk stratification and early prediction of the prognosis of OSCC patients. We collected the peripheral blood samples from the newly diagnosed treatment naïve OSCC patients and healthy controls with their consent. The circulating MALAT1 expression levels were determined from the blood plasma through qRT-PCR. Then we performed a comparative study to check the clinical association between circulating MALAT1 levels and actual disease outcome (recurrence and disease-free survival) compared to the conventional histopathological markers for risk stratification in OSCC treatment management. We found that the relative expression of MALAT1 is significantly upregulated in OSCC patients compared to healthy controls. Our results showed that MALAT1 is significantly upregulated in patients with recurrence compared to non-recurrence patients. Based on Mantel-Cox's survival analysis, patients with high MALAT1 levels experienced significantly shorter disease-free survival. Therefore, the highly expressed MALAT1 level in OSCC patients can be a potential predictive and prognostic biomarker for predicting recurrence and poor disease-free survival.

Key words: Liquid Biopsy, Blood-Based Biomarker, Recurrence, Disease Free Survival, Prognosis

Exploiting Lipid Metabolism Dependencies to overcome Therapy Resistance in Colorectal Cancer

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Colorectal cancer (CRC) remains a leading cause of cancer-related mortality, largely due to therapy resistance and disease relapse. These challenges are driven by drug-tolerant persister cells (DTPs) that survive initial treatment and sustain residual disease. Emerging evidence identifies metabolic reprogramming as a central driver of tumor progression, with dysregulated lipid metabolism and lipid droplet (LD) accumulation marking aggressive, therapy-resistant CRC. However, the mechanisms linking lipid storage to tumor progression under therapeutic stress remain poorly understood.

In this study, we found increased LDs contribute to tumor progression. CRC DTPs exhibit marked overexpression of Lipin1 (LPIN1), a key enzyme mediating fatty acid sequestration into LDs. LPIN1 upregulation is driven by the ETS1–PTPN1–c-Src–CEBPβ signaling axis. Inhibition of LD formation using statins or suppression of LPIN1 disrupts lipid homeostasis, inducing lipotoxicity and ferroptotic cell death in DTPs and patient-derived organoids (PDOs). This is accompanied by elevated lipid reactive oxygen species and rescued by ferroptosis

inhibitors or N-acetyl cysteine. Targeting LPIN1 also suppresses tumor growth in DTP-derived xenograft and PDX models.
These findings establish LPIN1-driven LD formation as a critical metabolic vulnerability in therapy-resistant CRC, revealing a targetable pathway to induce ferroptosis, impair tumor growth, and prevent relapse.

Key words: Drug-Tolerant Persister Cells, Therapy Resistance, Metabolic Reprogramming, Lipid Metabolism, Lipid Droplets, Lipin1 (Lpin1), Ferroptosis

IACR - 659 **POSTER**

Revealing the Potential Role of 3, 3'-Diindolylmethane to Enhance the Efficacy of 5-Fluorouracil Therapy in Colorectal Cancer through Modulation of Mitochondrial Apoptosis Pathway

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Colorectal cancer (CRC) is one of the most commonly diagnosed cancer worldwide and 30% of patients with CRC experience metastasis. CRC ranks third in case of incidence and second leading cause of death after lung cancer. 5-FU (Fluorouracil), an anti-metabolite drug, is commonly used as the first-line of treatment modalities in most CRC cases. The primary barriers that restrict 5-fluorouracil (5-FU) effectiveness in CRC treatment are chemoresistance and drug induced hepatotoxicity. Therefore, the objective of the present study is to improve the therapeutic efficacy and prevention of 5-FU-induced toxicity, by the concurrent use of 3,3′-diindolylmethane (DIM). In this study, DIM was administered (25 mg/kg b.w., p.o.) to colorectal carcinoma (CT26 cell line) induced solid tumor in Balb/C mice alone as well as in combination with 5-FU (5 mg/kg b.w., i.p.) in concomitant treatment schedule. Results of the present study we showed that natural compound DIM significantly ($P<0.05$) enhanced the therapeutic efficacy of 5-FU both *in vitro* and *in vivo*. DIM and 5-FU treatment markedly inhibited proliferation and promoted mitochondrial depolarization of HCT116 and CT26 cells. Combinatorial treatment further induced G0/G1 cell cycle arrest, apoptosis and DNA damage in CRC cells. Additionally, we also showed that co-administration of DIM and 5-FU significantly ($P<0.05$) reduced the tumor size and improved over all survival of the host. Moreover, we also showed that DIM provided additional host survival advantages by attenuated 5-FU induced toxicities through modulation of Nrf2/ARE pathway and promoted expression of cytoprotective proteins HO-1, NQO1 and GSTπ in hepatic tissue. Collectively, these findings demonstrate the sensitizing and protective roles of DIM, supporting its potential as a promising adjuvant to improve the efficacy and safety of 5-FU–based chemotherapy in CRC.

Key words: Colorectal Cancer (CRC); 3, 3-Diindolylmethane (DIM); 5-Fluorouracil (5-Fu); Cell Cycle Arrest; Apoptosis

IACR - 660 **POSTER**

Role of ACSL 4-Mediated Lipid Metabolism in Colorectal Cancer Drug Resistance and Metastasis

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Chemoresistance poses a major challenge to colorectal cancer therapy leading to tumour relapse, metastasis and poor clinical outcome. Understanding the molecular adaptations enabling residual tumour subpopulations to survive therapeutic stress and undergo metastasis is therefore of critical importance.

Ferroptosis is an iron-dependent mode of cell death. Long-chain acyl CoA synthetase 4 (ACSL4) is a central regulator and influences cellular susceptibility to ferroptosis. In this study, we investigated the role of ACSL4 in CRC progression, chemo-resistance and metastatic potential by analysing its expression in primary colorectal tumours and drug-tolerant persister cells.

We found that ACSL4 expression is elevated in colorectal tumours, consistent with increased lipid metabolism during tumour growth. However, DTP cells exhibit marked downregulation of ACSL4, suggesting an adaptive suppression of ferroptotic vulnerability. Notably, reduced ACSL4 expression in resistant cells implicates enhanced survival, increased migratory capacity, and acquisition of metastatic traits, indicating ACSL4 inhibition not only confers resistance to ferroptosis but also facilitates tumour cell dissemination.

Collectively, these findings identify ACSL4 downregulation as a dual survival strategy through which chemoresistant CRC cells evade ferroptotic cell death facilitating metastasis. Targeting ACSL4-dependent ferroptosis may therefore represent a promising therapeutic strategy to eliminate drug-resistant and metastasis-initiating cell populations in colorectal cancer.

Key words: Ferroptosis, Drug-Tolerant Persister Cells (DTP), ACSL 4, Chemoresistance

IACR - 661 **POSTER**

Fractionated Radiation Alters Epigenetic Signatures, Instrumental in Regulating DNA Repair in Breast Cancer Cells

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Radiotherapy is a cornerstone treatment in breast cancer; however, fractionated radiation can induce epigenetic alterations, including changes in histone acetylation and DNA methylation. These modifications influence chromatin organisation and DNA damage responses, contributing to variable radiation effects. Luminal, mild (MCF-7), and basal, aggressive triple-negative (MDA-MB-231) breast cancer cell lines were exposed to X-ray irradiation as a single dose of 2 Gy or a fractionated dose of 6 Gy (2 Gy × 3). Tumorigenic properties were evaluated using cell culture–based assays. Histone acetylation, DNA methylation and repair protein expression were assessed by western blotting. Fractionated radiation reduced histone acetylation with a greater decrease observed at 6 Gy, accompanied by reduced activity of key DNA repair proteins, including Ku70 and ATM. DNA methylation levels increased in the mild subtype, whereas a decrease was observed in the aggressive subtype. These findings indicate that fractionated radiation induces distinct epigenetic changes across breast cancer subtypes, where reduced histone acetylation correlates with chromatin compaction and reduced accessibility of DNA damage sites, leading to diminished DNA repair protein activity and altered DNA repair capacity. In aggressive cells, reduced DNA methylation may facilitate over-expression of specific transcription factors that alter differentiation status, potentially contributing to adaptive responses following radiation exposure. Overall, radiation-induced epigenetic alterations may promote mutation accumulation and enhanced epigenetic plasticity, ultimately contributing to the development of radio-resistance.

Key words: Radiation, Breast Cancer, DNA Repair, Epigenetic Changes

IACR - 663 **POSTER**

Role of Transforming Growth Factor Beta-Induced (TGFβI) in Cancer-Associated Fibroblast and its Influence on TME

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Non-small cell lung carcinoma has poor survival due to genetic alterations and heterogeneous tumor microenvironment (TME). Cancer-associated fibroblasts (CAFs) represent predominant cells in TME. Preliminary RNA sequence analysis has shown TGFβI /BigH3 to be up-regulated in Lung cancer patient-derived CAFs. Hence, it is important to study influence of TGFβI in TME. siRNA targeting of TGFβI was used to assess phenotypic changes in CAFs. Analysis of RNA sequencing was performed to understand genes, and pathways regulated by TGFβI at molecular level. Effect of TGFβI on tumorigenesis in vivo was studied. Higher expression of TGFβI was observed in CAFs compared to NF (Normal fibroblasts) at both the cellular and secretory levels. Upon TGFβI knockdown, CAF showed reduced migration and contractile property. upon TGFβI knockdown. From the transcriptomics analysis, we observed that immune-related pathways were up-regulated while cell cycle-related pathways were down-regulated upon knockdown of TGFβI in CAFs. Overexpression of TGFβI resulted in increased

tumor volume and weight in mice. Our study suggests that TGFβI may play a vital role in maintaining CAF phenotype and modulating immune response in TME. This study can highlight the understanding of CAF's expressed TGFβI role in TME and overall outcome on tumor growth. Since TGFBI is a secretory protein it will be a good choice for generating neutralizing antibody or small molecules to interfere with its functions.

Key words: NSCLC: Non-Small Cell Lung Carcinoma, NF: Normal Fibroblast, CAF: Cancer-Associated Fibroblasts, TGFβI: Transforming Growth Factor Beta-Induced, TME: Tumor Microenvironment

IACR - 664 **POSTER**

Study of the Anti-Cancer Effects of Quinacrine & Resveratrol Drug Combination against Breast Cancer

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Breast cancer remains the most prevalent malignancy among women globally, with standard treatments such as hormone therapy, chemotherapy, and radiation therapy constrained by cytotoxicity, off-target effects, drug resistance, and limited bioavailability. However, various plant-derived bioactive compounds showing lower toxicity have emerged as promising anti-cancer agents in cancers. Quinacrine (QC), an acridine antimalarial with DNA-intercalating action, and Resveratrol (Res), a mitochondrial disrupting polyphenol, each demonstrate potent anti-cancer activity against breast cancer cells. Their combination might overcome individual poor bioavailability, reducing doses for maximal efficacy while minimizing side effects and resistance. The present study focuses on the anti-cancer efficacy of QC in combination with Res against breast cancer cells. The detailed mechanism of anti-cancer action of QC and Res combination in breast cancer has been evaluated using cell survival assay, single cell gel electrophoresis assay (comet assay), apoptosis assay and immunoblot analysis in MCF7 breast cancer cell line. The result has revealed that QC and Res inhibit proliferation of MCF7 as monotherapies, and their combination showing enhanced anti-cancer efficacy. Res markedly enhanced anti-cancer activity, promoting DNA damage accumulation by comet assay, early apoptosis, and cell death in QC-pretreated MCF7 cells at substantially lower concentrations than individual treatments. The study suggests that combination of QC and Res shows anti-cancer potentiality against breast cancer cells, demonstrating that the combined treatment being more effective than QC or Res treated alone, suggesting the QC and Res combination therapy may offer superior therapeutic potential.

Key words: Breast Cancer; DNA Damage; Apoptosis; Quinacrine; Resveratrol

IACR - 665 **POSTER**

Gossypin Suppresses Mutant KRAS G12d Driven Oncogenic Activity by Considering NFκB Mediated Lipid Dysregulation in Pancreatic Cancer

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Pancreatic cancer is an aggressive malignancy driven largely by oncogenic KRAS signalling and constitutive activation of downstream NFκB pathway. Despite significant advances, synthetic drugs against KRAS have shown limited efficacy due to rapid drug resistance and systemic toxicity. These limitations highlight the need for safer, natural compounds capable of modulating KRAS driven oncogenic signalling. Through high-throughput screening of bioflavonoids, gossypin was identified as a lead compound targeting the KRAS G12D mutant over wild-type KRAS. Although gossypin has shown promising anticancer activity, its precise molecular mechanism and therapeutic relevance in pancreatic cancer remain unclear. This study elucidates the role of KRAS downstream target P65(A subunit of NFκB) in mediating the anti-tumorigenic and metabolic effects of gossypin in pancreatic cancer. Gossypin suppressed NF?B activation in PANC-1 cells, leading to reduced proliferation, clonogenic potential, migration, and invasion. Conversely, enforced P65 expression enhanced tumorigenic and adipogenic potential and reversed gossypin mediated oncogenic inhibition, confirming a P65 dependent mechanism in cancer suppression. In parallel, gossypin treatment resulted in a pronounced reduction in intracellular lipid accumulation, cholesterol and triacylglyceride levels. This suppression of adipogenic activity was accompanied by significant downregulation of key lipid regulatory genes, including SREBP1, HMGCoR and perilipin-1. Notably, ectopic P65 expression reversed these gossypin induced metabolic alterations, restoring both lipid content and gene expression level. Collectively, these findings demonstrate NFκB/P65 signalling as a central mediator of gossypin induced inhibition of tumorogenic and subsequent adipogenic activity in pancreatic cancer cells.

Key words: Pancreatic Ductal Adenocarcinoma, NFκB, KRAS G12D, Overexpression, Lipid Dysregulation

IACR - 667 **POSTER**

Quinacrine Suppresses Metastasis and Angiogenesis of Oral Squamous Cell Carcinoma by Inhibiting Tumor-Associated Macrophage-Derived Inflammatory Cytokines

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Tumor-associated macrophages (TAMs) in tumor microenvironment (TME) comprise of both M1 and M2 subtypes which are responsible for cancer growth and invasiveness through secretion of multiple cytokines. Although M2 are well-established drivers of cancer progression, M1 also promote the formation of cancer stem cells (CSCs), yet targeted therapies against M1-mediated CSC induction remain largely unexplored. Quinacrine (QC), a repurposed anti-malarial drug, has the ability to suppress M1-driven CSCs induction via inflammatory cytokines in oral squamous cell carcinoma, and its potentiality to reduce stemness, invasion, and angiogenesis in CSCs. A highly M1-like macrophage-enriched conditioned medium (CM) was generated by treating xed doses of PMA and LPS in THP1 cells. These M1-like macrophages increased the production of cytokines (TNF- α, IL-6, IL-1β). A CSCs population was generated after addition of cytokine enriched CM from M1

macrophage to SCC9 cells and patient derived primary oral cancer cells (PDOCs). After incubation with CM, enhancement of stemness, angiogenic and metastatic properties of both SCC9 and PDOCs were noted. QC decreased the cytokines level in CSCs-enriched cells and reduced the invasion, proliferation and growth of CSCs. Representative metastatic (CD133, ALDH1) and angiogenic markers (MMPs, iNOS, VEGF-A) were decreased after QC treatment in CSCs enriched oral cancer cells niche. It also disrupted angiogenesis, depleted nitric oxide production in fertilized chick embryos. Thus, this study inferred that CSC-mediated stemness is a cytokine dependent phenomena and QC treatment inhibits this process in *in vitro*, *in ovo* and *ex vivo* model systems highlighting its therapeutic potential against CSCs.

Key words: Oral Cancer; Cancer Stem Cells (CSCS); Cytokines; Macrophages; Angiogenesis; Quinacrine

IACR - 668 **POSTER**

Hepatitis B Virus X Protein Upregulates FoxM1, A Tumor Promoter in Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) is a leading cause of cancer-related deaths worldwide and chronic hepatitis B virus (HBV) infection is a major risk factor, however, the molecular mechanisms driving HBV related HCC remains unclear. HBV encoded oncogene X protein (HBx) is a key regulator hepatocarcinogenesis. Forkhead box M1 (FoxM1), an oncogene essential for cell cycle progression and tumorigenesis, is aberrantly overexpressed in many tumors, but its role in HBV-associated HCC is not fully understood. This study aimed to investigate the functional role of HBx in regulating FoxM1 and its contribution to HBx-induced HCC.Bioinformatic analysis of FoxM1 expression across cancer with a focus on HCC and Kaplan-Meier survival analysis were performed. FoxM1 was knockdown in HBx positive Hep3B cells and validated by western blot. Oncogenic functions were evaluated using proliferation, colony formation, migration, invasion and anchorage independent growth assays. Stemness and apoptotic markers were analyzed by western bloting. HBx-FoxM1 interaction and localization were examined using co-immunoprecipitation (Co-IP) and confocal microscopy. The impact of HBx knockdown on FoxM1 and downstream targets were evaluated at mRNA and protein levels. Domain mapping identified the HBx region regulating FoxM1. Co-depletion of HBx and FoxM1 was evaluated for effects on cell proliferation and apoptosis using BrdU incorporation and JC-1 aasays. Additionally, the interaction between HBx and Cdh1, a negative regulator of FoxM1 was examined using Co-IP and ubiquitination assays were performed to assess HBx mediated degradation of Cdh1 . FoxM1 expression was significantly upregulated in HBx positive HCC cells and HBx was identified as a key regulator of FoxM1 expression in HBV expressing HCC cells. Functional studies showed that FoxM1 knockdown impaired HBx mediated cell proliferation, migration, invasion and anchorage independent growth while co-depletion of HBx and FoxM1 synergistically reduced proliferation and enhanced apoptosis. Domain mapping analysis identidied the 21 -120 amino acid region of HBx as critical for FoxM1 upregulation. Mechanistically, HBx interacted with and destabilized Cdh1 through ubiquitin mediated degradation, resulting in aberrant FoxM1 expression. Overall, these findings establish the HBx-FoxM1 axis as a key driver of HBV associated hepatocarcinogenesis and highlight FoxM1 as a potential therapeutic target in HCC.

Key words: Hepatocellular Carcinoma, Foxm1, Hepatitis B Virus, Hbx, Cdh1, Tumorigenesis, And Therapeutic Target

IACR - 669 **POSTER**

PI3K Inhibition by Alpelisib Augments Cisplatin Induced Cell Death in Epithelial Ovarian Cancer Cells

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Epithelial Ovarian Cancer (EOC) patients often develop resistance to platinum-based drugs. The PI3K/Akt/mTOR signaling pathway is frequently dysregulated in EOC through *PIK3CA* amplifications/mutations, contributing to chemo-resistance and tumor progression. We recently reported that 30% of high-grade serous ovarian cancer (HGSOC) patients respond favorably to cisplatin when combined with alpelisib, a clinically approved PI3K inhibitor. However, the molecular mechanisms underlying this alpelisib-induced cisplatin sensitization is yet unknown. Thus, we aim to investigate the cisplatin-alpelisib combinatorial efficacy and its underlying molecular mechanism in EOC cell lines. We employed MTT cell viability assay, PI staining and flow cytometry, western blotting and Immunofluorescence assay to evaluate cytotoxic effect of cisplatin-alpelisib combination, cell cycle distribution and the key signalling proteins expression.

The cisplatin-alpelisib combination demonstrated significantly enhanced cytotoxicity in SKOV3 cells compared to cisplatin monotherapy, accompanied with robust S phase arrest upon sequential treatment of cisplatin, followed by alpelisib. Western blot analysis revealed decreased Akt phosphorylation, increased ERK activation with elevated markers of DNA damage and apoptosis, including PARP cleavage, γH2AX expression, and phospho-CHK1 levels in combination-treated cells. Kinetics of yH2AX foci resolution demonstrated delayed and sustained γH2AX nuclear foci in combination-treated cells compared to cisplatin monotherapy. Further experiments are in progress.

Key words: Platinum Resistance, Cisplatin-Alpelisib Combination, DNA Damage, Apoptosis

IACR - 670 **POSTER**

Care-Giving Burden and Suicidal Ideation among Caregivers of Cancer Patients: Moderating Role of Resilience and Socioeconomic Status

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Background: Cancer is not an isolated condition that only affects the patient but has an immense impact on caregivers. The contemporary psycho-oncology focuses on dyadic framework, where patients and caregivers act as an interdependent emotional dyad.

Objectives: The study has analysed relationship between the Care-giving Burden, Resilience, SES,& Suicidal Ideation among the caregivers of cancer patients. Examined the moderating effect of resilience in relationship between care-giving burden and suicidal ideation between SES groups. **Methods:** A cross-sectional design was used with a sample of 200 caregivers of cancer patients recruited through convenience sampling from the Department of Oncology, SMHS Hospital, Srinagar. Standardized tools were used, Informed consent was also given. **Results:** Suicidal ideation positively correlated with care-giving burden. Women caregivers and people with low SES reported more burden. Notably, upper-middle-class caregiver were also characterized by a high level of burden. Both caregiving burden & suicidal ideation correlated negatively with resilience which reveals a buffering effect. **Implications:** The study shows that Resilience acts as a buffer in the cancer care. Thus, Resilience-oriented interventions and policies to consider SES can improve the holistic cancer care outcomes.

Key words: Caregiving Burden, Cancer Caregivers, Resilience, Suicidal Ideation, Socioeconomic Status

IACR - 671 **POSTER**

Click-Enabled Design and Synthesis of Nitrogen-Containing Hybrid EGFR Inhibitors with in Silico Insights and Anticancer Evaluation

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Cancer is a multifactorial disease arising from complex interactions between genetic predisposition and environmental factors, and its global incidence continues to rise. Despite substantial progress in cancer therapeutics, many conventional chemotherapeutic agents lack target selectivity, resulting in dose-limiting toxicities and adverse side effects. Therefore, the development of selective small-molecule anticancer agents with improved efficacy and safety profiles remains a critical challenge. A novel series of 1,2,3-triazole-benzothiazole hybrid derivatives (6a-j) was rationally designed and synthesized via click chemistry. Structural characterization was performed using 1H NMR, 13C NMR, and HRMS. Antiproliferative activity was evaluated against human breast (MCF- 7), colon (HT-29), and lung (A-549) cancer cell lines, using celecoxib, erlotinib, and osimertinib as reference standards. Molecular docking studies were conducted to analyze binding interactions within the EGFR kinase domain. Mechanistic validation included EGFR kinase inhibition assays, ELISA, apoptosis and cell cycle analyses, and Western blot studies. All compounds exhibited varying antiproliferative activity. Compounds 6c, 6e, and 6i emerged as the most potent, displaying IC_{50} values of 1.20-2.73 μM, surpassing celecoxib and comparable to erlotinib and osimertinib. These leads effectively inhibited both EGFRWT and EGFRT790M kinases. Mechanistic studies revealed apoptosis induction via Bax upregulation and Bcl-2 downregulation, while compound 6c induced significant G2/M phase arrest (36.15%) in MCF-7 cells. Docking and Western blot analyses supported effective EGFR targeting. The 1,2,3-triazole-benzothiazole hybrids, particularly compounds 6c, 6e, and 6i, represent promising EGFR-targeted anticancer leads for further optimization and development.

Key words: EGFR, Cancer, Click Chemistry

Triple Jeopardy: Three Primary Synchronous Cancers and One Journey; A Single Woman and Surviving

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BACKGROUND: Synchronous multiple primary malignancies (MPM) are rare and diagnostically challenging entities that demand multidisciplinary individualized treatment strategies. **ABSTRACT**: A 74-year-old female presented with complaints of a lump in left breast for past 2 years along with persistent per vaginal discharge for 1 year. On evaluation, contrast MRI pelvis done revealed 13*12mm T2 hypointense lesion in endometrium. She underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy for the same. Surgical HPE was suggestive of endometrial carcinoma; stage IA. She was further subjected to contrast CT whole body which revealed a hypo-enhancing thickening in the gastric cardia and a soft tissue density thickening measuring 33*34mm in the left breast. She was further subjected to esophago-gastro-duodenoscopy which revealed an ulcero-proliferative growth at the GE junction; siewert-III, the HPE of which was suggestive of Adenocarcinoma. To characterize the breast lesion, a tru-cut biopsy was done which was suggestive of mucinous breast carcinoma. She is being planned for surgery for both the gastric and breast malignancy. **DISCUSSION**: The association of MPM is a rare occurrence, incidence ranging between 0.04% and 0.81%. Etiological factors may include genetic predisposition, familial cancer syndromes, immunosuppression, immunodeficiencies, environmental and lifestyle exposures. Treatment protocols for SPM are not well established. Successful treatment requires a good multidisciplinary collaboration to provide timely correct diagnosis and the best therapeutic strategies.

Key words: Synchronous Primary Malignancies, Triple Malignancy

Design, Synthesis, and Computational Evaluation of Novel Triazole Derivatives as EGFR-Targeted Anticancer Agents

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The epidermal growth factor receptor (EGFR), a prominent member of the receptor tyrosine kinase family, plays a critical role in tumor initiation, progression, and represents a well-established molecular target for anticancer therapy. Approximately 50% of breast cancer cases exhibit EGFR overexpression, while its limited expression in normal tissues makes it an attractive target for selective drug development. In this study, a novel series of triazole-based derivatives was rationally designed and synthesized. The chemical structures of synthesized compounds were confirmed using $^{1}H/^{13}C$ NMR spectroscopy and mass spectrometry. The anticancer potential of triazole derivatives was evaluated *in vitro* against MCF-7 breast cancer

cells using the MTT assay. Results demonstrated that the compounds exhibited dose-dependent cytotoxicity in micromolar range, with several derivatives showing activity comparable to or better than the reference EGFR inhibitor, Gefitinib. Selected compounds (6a, 6e, and 6f) emerged as the most potent candidates, displaying low-micromolar IC50 values, indicating enhanced antiproliferative activity. To elucidate the binding mode and molecular basis of activity, molecular docking was performed against the EGFR/HER2 kinase domain (PDB ID: 3W32) using Schrodinger Suite. The top-ranked compound was further subjected to molecular dynamics simulation alongside the co-crystallized ligand to assess complex stability, conformational behavior, and key binding interactions.

Key words: Tyrosine Kinase, EGFR, Inhibitors, Cancer, In Silico

IACR - 674 **POSTER**

To Study the Role of D-Limonene in Combination with Tamoxifen on DNA Damage Repair in Breast Cancer Cells

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Breast cancer remains a leading cause of cancer-related mortality worldwide, with estrogen receptor-positive (ER+) cases over 75% of instances, representing a prevalent subtype and a primary focus of research. Endocrine therapy targets estrogen signaling inhibit proliferation and induce cell death. Tamoxifen (Tam) a SERM standard treatment for ER+; however, 40-50% of cases exhibit resistance via altered ER signaling or escape pathways. This resistance not only enables estrogen-independent growth but also involves the adaptive upregulation of DNA damage response (DDR), allowing cancer cells to repair tamoxifen-induced oxidative lesions and evade apoptosis. D-limonene (DL), a bioactive compound from citrus oils, exhibits anticancer properties by inducing apoptosis, autophagy, and oxidative stress, while inhibiting proliferation, angiogenesis, and metastasis. Both DL and Tam monotherapies inhibited MCF7 proliferation, and their combination enhanced tamoxifen-mediated apoptosis and G1 arrest via cyclin D1/B1. Present study focuses on unexplored combined effects of DL and Tam on dysregulated DDR in ER+ cells. The DNA damage mechanism was assessed via Comet assay, Immunofluorescence (γH2AX), with key DDR proteins (PARP1, FEN1, XRCC1) expression via Immunoblot, docking interactions between DL and DDR proteins. MCF7 cells, when subjected to combined treatment, showed a notable decrease in repair proteins, resulting in increased sensitivity to DNA damage, implying a potential therapeutic strategy for breast cancer treatment.

Key words: Breast Cancer, Estrogen Receptor- Positive, DNA Damage Response, D-Limonene and Tamoxifen

IACR - 675 **POSTER**

5-FU in Combination with PARP Inhibitor ABT-888 Deregulates MGMT-Dependent Mismatch Repair (MMR) Pathway in MMR-Proficient Colorectal Cancer Stem Cells by Modulating MGMT/PARP1/MSH6 Complex

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Previously, it has been reported that PARP inhibitor ABT-888 potentiates the 5-fluorouracil (5-FU) cytotoxicity by inhibiting PARP1-mediated mismatch repair (MMR) pathway via deregulation of MSH6 in MMR-proficient colorectal cancer stem cells (CRC-CSCs). Emerging evidence indicates that 5-FU regulates the activity of DNA repair enzyme O6-methylguanine-DNA-methyltransferase (MGMT). The mechanistic basis for involvement of MGMT and PARP1-mediated MMR pathway following 5-FU treatment remains complex and poorly defined. This study aimed to delineate the role of MGMT in 5-FU induced MMR pathway, and also checked the effect of 5-FU and ABT-888 combination in MMR pathway inhibition via modulating MGMT against CRC-CSCs. The molecular mechanism of MGMT involvement after combinatorial drug exposure in CRC-CSCs has been studied by using colocalization, westen blot, co-immunoprecipitation, knockdown of MGMT gene, in *in vitro*, and *ex vivo* preclinical model systems, and performed molecular docking study as *in silico* model. Treatment with 5-FU in CRC-CSCs resulted in PARylated-PARP1 which further activated MGMT and MMR pathway by interacting with MSH6. However, PARylation was inhibited after ABT-888 treatment in 5-FU-pre-exposed CSCs. Therefore, PARP1 could not physically interact with both MGMT and MSH6, and complete abolishment of MGMT and MSH6 was observed in combination treatment. Thus, other MMR proteins were also found to be downregulated. The role of MGMT in PARP1-mediated MMR activation, was confirmed by silencing MGMT gene, which resulted in faulty MMR pathway. Further experimental confirmation was done using *ex vivo* model system and interestingly similar results were obtained. Combination of 5-FU with ABT-888 enhanced CRC-CSCs death by inhibiting the PARP1-MGMT-MSH6 interaction and simultaneously inhibiting the MGMT-dependent PARP1-mediated MMR pathway in MMR-proficient CRC-CSCs.

Key words: Colorectal Cancer Stem Cells, Mismatch Repair (MMR), O6-Methylguanine-Dna-Methyltransferase (MGMT), 5-Fluorouracil (5-Fu), PARP Inhibitor (Abt-888)

IACR - 676 **POSTER**

PHKA1 Orchestrated Glucose Metabolic Shift: A Novel Link between Diabetes and Breast Cancer

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Metabolic reprogramming is a defining hallmark of cancer, which is also intricately linked to insulin resistance and T2D. Tumor cells can meet the elevated bioenergetic demands while

maintaining homeostasis, due to metabolic reprogramming. The epidemiological link that exists between cancer and T2D suggests the presence of shared molecular drivers that couple metabolic dysfunction with tumor progression. This study identifies and functionally characterizes *PHKA1* as a novel metabolic driver at the intersection of glucose metabolism and breast cancer aggressiveness. Through systematic screening of 179 genes associated with glucose metabolism and insulin signalling, using TCGA dataset, *PHKA1* emerged as a significantly upregulated candidate across multiple cancer types. *PHKA1* was upregulated in malignant tissue samples compared to benign controls, finding further corroborated in T2D diabetes patient datasets (GSE144441). Experimental validation confirmed that *PHKA1* showed glucose and insulin-responsive elevated expression. Functional silencing of *PHKA1* attenuated proliferation, invasion, and stemness while reversing EMT, evidenced by decreased Vimentin and restored E-cadherin expression. To validate the role of *PHKA1* in metabolic dysregulation, we performed Seahorse metabolic profiling on *PHKA1*-silenced MDA-MB-231 cells. The knockdown of *PHKA1* resulted in impaired glycolytic capacity and mitochondrial respiration; there was a marked reduction in lactate, pyruvate levels and mitochondrial membrane potential, alongside downregulation of *GLUT1*, *GLUT4* and *HK-2*. These findings establish *PHKA1* not merely as a biomarker, but as a functional metabolic driver that coordinated glycolytic and mitochondrial activity to fuel cancer. Targeting *PHKA1* offers a novel therapeutic strategy to disrupt the bioenergetic machinery linking diabetic metabolic dysregulation to breast cancer progression.

Key words: PHKA1 (Phosphorylase Kinase Regulatory Subunit-1), ECAR (Extracellular Acidification Rate), OCR (Oxygen Consumption Rate), EMT (Epithelial-Mesenchymal Rate), Metabolic Reprogramming, Breast Cancer

IACR - 677 **POSTER**

Integrated Radiogenomic Framework for Prognosis and Biological Characterization of Lung Adenocarcinoma

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Tumour heterogeneity in lung adenocarcinoma (LUAD) is poorly captured by clinical variables or individual gene-level biomarkers, which often show strong cohort specificity and limited generalisability. We hypothesised that the variation in underlying tumour biology is more consistently reflected at the level of coordinated biological programs rather than isolated genes. Using TCGA data, we developed a systems-level framework organising pathway activity into stable modules (8 in number) representing coordinated disease programs and evaluated their relevance to prognosis. The composite risk score robustly stratified patients (median survival 71.4 vs 38.5 months, $p < 0.0001$; C-index = 0.673) and generalised across 10 other cancer types, supporting a conserved malignant progression axis. This risk was driven by a microenvironmental-influenced module core, while highly variable tumour-intrinsic modules showed limited association, indicating transcriptional variability alone does not explain clinical progression. Radiogenomic analysis in an independent cohort revealed a significant correlation between CT-derived radiomic features and this risk score ($\rho = 0.835$, 95% CI 0.768–0.889), suggesting that imaging-visible heterogeneity mirrors underlying biological organisation. Finally, single-cell analysis in a LUAD brain metastasis cohort demonstrated that although the complex risk program originates in malignant cells, it eventually embeds across immune compartments during metastatic progression, explaining its robustness in bulk data. These

results indicate that modelling coordinated biological programs provides a generalisable framework for studying tumour progression beyond gene-centric analyses.

Key words: Lung Adenocarcinoma, Radiogenomics, Tumour Heterogeneity, Systems Biology, Tumour Microenvironment, Single-Cell Analysis, Prognosis

IACR - 678 **POSTER**

Modulation of ZNF726 Oncogene Reveals Metabolic Shift and Concurrent Regulation of Various Unexplored Gene Expressions

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ZNF726 has recently emerged as a potential oncogene, but its role in controlling cellular metabolism and downstream gene expression remains poorly understood. In this study, we aimed to investigate how modulation of ZNF726 influences metabolic reprogramming and overall gene expression in cancer cells. ZNF726 expression was altered through overexpression and knockdown methods, followed by transcriptomic analysis. Changes in ZNF726 levels caused significant metabolic shifts, including deregulation of glucose, lipid metabolism and mitochondrial activity, indicating its involvement in key pathways that support tumor growth and survival. Concurrently, transcriptomic profiling revealed widespread gene expression changes. Notably, several differentially expressed genes had not been previously linked to ZNF726, suggesting the involvement of novel regulatory pathways. Differential gene expression and KEGG pathway enrichment analyses showed that these genes are associated to oncogenic signalling and metabolic pathways. For validation, metabolism-related genes were examined using real-time PCR, and functional assays such as Nile Red staining, JC-10, and TMRE were performed in breast cancer cells following ZNF726 overexpression. The results demonstrated consistent upregulation across all assays, further supporting ZNF726's role in regulating metabolic pathways. The combined impact on metabolism and gene expression implies that ZNF726 may function as a central regulator, coordinating transcriptional programs with the metabolic needs of tumor progression. Overall, our findings reveal a previously unrecognised role of ZNF726 in metabolic remodelling and gene regulation in cancer, offering new insights into its oncogenic function.

Key words: Breast Cancer, ZNF726, Transcriptomic Analysis, Differential Genes, KEGG Pathways, Metabolic Pathways

IACR - 679 **POSTER**

Talazoparib Enhances the Anti-Angiogenic Potential of Quinacrine through the Deregulation of P300 And GCN5 Chromatin Remodelers in Patient-Derived Oral Cancer Stem Cells

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Angiogenesis plays a crucial role in cancer progression. However, the role of PARP1 in regulating chromatin remodelers and activating pro-angiogenic factors in cancer stem cells (CSCs) remains poorly understood. This study systematically investigates the detailed molecular mechanism through which PARP1 and its associated chromatin remodelers, P300 and GCN5, regulate angiogenesis in ex vivo patient-derived oral mucosa cancer stem cells (PD-OMCSCs). To investigate this mechanism, we used a combination of experimental approaches, including CAM assays, tube formation assays, biochemical analyses (western blot, gelatin zymography, and ELISA), molecular imaging (tissue immunofluorescence), and protein–protein interaction (co-immunoprecipitation and in silico study). Comparative analyses revealed significantly higher expression of PARP1, P300, and GCN5 in oral cancer tissues compared to normal ones. Co-immunoprecipitation and docking studies confirmed their mutual interactions, forming a chromatin-remodeling complex (PARP1-P300-GCN5) that facilitates angiogenic gene activation and expression. Quinacrine (QC), in combination with PARP inhibitor Talazoparib, disrupted this complex, leading to significant downregulation of VEGFA expression, reduced MMP activity, and suppression of angiogenic markers (Ang-1, Ang-2, TGF-β, CXCL-12, VEGFC, HIF-1α, and IL-6). These effects collectively impaired endothelial cell tube formation and blood vessel development in both HUVECs and CAM models. Furthermore, individual knockdown of PARP1, P300, or GCN5 reduced VEGFA expression, indicating their important role in regulating tumor angiogenesis. In conclusion, the QC and Talazoparib combination effectively prevents the activation and secretion of angiogenic factors, thereby suppressing angiogenesis, and may serve as a promising therapeutic approach for oral cancer by targeting PARP1 and associated chromatin remodelers.

Key words: Patient-Derived Oral Mucosa Cancer, Angiogenesis, Cancer Stem Cells, Chromatin Remodeling, Quinacrine, Talazoparib

IACR - 680 **POSTER**

Reshaping the Stromal Landscape-IGFBPS as Critical Mediators of CAF-Driven Tumour Progression

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The tumour microenvironment is orchestrated by dynamic interactions between cancer cells and stromal components, with cancer-associated fibroblasts (CAFs) playing a central role in supporting tumour progression. However, their highly heterogeneous nature presents a limiting challenge to effective stromal targets. Thus, there is a need to identify the main drivers and understand the mechanisms behind heterogeneity that promote tumour development. In this study, we identified certain members of the Insulin-like Growth Factor Binding Protein

(IGFBP) family, specifically IGFBP5, IGFBP6, and IGFBP7, as highly upregulated genes in lung cancer-associated fibroblasts. Using genetic knockdown experiments, we demonstrate that these IGFBPs are essential for maintaining core CAF properties. Mechanistically, their expression is induced by tumour-derived signals, particularly TGFβ and IL6. Strikingly, individual knockdown of each IGFBP drove CAFs toward distinct phenotypic states, revealing non-redundant roles in shaping CAF heterogeneity. Furthermore, IGFBP-expressing CAFs exerted potent pro-tumorigenic effects in a cell non-autonomous manner, enhancing cancer cell growth, migration, invasion, and chemoresistance. Clinically, gene signatures associated with these IGFBPs correlate with poorer patient prognosis. Taken together, our findings establish these binding proteins as critical mediators of CAF biology and function, providing new mechanistic insight into how the tumour microenvironment is reprogrammed to support malignancy.

Key words: Cancer-Associated Fibroblasts, Tumor-Microenvironment, IGFBPS, CAF-Subtypes, CAF Heterogeneity

IACR - 682 **POSTER**

Poly (ADP-Ribose) Polymerase 1 (PARP1) as a Diagnostic Biomarker in Oral Cancer and Cervical Cancer: A Comparative Expression Analysis

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Oral cancer and cervical cancers are among the most prevalent malignancies in developing countries, often diagnosed at an advanced stage due to a lack of reliable early biomarkers. Poly (ADP-ribose) polymerase 1 (PARP1), a nuclear enzyme involved in DNA repair and chromatin remodeling, has emerged as a potential diagnostic and therapeutic target in various malignancies. Its overexpression has been correlated with genomic instability and tumor progression. We aim to evaluate the expression profile of PARP1 in oral and cervical cancer tissues, and assess its potential as a diagnostic biomarker for early detection and disease stratification. A cross-sectional study was conducted on biopsy-confirmed cases of cervical (n=30) and oral cancer (n=30). Immunohistochemistry (IHC) and quantitative real-time PCR (qRT-PCR) were used to analyze PARP1 expression. Statistical analysis included ROC curve assessment to determine diagnostic sensitivity and specificity. PARP1 expression was significantly upregulated in both cervical and oral cancer tissues compared with adjacent non-malignant controls in both cancer types, with notably stronger staining intensity and higher H-scores in advanced pathological grades. Overexpression correlated positively with tumor grade and lymph node involvement. PARP1 shows promise as a non-invasive diagnostic biomarker for both cervical and oral cancers. Its elevated expression in early stages supports its utility in screening and prognosis, and it may serve as a candidate for targeted therapies using PARP inhibitors. Further validation in larger cohorts is warranted.

Key words: Parp1, Oral Cancer, Cervical Cancer, Biomarker, Early Diagnosis, Immunohistochemistry

IACR – 683 **POSTER**

Revealing the Potential of miR-154-5p in Blood Plasma as a Groundbreaking, Non-Invasive Tool in Liquid Biopsy for Predicting Patient Outcomes in Oral Squamous Cell Carcinoma

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OSCC lacks reliable blood-based prognostic biomarkers Emerging evidence suggests that dysregulated hsa-miR-154-5p levels contribute to OSCC pathogenesis; however, its clinical relevance remains unexplored. The present study aims to evaluate the expression signature of circulating miR-154-5p in blood plasma as a potential biomarker for liquid biopsy for risk stratification and early prediction of prognosis of OSCC patients. Peripheral blood samples were collected from newly diagnosed, treatmentnaïve OSCC patients following ethical approval and informed consent. In each patient, the expression levels of miR-154-5p were checked from cell-free blood plasma samples through qRT-PCR. After surgery, the follow-up data were collected for the next two years. In the present investigation, reanalysis of publicly available datasets consistently demonstrated dysregulated miR-154-5p expression in OSCC. Subsequent qPCR analysis confirmed a significant downregulation of circulating miR-154-5p in OSCC patients compared to healthy controls. A comparative clinical analysis further revealed significant associations between circulating miR-154-5p levels, conventional histopathological parameters, and patient outcomes (recurrence and survival). Importantly, reduced miR-154-5p expression was associated with poorer survival and shorter lifespan in patients. Collectively, these findings highlight the clinical relevance of circulating miR-154-5p as a minimally invasive liquid biopsy biomarker for early prognostic stratification and outcome prediction in OSCC.

Key words: Liquid Biopsy, Biomarker, miRNA, Prognosis, Survival, OSCC

IACR – 684 **POSTER**

Evaluation of Bacopa Monnieri Derived Saponins for Anti-Glioblastoma Activity, Brain Biodistribution, and Neuroprotective Potential

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Glioblastoma is the most aggressive primary brain tumor, characterized by poor survival outcomes and therapy-induced neurocognitive impairment. There is a critical need for

therapeutic strategies that combine anti-tumor efficacy with neuroprotective potential. This study evaluates the anti-glioblastoma activity, brain biodistribution, and safety profile of Bacopa monnieri derived bioactive saponins. *In vitro* assays using human (U87MG) and rat (C6) glioblastoma cell lines demonstrated that crude Bacopa monnieri extract exerted dose-dependent cytotoxicity (IC50: 46 µg/mL), significantly inhibiting clonogenic survival and cell migration. Notably, Bacoside A, a defined mixture of Bacoside A3, Bacosaponin C, and Bacopaside II exhibited enhanced potency with a lower IC50 (17.63 µg/mL) and marked suppression of long-term colony formation and migratory capacity. Using an orthotopic rat glioma model, LC–MS analysis confirmed the accumulation of major Bacopa saponins within tumor-bearing brain tissue, supported by histopathological validation of tumor architecture. Structural profiling identified Bacoside A3, Bacosaponin C, and Bacopaside II as the predominant constituents. *In silico* ADMET analysis predicted favorable pharmacokinetics, high intestinal absorption, low toxicity, and acceptable clearance. These findings establish Bacopa monnieri derived saponins as promising brain-accessible anti-glioblastoma agents with potential neuroprotective advantages, warranting further *in vivo* efficacy and cognitive outcome investigations.

Key words: Glioblastoma, Bacopa Monnieri, Bacoside A, Brain, Biodistribution, Antitumor Activity

IACR - 685 **POSTER**

A Novel Exosome-Based Nanotherapeutic Strategy to Inhibit Cancer Stem Cell "driven EMT in Triple-Negative Breast Cancer

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Triple-negative breast cancer (TNBC) is an aggressive malignancy with limited treatment options, particularly in advanced and metastatic disease where chemoresistance is common. Metastasis accounts for over 90% of breast cancer–related mortality and is largely driven by cancer stem cells (CSCs) undergoing epithelial-to-mesenchymal transition (EMT). Doxorubicin (DOX), a frontline chemotherapeutic agent for TNBC, has been reported to paradoxically promote CSC survival and EMT-associated traits, potentially increasing metastatic risk and tumor recurrence.
Recent advances in nanomedicine provide new opportunities to target CSC populations more effectively. The dietary indole compound 3,3′-diindolylmethane (DIM) has emerged as a promising adjuvant capable of modulating CSC-associated signaling and EMT processes. This study proposes a novel combinatorial strategy integrating DOX and DIM to counteract CSC-mediated EMT in TNBC. To enhance tumor-specific delivery, an advanced drug delivery system employing exosome-sheathed mesoporous silica nanoparticles is envisioned, aiming to improve bioavailability, reduce systemic toxicity, and selectively target the CSC niche. This approach holds promise for limiting metastasis and overcoming chemoresistance in TNBC.

Key words: Triple Negative Breast Cancer, Cancer Stem Cells, epithelial Mesenchymal Transition, Exosome-Based Nanotherapy, doxorubicin, Dim Co-Delivery

IACR - 686 **POSTER**

Circulating Exosomal Thrombospondin-1 as a Minimally Invasive Biomarker for Breast Cancer Aggressiveness and Metastatic Potential

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Breast cancer mortality is largely driven by metastasis and tumor heterogeneity, highlighting the limitations of invasive tissue biopsies and the need for minimally invasive prognostic tools. Liquid biopsy approaches, especially Exosomes offer a strong clinical potential. This study evaluates thrombospondin-1 (THBS1), a matricellular protein involved in tumor progression, as an exosome-associated biomarker of breast cancer aggressiveness. THBS1 expression across breast cancer subtypes was assessed by Western blotting. Exosomes isolated from breast cancer cell lines, preclinical mouse models, and patient plasma were characterized using nanoparticle tracking analysis, TEM, and immunoblotting for exosomal markers. Exosome burden and THBS1 enrichment were quantified in plasma and purified exosomal fractions. THBS1 was markedly enriched within exosomes across models, with the highest levels observed in metastatic triple-negative breast cancer (TNBC; MDA-MB-231). Genetic silencing of THBS1 delayed tumor onset and significantly reduced circulating exosome burden in vivo, indicating tumor cells as a major source of circulating exosomes. Isolated vesicles exhibited canonical exosomal features, including 100–130 nm size, CD63/Alix expression, and cup-shaped morphology. Clinically, THBS1 was predominantly exosome-associated rather than soluble, with exosomal THBS1 levels increasing in a stage-dependent manner, particularly in TNBC patients. Collectively, these findings support exosomal THBS1 as a promising circulating prognostic biomarker of breast cancer progression.

Key words: Breast Cancer, Exosomes, Thrombospondin 1

IACR - 687 **POSTER**

Uptake and Accumulation of Antibiotics in Leafy Vegetables - A Comprehensive Review

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The widespread and increasing use of antibiotics in agriculture, livestock, and wastewater irrigation has contributed to the increased concentration of pharmaceuticals in soil, water, and edible crops. Leafy vegetables, with their large leaf area, high turnover rate, and continuous irrigation, serve as major pathways for the entry of antibiotics into the human food chain. This review critically integrates current knowledge on the uptake, translocation, and bioaccumulation of major classes of antibiotics in leafy vegetables such as spinach, lettuce, kale, and pak choi. Antibiotic uptake, via passive diffusion and active transport, is greatly influenced by physicochemical properties (pKa, log Kow), soil properties (pH, organic carbon content), and plant-specific physiological processes. High translocation factors (TF ≈ 0.9-1.3) have been reported for sulfamethoxazole and erythromycin, moderate translocation factors (TF

≈ 0.4-0.8) for tetracycline, doxycycline, and amoxicillin, and low translocation factors (TF ≈ 0.1-0.3) for ciprofloxacin and enrofloxacin. Bioaccumulation factors (BAF ≈ 1.9-2.4) indicate high uptake of sulfonamides and macrolides, moderate uptake of tetracyclines and β-lactams (BAF ≈ 1.2-1.8), and very low foliar uptake of fluoroquinolones (<0.9). The accumulation of these residues in edible crops increases the risk of antimicrobial resistance, microbiome imbalance, and toxicity. This review highlights the pressing need for a comprehensive approach to mitigate these residues through biochar amendment, compost management, advanced water treatment, and effective regulatory policies to ensure food safety and public health.

Key words: Pharmaceuticals, Drug Residues, Antibiotic Contamination, Tetracycline, Uptake, Translocation, Bioaccumulation

IACR - 688 **POSTER**

Targeting Cell Cycle Checkpoints: Emerging Strategies to Overcome Cancer Proliferation

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The cell cycle checkpoints G1/S, intra-S, and G2/M are critical protective mechanisms against genomic instability, but their disruption is the driving force behind uncontrolled cancer cell proliferation. This is a comprehensive review of novel approaches that focus on these checkpoints to suppress tumor progression with a reduced impact on normal cells. CDK4/6 inhibitors, such as palbociclib, primarily act on the G1/S transition by inducing Rb-mediated cell cycle arrest in hormone receptor-positive (HR+) breast cancer, with active development of CDK2 inhibitors to overcome resistance. Recent progress in G2/M checkpoint inhibitors includes WEE1 inhibitors (adavosertib) and ATR/CHK1 inhibitors (berzosertib), which induce premature mitosis in response to replication stress and have shown synergistic effects when combined with DNA-damaging chemotherapeutic agents. Mitotic kinase inhibitors PLK1 and Aurora, such as volasertib, have shown efficacy in acute myeloid leukemia (AML) and solid malignancies. Combination therapies have been shown to enhance therapeutic potency: CDK4/6 inhibition in combination with endocrine therapy has improved survival outcomes, and checkpoint inhibition combined with PARP inhibitors has shown promise in homologous recombination-deficient (HRD) cancers. New approaches include the use of PROTACs to target cyclin degradation and non-coding RNA modulation. Response rates of 50-70% have been reported in clinical trials, and biomarker-based stratification (notably Rb status) has been used to select patients, although neutropenia and bypass mechanisms have been identified as challenges. Future research will focus on AI-optimized inhibitor design, combination with immunotherapy, and precision modeling to overcome resistance. By capitalizing on cancer cell vulnerabilities, checkpoint inhibitors promise a new era in the regulation of cellular proliferation.

Key words: Cell Cycle Checkpoints, Cancer Proliferation, Cdk4/6 Inhibitors, G2/M Checkpoint, Wee1 Inhibitors, Palbociclib, ATR/CHK1 Inhibitors, Rb Phosphorylation

Spirometry as Response Assessment Criteria in Non-Small Cell Lung Cancer Patients Treated with Chemotherapy

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Non-small cell lung cancer is a major global cause of cancer deaths and it has a complicated treatment scenario. Chemotherapy remains a key component of the treatment approach for numerous patients with advanced or metastatic non-small cell lung cancer. Accurate assessment of treatment response is crucial for informing clinical decisions.

Treatment response evaluation is mainly done using radiological imaging methods but they may not be sufficient for identifying early biological and functional alterations in tumors. Spirometry is regularly employed to evaluate lung mechanics and air flow. Chemotherapy may cause lung damage but spirometry test could potentially provide valuable information about how well a treatment is working.

This study aims to examine the effectiveness of spirometry as a method for assessing treatment response in patients with non-small cell lung cancer who are receiving chemotherapy. This study suggest that spirometry could be useful and non-invasive technique for assessing the response to treatment in patients with non-small lung cancer. It can be useful supplement of radiological imaging with the aim of monitoring the treatment response and functional changes in the lungs of the patients with non-small lung cancer undergoing chemotherapy.

Key words: Non-Small Lung Cancer, Spirometry, Chemotherapy

Molecular Characterization of circRNA Expression in Human Small-Cell Lung Cancer

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Introduction: Small-cell lung cancer (SCLC) is a highly aggressive neuroendocrine tumor, categorized into four molecular subtypes, each defined by unique biological characteristics and therapeutic responses. While gene expression profiles are well defined, circular RNAs (circRNAs) remain poorly understood.
Methodology: This study investigates circRNA expression in SCLC biopsies through whole-transcriptome sequencing of SCLC tumor and normal lung tissues (n=5 each). Using CircInteractome and miRTarBase, potential miRNA partners and downstream mRNA targets were identified to construct circRNA–miRNA–mRNA networks. The differential expression of circRNAs, along with selected interacting miRNAs, was subsequently validated using qRT-PCR, and their diagnostic utility was evaluated.
Results: We identified 23 differentially expressed circRNAs (DECs) in SCLC biopsies, of which 13 were upregulated, and 10 were downregulated. Computational predictions indicated that these DECs could interact with 241 miRNAs, collectively influencing 7,804 potential mRNA targets. Experimental validation confirmed marked downregulation of circLIFR and overexpression of circCAMSAP1 in SCLC samples. The circLIFR-associated regulatory network encompassed 26 miRNAs and 2,447 mRNA targets, with miR-1234-3p and miR-375-3p significantly upregulated. In contrast, the circCAMSAP1-associated network comprised 14 miRNAs and 553 mRNA targets, with miR-145-5p significantly downregulated. Notably, circCAMSAP1 expression showed a strong correlation with therapeutic response. As diagnostic biomarkers, circLIFR and circCAMSAP1 demonstrated robust performance, with AUC values of 0.9177 and 0.764, respectively.
Conclusion: Our bulk RNA sequencing analysis revealed aberrant expression of multiple circRNAs in human SCLC. Several of these circRNAs may be involved in circRNA–miRNA–mRNA regulatory networks and potentially contribute to SCLC pathogenesis, a hypothesis that requires experimental validation.

Key words: Circular RNA, SCLC, Biomarker, microRNA, circLIFR, circCAMSAP1

IACR - 691 **POSTER**

Hsp90 Isoforms Modulate Cellular Heterogeneity and Disease Aggression in Cancer

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In the context of survival and fitness, canalization refers to the ability of a cell to resist phenotypic changes, regardless of perturbations in its micro-environment. Strong canalization results in limited phenotypes while weak canalization results in phenotypic diversity. In cancer induced phenotypic variability favors, disease relapse and tumor aggression. In the models such as *Drosophila* and *Arabidopsis*, the Hsp90 chaperone regulates canalization by buffering mutations and alerting the epigenetic landscape; however, its impact on tumor heterogeneity is unclear. Here, we show that Hsp90 isoforms Hsp90a and Hsp90b, differentially regulate canalization in response to Hsp90 inhibition or chemotherapeutic interventions. Hsp90a favors proliferation stabilizing, the mutated oncogenes, while Hsp90b favors induced pluripotency and differentiation. The differential chromatin occupancy exposes Hsp90 role in altering the chromatin landscape. The increased Hsp90b occupancy on the *NOTCH2* genomic region is

found to be unique upon therapeutic intervention. We demonstrated that induce heat shock response (HSR) mediated by heat shock transcription factor, HSF1 induces Hsp90b, where the latter modulates *NOTCH2* expression. We expose the Hsp90b-Notch2 axis in the induced intra-tumor heterogeneity and tumor aggression. Interfering with HSF1 functions sensitizes cancer cells to chemotherapy by decreasing the tumor heterogeneity *in vitro* and mouse xenografts. Since Notch2 is a critical for maintenance of induced pluripotency stem cell maintenance and EMT, our findings gain importance in establishing unexposed molecular crosstalk on tumor evolution and treatment resistance. We propose that chemotherapeutic drugs, including Hsp90 inhibitors in combination can combat cancer and pave the way for novel combinatorial anti-cancer treatment regimens.

Key words: Hsp90, Tumor Heterogeneity, Heat Shock Response

IACR - 692 **POSTER**

TRAP1 Modulates Iron Metabolism in Cancer Cells

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Iron regulates several cellular processes, including mitochondrial energy metabolism, DNA synthesis and repair, oxidative stress management, iron sulphur cluster (ISC) and heme biosynthesis, etc. While glucose oxidation contributes to cellular ATP production, the oxidative phosphorylation (OXPHOS) complexes I, II, III & IV require ISC and heme as co-factors. Cellular iron homeostasis is tightly regulated by absorption, storage, utilization and recycling. Dysregulated iron metabolism is associated with several human pathologies, including cancer. Since mitochondrial chaperone TRAP1 regulate metabolic rewiring by favoring aerobic glycolysis over OXPHOS, we examined whether it also modulates iron metabolism. Strengthening our assumption, TRAP1 interactome analysis identified iron and heme dependant respiratory complex subunits. Next, we examined the crosstalk between TRAP1 and iron metabolism using TRAP1 overexpression (OE) and TRAP1 knockdown (KD) systems, and found that TRAP1 favors iron absorption and accumulation. This correlated with enhanced ISC and heme biosynthesis, but did not corelated with OCR. Further, OE cells sustained iron overload, while KD cells succumbed to iron toxicity leading to ferroptosis. TRAP1 retained mitochondrial integrity and anti-oxidative potential of cancer cells; however, it selectively downregulates OCR. Using DNA damaging agents, we confirmed that enhanced ISC and heme levels favour DNA synthesis and repair mechanisms to meet the proliferative and metastatic demands of cancer cells over OXPHOS. We exposed TRAP1 involvement not only in metabolic rewiring but also in modulating iron metabolism, and propose TRAP1 targeting to interfere with cancer metabolism.

Key words: TRAP1, Iron Metabolism, Metabolic Rewiring, Ferroptosis, Cancer Therapeutics

IACR - 693 **POSTER**

Hsp90 Chaperone Modulates the Epigenetic Landscape of MDR1 (Multidrug Resistance 1) Promoter in Drug-Adapted Cancer Cells

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The acquired multidrug resistance in cancer cells has become a significant challenge in conventional therapeutics. The altered cellular and epigenetic networks often drive chemotherapeutic adaptations, where regulation of the ABC-family of proteins (drug efflux pumps), especially the P-glycoprotein (P-gp) with diverse substrate specificities, decides chemotherapeutic resistance. The 90-kDa cancer chaperone, Hsp90, has been implicated in organismal and cellular adaptations. Earlier, we established that enhanced P-glycoprotein-mediated efflux activity, which imparts drug resistance, relies on Hsp90 isoforms in modulating the MDR1 transcription and thus cell fate. We also show that between the two isoforms of Hsp90, Hsp90α modulates the proliferative potential, and Hsp90β modulates chromatin transcription. We observed that both drug adaptation and enforced Hsp90α inhibition induce Hsp90β by a feedback loop mechanism that activates the shock transcription factor 1 (HSF1). Induced Hsp90β interacted with the promoter regions of *MDR1* and enhanced its transcription. Furthermore, increased Hsp90α function reversed CpG-mediated transcriptional repression of *MDR1* at the 1st exonic-intronic regions. These results suggest that Hsp90β plays an adaptive role during therapeutic intervention. In agreement with this, drug-adapted cells were found to be sensitive to Hsp90β inhibition. We expose two key mechanisms that modulate Hsp90β-P-gp regulation: (1) Hsp90α-mediated HSF1 and (2) chromatin repression. Interfering with HSF1 functions interfered with enhanced *MDR1* transcription via decreased Hsp90β occupancy on the *MDR1* promoter. Subsequently, the nuclear proteome analysis suggested that Hsp90β negatively regulates NuRD and PRC2 complexes that are involved in chromatin repression. We conclude that Hsp90β modulates drug adaptation. Therefore, we propose that interfering with the Hsp90β-HSF1 axis interferes with the adaptation of cancer cells.

Key words: Hsp90, Acquired Multidrug Resistance, MDR1, Epigenetics

IACR - 694 **POSTER**

Modifications of Free Tyrosine, a Form of Metabolic Reprogramming in Cancer Cells and Mimetic of Tyrosine as an Inhibitor of PI3K Enzyme

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Background: Alterations in metabolic pathways due to metabolic reprogramming are increasingly recognized in cancer biology. Among these, free aromatic amino acids like tyrosine and tryptophan play critical roles as diagnostic biomarkers. However, studies exploring tyrosine modifications; specifically nitro tyrosine, phosphotyrosine and their relevance in oral cancer remain limited. **Methods:** We utilized an in-house developed vertical tube gel electrophoresis (VTGE) system to purify metabolites from urine and nail clippings of oral cancer patients and healthy individuals. The purified samples were analyzed using a modified 96-well plate–based Lowry colorimetric assay to quantify free tyrosine. This assay was also employed to assess tyrosine levels in cultured cancer cells. Furthermore, a tyrosine

mimetic was evaluated as a potential PI3K inhibitor through computational approaches, including AutoDock Vina, molecular dynamics simulations, and ADMET profiling. **Results:** Urine samples from oral cancer patients exhibited elevated levels of nitro tyrosine and phosphotyrosine, while tyrosine levels in nail clippings were reduced compared to healthy controls. Tyrosine levels also changed during drug-induced cell death *in vitro*. ADMET analysis suggested that the tyrosine mimetic has a favorable safety profile, with low risks of DILI, carcinogenicity, and toxicity. The mimetic showed strong binding affinity for PI3K, a key enzyme in cancer-associated tyrosine modification. **Conclusion:** Tyrosine metabolism profiling revealed amino acid alterations associated with tumor activity. This supported the design of a tyrosine mimetic targeting PI3K, potentially disrupting tyrosine phosphorylation and oncogenic signaling in cancer cells.

Key words: Oral Cancer, Tyrosine, Phosphorylation, Metabolic Reprogramming, Therapies, Mimetic.

IACR - 695 **POSTER**

SIN3A Mediated Estrogen Receptor a Repression by Cyanidin-3-Rutinoside Sensitizes Hormone Positive Breast Cancer to Chemo/ Radiotherapy

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Resistance to chemotherapy and radiotherapy remains a remains a major challenge for the treatment in estrogen receptor (ER) positive breast cancer, due to persistent ER signaling that enhances tumor survival by facilitating DNA damage repair. Cyanidin 3 rutinoside (C3R) is a naturally occurring anthocyanin and a food colorant. Despite its known estrogenic properties, its influence on therapeutic response with respect of estrogen signaling has not been well explored. The present study investigates the chemo/ radio sensitizing potential of C3R by modulating estrogen signaling in hormone positive breast cancer cell line.

Using ERα positive breast cancer cells, we demonstrate that C3R functions as an ERα antagonist through interference with the nuclear corepressor SIN3A. Importantly, C3R markedly increased sensitivity to chemotherapeutic drugs and ionizing radiation by suppressing ERα transcriptional activity and downregulating ERα responsive genes involved in cell proliferation. C3R treatment led to enhanced DNA damage accumulation, G2/M cell-cycle arrest, and reduced expression of key proteins involved in DNA damage repair and cell invasion. Additionally, C3R elevated reactive oxygen species production in the X-ray treated cells and triggered mitochondrial mediated apoptosis. These effects were selective to ERα positive cells, highlighting the hormone dependent action of C3R.

Overall, this study identifies C3R as a selective estrogen receptor modulator and enhances chemo/ radio sensitivity via SIN3A dependent ERα repression, supporting its potential as a dietary adjuvant for improving therapeutic outcomes in ER positive breast cancer.

Key words: Estrogen Receptors, Cyanidin-3-Rutinoside, SIN3A, DNA-PKCS, Aid

IACR – 696 **POSTER**

Vitamin D VDR Signaling as an Adjuvant Strategy to Limit Estrogen-Driven EMT and Invasiveness in ER-Positive Breast Cancer

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Estrogen receptor–positive (ER+) breast cancer progression is driven by estrogen-dependent signaling pathways that promote tumor growth and metastatic potential. Vitamin D deficiency is frequently observed in breast cancer patients, yet its functional relevance to estrogen-mediated tumor aggressiveness remains unclear. ER? MCF-7 breast cancer cells were treated with 17β-estradiol (E2), Vitamin D (VD), and VD+E2. Cell viability was evaluated using AO/EtBr staining, DNA damage by comet assay, migratory and invasive capacity by wound healing and transwell assays, and epithelial–mesenchymal transition (EMT) markers by Western blotting. Vitamin D receptor (VDR) dependency was assessed using siRNA-mediated knockdown. E2 significantly enhanced cell viability, migration, invasion, and EMT, characterized by reduced E-cadherin and increased N-cadherin expression. Vitamin D treatment markedly attenuated estrogen-induced proliferative and metastatic traits and reversed EMT-associated molecular changes. VDR silencing potentiated estrogen-induced c-MYC expression, confirming a VDR-dependent inhibitory mechanism. These findings highlight Vitamin D–VDR signaling as a negative regulator of estrogen-driven breast cancer progression and support its potential utility as an adjuvant strategy in ER+ breast cancer management.

Key words: Vitamin D Receptor, Estrogen Receptor, ER-Positive Breast Cancer, Epithelial mesenchymal, Transition adjuvant Therapy

IACR – 697 **POSTER**

Butylated Hydroxyanisole Alleviates Radiation Induced DNA Damage While Amplifies DNA Damage Response and Repair in Breast Cancer Leading to Cell Survival and Radioresistance

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Radiotherapy efficacy in breast cancer is limited by intrinsic radioresistance, a process potentiated by estrogen receptor alpha (ERα)-mediated enhancement of DNA repair. Given the ubiquitous presence of the synthetic antioxidant butylated hydroxyanisole (BHA) in human serum, we investigated its potential to disrupt the radiation response. Current study we found that BHA, induces radioresistance in breast cancer cell lines through two distinct mechanisms: (1) scavenging ionizing radiation (IR)-induced reactive oxygen species (ROS), thereby minimizing DNA damage and preventing cell cycle arrest and apoptosis; and (2) upregulating key non-homologous end joining (NHEJ) repair proteins, including p53, DNA-PKcs, Ku70, and Ku80, which are associated with estrogen-responsive genes and interact with estrogen receptor alpha (ERα). Furthermore, BHA functions as an ERα agonist, enhancing its expression while simultaneously suppressing ERβ, a critical regulator of apoptosis. This ERα/ERβ imbalance promotes cancer cell survival and proliferation, as evidenced by increased mitochondrial membrane potential. The ER α agonistic activity of BHA enhances cell invasion and migration in ER+ ve cells leading to epithelial to mesenchymal transition and prevent IR

induced apoptosis. These findings underscore the role of BHA in promoting radioresistance in breast cancer through ROS scavenging and enhanced DNA repair via NHEJ, coupled with altered estrogen receptor signalling. Understanding this mechanism is critical for assessing the impact of dietary antioxidants on cancer therapy outcomes and developing targeted strategies to mitigate radiation resistance.

Key words: Butylated Hydroxyanisole, Radioresistance, Breast Cancer, Reactive Oxygen Species, Non-Homologous End Joining, Estrogen Receptor

IACR – 698 **POSTER**

Targeting Antigen Heterogeneous B Cell Malignancies with Multi-Specific Car Molecules

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CAR-T cell therapy has transformed the treatment landscape, however, long-term outcomes remain limited by antigen-loss-mediated escape and inadequate CAR-T cell persistence. The study focuses on the rational design and optimization of bispecific third-generation CAR-T cell constructs to effectively target antigen-heterogenous B-cell malignancies. Bispecific CAR constructs targeting combinations of key B-cell antigens were designed and systematically evaluated to mitigate antigen escape. *In silico* structural analyses were integrated to guide scFv orientation with optimal structural stability. Antigen-loss model systems were generated using CRISPR-Cas9 engineered B-cell lymphoma cell lines to facilitate screening of bispecific CAR constructs. Functional evaluation in these models revealed that not all bispecific CAR constructs perform equivalently under antigen-loss conditions. The study also aimed to enhance CAR-T cell persistence and functional efficacy using a comprehensive, multi-parametric screening of dual costimulatory domain combinations. Unlike conventional approaches, this screening evaluated multiple functional parameters under repeated antigen exposure. This integrated analysis revealed that certain costimulatory combinations excelled in one parameter but underperformed in others, emphasizing the necessity of multi-parameter evaluation for rational CAR design. Overall, this study underscores the importance of scFv pairing and rational costimulatory selection, providing a framework for developing effective and persistent CAR-T cells with translational potential in antigen-heterogenous B-cell malignancies.

Key words: Car-T Therapy, Crispr-Cas9, B-Cell Malignancies, Antigen Loss, Bispecific, Third-Generation Car-T

IACR – 699 **POSTER**

Investigating the Effect of Mitocurcumin on Metastatic Potential of Non-Small Cell Lung Cancer (NSCLC)

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Lung cancer remains the leading cause of global cancer mortality, largely due to metastasis and chemoresistance. While only 0.01% of shed tumor cells successfully colonize distant sites, metastasis accounts for 90% of cancer deaths. Current treatments are hampered by toxicity and tumor heterogeneity, highlighting an urgent need for targeted strategies.
Mitochondria have emerged as pivotal targets because mitochondrial dynamics—the balance of fusion and fission—regulate all hallmarks of metastasis, including motility, plasticity, and colonization. However, the clinical utility of "mitocans" is often limited by poor bioavailability. To overcome this, Mitocurcumin-1 (MiC) utilizes a delocalized lipophilic cation (DLC) strategy. By incorporating two triphenylphosphonium (TPP) moieties, MiC exploits the hyper-negative mitochondrial membrane potential of cancer cells to achieve 100–1000-fold higher accumulation than in normal cells.
MiC exerts anticancer effects by inhibiting TrxR2 and modulating reactive oxygen species (ROS), which are key regulators of mitochondrial dynamics. Preliminary data show that MiC reduces migration, invasion, and mesenchymal markers in non-small cell lung carcinoma (NSCLC) lines. This study will further investigate MiC's impact on metastasis and mitochondrial dynamics to evaluate its potential as a robust therapeutic strategy against NSCLC progression.

Key words: Lung Cancer, Metastasis, Mitocurcumin

IACR – 700 **POSTER**

Association between Oral and Gut Microbiome Dysbiosis in Various Types of Cancer: An Umbrella Review of Systematic Reviews and Meta-Analysis

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The state of eubiosis is maintained by the diverse nature of the gut and oral microbial communities that turn into dysbiosis to the disruption of the barrier and altered proportions of the microbiota. Hence, this umbrella review composes the systematic reviews on oral and gut microbiome dysbiosis in various types of cancer. Various databases were searched to include ten systematic reviews upon exclusion of irrelevant studies with substantial inter-reviewer agreement. The reviews were related to Colorectal, Gastric, Oral, digestive, breast, pancreatic and prostate cancers. Meta-analysis was performed in five of the included reviews, methodological rigor revealed strong evidences in five and moderate in three of the reviews with one study reporting the GRADE. Moderate duplication with an overlap percentage of 23.97 was calculated amongst the included systematic reviews and AMSTAR-2 scale was used for the assessment of risk of bias which verified reporting of moderate to high evidence. Abundance of *Fusobacterium nucleatum, Porphyromonas gingivalis* and *Prevotella intermedia* and reduced *Faecalibacterium* and *Bifidobacterium* was observed across most of the types of cancer. Crucial role has been played by the periodontopathogens present in the oral cavity which translocate to the gut through oral-gut axis acting as the major factor in these cancers. Further species-specific analytical studies could address the heterogeneity present in this umbrella review.

Key words: Cancer, Dysbiosis, Gut Microbiome, Microbiota, Oral Microbiome, Umbrella Review

IACR – 701 **POSTER**

Natures Shield: Phytochemicals as Guardians against Cancer

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Each year approximately 400000 children develop cancer. About 30-50% of cancers can currently be prevented by avoiding risk factors and implementing existing evidence-based prevention strategies. Chemoprevention, a relatively new and promising strategy to prevent cancer, is defined as the use of either natural or synthetic substances or their combinations to block, reverse or retard the process of carcinogenesis. Naturally occurring compounds from plants known as phytochemicals, serve as vital resources for novel drugs and also sources for cancer therapy. Phytochemicals, are not regarded as essential nutrients in humans although an increasing number of well-conducted studies are linking higher intake with a lower risk of developing cancer, as well as lower relapse after initial treatment completion. Phytochemicals have shown specific and non-specific anticarcinogenic properties, such as anti-inflammatory and estrogenic activities, reduction of oxidative damage to lipids and DNA, induction of phase I and II enzymes, inhibition of angiogenesis, and stimulation of DNA repair and apoptosis. Their anti-oxidant properties help to protect our DNA from ingested or environmental carcinogens. Not only do they improve our daily lives by helping our food taste, smell and look appetizing, they also reduce our risk of cancer and help people living with and beyond treatments. This poster presentation focuses on the role of phytochemicals in cancer prevention.

Key words: Phytochemicals, Cancer

IACR - 702 **POSTER**

Hybrid Epithelial/ Mesenchymal States Contribute to Endocrine Resistance in ER+ Breast Cancer

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Estrogen receptor-positive (ER?) breast cancer constitutes ~70% of cases and is primarily treated with endocrine therapies, yet ~30% of patients relapse within 5-10 years. EMT is now understood as a plastic continuum, with hybrid epithelial/mesenchymal (E/M) states enabling tumour adaptation under therapeutic stress. We established a graded TGF-β driven EMT model in MCF-7 cells spanning epithelial, hybrid, and mesenchymal states. Integrated morphological, transcriptional, and functional analyses reveal that hybrid and mesenchymal states display enhanced endocrine tolerance and altered immune-modulatory features. Using optimized Jurkat T-cell activation assays, we investigate how hybrid EMT states influence T-cell function, offering insight into the limited efficacy of endocrine-immunotherapy combinations in ER? disease.

We propose that hybrid EMT states function as a plasticity checkpoint that allows tumour cells to evade both endocrine therapy and immune attack. Using our scalable tumour T-cell co-culture system, we will test rational combination strategies such as low-dose TGF-β receptor inhibition together with PD-1 blockade to re-sensitise tumours to T-cell killing. This platform will also help identify clinically relevant biomarkers (for example, ZEB1/OVOL2 ratios) to flag high-risk ER+ patients, explain why some immunotherapy trials have failed, and guide the

design of next-generation combination therapies aimed at durable disease control in relapsing ER+ breast cancer.

Key words: Hybrid E/M States, Endocrine Resistance, ER+ Breast Cancer, EMT Plasticity, TGF-β, Immune Evasion

IACR - 704 **POSTER**

Comprehensive Genomic Profiling of Gastric Cancer in Patients from North East India

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Gastric cancer is the fifth most common malignancy and fourth leading cause of cancer-related mortality globally. North East India shows a consistent higher incidence and mortality than national average, particularly in regions like Aizawl and Papumpare with a remarkably higher risk among male patients. Major risk factors include *Helicobacter pylori* infection, dietary practices such as consumption of smoked foods, and genetic predispositions. However, somatic mutational data from this region remain limited despite indications of region-specific mutational patterns accounting from unique cultural practices and ethnic heterogeneity. To address this gap, a case-based observational study is designed to detect somatic mutations and identify molecular tissue subtypes of gastric cancer using whole-exome sequencing in patients recruited from hospitals across Assam, Mizoram, Nagaland, and Manipur, following ethical approval and informed consent. This includes systematic collection of demographic, lifestyle, dietary, and clinical information, paired tumor and peripheral blood sampling, histopathological evaluation, genomic DNA extraction and quality assessment, and high-throughput sequencing using the Roche KAPA HyperExome V2 on Illumina NovaSeq 6000 platform. It is followed by integrative analysis of somatic variants, tumor mutational burden, and mutational signatures with reference to global databases. The study aims to delineate regional molecular characteristics to inform precision and immunotherapeutic strategies.

Key words: Gastric Cancer; Whole-Exome Sequencing; Somatic Mutations; North East India; Molecular Subtypes; Tumor Mutational Burden; Precision Oncology; Genomic Profiling

IACR - 705 **POSTER**

Design and Biological Evaluation of a Pyrazole-Thiazolidinedione-Based EGFR Tyrosine Kinase Inhibitor for Breast Cancer Therapy

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Breast cancer is one of the most prevalent malignancies among women, and dysregulation of epidermal growth factor receptor (EGFR) signalling is closely associated with tumour proliferation, survival, and therapeutic resistance, particularly in aggressive subtypes. The development of novel small-molecule EGFR tyrosine kinase inhibitors (TKIs) with improved efficacy and safety profiles remains a major focus in anticancer drug discovery. Pyrazole and

thiazolidinedione scaffolds are individually recognised for their anticancer potential, prompting the design of hybrid molecules to enhance biological activity. A novel pyrazolthiazolidinedione based compound was designed and evaluated using an integrated in silico, in vitro, and in vivo approach. Molecular docking studies were performed to assess binding interactions with the EGFR kinase domain. In vitro cytotoxicity was evaluated using the MTT assay against MCF-7 and MDA-MB-231 breast cancer cell lines. A hemolysis assay evaluated hemocompatibility, while antioxidant potential was determined using the DPPH radical scavenging assay. In vivo acute toxicity studies were conducted, followed by biochemical estimation of liver and kidney function markers and histopathological examination of hepatic and renal tissues. Glide XP molecular docking studies against the EGFR tyrosine kinase domain (PDB ID: 1M17) demonstrated strong binding affinity of the pyrazolethiazolidinedione-based compound, with a docking score of-8.19 kcal/mol, indicating favourable ligand-receptor interactions within the ATP-binding pocket. The compound exhibited significant, dose-dependent cytotoxicity against MCF-7 and MDA-MB-231 breast cancer cell lines in the MTT assay. Minimal hemolytic activity confirmed good hemocompatibility, while notable antioxidant activity was observed in the DPPH radical scavenging assay. In vivo acute toxicity studies revealed no significant adverse effects, supported by normal liver and kidney biochemical parameters and the absence of histopathological alterations in hepatic and renal tissues. The pyrazole-thiazolidinedione-based compound demonstrates potent EGFR-targeted anticancer activity. These findings support its potential as a promising lead candidate for further development as a therapeutic agent for breast cancer.

Key words: Breast Cancer, Heterocyclic Compounds, Pyrazole, EGFR.

IACR - 708 **POSTER**

Nutrient Stress Drives Dual Metabolic-Structural Evolution in Tumours: Insights from a Calorie-Restriction Model

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Calorie restriction (CR) is well-established to improve metabolic health and reduce long-term cancer risk, yet how tumours adapt to grow in this situation remains poorly understood. The study was aimed to develop a calorie-restriction tumour model specifically designed to map the adaptive metabolic and structural remodelling in the immune system. Mice were maintained under calorie restriction prior to solid tumour induction with ehrlich ascitic carcinoma cells. Quantitative proteomic profiling of the tumour tissues were done to identify CR-driven metabolic remodelling. Pathway enrichment and functional clustering were performed to uncover integrated survival strategies. Calorie-restricted mice developed metastasis significantly earlier than mice fed normal diet. Tumours in calorie-restricted hosts exhibited a distinct, coordinated metabolic program that diverged sharply from tumours in normally fed controls. Proteomic analysis revealed a marked induction of *de novo* fatty-acid biosynthesis, including strong upregulation of fatty acid synthase (FASN) and enzymes of the fatty acid synthase complex, enabling tumours to maintain membrane production and energy storage despite dietary lipid scarcity. This was accompanied by enhanced expression of acetoacetyl-CoA synthetase, indicating that tumour cells increasingly relied on ketone bodies as an

auxiliary fuel source, reflecting a shift toward lipid-driven metabolic autonomy. In parallel with this anabolic adaptation, CR tumours displayed stress-induced cytoskeletal and membrane-remodelling adaptations. These changes, combined with proteomic indicators of oxidative-stress tolerance and modulation of apoptotic signalling, collectively suggests that nutrient scarcity selects tumour cells capable not only of sustaining biosynthetic independence but also enhancing metastatic capability and early mortality-related traits. This mechanistically driven CR tumour model demonstrates that calorie restriction does not merely alter tumour growth rate but it reprograms tumour biology through lipid-based metabolic self-sufficiency and cytoskeletal stress adaptation. Calorie restriction generates metabolically flexible, structurally resilient phenotype with potential implications for early metastasis. These findings highlight the need to critically evaluate dietary interventions not only for prevention but also for their capacity to reshape tumour evolution during oncogenesis and progression.

Key words: Calorie Restriction, Tumour Metabolic Rewiring, Fatty-Acid Biosynthesis, Ketone Utilisation, Cytoskeletal Adaptation, Metabolic Stress, Tumour Evolution, Proteomics

IACR - 709 **POSTER**

The Role of OAS-ISG-GBP Antiviral Axis in Spontaneously Regressing 4T1 Tumours

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Background: Spontaneous regression of 4T1 mammary carcinoma is exceptionally rare, as this tumour model is typically aggressive. In a subset of our BALB/c colonies, however, 4T1 tumours displayed progressive growth during the first few weeks followed by sudden and complete regression thereafter. **Aim:** To understand molecular mechanisms associated with the spontaneous regression of 4T1 tumours by conducting proteomic profiling of regressing tumours. **Methods:** Tumours were collected from BALB/c colonies showing tumour regression. Differential proteomic analysis focusing proteins enriched in the regressing tumours were performed. **Results:** Regressing tumours showed large fold increases in multiple classical type-I interferon stimulated genes (ISGs), which together generated a high-fidelity antiviral signature. Key antiviral enzymes OAS1, OAS2, OAS3, and ISG20 demonstrated some of the highest fold changes, indicating activation of the OAS–RNase L antiviral pathway. In parallel, guanylate-binding proteins (GBPs) and immunity-related GTPases (IRGs) were markedly induced, reflecting robust IFN-γ–driven intracellular pathogen–defence mechanisms. The consistency of these ISGs, combined with their magnitude and coordinated behaviour, forms a unified OAS–ISG–GBP antiviral axis. **Discussion:** The regressing 4T1 tumours showed a clear and coordinated increase in several antiviral gene families. These proteins are typically activated when cells detect unusual or foreign nucleic acids, which trigger type-I interferon signalling. Their high fold changes indicate that the tumour cells were responding to strong interferon-driven signals at the time of regression. GBP and IRG GTPases are known for their roles in intracellular defence and are commonly activated when cells attempt to contain or eliminate structures they identify as abnormal. The joint appearance of OAS, ISG, GBP, and IRG families shows that multiple antiviral defence pathways were switched on together. This suggests that the tumour microenvironment had shifted into a state where antiviral responses became dominant, more visible to immune attack, which increase the likelihood of their

elimination. \ The coordinated activation of the OAS–ISG–GBP axis provides an explanation for the regression phenotype.

Key words: Spontaneous Regression, Antiviral Immune Priming, OAS-ISG-GBP Axis, Interferon-Stimulated Genes

IACR - 710 **POSTER**

In Silico Induction of Immunogenic Cell Death in TNBC by Phytochemicals from *Gloriosa Superba* and *Artocarpus Heterophyllus*

D Raksan
Vel Tech High Tech

Triple-Negative Breast Cancer (TNBC) remains a clinical challenge due to its aggressive nature and lack of specific therapeutic targets. Immunogenic Cell Death (ICD) offers a novel strategy to convert "cold" tumors into "hot" immunological targets by releasing Danger-Associated Molecular Patterns (DAMPs) like Calreticulin (CALR) and HMGB1. This study investigates the potential of bioactive phytocompounds from *Gloriosa superba* and *Artocarpus heterophyllus* as potent ICD inducers in TNBC.

Using an *in silico* approach, major phytochemicals including Gloriosine and Artocarpin were screened against the Tubulin-Colchicine binding site (PDB ID: 1SA0), a critical target for microtubule destabilization and subsequent ICD triggering. Molecular docking analysis revealed that *Gloriosa superba* derivatives exhibited superior binding affinity (Binding Energy: **-9.8 kcal/mol**) compared to standard chemotherapeutic controls, forming stable hydrogen bonds with key residues in the colchicine-binding pocket.

ADMET profiling further validated the drug-likeness and pharmacokinetic safety of these leads. The study predicts that these phytochemicals can effectively destabilize microtubules, potentially triggering the endoplasmic reticulum (ER) stress pathway required for CALR surface translocation. These findings suggest that *Gloriosa superba* and *Artocarpus heterophyllus* are promising sources of novel ICD-inducing agents, offering a synergistic immunotherapeutic approach for managing chemoresistant TNBC.

Key words: Triple-Negative Breast Cancer, Immunogenic Cell Death, *Gloriosa Superba*, Molecular Docking, Phytochemicals

IACR - 711 **POSTER**

Host-Directed Therapy using Dehydrozingerone Diaryl Ethers and Repurposed Drugs Suppresses Macrophage Mycobacterial Growth Via Nf-κB Inhibition

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Chronic inflammation drives tissue damage and disease severity in tuberculosis (TB), highlighting the need for host-directed therapies (HDT) that rebalance dysregulated immunity while preserving antimicrobial defense. This study evaluated the immunomodulatory potential of the repurposed drugs Sofalcone and Rebamipide together with a novel diaryl ether dehydrozingerone derivative, DHZ (6), targeting the central inflammatory regulator NF-κB. Using THP-1 macrophages infected with Mycobacterium smegmatis, safety, antimicrobial efficacy, and mechanistic responses were assessed through Western blotting, immunofluorescence, and ELISA to monitor NF-κB signaling. Matrix metalloproteinase activity was examined by gelatin zymography, and intracellular reactive oxygen species were quantified using the DCFH-DA assay. All compounds displayed minimal cytotoxicity and significantly reduced intracellular bacterial survival ($p<0.05$). Mechanistically, treatment markedly suppressed NF-κB activation, including approximately 83% inhibition of upstream P-IKKα/IKKβ and nearly 89% reduction in p65 phosphorylation, preventing nuclear translocation. Functional outcomes included near-complete inhibition of MMP-2/9 activity and about 71% reduction in ROS production ($p\leq0.0001$), demonstrating potent anti-inflammatory action. Collectively, these findings position DHZ (6), Sofalcone, and Rebamipide as promising NF-κB–targeted HDT candidates to limit inflammatory damage and intracellular mycobacterial persistence. These results support further translational validation, preclinical evaluation, and future clinical exploration of adjunct host-directed strategies for tuberculosis and broader inflammatory diseases worldwide today.

Key words: Macrophages, Rebamipide, Sofalcone, Diaryl Ether Derivative of Dehydrozingerone DHZ (6), NF-κB, MMP-2, MMP-9, Reactive Oxygen Species, Immunomodulation

IACR - 712 **POSTER**

Kanchanar Guggulu Promotes P-ERK-dependent Apoptosis and Inhibits Tumor Growth in Ovcar-3 Xenografts

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Kanchanar Guggulu (KG), an Ayurvedic formulation, has shown therapeutic potential against various diseases, including cancer; however, its in vivo efficacy and mechanisms remain unclear. This study investigated the antitumor effects of KG in multiple cancer cell lines and an ovarian tumor xenograft model. Cell viability and clonogenic survival were assessed using MTT and colony formation assays. Apoptosis was evaluated through ROS analysis by flow cytometry, DAPI staining, gene expression studies, and Western blotting. An ovarian xenograft model was established by subcutaneous injection of OVCAR-3 cells into athymic nude female mice, followed by KG administration for six weeks. KG treatment significantly inhibited tumor cell growth and induced apoptosis in a dose-dependent manner. It also reduced the cancer stem cell population, as indicated by decreased CD44-CD117 cells and impaired sphere formation. Mechanistically, KG induced ROS generation, leading to ERK activation and upregulation of apoptosis-related proteins, including caspase-3 and PARP. In vivo, KG significantly reduced tumor volume and weight compared to controls. Immunohistochemical analysis demonstrated decreased Ki-67 expression, confirming its anti-proliferative effect. These findings indicate

that KG exerts potent antitumor activity through ROS-mediated ERK activation and apoptosis induction.

Key words: Kanchanar Guggulu, Ayurveda, Ovarian Cancer, Perk

IACR - 713 **POSTER**

Replication Stress Adaptation and Genome Instability Drive Endocrine Therapy Resistance in Breast Cancer

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Although endocrine resistance in hormone receptor-positive breast cancer is linked to genomic instability, the mechanisms underpinning resistant cell survival remain unclear. Using functional and integrated genomic analyses, we examined DNA damage response (DDR) pathways, repair efficiency, and replication fork dynamics across MCF7 wild-type (WT), tamoxifen-resistant (TamR), and fulvestrant-resistant (FulR) cellular models.

Resistant cells exhibited constitutively elevated γH2AX, indicative of persistent endogenous DNA damage and replication-associated stress. Despite this basal damage, resistant cells demonstrate significantly efficient γH2AX resolution following doxorubicin release, consistent with enhanced DNA break repair capacity as supported by neutral comet assays showing minimal DNA fragmentation in resistant cells. DNA fibre analysis revealed increased basal replication fork speed in resistant cells. Upon hydroxyurea-induced fork stalling, resistant cells showed significant fork slowing, suggesting active fork stabilization. Concordantly, basal CHK1 phosphorylation was elevated in resistant cells, indicating constitutive ATR-CHK1 pathway activation. Resistant cells displayed increased γH2AX-positive micronuclei, reflecting ongoing chromosomal instability despite efficient repair, highlighting a cellular compromise between therapeutic survival and genome integrity. Integrated whole-exome and transcriptome analyses identified alterations in DDR and chromatin remodeling genes in resistant cells. Collectively, these findings reveal adaptive rewiring of DDR and replication stress checkpoint signaling that promotes endocrine resistance and genomic instability.

Key words: Endocrine Resistance, Hormone Receptor-Positive Breast Cancer, DNA Damage, Replication Stress, ATR-CHK1 Signaling, Genomic Instability

IACR - 714 **POSTER**

Nimbolide Suppresses Lung Metastasis and Inflammatory Signaling in Experimental Hepatocarcinogenesis

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Background: Hepatocellular carcinoma (HCC), the fourth leading cause of cancer-related deaths worldwide, is characterized by high aggressiveness, inflammation, and frequent lung metastasis. Despite advances in therapy, the molecular mechanisms underlying HCC lung metastasis remain unclear. This study investigates the effect of Nimbolide on lung metastasis and inflammation in HCC mice. **Methods:** HCC was induced in one-month-old CD-1 mice using diethylnitrosamine (DEN; 100 mg/kg, i.p.) and N-nitrosomorpholine (NMOR; 80 ppm in drinking water) for 28 weeks. From week 28 to 32, mice received Nimbolide (6 mg/kg) or vehicle. At week 32, blood, liver, and lung tissues were collected for molecular analyses. **Results:** Nimbolide treatment significantly increased body weight and reduced tumor burden in liver and lung tissues compared to untreated HCC mice. Nimbolide also suppressed hepatic proinflammatory cytokines and the NF-κB/TLR4 signaling pathway. Expression of thyroid transcription factor 1 (TTF-1), elevated in the lungs but reduced in the livers of HCC mice, was normalized by Nimbolide ($p < 0.01$). Moreover, it downregulated MMP-9 while upregulating TIMP-1 in both liver and lung tissues. In HCC mice, Nimbolide reversed epithelial–mesenchymal transition (EMT) by restoring E-cadherin and reducing N-cadherin expression ($p < 0.05$). **Conclusion:** This study provides the first evidence that Nimbolide mitigates inflammation and lung metastasis in HCC, underscoring its potential as a promising therapeutic agent for managing metastatic HCC.

Key words: EMT, Inflammation, Liver Cancer, Metastasis, Nimbolide

IACR - 715 **POSTER**

Multi-Level Transcriptomic Profiling Reveals Dysregulation of LncRNA Fal1 with Prognostic and Therapeutic Significance in Indian Oral Squamous Cell Carcinomas

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Oral squamous cell carcinoma (OSCC) ranks among the leading global malignancies, particularly in India, where it is associated with dismal overall survival rates. Long non-coding RNAs (lncRNAs) have emerged as key regulators of OSCC progression and therapeutic response, yet their roles in Indian cohorts remain underexplored. This study aimed to delineate lncRNA dysregulation in OSCC among Indian patients. TCGA head and neck cancer datasets (n=43 paired samples) were interrogated using R packages and GEPIA. Validation involved qRT-PCR and RNA sequencing of matched OSCC tissues (n=3) from Indian patients, alongside doxorubicin-treated HEp-2 cells to evaluate therapeutic implications. TCGA analysis identified 523 upregulated and 179 downregulated lncRNAs ($p<0.05$). KEGG enrichment highlighted the PI3K-Akt signaling pathway as prominently dysregulated. FAL1 exhibited profound downregulation (log2FC = -3.2), correlating with poorer overall survival. RNA sequencing and qRT-PCR confirmed significant downregulation of FAL1 in Indian OSCC tissues and in HEp-2 cells. Treatment with doxorubicin for 48 hours caused cytotoxicity and increased FAL1 expression in HEp-2 cells, suggesting possible

therapeutic importance. Further analysis showed that FAL1 may interact with CCND2, a key gene in the PI3K-Akt pathway, which was found to be overexpressed in OSCC (log2FC = 3). Reduced FAL1 expression may fail to recruit EZH2 to the CCND2 promoter, leading to increased CCND2 expression, as reported previously. This study is the first to report the clinical significance of FAL1 in Indian OSCC patients. Restoring FAL1 may inhibit CCND2-driven tumor growth and improve treatment response. Further studies with larger patient groups are ongoing.

Key words: Oral Squamous Cell Carcinoma (OSCC), Long Non-Coding RNA (LncRNA), Fal1, Cancer Diagnosis, Cancer Therapy

IACR - 716 **POSTER**

Investigating the Role of the miR-127/136 Cluster in Regulating Tumour Behaviour and Stemness in Cervical Cancer

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Cervical cancer progression and therapeutic resistance are increasingly linked to the persistence of cancer stem–like cells (CSCs), which sustain tumor growth and recurrence. MicroRNAs (miRNAs) play pivotal roles in regulating oncogenic and tumor-suppressive pathways, including those governing stemness. In our previous studies, the miR-127/136 cluster was identified as significantly downregulated in cervical cancer cell lines, indicating a potential tumor-suppressive role. However, the functional relevance of this cluster in modulating tumor behavior and stemness properties remains poorly understood.

In the present study, we investigated the functional significance of the miR-127/136 cluster through a gain-of-function approach using a lentiviral delivery system, and successful overexpression was confirmed by quantitative PCR. Functional characterization revealed that miR-127/136 overexpression significantly altered tumor-associated phenotypes. Overexpression of this cluster resulted in reduced colony-forming ability, suppressed cell proliferation, impaired migration and invasion, and increased apoptosis with notable changes in cell cycle distribution. These findings collectively suggest that the miR-127/136 cluster functions as a tumor suppressor in cervical cancer. To further delineate its role in regulating stemness, future studies will employ spheroid-based culture systems to enrich CSC populations, followed by functional assays to assess stemness properties, which will be further extended to *in vivo* validation models. Additionally, comprehensive transcriptomic profiling and target validation studies will be performed to elucidate the downstream molecular pathways regulated by this miRNA cluster.

Overall, this study highlights the tumor-suppressive potential of the miR-127/136 cluster and provides a foundation for exploring its therapeutic relevance in targeting stemness properties in cervical cancer cells.

Key words: Cervical Carcinoma, Cancer Stem-Like Cells, Tumor Suppressor, miRNA Cluster, Overexpression, Stemness Regulation

IACR - 717 **POSTER**

Targeting Chemoresistant Heterogenous Tumor Populations in Metastatic Breast Cancer using Combination Therapy

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Metastatic breast cancer (mBC) remains incurable till date with combination therapies being the mainstay for management of the disease. One of the major reasons for therapeutic failures, is intratumoral heterogeneity (ITH), which refers to the coexistence of diverse cellular populations within a single tumor. This heterogeneity contributes to therapeutic resistance, metastatic potential, and drives disease relapse. Using the 4T1 murine metastatic model, we previously obtained heterogenous tumor subpopulations from primary tumor (T1) and matched lung metastases (L1) exhibiting aggressive and metastatic phenotype. RNA sequencing revealed that the highly metastatic T1 cells overexpress Macc1 (Metastasis Associated in Colon Cancer 1), a gene associated with tumor progression and chemoresistance. We targeted the Macc1 enriched cells using lovastatin, a widely used statin drug and a known transcriptional regulator of Macc1, which resulted in decreased cell viability in T1 and L1 cells compared to the bulk tumor populations. We now explore the efficacy of using lovastatin, in combination with a conventional chemotherapeutic drug 5-fluorouracil (5-FU) to target heterogenous chemoresistant T1 and L1 cells. Monotherapy with 5-FU led to a significant increase in the IC50 and Macc1 expression in T1 and L1 cells compared to the bulk, indicating its role in chemoresistance. Furthermore, monotherapy with lovastatin inhibited cell proliferation and significantly reduced Macc1 expression, particularly in L1 cells. Compared to the monotherapy, concurrent combination therapy with 5-FU and lovastatin resulted in significant reduction in cell viability , effectively targeting chemoresistant high Macc1 cells. Our findings suggest a promising strategy to overcome resistance due to ITH and improve therapeutic efficacy in mBC.

Key words: Metastatic Breast Cancer (mBC), Intratumoral Heterogeneity, MACC1 (Metastasis Associated in Colon Cancer, Lung Metastasis combination Therapy, TNBC (Triple Negative Breast Cancer)

IACR - 718 **POSTER**

Antitumor Efficacy of Graveoline, A Quinoline Alkaloid from *Ruta Graveolens*, in Solid Tumor Systems

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Graveoline, a 2-phenyl quinolinone alkaloid from Ruta species and other rutaceous plants, has emerged as a promising natural product for cancer therapeutics. Quinoline alkaloids represent a structurally diverse class of nitrogen-based heterocyclic compounds with established antimicrobial, anti-inflammatory, and antitumor properties. Prior studies document graveoline's capacity to induce both apoptosis and Beclin-1-associated autophagy in melanoma cells through independent signaling pathways, thereby circumventing apoptosis-resistant phenotypes. Recent biophysical investigations reveal that graveoline modulates KRAS membrane association through cooperative binding to the hypervariable region and G domain, a critical oncogenic driver in pancreatic, lung, and colorectal malignancies. However, systematic characterization of graveoline differential cytotoxic profile across diverse solid tumors remains unexplored. To address this knowledge gap, we evaluated graveoline against a panel of solid tumor-derived human cancer cell lines including cervical (HeLa), breast (MCF-7, MDA-MB-231), colon (HCT-116), and pancreatic (MiaPaCa-2) cancer models. Graveoline demonstrates selective targeting with pronounced sensitivity in certain cell lines concurrent with elevated apoptotic and autophagy markers, while other cell types show attenuated responsiveness. Differential sensitivity likely reflects variations in cellular uptake, metabolic pathways, and survival signaling architecture across distinct tumor types. Our preliminary data support graveoline potential as a selective anticancer agent, particularly for breast, colon, and pancreatic malignancies. Mechanistic studies including cell cycle analysis, signaling pathway evaluation, and combination strategies are currently underway to elucidate the molecular basis of selectivity and optimize therapeutic potential. These results support further preclinical evaluation and optimization toward potential clinical development.

Key words: Therapeutics, Anticancer Agent

IACR - 719 **POSTER**

ECM Stiffness Dictates Radio-Resistance in TNBC via Translational Reprogramming

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Background: Extracellular matrix (ECM) stiffening is a peculiar feature of breast tumor microenvironment that facilitates cancer progression. Stiff ECM is instrumental in potentiating survival, proliferation, contractility, invasion and stemness of cancer cells. However, the role of ECM rigidity in regulating radio-response of cancer cells remains largely intangible and needs in-depth investigation. **Methods and Materials:** To recapitulate the stiffness of normal breast stroma (0.5kPa) and metastatic breast tumor (5kPa), stiffness-tunable hydrogels were fabricated. To elucidate the impact of ECM-stiffness on radio-response of cancer cells, various functional and molecular assays including cell survival, cell cycle profiling, apoptosis, migration, immunofluorescence, immunoblotting, RT-PCR and RNA sequencing were performed. **Results:** The stiff scaffold primed cells showed significantly decreased apoptosis with higher survival and sustained proliferation index post-IR compared to that of soft ECM. Post-IR, the low level of γH2AX and early recruitment of DDR proteins (pATM, pDNA-pk and 53BP1) at DSBs showcase attenuated DNA damage in stiff ECM primed cells.

Transcriptomic profile of stiff ECM primed cells showed genes involved in ribosome biogenesis, organelle assembly and translation were differentially regulated. Upon investigation we found rigid ECM activates integrated stress response (ISR) as an adaptive mechanism which further potentiate stiffness acquired radio-resistance in breast cancer cells.

Key words: ECM Stiffness, Breast Cancer Radio Resistance, Translation, ISR

IACR - 720 **POSTER**

Engineered Mirror-Image Peptide Nanopores Induce Selective Cytotoxicity via Membrane Disruption in Breast Cancer

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Metastatic breast cancer (mBC) remains a major clinical challenge due to the lack of effective targeted therapies. Peptide-based therapeutics offer a promising strategy by targeting cancer cells through membrane-specific mechanisms. We report on a class of synthetic mirror-image peptides, pPorA, which self-assemble into stable, large-conductance pores in lipid bilayers. Building on this design, a charge-modified variant, pPorA DE was developed, resulting in increased conductance and enhanced anion selectivity. In this study, we investigated the cytotoxic potential of pPorA DE against MDA-MB-231 mBC cells by examining its interaction with cancer cell membranes. Compared to its L-enantiomer, DpPorA DE exhibited greater protease resistance and a preferential affinity for negatively charged cancer cell membranes. Treatment with DpPorA DE led to a concentration-dependent reduction in the viability of cancer cells, while having minimal effects on normal MCF10A mammary epithelial cells. Immunofluorescence analysis revealed significant disruption of membrane integrity following peptide exposure and fluorescently labelled DpPorA DE exhibited time-dependent incorporation into cancer cell membranes. These findings highlight the potential of mirror-image peptide pores to selectively disrupt cancer cell membranes, paving the way for the development of targeted anticancer therapies that exploit membrane fluidity and charge differences.

Key words: Metastatic Breast Cancer, Peptide Therapeutics, Membrane Disruption

IACR - 721 **POSTER**

The Goldilocks Relationship of Nutrient and Wnt Signalling Pathway

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The canonical Wnt signalling pathway, the primary contributor of colorectal cancer, operates via stabilization of the effector protein β-catenin, which translocates to the nucleus and regulates gene expression. There are multiple levels of regulations to manipulate the signalling, like at the ligand-receptor level, at the level of destruction complex of β-catenin and the translocation of β-catenin to the nucleus. In most of the colorectal cancers, APC (adenomatous polyposis coli) is found to be mutated, which is a component of β-catenin destruction complex. On the other hand, nutrient stress is a hallmark of tumour microenvironment where depletion of glucose, lipids and amino acids induce homeostatic feedback pathways. We used three cell

lines, HEK293T, CACO-2 and HCT116 expressing a luciferase based Wnt reporter system to study the starvation effect of these nutrients on Wnt output. While HEK293T shows an effect of NEAA starvation on Wnt output, each of them shows an altered Wnt output upon glucose stress regardless of their mutational differences. This indicates a cross talk between Nutrient and Wnt signalling. Whether this acts as a cue of metabolic rewiring in tumorigenesis is to be unfolded.

Key words: Colorectal Cancer; Nutrient Stress; Wnt Signalling; Adenomatous Polyposis Coli

IACR - 723 **POSTER**

Identification of Synthetic Lethal Interactions of *MEN1* in Pancreatic Neuroendocrine Tumors

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Pancreatic neuroendocrine tumors represent a rare, heterogeneous neoplasm of endocrine pancreas, accounting for ~1-2% of pancreatic cancer. Mutations in the *MEN1* gene encoding the scaffold protein menin, are prevalent in PanNETs, with over 35% of patients exhibiting loss of function mutations. Synthetic lethality offers a promising therapeutic strategy for targeting such tumors where protein expression is compromised. A synthetic lethal interaction occurs when simultaneous mutations in two genes result in cell death, while a mutation in only one of these genes is non-lethal. Therapeutic strategies that exploit synthetic lethal interactions would selectively target cancer cells harboring specific mutations, thereby enhancing therapeutic efficacy and minimizing off-target effects. This study aims to identify synthetic lethal interactors of menin, which could delineate the development of novel therapeutic strategies for PanNETs. We generated *MEN1* knockout and *MEN1* wild type cell lines that stably express CAS9 and utilized CRISPR-based kinome screening to identify kinases essential for the survival of MEN1 knockout cells but non-lethal in MEN1 wild-type cells. 18 target kinases were found to be essential for the survival of *MEN1* knock out cells. Further validation will elucidate pathway dependencies in PanNETs and facilitate the development of targeted therapies for tumors with MEN1 mutations.

Key words: Pancreatic Cancer, Pancreatic Neuroendocrine Tumor, Menin, Synthetic Lethality, CRISPR-Based Kinome Screen

IACR - 724 **POSTER**

Prognostic Significance of Mitochondrial Ferroptosis Signalling in the Pathogenesis of Retinoblastoma

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Retinoblastoma (Rb) is the most common intraocular malignancy of childhood. Previous studies indicate that mitochondrial dysfunction and elevated reactive oxygen species (ROS)

contribute to Rb pathogenesis. Ferroptosis, an iron-dependent form of regulated cell death associated with redox imbalance, is closely linked to mitochondrial metabolism. This study investigated the mitochondrial-mediated pro- and anti-ferroptotic gene expression in Rb tissues. **Methods:** Fifty primary Rb cases were prospectively analysed and divided into Group I (without high-risk factors [HRFs], n=30) and Group II (with HRFs, n=20). HRFs included massive choroidal invasion, scleral invasion, and post-laminar optic nerve invasion (PLONI). Quantitative Real Time-PCR (qRT-PCR) assessed mitochondrial, pro-ferroptotic, and anti-ferroptotic genes. GPX4 expression was validated by immunohistochemistry and western blotting, and mitochondrial ultrastructure was examined by transmission electron microscopy (TEM). **Results:** HRF-positive cases showed upregulation of MFRN1, BAX, LONP1, TFR1, RAS, NOX, GPX4, GSH, and SLC7A11, while ACSF2, MFRN2, CISD1, SOD2, VDAC2/3, NRF2, and HSPB1 were downregulated. SOD2 and VDAC3 were significantly associated with choroidal invasion, and SOD2 also correlated with PLONI. **Conclusion:** Mitochondrial ferroptosis pathway dysregulation is associated with aggressive Rb features. Targeting mitochondrial ferroptosis signalling may offer novel therapeutic strategies for high-risk retinoblastoma**.**

Key words: Retinoblastoma, Ferroptosis, Mitochondria, QRT-PCR, Invasion

IACR - 725 **POSTER**

Identification of Prognostic Genes Associated with Mitochondrial Biogenesis in Pediatric Ocular Malignancy

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Background: Retinoblastoma (Rb) is a common childhood cancer in India. The genetic foundation of the disease is well-documented; however, the subsequent metabolic adaptations, especially those related to mitochondria, are increasingly acknowledged as crucial in facilitating retinoblastoma progression and therapeutic chemoresistance. This study therefore aims to measure the mitochondrial copy number and expression of its biogenesis genes in Rb. **Methods:** This was the prospective study which includes 51 Rb patients. Mitochondrial DNA copy number (mtDNA) and biogenesis genes expression (PGC1-α, NRF1, NRF2, TFAM and POLRMT gene) were analysed using quantitative real-time PCR (qRT-PCR). Protein expression was evaluated by immunohistochemistry (IHC) and western blotting. Statistical analysis was performed to correlate their expression with clinicopathological parameters and patient outcome. **Results:** There was a male preponderance. Histopathology revealed high-risk features in 50.98% cases, with necrosis and calcification in 43.13% and 50.98% cases, respectively. Poorly differentiated Rb (PDRB) were found in more than 90% of cases. qRT-PCR results showed significant upregulation of PGC1-α, TFAM and POLRMT genes in more than 80% of cases. Western blotting and IHC results were consistent with qRT-PCR for PGC1-α and TFAM protein. mtDNA copy number was significantly higher in primary Rb. On statistical analysis, PDRB and HRFs ≥1 was positively significant with PGC1-α, TFAM and POLRMT expression. **Conclusion:** This is the first of its kind study showing the evidence of differential expression of mitochondrial biogenesis genes and altered mtDNA copy number in Rb patients.

Key words: Retinoblastoma, Mitochondria, Biogenesis, Chemoresistance, High-Risk Parameters

Dysregulated Hippo-Yap Signaling Drives Tumor Progression in Uveal Melanoma

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Introduction: Dysregulation of Hippo pathway contributes to chemoresistance and tumor progression in several cancers, including uveal melanoma (UM). In UM, GNAQ/11 driver mutations activate YAP by inhibiting Hippo kinases, promoting proliferation and metastasis. This study evaluated the role of Hippo pathway components in cell cycle regulation as potential therapeutic targets. **Methods:** Whole Exome Sequencing was performed on 70 UM cases. Real-Time PCR, immunohistochemistry, and western blotting were used to assess mRNA and protein expression of Hippo and cell cycle components, while cytokine levels were measured using ELISA. Molecular findings were correlated with clinical outcomes. **Results:** Mutually exclusive *GNAQ (38/70)* and *GNA11 (30/70)* mutations were identified, with *BAP1* alterations in 22.9% of cases. Upstream Hippo components (MST1, MOB1A, LATS1/2) and YAP/TAZ were downregulated in over 60% of tumors, whereas TEAD and VGLL4 were upregulated in more than 70%. Nuclear YAP was detected in 41.4% of cases and was associated with reduced metastasis-free survival. Elevated Cyclins/CDKs correlated with YAP activation and high-risk tumors. Cytokine profiling showed dynamic postoperative changes. Protein expression correlated with advanced stage, epithelioid morphology, high pigmentation, and BAP1 loss. **Conclusion:** Dysregulation of Hippo pathway contributes to metastatic progression in UM. Targeting YAP-CDK axis may represent promising combinatorial therapeutic strategy.

Key words: Uveal Melanoma, Distant Metastasis, Hippo Signaling, Exome Sequencing, Real-Time PCR

Disruption of the NOSIP-INOS Axis Sensitizes Colorectal Cancer to 5-Fluorouracil via Nitrosative Stress Signalling

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Colorectal cancer (CRC) exhibits frequent resistance to first-line chemotherapy regimens such as FOLFOX, limiting durable clinical responses. Nitric oxide (NO) exerts pleiotropic roles in tumor biology; sustained high-output NO can induce nitrosative stress, mitochondrial

dysfunction, and tumor cell death. We hypothesized that disrupting the NOSIP–iNOS interaction enhances intracellular NO accumulation and reverses chemoresistance in CRC.
NOSIP was inhibited via lentiviral-mediated stable knockdown and a small-molecule inhibitor (NOSIAN). Functional consequences were assessed in HT29 and SW620 cells using quantitative NO measurements, clonogenic assays, viability profiling, and Annexin V/7-AAD apoptosis analysis. In vivo efficacy was evaluated in tumor-bearing mouse models. Mechanistic insights were obtained through bulk RNA sequencing with pathway enrichment analysis and mitochondrial membrane potential assessment.
NOSIP disruption markedly elevated intracellular NO, resulting in reduced clonogenic potential, impaired viability, and enhanced apoptosis, particularly in combination with 5-fluorouracil (5-FU). In vivo NOSIP targeting significantly reduced tumor burden without overt systemic toxicity. Pharmacological inhibition phenocopied genetic depletion and potentiated 5-FU responses. Transcriptomic profiling revealed enrichment of type I interferon signalling, accompanied by mitochondrial depolarization, consistent with NO-driven mitochondrial stress and innate immune activation.
Collectively, these findings position NOSIP as a redox-immune checkpoint whose targeting enhances nitrosative stress and sensitizes CRC to 5-FU-based chemotherapy.

Key words: Colorectal Cancer, Chemoresistance, NOSIP, INOS, Nitric Oxide

IACR - 728 **POSTER**

Anticancer Potential of *Indigofera Longiracemosa* Stem Ether Extract

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Indigofera longiracemosa, a member of the Fabaceae family documented in traditional medicine for its therapeutic potential, holds promise as a viable natural indigo source. The anticancer potential of the stem ether extract (SEE) of this plant was evaluated in cancer cell lines, and SEE demonstrated cytotoxicity towards cancer cell lines in both short-term and extended (48-hour) exposure periods. Subsequently, the anticancer potential of the extract was examined in a DLA-induced solid tumor model using BALB/c mice. The animals were administered SEE at doses of 100 mg/kg b.wt (SEE LD) and 400 mg/kg b. wt (SEE HD) twice weekly for three weeks. The standard drug, cyclophosphamide (CTX), was administered at a dose of 15 mg/kg b. wt. On day 29, the animals were euthanized, and blood and tumor samples were collected for subsequent analysis. SEE effectively reduced tumor volume in DLA-induced animals. In addition, the elevated total leukocyte count (TC), indicative of tumor-induced leukocytosis in DLA-bearing animals, was markedly reduced to normal levels following treatment with SEE. Marked tumor cell proliferation in the untreated tumor-bearing group was reduced in the SEE-administered groups, as evidenced by hematoxylin and eosin staining and Ki-67 immunostaining. Furthermore, SEE altered the tumor microenvironment by downregulating IL-6 levels and upregulating TGF-β expression, as assessed using qRT-PCR. The observed reduction in tumor cellularity, together with increased necrotic areas and inflammatory cell infiltration in the SEE-treated groups, was consistent with therapy-

associated tumor remodeling, a pattern commonly reported following successful anticancer interventions.

Key words: Cytotoxicity, Solid Tumor Model, Anti-Cancer Therapy, *I. Longiracemosa*

IACR - 729 **POSTER**

When to Let Go: 14-3-3ε as a Gatekeeper of Centriole Disengagement

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The 14-3-3 protein family regulates several pathways in mammalian cells, including cell division and centrosome duplication. However, the precise mechanisms by which 14-3-3 paralogs regulate the centrosome cycle remain unclear. To identify the mechanisms by which 14-3-3ε regulates centrosome duplication, we altered two conserved acidic residues in the 14-3-3ε phospho-peptide-binding pocket that regulate complex formation and dissociation with the associated ligands, D127 and E134, to Alanine. Using Live cell imaging we demonstrated that altering these residues to Alanine led to opposing effects on centrosome duplication; the D127A mutant inhibited centrosome duplication (Monopolar Spindle), while cells expressing the E134A mutant showed the presence of supernumerary centrosomes (Multipolar Spindle). We demonstrate that 14-3-3ε does not inhibit centriole duplication, as reported for 14-3-3γ, but inhibits centriole disengagement. Using a combination of pharmacological and genetic approaches, we demonstrate that 14-3-3ε inhibits the activity of Plk1 and Separase, leading to disengagement defects that ultimately lead to decreased proliferation and cell death. Our work demonstrates that different 14-3-3 paralogs regulate different steps in the centrosome cycle, and disrupting complex formation between 14-3-3ε and Plk1 or Separase could be a novel therapeutic strategy in tumor cells.

Key words: 14-3-3e, Centrosome, Centriole Disengagement, Cell Division, Plk1, Separase, Bi2536, Sepin1

IACR - 731 **POSTER**

Comprehensive Expression and Prognostic Analysis of COMMD10 in Pan Cancer

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Colorectal cancer (CRC) continues to be a significant global cause of cancer-related morbidity and mortality, highlighting the necessity for reliable prognostic biomarkers. Copper metabolism MURR1 domain-containing protein 10 (COMMD10) is one of the members of the COMMD protein family, mainly involved in cellular homeostasis, transcriptional regulation, and NF-κB signalling. Given the central role of NF-κB signalling in colorectal tumorigenesis

and limited studies on the prognostic and expression landscape of COMMD10 in CRC, we selected this for comprehensive pan-cancer and CRC-specific analysis. Herein, we analysed the Cancer Genome Atlas (TCGA) and Gene Expression Omnibus (GEO) to evaluate the expression status of the COMMD10 in Pan Cancer. COMMD10 expression varied significantly across tumour types, showing both tumor-suppressive and promoting associations depending on cancer context. Kaplan–Meier survival analysis showed a trend toward shorter overall survival in patients with low COMMD10 expression compared with those with high expression (HR = 0.45, p = 0.13). The interacting genes of COMMD10 were analysed via the STRING tool. Functional enrichment analyses were performed to explore the biological pathways associated with expression, mentioning that its involvement in cancer-related signalling pathways, including inflammatory response, cell proliferation, and transcriptional regulation. Furthermore, COMMD10 expression was examined in CRC tissue samples, showing downregulation in the majority of tumour tissues. Additionally, in the CRC cell line, higher expression of COMMD10 was observed in HCT116 cells compared with SW480 and SW620 cells. In literature, COMMD10 has been identified as a biomarker for the prognosis of several cancers, including Gastric and hepatocellular carcinoma. Our study suggests that COMMD10 may be a potential biomarker for CRC patients, warranting further validation in larger cohorts.

Key words: Cancer; CRC; COMMD10; Biomarker; Prognosis

IACR - 732 **POSTER**

Epithelial to Neuroendocrine Transition in PDAC: Neuroendocrine Plasticity as a Driver of Aggressive Pancreatic Cancer

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Pancreatic ductal adenocarcinoma (PDAC) is a highly malignant cancer with the overall survival rate of less than 10 %. According to GLOBOCAN 2022 estimates, PDAC ranks as the seventh leading cause of cancer-related death in men and women worldwide and is projected to become the second leading cause in the coming years. This poor prognosis could be attributed to tumor cell plasticity, which promotes intratumoral heterogeneity, drug resistance, and disease recurrence. In several cancers, including prostate and small cell lung cancer, neuroendocrine differentiation has emerged as a key mechanism of therapeutic resistance. Similarly, lineage plasticity in PDAC may enable epithelial tumor cells to undergo epithelial-to-neuroendocrine transition, acquiring neuroendocrine marker expression and more aggressive phenotypes following chemotherapy. However, the molecular mechanisms driving this epithelial-to-neuroendocrine lineage switch in PDAC remain poorly understood.
This study aims to elucidate the mechanisms underlying neuroendocrine plasticity in PDAC and define its role in chemoresistance. Understanding these pathways may identify the potential targets to prevent lineage switching, enhance chemosensitivity, and ultimately improve clinical outcomes for patients with pancreatic cancer.

Key words: Pancreatic Ductal Adenocarcinoma, Lineage Plasticity, Ductal to Neuroendocrine Transition, Intratumoral Heterogeneity, Drug Resistance

IACR - 734 **POSTER**

Immunohistochemical Evaluation of MTA1 Expression in Canine Mammary Tumours: Correlation with Tumour Type and Grade

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Metastasis-associated protein 1 (MTA1) is a pivotal oncogenic regulator that promotes cancer progression by modulating oncogenesis, angiogenesis, metastasis and apoptosis. MTA1 modulates estrogen receptor α (ERα) via histone acetylation, activates Ras, Wnt1 and STAT3 pathways, inhibits p53-dependent apoptosis, stabilises hypoxia-inducible factor 1α (HIF-1α) and triggers epithelial mesenchymal transition (EMT) by downregulating E-cadherin expression. Its overexpression has been documented in several human cancers, including breast, colorectal, gastric, lung and prostate cancers. Canine mammary tumours (CMTs) represent invaluable spontaneous animal models for studying human breast cancer, sharing similar histopathological characteristics, hormonal dependencies and molecular signatures. The present study investigated MTA1 expression in CMTs using immunohistochemistry to evaluate its role as a biomarker of tumour aggressiveness and grade. MTA1 immunostaining was detected in 23/25 cases of CMTs, with 4/25 cases showing strong positivity, 13/25 cases moderate positivity and 5/25 cases weak positivity. Cytoplasmic localisation predominated (19/23 cases), with nuclear localisation restricted to grade III carcinosarcoma and dual localisation noted in anaplastic carcinoma and fibrosarcoma. Aggressive histological subtypes exhibited moderate to strong MTA1 immunostaining and a significant association was observed between the number of MTA1-positive cells and tumour grade, highlighting the diagnostic value of quantitative immunohistochemical assessment. These findings support MTA1 as a reliable biomarker for tumour progression and aggressiveness in CMTs, mirroring its oncogenic role in human breast cancer.

Key words: Metastasis-Associated Protein 1, Canine Mammary Tumours, Immunohistochemistry, Tumour Biomarker, Comparative Oncology, Tumour Aggressiveness

IACR - 735 **POSTER**

Identification of Insulin-Like Growth Factor-1 Receptor (IGF1R) Specific Small Molecule Allosteric Inhibitors as Novel Anti-Cancer Agents

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The insulin-like growth factor-1 receptor (IGF1R) is a member of the receptor tyrosine kinase family and is pivotal in regulating cell differentiation, cell growth, and survival during various stages of embryonic and adult development. The IGF1R pathway is commonly dysregulated in many cancers, primarily via increased expression of IGF1R or its ligands, IGF-1 and IGF-2. The IGF1R and insulin receptor (IR) are closely related receptor tyrosine kinases sharing 84% overall homology, and 100% homology in their kinase domains. The homology between IGF1R and IR makes selective targeting of one of the receptors very difficult and thus creates a special challenge for IGF1R inhibitor design. Therefore, scientists are exploring to develop allosteric small molecule inhibitors; although finding allosteric inhibitor binding sites are proving very daunting in these complex kinases. We identified and validated the presence of an allosteric inhibitor binding pocket in IGF1R using multiple approaches which included molecular biology, cell biology, and bio-informatics. In an effort to discover allosteric small molecule(s) that can fit into this pocket, virtual screening of a library of 1.48 lac drug-like molecules was carried out, and ZINC000009985567, ZINC000005757555 and ZINC000005158416 were identified as three most potent hit compounds binding to this pocket as allosteric inhibitors.

Key words: Allosteric Inhibitor, Insulin-Like Growth Factor-1 Receptor, Tyrosine Kinases

IACR - 736 **POSTER**

Emerging Frontiers in Organoid Modeling of Epithelial-Mesenchymal Transition (EMT)

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Epithelial-mesenchymal transition (EMT) is a dynamic and reversible biological process that enables epithelial cells to acquire mesenchymal traits, playing a central role in cancer metastasis and fibrosis. However, traditional two-dimensional (2D) monolayer cultures fail to capture the spatial complexity, extracellular matrix (ECM) stiffness, and multicellular interactions that regulate EMT *in vivo*. In contrast, three-dimensional (3D) patient-derived organoids provide a more physiologically relevant platform, preserving tissue architecture, stem cell hierarchies and tumor heterogeneity. When stimulated with cytokines such as TGF-β and TNF-α, organoids effectively replicate hallmark EMT events, including cytoskeletal remodeling, cadherin switching, and ECM reorganization. These changes are accompanied by increased expression of mesenchymal markers like vimentin and N-cadherin, along with activation of key signaling pathways such as p38 MAPK, PI3K/AKT, and SMAD-dependent cascades. Such models have proven particularly valuable in studying intestinal fibrosis, breast cancer invasion and non-small cell lung cancer (NSCLC). Patient-derived organoids (PDOs) have become powerful tools in precision oncology, especially for investigating EMT-mediated therapeutic resistance. They allow researchers to examine hybrid epithelial/mesenchymal states, cancer stemness and drug resistance under therapeutic pressure. Integrated transcriptomic and single-cell analyses further enable real-time monitoring of EMT plasticity and mesenchymal-epithelial transition (MET). With advances in bioengineering- such as microfluidic systems, organs-on-chips, 3D bioprinting, and CRISPR-based editing- organoid

platforms are becoming increasingly sophisticated. Despite challenges like scalability and matrix variability, these systems offer a more predictive and human-relevant framework for metastasis research and personalized cancer therapy.

Key words: Epithelial Mesenchymal Transition (EMT), Tumor Heterogeneity, Patient-Derived Organoids, Organs-On-Chip, Personalized Medicine

IACR - 737 **POSTER**

Hematopoietic Stem Cells -Conditioned Media Modulate Cellular Energetics via Mitochondrial Dysfunction and Dynamics to Eliminate Colorectal Cancer Cells

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Mitochondrial fusion-fission dynamics play a critical role in regulating the signaling and metabolic landscape of colorectal cancer (CRC). While moderate mitochondrial fission typically supports CRC progression and chemoresistance, excessive fission can shift the cellular balance toward apoptosis. Our previous research established that hematopoietic stem cell-derived conditioned media (HSCs-CM) can alter the tumor microenvironment and in this study, we have investigated the specific mechanisms by which HSCs-CM influence mitochondrial dynamics and cell fate in the HCT-116 CRC cell line. Using HSCs-CM derived from sorted HSCs, we performed a comprehensive multi-omics analysis integrating RNA sequencing, proteomics, and metabolomics validated through molecular biology approaches. Our results demonstrate that HSCs-CM induces lethal, excessive mitochondrial fission by modulating DRP-1 protein levels. This fission triggers a mitophagy-mediated apoptotic pathway, leading to effective cancer cell clearance. Proteomic profiling revealed significant dysregulation of electron transport chain complexes III and IV, while complementary metabolomics and transcriptomics confirmed the disruption of mitochondrial bioenergetics and autophagy pathways. These findings delineate the therapeutic potential of HSC-conditioned media in treating colorectal cancer by promoting mitochondrial dysfunction and programmed cell death.

Key words: Mitochondrial Dynamics; Colorectal Cancer; Hematopoietic Stem Cell-Conditioned Media (HSCs-CM); Apoptosis; Mitophagy; DRP-1; Metabolic Reprogramming; Multi-Omics

The Molecular Glue an Innovative Approach Better than Inhibitors against Cancer and Neurological Disorders

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Small-molecule inhibition has long been central to drug discovery in oncology and neurology, but occupancy driven therapies inhibition often causes incomplete target suppression, dose related toxicity, and rapid therapeutic resistance. These limitations are particularly evident in complex oncogenic signaling pathways, including the RAS-RAF-MEK-ERK cascade as well as neurodegenerative diseases were accumulation of protein driven disease progression. To overcome these challenges, molecular glue degraders have emerged as fundamentally distinct and potentially transformative approach. Rather than inhibiting protein activity, these compound exploits the cellular ubiquitin-proteasome system to selectively eliminate disease-associated proteins. Molecular glues such as IK-595 function by promoting interactions between a target protein and an E3 ubiquitin ligase, leading to ubiquitination and subsequent proteasomal degradation. This event-driven, catalytic mechanisms, enables sustained protein removal instead of temporary functional blockade. In oncology, this strategy permits more complete suppression of oncogenic proteins by eliminating both catalytic and non-enzymatic scaffolding functions, potentially overcoming resistance mechanisms associated with kinase reactivation, compensatory feedback loops, and mutations that reduce inhibitor binding affinity. In neurological diseases, many pathogenic proteins lack clear active sites, molecular glue degraders expand the druggable proteome by targeting conformational regions and protein-protein interaction interfaces. Furthermore, catalytic degradation may achieve sustained biological effects with lower systemic exposure. Emerging preclinical and early clinical evidence indicates that molecular glue-based therapies can induce deeper and more durable modulation of disease pathways compared with traditional inhibitors, establishes targeted protein degradation as next-generation therapeutic platform for treatment resistant cancers and proteinopathies and offering scalable strategy to address previously undruggable disease drivers.

Key words: RAS-RAF-MEK-ERK Signaling, Inhibitors, Molecular Glue Degraders, Targeted Protein Degradation, Next-Generation Therapeutics

C14MC-Driven Metabolic Reprogramming Modulates Cisplatin Sensitivity in Cervical Cancer

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Cisplatin-based chemotherapy is a standard treatment modality; however, resistance, recurrence, and systemic toxicity remain major clinical challenges. Metabolic rewiring reduces cisplatin efficacy by promoting enhanced cellular fitness and survival. Epigenetic regulation plays a critical role in modulating tumorigenesis and cisplatin sensitivity. Several studies have reported the downregulation of multiple members of the miR-379/miR-656 cluster (C14MC) in cervical cancer; however, its role in metabolic reprogramming and cisplatin sensitivity remains unclear. This study aimed to investigate the role of C14MC in modulating cellular metabolism and its implications for cisplatin response in cervical cancer cell lines. We performed C14MC activation in cervical cancer (CC) cell line (C33A) by a CRISPR/Cas9-activation. To evaluate its functional role in cisplatin response, we performed colony formation, cell proliferation, and cytotoxicity assays. To elucidate the underlying mechanisms, we conducted untargeted metabolomic profiling to identify metabolic alterations associated with C14MC activation. Additionally, confocal microscopy was employed to assess structural cellular changes and to quantify reactive oxygen species (ROS) levels. C14MC cluster activation significantly enhanced cisplatin cytotoxicity growth and proliferation in CC. Metabolomic analysis revealed pronounced metabolic reprogramming characterized by disrupted energy metabolism and compromised redox buffering capacity. Confocal microscopy further demonstrated elevated ROS accumulation and altered mitochondrial morphology, corroborating the observed metabolic perturbations. C14MC activation enhanced cisplatin sensitivity via energy catastrophe and mitochondrial damage.

Key words: C14MC, Therapy Resistance, Metabolic Reprogramming, Cervical Cancer

IACR - 740 **POSTER**

SAM-Competitive Inhibition of EHMT2, SUV39H1, and EZH2 Reveals a Shared Epigenetic Vulnerability in Cancer and Sickle Cell Disease

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Histone methylation is a critical epigenetic regulator of chromatin and gene expression, and its dysregulation contributes to oncogene activation, tumor suppressor silencing, and impaired developmental gene control. Therapeutic targeting of repressive histone methyltransferases (HMTs), therefore represents a compelling strategy in cancer and hemoglobinopathies. Here, we report the identification and comprehensive characterization of compound 5g, an isoquinolinium bromide–based, S-adenosyl methionine (SAM)-competitive inhibitor of key repressive HMTs. Compound 5g potently inhibited SUV39H1 (IC50 = 1.5 μM), EZH2 (IC50 = 2.5 μM), EHMT2 (IC50 = 3 μM), and SUV20H1 (IC50 = 8 μM), while demonstrating marked selectivity over additional HMTs and DNMT1. Functionally, 5g induced erythroid differentiation and robust fetal γ-globin expression in K562 cells, underscoring its potential relevance to sickle cell disease. In triple-negative breast cancer (MDA-MB-231) cells, 5g suppressed clonogenic growth, enforced G1-phase arrest, and activated intrinsic apoptotic signaling. Furthermore, it impaired induced pluripotent stem cell reprogramming and zebrafish

fin regeneration, highlighting its impact on epigenetic plasticity. Collectively, these findings establish 5g as a mechanistically defined, multi-target epigenetic modulator with promising translational implications across oncology and hemoglobinopathies. Hence, Coordinated inhibition of repressive histone methyltransferases represents a unifying epigenetic therapeutic strategy across malignancy and hemoglobinopathies.

Key words: EZH2, EHMT2, Sam-Competitive, Apoptosis, γ -Globin, Regeneration

IACR - 741 **POSTER**

Understanding Cross-Talk Between β-Catenin, GSK-3β and JNK3 Signaling to Develop Therapeutic Strategies for the Treatment of Neurodegenerative Disorders

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The Wnt/β-catenin Signaling pathway is central pathway for maintaining tissue homeostasis, embryonic development, cell proliferation, differentiation, neurogenesis and stem cell renewal. Various illnesses, such as cancer and neurological conditions, are linked to the dysregulation of this pathway. The Wnt/β-catenin Signaling is upregulated in many cancers, whereas it is downregulated in neurological disorders. Despite intense examination this pathway has not been effectively manipulated for therapy owing its complexity of structure, multiple regulation system, complex interconnections with other Signaling pathways. GSK-3β is the master regulator of this pathway. Upregulation of GSK-3β has been observed in may cancers and its downregulation in many neurodegenerative disorders like AD and PD. GSK-3β has been reported to cause the accumulation of tau protein, suppresses Wnt/ β-catenin pathway, enhances neuroinflammation, and drives neuronal apoptosis collectively leading to neurodegeneration.We identified a very potent highly selective GSK-3β inhibitor, MJ34. ?Presently, we are exploring the impact of MJ34 on the Wnt/β-catenin pathway cross-regulation with GSK-3β and JNK3 in neurodegenerative diseases. This study will explain the role of β-catenin in neurogenesis and establishing its connections to tau hyperphosphorylation and JNK3 activity, that would contribute to the identification of novel regulatory nodes that may have potential therapeutic relevance in neurological disorders.

Key words: Wnt/β-Catenin Signaling, Neurogenesis, Gsk-3β,Mj34, Neuroinflammation, Tau Hyperphosphorylation

IACR - 742 **POSTER**

Elucidating the Role Of Mj04 as Janus Kinase (JAK) Inhibitor, Regulating Pro-Inflammatory Cytokines against the Pathogenesis of *Alopecia Areata*

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The pathogenesis of AA is associated with the steady activation of the JAK/STAT pathway in the catagen and telogen phases, preventing HFSC activation and anagen re-entry. The upsurge in the surrounding pro-inflammatory cells (CD8+NKG2D, macrophages, etc.), cytokines (IL-15, IFN- γ, IL-6, IL-2, and TNF-α), chemokines, and MHC-1 expression contribute to the collapse of the immune-privileged state of HFs, thus leading to AA pathogenesis. No specific treatment for AA is available to date, but several steroid-based drugs and vasodilators have been incorporated into the treatment regimen of AA. In recent years, JAK/STAT inhibitors have come into the limelight and are used as a strategy to overcome the burden of alopecia and re-growth of new hair. Several non-selective JAK inhibitors (Tofacitinib, Baricitinib, Ruxolitinib) have been reported to promote hair regrowth in human and mice subjects, but their non-selectivity and specificity leave a huge gap in overcoming the safety and efficacy of these drugs. With a similar aim, our lab has discovered a selective JAK-3 small molecular inhibitor; thus, the prospect of my study is to understand the role of this small molecule inhibitor on the selective inhibition of JAK-3 and to investigate the mechanistic pathways of several pro-inflammatory cytokines involved in the collapse of IP. Moreover, the data from the ongoing cell-free and in-vitro studies suggest a significant downregulation of the phosphorylated form of JAK-3 and the associated pro-inflammatory cytokines.

Key words: JAK, STAT, Alopecia, Cytokines, Pro-Inflammatory, Immune Privilege

IACR - 743 **POSTER**

Heterochiral Dipeptide Drives Proteostasis-Mediated NM23H1 Stabilization to Suppress Metastasis in P53-Diverse Solid Tumors

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Metastatic progression remains a principal driver of cancer-related mortality, highlighting the pressing need for therapeutic strategies that effectively curb invasion and systemic dissemination. Despite advances in oncology, epithelial-mesenchymal transition (EMT) and functional loss of metastasis suppressors continue to fuel tumor relapse and distant colonization. NM23H1, a prototypical metastasis suppressor, is frequently downregulated or epigenetically silenced in aggressive cancers, a deficiency that facilitates EMT and metastatic spread, thereby positioning its pharmacological restoration as an attractive yet underexploited therapeutic avenue. Here, we report a rationally designed phenylalanine-based heterochiral dipeptide, D-phenylalanyl-L-phenylalanine, as a small-molecule scaffold capable of reactivating NM23H1 and restraining metastatic progression. Using colorectal cancer as the primary model, with validation in breast, prostate, and lung cancer systems encompassing diverse p53 backgrounds, we demonstrate that this dipeptide enhances NM23H1 stability by attenuating ubiquitin-mediated proteasomal degradation. Stabilization of NM23H1 reinstated epithelial characteristics, marked by E-cadherin upregulation and suppression of Vimentin, Snail, and Twist, culminating in significant inhibition of migration, invasion, and clonogenic expansion. Mechanistic analyses revealed that NM23H1 reactivation occurred independently

of p53 status, whereas induction of apoptosis and G_2/M cell cycle arrest required functional p53 signalling. *In vivo,* administration in orthotopic and experimental 4T-1 mouse models substantially reduced primary tumor burden and distant metastases. Collectively, these findings establish this first-in-class heterochiral dipeptide as a translationally relevant metastasis-suppressing scaffold and provide a rationale for combinatorial strategies integrating proteasome inhibitors, p53 reactivators, or EMT-targeted therapies in solid malignancies.

Key words: Heterochiral Dipeptide, NM23H1 Stabilization, Metastasis Suppression, P53 Signalling, Cancer Therapy

IACR - 744 **POSTER**

Targeting Hsp90-Mediated Autophagy-Apoptosis Crosstalk in KRAS-Mutant Non-Small Cell Lung Cancer: Synergistic Anticancer Effects of Gedunin And Metformin

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Lung cancer, predominantly non-small cell lung cancer (NSCLC), remains the leading cause of cancer-related mortality worldwide, accounting for nearly 1.8 million deaths annually. Despite advances in targeted therapies, mutations in KRAS and EGFR sustain tumor survival and therapy resistance by activating the EGFR/PI3K/AKT axis and modulating autophagy-apoptosis crosstalk. Heat shock protein 90 (Hsp90), a central molecular chaperone, stabilizes multiple oncogenic client proteins, including Beclin-1, EGFR, PI3K, and AKT, thereby promoting tumor progression, poor prognosis, and resistance to treatment. Targeting Hsp90, therefore, represents a promising strategy to disrupt these interconnected survival pathways. Building on our previous findings, the combination of Gedunin and Metformin led to disruption of the Hsp90:Beclin-1:Bcl-2 complex, induced endoplasmic reticulum (ER) stress, and promoted apoptosis in KRAS-mutant A549 lung cancer cells. We further tried to understand the role of Hsp90 after autophagy inhibition. 3-methyladenine-treated cells under serum starvation confirmed reduced LC3 expression without mitochondrial or genomic damage, highlighting redox-regulated autophagy. Notably, early autophagy blockade promoted drug resistance through Hsp90α/GRP78/PIK3CA upregulation and attenuation of p53-caspase signaling. Combination therapy with metformin and gedunin demonstrated synergistic cytotoxicity by amplifying ROS generation, activating AMPKα1, suppressing Hsp90 and its client proteins, and reactivating apoptotic pathways. Collectively, these findings suggest that targeting Hsp90 with gedunin, particularly in combination with metformin, effectively overrides autophagy-mediated resistance and enhances apoptosis in KRAS-mutant NSCLC, offering promising avenues for precision cancer therapeutics.

Key words: Lung Cancer, Hsp90, Autophagy, Apoptosis

IACR - 745 **POSTER**

Discovery of a Novel S-Triazine-based PI3K-a Inhibitor with Potent Antitumor Activity in PIK3CA-Mutant Hr? Breast Cancer

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The phosphoinositide 3-kinase (PI3K)/Akt/mTOR plays an indispensable role in regulating cell growth, proliferation, survival and metabolism. Dysregulation and constitutive activation of PI3K signaling pathway, most frequently driven by *PIK3CA* mutations, are strongly associated with hyperactivation of Akt and mTOR and have been reported in approximately 40% of HR? breast cancer cases. Therefore, targeting PI3K-α represents a promising strategy to treat PI3K-mutant, HR? breast cancer. In our work, we report the identification and preclinical characterization of a novel s-triazine scaffold based PI3K inhibitor that exhibits nanomolar potency in both cell-free and cell-based assays. Mechanistic studies conducted on HR?, PI3K-mutant MCF-7 breast cancer cells revealed a significant downregulation of phosphorylated Akt and mTOR, important regulators of cell growth, proliferation, and survival, demonstrating a significant inhibition of the PI3K/AKT/mTOR signalling axis. Western blotting and flow cytometry analysis confirmed that the compound induced G1 phase cell cycle arrest and triggered apoptosis in MCF-7 cells. *In vivo* efficacy study in 4T1 syngeneic mice model revealed a significant antitumor activity and a favorable therapeutic window. Collectively, these findings establish this novel s-triazine-based PI3K inhibitor as a promising anticancer candidate with promising *in vitro* and *in vivo* efficacy.

Key words: Pi3k, Akt, Hr?, PI3K-Mutant, S-Triazine, 4t1 Syngeneic Mice Model

IACR - 746 **POSTER**

Targeting TMPRSS2-ERG Fusion-Driven Prostate Cancer Using Novel HBS-α-Helicomimics

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Prostate cancer (PCa) is characterized by frequent occurrence of *TMPRSS2-ERG* gene fusion, found in over 50% of Indian and Caucasian patients. This fusion event places androgen receptor (AR)-regulated *TMPRSS2* promoter upstream of *ERG*, drives aberrant ERG expression and is strongly associated with advanced tumor stage, higher Gleason scores, and metastasis. Despite its prevalence, pharmacological targeting of ERG transcription factor remains challenging. We developed HBS-α-helicomimic, a novel class of chemically engineered, designed to specifically bind to the ETS consensus DNA motif, thereby blocking ERG-DNA interaction. Two helicomimics with anti-cancer efficacy were identified for functional validation. Mechanistic studies confirmed that these helicomimics disrupt ERG binding and its interactions with key partners such as AR in ERG-positive PCa cell lines. Additionally,

luciferase-based promoter-reporter assay demonstrated a marked reduction in ERG transcriptional activity upon helicomimics treatment and chromatin immunoprecipitation-PCR (ChIP-PCR) showed helicomimics disrupts ERG occupancy at its target gene, leading to decrease in its oncogenic potential. Finally, cell-based functional assays showed marked reduction in cell proliferative, migratory, and invasive potential of ERG-expressing PCa cells. To validate these findings, we genererated a murine xenograft model, which demonstrated anticancer effects of HBS-α-helicomimics suppressing ERG mediated tumorigenesis. Our findings establish HBS-α-helicomimics as a transformative therapeutic strategy that directly impedes oncogenic function of ERG, offering a novel and promising therapeutic avenue for treatment of *TMPRSS2-ERG* driven prostate cancer.

Key words: Prostate Cancer, TMPRSS2-ERG Fusion, HBS-α-Helicomimic, ERG Transcription Factor

IACR - 747 **POSTER**

Differential Telomere Repeat Binding Factor-1 Expression in Breast Cancer Molecular Subtypes: A Possible ER Mediated Telomere Regulation

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Background: Telomere repeat binding factor-1 (TRF1) is a telomere associated protein that binds and stabilizes the chromosome ends/telomeres, hence imperative for genomic stability. The contribution of telomere-associated proteins to breast cancer biology has not studied. Therefore, in the present study we have investigated the TRF1 expression in different breast cancer molecular subtypes. Also, through *in-silico* analysis TRF1 correlation with hormone receptor signalling and survival analysis was evaluated. **Methods:** TRF1 protein expression was evaluated by immunohistochemistry across molecular subtypes of breast cancer (Luminal A, Luminal B, HER2-positive, and triple-negative breast cancer [TNBC]). Expression was quantified using H-score and percentage of positive tumor cells. Transcriptomic correlation analysis between TERF1 and ESR1 was performed. Kaplan–Meier analyses were used to assess the prognostic significance of TERF1 expression. **Results:** In the present study, we observed subtype-specific pattern of TRF1 expression across breast cancer molecular subtypes. TRF1 expression demonstrated significant enrichment (high H scores & large tumor cell populations) in Luminal B tumors compared to HER2-positive and TNBC subtypes. Transcriptomic analysis revealed a significant positive correlation between TRF1 and ESR1 expression ($R = 0.28$, $p < 0.001$). Survival analysis demonstrated a non-significant overall survival and disease-free survival in patients with high TRF1 expression. **Conclusion:** TRF1 as a subtype-restricted telomere regulator preferentially upregulated in ER-positive,

particularly Luminal B, breast cancer. The positive association between TERF1 and ESR1 suggests that estrogen signalling may be involved in telomere stabilization via TRF1 to sustain proliferative capacity.

Key words: Telomere Repeat Binding Factor, Breast Cancer, TNBC, Luminal A, Luminal B

IACR - 748 **POSTER**

Expression of the *Forkhead Box M1* (FOXM1) in Human Urinary Bladder Transitional Cell Carcinoma

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Forkhead box M1 (FOXM1) is a transcription factor required for a wide spectrum of essential biological functions, including DNA damage repair, cell proliferation, cell cycle progression, cell differentiation and tissue homeostasis. The study aim is to evaluate mRNA/protein expression of *FOXM1* in transitional cell carcinomas (TCCs) of urinary bladder and correlate its expression with the clinicopathological characteristics of patients. In this study, the methods of qRT-PCR and immunohistochemistry (IHC) were utilized to evaluate mRNA/protein expression of *FOXM1* in TCC. Independent Student's t test, ANOVA and Chi-square were used to analyze the data statistically. Overexpression of FOXM1 mRNA in majority (77.6%) of TCC patients. Relative mean fold expression of *FOXM1* mRNA was found to be significantly ($p<0.0001$) higher in muscle-invasive bladder cancer (MIBC) as compared to non-muscle-invasive bladder cancer (NMIBC) patients. (8.06 ± 3.19 vs. 4.66 ± 2.75, $p<0.0001$). *FOXM1* protein expression was demonstrated on archival formalin-fixed, paraffin-embedded (FFPE) bladder tissues and cytoplasmic staining pattern was detected. Significant difference was observed in protein expression of FOXM1 between the two groups (NMIBC and MIBC patients) (82.8% vs. 100%, $p=0.014$). Our study results suggest that *FOXM1*mRNA/protein expression was observed in TCC of UBC and might be used as a novel diagnostic biomarker.

Key words: Bladder Tumorigenesis, Transcription Factor, Immunotherapy, Peptide Vaccines, Transitional Cell Carcinoma, FOXM1

IACR - 751 **POSTER**

Targeting Downstream of Tryptophan Catabolism to Overcome Immune Checkpoint Blockade (ICB) Resistance in Oral Squamous Cell Carcinomas

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Oral squamous cell carcinoma (OSCC) demonstrates limited responsiveness to immune checkpoint blockade (ICB), necessitating mechanistic insights into immunotherapy resistance. Dysregulated tryptophan metabolism and activation of the Aryl Hydrocarbon Receptor (AhR) have emerged as critical mediators of tumor immune evasion. Here, we investigated TAM-driven regulation of tryptophan catabolizing enzymes (TCEs) and AhR signaling in OSCC. Human OSCC cell lines (SCC9 and H357) were cultured as stem-enriched 3D orospheres and co-cultured with polarized M1 and M2 macrophages to model tumor–immune crosstalk. Expression of TCEs (IDO1, TDO2, IL4I1) and AhR target genes was assessed by quantitative RT-PCR and immunoblotting. Stem-like orospheres exhibited intrinsic upregulation of TDO2 and enhanced AhR transcriptional activity. M2-polarized macrophages further amplified TCE expression and sustained AhR signaling, establishing a cooperative immunosuppressive circuit. Pharmacologic inhibition of AhR using CH-223191 attenuated M2-induced signaling. Notably, combined AhR inhibition and PD-1/PD-L1 blockade resulted in superior suppression of pro-tumorigenic immunometabolic signatures compared to monotherapy. Collectively, these findings identify the TAM–TCE–AhR axis as a critical driver of immunometabolic resistance in OSCC and provide a mechanistic rationale for combinatorial AhR-targeted immunotherapy strategies.

Key words: Oral Cancer, Tryptophan Metabolism, Aryl Hydrocarbon Receptor, Immune Checkpoint Blockade, Tumor-Associated Macrophages

IACR - 752 **POSTER**

Characterization of FRG1 Mutation in Pancreatic Cancer

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Pancreatic ductal adenocarcinoma is a highly lethal malignancy, primarily because of its intricate genetic makeup and diagnosis at advanced stages. Whole-exome sequencing of Indian PDAC patients revealed mutations in the *Facioscapulohumeral muscular dystrophy region gene 1 (FRG1)*, specifically P→A, P→T, and N→D. While *FRG1* has been implicated in diverse cancers and cellular processes, including splicing, actin bundling, and DNA repair, its precise function in pancreatic cancer remains largely uncharacterized. This research examines the functional consequences of FRG1 mutations in pancreatic cancer cell lines. The data indicate that FRG1 mutations do not impact proliferation or colony formation in PDAC cell lines; however, the P→A mutant enhances colony formation in normal pancreatic cells, and the N→D mutant significantly promotes cell migration in DanG cells. Notably, the FRG1 N→D variant exhibits reduced protein expression independent of proteasomal degradation, suggesting the involvement of alternative degradation pathways. Furthermore, proximity-based interactome profiling shows interactors involved in RNA binding, the spliceosomal complex, and regulators of RNA splicing. These results offer new insights into the mechanisms of action of FRG1 and lay the foundation for subsequent investigations to clarify its role in metastasis.

Key words: Pancreatic Cancer, FRG1, Metastasis

Targeting Aromatic Amino Acid Metabolism via Synthetic Biology-Based Gene Silencing Methods in Glioma

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Gliomas use tryptophan metabolism to increase kynurenine (KYN) flux, coupling tumor-intrinsic survival with immune escape. It has been demonstrated that KYN is an endogenous ligand of aryl hydrocarbon receptor (AHR), which is a transcription factor that regulates multiple genes involved in immune response modulation and tumorigenesis. KYN–AHR pathway is active in human brain tumors, which are associated with malignant progression and tumor-derived immunosuppression. In glioblastoma, elevated TDO2/IDO-driven KYN can activate AHR, which (upon heterodimerization with ARNT) enforces transcriptional programs that support motility/invasiveness while concurrently limiting immune-cell proliferation and function in the tumor microenvironment. Against this backdrop, RNAi-based gene silencing offers a direct way to target and halt the AHR-ARNT-KYN axis at its transcriptional control node by suppressing AHR itself, rather than only modulating upstream metabolism. The central premise of this project is that shRNA-mediated AHR knockdown can dampen AHR–ARNT–dependent transcription and weaken the KYN-driven feed-forward logic that sustains tumor progression and immune suppression. This is conceptually aligned with the broader oncology literature linking tumor AHR activity to malignant phenotypes and tumor-immune dysregulation, making AHR an actionable metabolic–immunologic lever in glioma. This project aims to establish a programmable, metabolism-linked gene-silencing framework for glioma therapy and rational combination opportunities with upstream kynurenine-pathway interventions. We began with cloning shAhR into a lentiviral plasmid, then transfecting glioblastoma cells. We hypothesize that it suppresses cell proliferation and restoring T-cells proliferation and enhances immune surveillance.

Key words: Glioblastoma, Glioma, Kynurenine, Aryl Hydrocarbon Receptor, Tryptophan Metabolism, Aryl Hydrocarbon Receptor Nuclear Translocator

A DNA Topology encoded P53-TERF2 Axis Enforces G-Quadruplex Directed Transcriptional Repression and Proteostatic Control

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Telomeres embody a fundamental paradox in cancer evolution, safeguarding genome stability yet limiting unchecked proliferation. To sustain replicative immortality while evading DNA damage signalling, tumour cells exploit the shelterin complex, with TERF2 (TRF2) serving as a pivotal repressor of telomere deprotection and checkpoint activation. Elevated TERF2 marks aggressive breast cancer subsets and portends inferior clinical outcome, yet its upstream regulation restraining TERF2 under tumour suppressor control remains unclear. Here, we delineate TERF2 as a direct and stringently regulated target of p53. Either activation of endogenous p53 by genotoxic stress (camptothecin), non-genotoxic MDM2 inhibition (Nutlin-3a), or ectopic overexpression elicited repression of TERF2 across human and murine breast

cancer cells. By contrast, siRNA-mediated ablation of p53 in MCF-7 rescued TRF2, indicating p53 dependence. Importantly, TERF2 repression strictly contingent upon intact p53 function, as canonical oncogenic and transactivation-defective variants were inert, reinforcing mechanistic exclusivity. Functionally, we posit that p53-mediated TERF2 attenuation may unleash CDKN1A to intensify p21-driven arrest; paradoxically, elevated TERF2 constrained this axis to favour tumorigenesis. Mechanistically, TERF2 restraint is executed through dual convergence. Structural interrogation of the locus revealed dense enrichment of high-scoring G-quadruplex (G4) motifs co-localising with canonical p53 response elements across the promoter and 5′UTR. Chromatin immunoprecipitation revealed selective p53 occupancy at these regions, supporting topology-encoded transcriptional silencing. Concurrently, integrative computational analyses, alongside endogenous or ectopic p53 activation ±MG132, convergently diminished TERF2 levels across cell lines, implicating proteostasis control beyond Siah1.Translationally, multi-cohort transcriptomic and proteomic analyses indicate clinical elevation of TERF2 correlates with *TP53* status and inferior overall survival (TCGA-BRCA HR 1.32, P = 0.024). Collectively, these findings position p53 as a bifunctional enforcer of TERF2 restraint and unveil telomere checkpoint vulnerability in *TP53*-altered breast cancer.

Key words: P53; TERF2; G4-Quadrupex; Proteostasis; Tp53 Status; Breast Cancer

IACR - 757 **POSTER**

Reciprocal Cooperation of Type A Procyanidin and Nitrofurantoin against Multi-Drug Resistant (MDR) UPEC: A pH-Dependent Study

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Uropathogenic Escherichia coli (UPEC) accounts for the majority of complicated and uncomplicated urinary tract infections. The use of phytomolecules in the treatment of UTI is fast gaining attention. The current report identifies a multidrug-resistant strain (QSLUPEC7), which is a strong biofilm producer, among the considered clinical isolates. The antimicrobial and antibiofilm activity was evaluated for the phytomolecule, Type A procyanidin (TAP) from Cinnamomum zeylanicum against QSLUPEC7. TAP treatment did not affect the growth of the MDR strain but affected the biofilm formation (~70% inhibition). The confocal microscopic examination reveals the biofilm inhibition and the live cells in the biofilm corroborates the antimicrobial results. Further, the synergy studies of TAP and nitrofurantoin (NIT) were carried out at different pH. TAP acts synergistically with nitrofurantoin at different pH considered. A closer look in the results reveals that at pH 5.8, maximum growth inhibition is recorded. The gene expression analysis shows that TAP alone and in combination with NIT downregulates the major fimbriae adhesins of UPEC. The results conclude that the TAP has an antibiofilm activity against the multidrug-resistant strain of UPEC, without affecting the growth.

Key words: Uropathogenic Escherichia coli (UPEC), Phytomolecules, Type A procyanidin (TAP), pH, Multidrug-resistant strain (QSLUPEC7)

IACR - 758 **POSTER**

Bio-Mimetic Dehiscence: A Novel pH-Responsive Nanocarrier Derived from *Ruellia Tuberosa* Mucilage for Targeted Immunogenic Cell Death in TNBC

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The acidic and high interstitial fluid pressure conditions of the tumor microenvironment (TME) in Triple-Negative Breast Cancer (TNBC) limit the effectiveness of systemic chemotherapy, highlighting the need for stimuli-responsive drug delivery systems. This study presents a bio-mimetic nanocarrier engineered from the high-tension mucilage of Ruellia tuberosa seed pods, designed for pH-responsive dehiscence and localized drug release to induce Immunogenic Cell Death (ICD) while reducing systemic toxicity.

Silver nanoparticles (AgNPs) were green-synthesized using cold-macerated mucilage extracts from immature pods to preserve tension-active pectins. These mucilage-capped nanocarriers were loaded with colchicine-rich extracts from *Gloriosa superba*. In vitro release studies were conducted under physiological (pH 7.4) and acidic TME (pH 5.0–5.5) conditions.

Characterization by UV-Vis and FTIR confirmed successful synthesis and stable encapsulation. The nanocarriers remained structurally stable at pH 7.4, preventing premature release. Under acidic conditions, rapid mucilage swelling and structural rupture mimicked natural seed pod dehiscence, triggering burst release of the payload. This targeted pH-responsive mechanism enhances localized cytotoxicity in TNBC cells while minimizing damage to healthy tissues.

Key words: tumor microenvironment (TME), Triple-Negative Breast Cancer (TNBC), Immunogenic Cell Death (ICD), *Gloriosa superba,* Silver nanoparticles (AgNPs)

IACR - 759 **POSTER**

Triggering the Anti-Tumor Immune Response: A Review of ICD-Inducing Phytochemicals from South Indian Flora

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The tumor microenvironment (TME) plays a critical role in cancer progression, immune evasion, and therapeutic resistance. Immunogenic cell death (ICD) has emerged as a promising anticancer strategy, as it converts dying tumor cells into a source of tumor antigens and danger-associated molecular patterns that stimulate antitumor immune responses. Recent evidence highlights the potential of phytochemicals—bioactive compounds derived from plants—as modulators of the TME capable of inducing ICD. Phytochemicals such as polyphenols, flavonoids, alkaloids, and terpenoids can trigger endoplasmic reticulum stress, reactive oxygen species generation, and calreticulin exposure, leading to the release of ICD hallmarks including ATP and HMGB1. In addition to directly inducing tumor cell death, these compounds can remodel the immunosuppressive TME by enhancing dendritic cell maturation, promoting cytotoxic T-cell activation, and inhibiting pro-tumorigenic inflammatory signaling. This abstract summarizes emerging insights into the mechanisms by which phytochemicals target the TME to promote immunogenic cell death and discusses their potential as safe, cost-effective adjuvants in cancer immunotherapy.

Key words: Immunogenic Cell Death (ICD); Tumor Microenvironment (TME); Tamil Nadu Ethnomedicine

Sustainable Oncology from Agro-Waste: Apoptotic Potential of Phenolic Phytochemicals Derived from Tamil Nadu Agricultural Residues

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The pursuit of sustainable oncology strategies has intensified interest in low-cost, bioactive resources derived from agricultural residues. Tamil Nadu, a leading agrarian state of India, generates substantial quantities of agro-waste annually, including banana peduncle, sugarcane bagasse, and rice bran. These residues represent an underexploited reservoir of phenolic compounds and flavonoids with demonstrated anti-cancer potential. This review systematically examines recent evidence on phytochemicals extracted from these region-specific agro-wastes and their ability to induce apoptosis in malignant cells. High concentrations of polyphenols isolated from these materials disrupt mitochondrial membrane potential, facilitating cytochrome c release into the cytosol and activating the intrinsic apoptotic pathway. This process involves caspase-9 and caspase-3 activation alongside the downregulation of anti-apoptotic Bcl-2 proteins, ultimately promoting programmed cell death. Additionally, the review highlights advancements in green extraction and synthesis techniques that enhance the yield and stability of pro-apoptotic fractions while preserving structural integrity. Collectively, agro-waste-derived phytochemicals from Tamil Nadu offer a promising, sustainable avenue for developing cost-effective chemotherapeutic adjuncts with targeted apoptotic efficacy.

Key words: Bioactive resources, Phytochemicals, Apoptosis, Chemotherapeutic adjuncts

Turning Undervalued Weeds to Nanotherapeutics: Tridax Procumbens Derived EVs Deliver Temozolamide and Induce Cell Death in Glioma Cells

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Extracellular Vesicles (EVs) are tiny, naturally occurring particles that can carry biological signals and therapeutic molecules between cells. These EVs emerged as promising nanocarriers for the delivery of various therapeutic molecules. In this study, we introduce, for the first time, EVs isolated from *Tridex procumbens* (TPEVs), a plant often considered a weed. These TPEVs have been revealed as a novel source of bioactive vesicles. We characterized these vesicles using dynamic light scattering, zeta potential analysis, Field-Emission Scanning Electron Microscopy, and nanoparticle tracking analysis, which confirmed their nanoscale size and stability. Their cellular internalization was validated in glioma cells by confocal microscopy labelling with lipophilic dye Oil Red O (ORO). To explore the therapeutic potential of TPEVs, we evaluated their use as drug carriers by loading them with temozolomide, a frontline chemotherapeutic drug used to treat glioblastoma. The vesicles showed efficient drug encapsulation, controlled release, and enhanced anticancer activity. Importantly, they also triggered autophagy-mediated cell death, suggesting a dual role as both delivery vehicles and active modulators of tumor biology. This work highlights *Tridex procumbens* EVs as a sustainable, plant-derived nanoplatform with promising applications in glioma treatment and opens a new avenue in plant-derived nanomedicine.

Key words: Extracellular Vesicles (EVs), Nanovesicles, Glioblastoma, Temozolamide, Anti-Cancer, Autophagy

IACR - 762 **POSTER**

Multicentric Osteolysis Nodulosis and Arthropathy Mimicking as Juvenile Idiopathic Arthropathy

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Multicentric Osteolysis, Nodulosis, and Arthropathy (MONA) syndrome is a rare autosomal recessive skeletal disorder caused by mutations in the *MMP2* gene, characterized by progressive osteolysis, joint destruction, and subcutaneous nodules. We report two sibling cases born to consanguineous parents who presented with progressive joint swelling and pain beginning in early childhood. The elder sibling, a 9-year-old girl, developed painless swelling of the wrists and ankles at age four, followed by progressive limitation of movement and deformities of the hands and feet. The younger sibling, a 6-year-old boy, exhibited similar symptoms starting at age three, with additional gingival hypertrophy and reduced mobility. Radiographic evaluation in both cases revealed marked osteolysis of carpal and tarsal bones, generalized osteopenia, and joint space narrowing. Laboratory investigations showed normal inflammatory markers, helping differentiate the condition from juvenile idiopathic arthritis. Genetic analysis confirmed pathogenic variants in the *MMP2* gene in both siblings, consistent with MONA syndrome. Management was supportive, including physiotherapy, orthopedic monitoring, and bisphosphonate therapy to improve bone density. These cases highlight the importance of early recognition of MONA syndrome in children presenting with progressive arthropathy and osteolysis, particularly in consanguineous families, to enable appropriate genetic counseling and multidisciplinary care.

Key words: Multicentric Osteolysis; Nodulosis; Arthropathy; Mona Syndrome; MMP2 Gene Mutation; Autosomal Recessive Disorder; Progressive Osteolysis; Pediatric Skeletal Dysplasia; Subcutaneous Nodules; Consanguinity; Sibling Cases; Genetic Counseling

IACR - 763 **POSTER**

Impact of Di(2-ethylhexyl) Phthalate on Cellular Dynamics in Head and Neck Cancer

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Di(2-ethylhexyl) phthalate (DEHP), a plasticizer used widely in high volumes to provide smoothness and elasticity to polyvinyl chloride (PVC) plastics, is present in household plastics, food packaging, and medical devices. DEHP is a carcinogen and induces alterations in cellular behavior and modifications at the molecular level. In this study, we explored the effects of DEHP on head and neck cancer (HNC) progression. CAL-27 and HSC-3 cells were treated with DEHP, and MTT was performed. The desired concentration of DEHP was used, and

several biological assays were performed. Furthermore, the cells were treated with DEHP; stained with actin-phalloidin, EdU and DCFDA; and examined by confocal microscopy. The results of the MTT and proliferation assays suggest that DEHP enhances proliferation, which is supported by the increase in the number of EdU positive cells. Additionally, we observed enhanced colony formation and migration in both cell lines after treatment with DEHP. Furthermore, actin–phalloidin staining revealed the rearrangement of F-actin filaments. Additionally, we also observed that DEHP increased the intracellular ROS levels and intracellular Calcium, which provides more support for the proliferation and migration effects in both cell lines. DEHP has received significant attention because of its potential effects on human health, particularly in cancer development. Overall, the results of functional studies indicated that DEHP significantly alters cancer cell behavior.

Key words: Head and Neck Cancer, DEHP, Plasticisers, PVC, Carcinogen, Proliferation, Migration.

IACR - 764 **POSTER**

TCN2(Transcobalamin2) Deficiency as a Critical Differential Diagnosis in Young Infants with Pancytopenia, Neurological Manifestations, and Immune Dysfunction

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TCN2 deficiency (Transcobalamin II deficiency) is a rare autosomal recessive disorder of intracellular cobalamin transport. Despite normal or near-normal serum vitamin B12 levels, affected infants develop functional cobalamin deficiency leading to multisystem involvement. Young infants may present with pancytopenia, developmental delay, hypotonia or regression, recurrent infections, and failure to thrive. Neurological manifestations and immune dysfunction may precede or accompany hematologic abnormalities, often mimicking primary bone marrow failure syndromes, severe combined immunodeficiency, or inborn errors of metabolism.
Recognition of this treatable condition is crucial, particularly when macrocytosis and elevated homocysteine are present despite normal serum vitamin B12 levels. Early genetic confirmation and prompt initiation of parenteral hydroxocobalamin can result in rapid hematologic recovery and improved neurological outcomes.
TCN2 deficiency should be considered in the differential diagnosis of infants presenting with pancytopenia, neurological manifestations, and immune dysfunction, as timely therapy can be lifesaving and prevent irreversible sequelae.

Key words: Transcobalamin-2 Deficiency, Pancytopenia, Developmental Delay, Failure To Thrive, Immunodeficiency, Young Infants

IACR - 765 **POSTER**

Infantile Hypercalcemia Secondary to Subcutaneous Fat Necrosis

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Subcutaneous fat necrosis (SCFN) is a rare panniculitis of term neonates that may result in significant metabolic complications. Although the cutaneous lesions are usually self-limiting,

dysregulated calcium homeostasis due to increased extrarenal production of 1,25-dihydroxy vitamin D by activated macrophages can lead to severe hypercalcemia. We report a 40-day-old female infant with a history of meconium aspiration who presented with persistent vomiting, lethargy, and multiple firm, non-tender subcutaneous nodules over the face, trunk, neck, and thighs. Laboratory evaluation revealed severe hypercalcemia (21.5 mg/dL), elevated 1,25-dihydroxy vitamin D levels, suppressed parathyroid hormone, and normal 25-hydroxy vitamin D levels. Renal ultrasonography demonstrated bilateral medullary nephrocalcinosis. The infant was managed with intravenous hydration, loop diuretics, low-calcium feeds, and systemic corticosteroids. Serum calcium levels initially declined but rebounded during steroid tapering, necessitating prolonged therapy. This case underscores the importance of early recognition and vigilant follow-up to prevent renal complications and ensure favorable clinical outcomes.

Key words: Subcutaneous Fat Necrosis,Panniculitis, 1,25-Dihydroxy Vitamin D, Bilateral Medullary Nephrocalcinosis

IACR - 766 **POSTER**

Hepatitis A Virus Induced Severe Hemolysis in a Patient with G6PD Deficiency

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Hepatitis A virus (HAV) infection is generally self-limiting in children; however, it may be complicated by hematological manifestations such as hemolytic anemia. Glucose-6-phosphate dehydrogenase (G6PD) deficiency, an X-linked recessive enzymopathy, predisposes red blood cells to oxidative injury and acute hemolysis during infections. We report an eight-year-old male who presented with jaundice, dark urine, vomiting, and right hypochondrial pain for ten days. Examination revealed pallor, icterus, and hepatosplenomegaly without signs of hepatic encephalopathy. Laboratory evaluation showed elevated bilirubin and transaminases, markedly raised lactate dehydrogenase, hyperferritinemia, and peripheral smear evidence of hemolysis. Direct and indirect Coombs tests were negative. Hepatitis A IgM was positive, and G6PD levels were reduced, confirming underlying enzymatic deficiency. The child was managed conservatively with close monitoring, supportive care, and strict avoidance of oxidative triggers. Despite severe anemia, transfusion was avoided as hemolysis gradually subsided. Clinical and biochemical recovery occurred over four weeks. This case highlights the importance of distinguishing hepatic dysfunction from superimposed hemolysis and considering G6PD deficiency in jaundiced pediatric patients with anemia, particularly in regions where both conditions are prevalent.

Key words: G6PD-Glucose-6-Phosphate Dehydrogenase

IACR - 767 **POSTER**

Congenital Stridor due to Bilateral Vocal Cord Paralysis

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Bilateral vocal cord paralysis (BVCP) is a rare but potentially life-threatening cause of congenital stridor in neonates. It accounts for a significant proportion of congenital laryngeal

anomalies and commonly presents within the first weeks of life with stridor, weak cry, respiratory distress, and feeding difficulties. Early identification is essential to prevent airway compromise and aspiration. We report a 3-day-old term male neonate (41 weeks gestation), delivered via lower segment cesarean section to non-consanguineous healthy parents, who developed stridor and increased work of breathing immediately after birth. The infant required respiratory support with nasal continuous positive airway pressure (CPAP). Baseline investigations, including infection markers, arterial blood gas analysis, chest radiography, echocardiography, and computed tomography of the chest, were normal. Persistent symptoms despite CPAP, high-flow oxygen therapy, and non-invasive ventilation prompted further evaluation. Direct laryngoscopy and bronchoscopy confirmed bilateral vocal cord paralysis with mild laryngomalacia. Due to worsening respiratory distress and feeding difficulty, tracheostomy was performed. The postoperative course was uneventful, and the infant was discharged in stable condition. We report a 3-day-old term male neonate (41 weeks gestation), delivered via lower segment cesarean section to non-consanguineous healthy parents, who developed stridor and increased work of breathing immediately after birth. The infant required respiratory support with nasal continuous positive airway pressure (CPAP). Baseline investigations, including infection markers, arterial blood gas analysis, chest radiography, echocardiography, and computed tomography of the chest, were normal. Persistent symptoms despite CPAP, high-flow oxygen therapy, and non-invasive ventilation prompted further evaluation. Direct laryngoscopy and bronchoscopy confirmed bilateral vocal cord paralysis with mild laryngomalacia. Due to worsening respiratory distress and feeding difficulty, tracheostomy was performed. The postoperative course was uneventful, and the infant was discharged in stable condition.

Key words: Bilateral Vocal Cord Paralysis, Congenital Stridor, Stridor, Weak Cry, Respiratory Distress, CPAP, Direct Laryngoscopy, Bronchoscopy, Laryngomalacia, Tracheostomy

IACR - 768 **POSTER**

Integrated Molecular And Bioinformatic Characterization of HSA-miR-125b-5p Suggests a Tumor Suppressor Role in Cervical Cancer

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Cervical cancer is driven by molecular alterations promoting sustained proliferation and dysregulated signaling. While microRNAs are key post-transcriptional regulators, the specific contribution of hsa-miR-125b-5p to cervical carcinogenesis remains incompletely defined. Microarray profiling and TaqMan validation identified hsa-miR-125b-5p as significantly downregulated in cervical cancer cells. To evaluate viral influence, HPV-negative C33A cells were transfected with the full length HPV16 and 18 plasmids and HPV16 and 18 E6/E7 expression plasmids. An integrative multi-omics strategy prioritized targets among 430

candidate genes by fusing miRNA-target predictions, functional networks, and transcriptomic data from SiHa and HeLa cell lines. HPV oncogene expression significantly suppressed hsamiR-125b-5p, establishing a direct link between viral activity and host miRNA depletion. Bioinformatic integration prioritized high-confidence targets, including KRAS and RPS3A. Enrichment profiling revealed significant associations with the p53 signaling pathway (P = 1.10 x 10-7), MicroRNAs in cancer (P = 5.57 x 10-8), Human papilloma Virus infection (P = 0.0425) and Cell cycle (P = 2.95 x 10-5). Crucially, targets were enriched in Apoptosis (P = 5.64 x 10-12), Viral carcinogenesis (P = 0.0044) and Autophagy (P = 0.01 86). These results support a model where hsa-miR-125b-5p loss dysregulates the balance between cell survival and death. The study points that hsa-miR-125b-5p may functions as a tumor suppressor by modulating critical proliferative and survival pathways. The integration of experimental transfection data and multi-omics prioritization establishes this miRNA as a central node in the HPV-mediated remodeling of host gene expression networks.

Key words: HPV, microRNA, QRT-PCR, Systems Biology, Integrative Multi-Omics

IACR - 769 **POSTER**

Fanconi Anemia: A Rare Inherited Bone Marrow Failure Syndrome

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A 7-year-old female presented with short stature, hypoplastic thumb, generalized hyperpigmentation, and recurrent episodes of bruising and bleeding. Hematological evaluation revealed pancytopenia with anemia, leukopenia, and thrombocytopenia. The child had a history of multiple blood transfusions. Given the clinical suspicion of inherited bone marrow failure, Whole Exome Sequencing was performed, which identified a homozygous pathogenic truncating variant in the FANCA gene, confirming the diagnosis of Fanconi Anemia (FA-A). FA is a rare autosomal recessive disorder characterized by congenital malformations, progressive bone marrow failure, and cancer predisposition. Early diagnosis is crucial for surveillance and timely hematopoietic stem cell transplantation (HSCT). This case highlights the importance of recognizing phenotypic clues, bone marrow assessment and integrating genetic testing for prompt diagnosis of FA.

Key words: Hyperpigmentation, Hypoplastic Thumb, Short Stature, Bruises, Bleeding, Pancytopenia, Bone Marrow Failure, Fanconi Anemia, Hematopoietic Stem Cell Transplantation

IACR - 770 **POSTER**

Clinical Profile of Neonate Born With Edward Syndrome

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Edward syndrome (Trisomy 18) is the second most common trisomy among live births and results from the presence of an extra chromosome 18 due to nondisjunction, mosaicism, or unbalanced translocation. It is characterized by intrauterine growth restriction, small for

gestational age, severe developmental delay, craniofacial dysmorphism, overlapping fingers, rocker-bottom feet, congenital heart defects (VSD/PDA), and high perinatal mortality.
We report a 3-hour-old female neonate born at 38 weeks via LSCS to a 34-year-old mother with polyhydramnios and pregnancy-induced hypertension. The newborn presented with typical dysmorphic features including micrognathia, prominent occiput, microphthalmia, clenched hands with overlapping fingers, syndactyly of second and third toes, and rocker-bottom feet. Echocardiography revealed a large non-restrictive perimembranous VSD with bidirectional shunting, PDA, and pulmonary artery hypertension. Karyotyping confirmed 47 chromosomes with Trisomy 18.
Edwards syndrome carries a poor prognosis, with most affected infants dying within the first weeks of life due to central apnea, cardiac failure, or respiratory complications. This case highlights the importance of early clinical recognition, cardiac evaluation, and cytogenetic confirmation. Prenatal diagnosis and timely parental counselling remain crucial for appropriate management and decision-making.

Key words: Trisomy, Dysmorphism, Prominent Occiput, Iugr, Sga, Rocker Bottom Foot, VSD, PDA, Karyotyping, Counselling

IACR - 771 **POSTER**

Eruptive Xanthomas as the Initial Manifestation of Severe Familial Hypercholesterolemia in a 3-Year-Old Child

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Eruptive xanthomas are uncommon in early childhood and usually indicate a severe underlying disorder of lipid metabolism. Early recognition is essential, as inherited dyslipidemias are associated with accelerated atherosclerosis and premature cardiovascular disease.
Case Presentation: We report a 3-year-old male child who presented with multiple yellowish, papular lesions over the extensor surfaces, clinically consistent with eruptive xanthomas. The child had normal growth and developmental milestones and no systemic symptoms. Lipid profile revealed markedly elevated total cholesterol of 951 mg/dL and low-density lipoprotein cholesterol (LDL-C) of 849 mg/dL, with triglycerides of 198 mg/dL and high-density lipoprotein cholesterol (HDL-C) of 32 mg/dL. Family history was significant for premature cardiovascular disease in the father, raising strong suspicion of an inherited lipid disorder.
Conclusion: The extreme elevation of LDL cholesterol in a young child, along with characteristic cutaneous manifestations and a positive family history, strongly suggests severe familial hypercholesterolemia, possibly homozygous in nature. This case highlights the importance of recognizing eruptive xanthomas as an early clinical marker of severe dyslipidemia in children. Prompt diagnosis, family screening, and early initiation of appropriate lipid-lowering strategies are crucial to reduce long-term cardiovascular morbidity and mortality.

Key words: Eruptive Xanthoma, familial Hypercholesterolemia

Bilateral Frontoparietal Polymicrogyria Associated with ADGRG1 Mutation: A Rare Case Report

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Mutations in the ADGRG1 gene (also known as GPR56) is associated with several neurological and developmental disorders, most notably bilateral frontoparietal polymicrogyria (BFPP). Bilateral frontoparietal polymicrogyria is a severe form of polymicrogyria. BFPP is a neuronal migration defect mainly characterized by severe mental retardation, motor developmental delay, language difficulties, seizures, dysconjugate gaze, ataxia, bilateral polymicrogyria (cobblestone malformation) with anterior to posterior gradient, bilateral patchy white matter signal changes, and brainstem and cerebellar hypoplasia.

Case description: A 16 months old female, born to consanguineous parents presented with delay in achieving milestones. On detailed examination, the child had global developmental delay along with hypotonia and hyporeflexia. MRI Brain was suggestive of bilateral cerebral hemispheres showing simplified gyral pattern, with microlobulated surface suggestive of Type 2 lissencephaly along with dysmyelination and hypoplastic pons with kinked brainstem, prominent ventricular system & extra axial spaces.

Genetic analysis revealed pathogenic variant of ADGRG1 gene.

Conclusion: Early diagnosis through neuroimaging and genetic testing facilitates targeted management, including seizure control, developmental support, and rehabilitation. Multidisciplinary care remains essential in improving the quality of life for individuals with polymicrogyria.

Key words: Mutation in ADGRG1 Mutation

Prevalence of Colistin Resistance among Carbapenem Resistant Gram-Negative Isolates in a Tertiary Care Hospital in Kashmir Valley using Colistin Broth Disc Elution (CBDE) and Colistin Agar Test (CAT)

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Antimicrobial resistance (AMR) is an escalating global health threat, with Asia—particularly India—emerging as a major hotspot. Carbapenems have long been considered the last-resort antibiotics for treating infections caused by multidrug-resistant Gram-negative bacteria; however, the increasing prevalence of carbapenem-resistant organisms (CROs) has significantly compromised their effectiveness. In response, colistin has re-emerged as a critical therapeutic option for such infections. Alarmingly, resistance to colistin is also rising, posing a serious challenge to clinicians and further limiting available treatment options. Detection of colistin resistance remains problematic, as the reference method, broth microdilution (BMD), recommended by CLSI, is technically demanding, labor-intensive, and often not feasible in routine diagnostic laboratories, especially in resource-limited settings. This study aims to determine the prevalence of colistin resistance among carbapenem-resistant Gram-negative isolates obtained from clinical specimens in a tertiary care hospital in the Kashmir Valley. Additionally, it evaluates the utility of two alternative, cost-effective phenotypic methods—Colistin Broth Disc Elution (CBDE) and Colistin Agar Test (CAT)—for the detection of

colistin resistance. The findings of this study are expected to provide valuable local epidemiological data and assess the feasibility of implementing these alternative methods in routine microbiology laboratories, thereby aiding in timely detection of resistance and strengthening antimicrobial stewardship efforts.

Key words: CBDE-Colistin Broth Disc Elution, CAT-Colistin Agar Test, CRE-Carbapenem Resistant Enterobacterales, MDR-GNB-Multi-Drug-Resistant Gram-Negative Bacilli, CRPA-Carbapenem Resistant *Pseudomonas Aeruginosa*

IACR - 774 **POSTER**

The Hartnup's Disease

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Hartnup disease is a rare autosomal recessive disorder caused by mutations in the SLC6A19 gene, resulting in impaired transport of neutral amino acids in the intestine and renal proximal tubules. This leads to neutral aminoaciduria and secondary niacin deficiency, producing pellagra-like dermatological and neurological manifestations. We report a 14-year-old male, born to a non-consanguineous marriage, who presented with progressive abdominal distension and chronic diarrhea since 3 years of age. He developed seizures at 4 years and was on antiepileptic therapy. On examination, he had short stature, massive splenomegaly, ascites, cerebellar ataxia, and photosensitive dermatitis, with preserved cognition. MRI brain showed right hippocampal atrophy. Based on clinical suspicion of a neutral amino acid transport defect, genetic testing was performed. Clinical exome sequencing revealed a pathogenic SLC6A19 mutation, confirming the diagnosis of Hartnup disease. The patient was managed with oral niacin supplementation and a high-proteindiet, following which improvement was noted in dermatological and gastrointestinal symptoms with stabilization of neurological features. This case highlights the importance of considering Hartnup disease in children with chronic diarrhea and neurocutaneous manifestations, even in the absence of consanguinity.

Key words: Hartnup's Disease, SLC6A19, Neutral Aminoaciduria, Pellagra-Like Dermatitis, Niacin Deficiency, Adolescent

IACR - 775 **POSTER**

Clinical and Genetic Characterization of Mitochondrial DNA Depletion Syndrome: Identification of Pathogenic Mutation and its Phenotypic Correlation in Pediatric Patients

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Mitochondrial DNA depletion syndrome (MDDS) is a heterogeneous group of autosomal recessive disorders characterized by a significant reduction in mitochondrial DNA (mtDNA) copy number in affected tissues, leading to impaired oxidative phosphorylation. These disorders primarily affect organs with high energy demands, including the brain, liver, and skeletal muscles. Early diagnosis is essential for prognostication, genetic counseling, and management.
The objective is to identify and characterize the pathogenic mutation responsible for mitochondrial DNA depletion syndrome and to correlate genetic findings with clinical presentation.
Genetic analysis revealing a pathogenic mutation in a nuclear gene associated with mitochondrial DNA maintenance, confirming the diagnosis of mitochondrial DNA depletion syndrome. The mutation resulting in impaired mtDNA replication, leading to reduced mtDNA copy number and defective mitochondrial respiratory chain function. Clinical features correlated with known phenotypic manifestations of MDDS.

Key words: Mitochondrial Disorder, Whole Exome Sequencing, Autosomal Recessive Disorder, Mitochondrial Dysfunction, Pediatric Metabolic Disorder, Inborn Error of Metabolism

IACR - 776 **POSTER**

Biotinidase Deficiency: A Rare Treatable Neurocutaneous Disorder

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Biotinidase deficiency (BTD) is a rare autosomal recessive neurometabolic disorder with an incidence of approximately 1:60,000, characterized by impaired recycling of biotin, an essential cofactor for carboxylase enzymes involved in gluconeogenesis, amino acid metabolism, and fatty acid synthesis. We report a case of a 2-month-old male infant, born of a consanguineous marriage, who presented with decreased feeding, irritability, lethargy, metabolic acidosis, and skin rash. Arterial blood gas analysis revealed severe metabolic acidosis. Laboratory investigations showed hyperammonemia and elevated lactate levels. Tandem mass spectrometry (TMS) demonstrated increased hydroxyisovaleryl carnitine and free acylcarnitine, while urine GCMS revealed elevated 3-hydroxyisovaleric acid, confirming biotinidase deficiency. The infant required ventilatory support and peritoneal dialysis for persistent acidosis. Oral biotin therapy (10 mg/day) was initiated, with advice for lifelong supplementation and parental genetic counseling.
BTD, though rare, is a treatable cause of acute neonatal encephalopathy. Early recognition, newborn screening, and prompt biotin supplementation are crucial to prevent irreversible neurological sequelae and reduce long-term morbidity and mortality

Key words: BTD-Biotinidase Deficiency

IACR - 777 **POSTER**

Impact of Traditional Fermentation and Agro-Climatic Variation on Arecoline Content in Betel Nut And its Association with Site-Specific Cancer Patterns in Northeast India

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In Northeast India, especially Assam, chewing areca nut is more than a habit, it is part of daily life and cultural identity. However, arecoline, the major alkaloid present in areca nut, is a known carcinogenic compound. This study examines how traditional fermentation practices and regional environmental differences influence arecoline levels and how these variations may relate to site-specific cancer patterns in the population. Areca nut samples were collected from six agro-climatic zones of Assam and analyzed for arecoline content using High-Performance Liquid Chromatography (HPLC). Following methanolic extraction, fermented nuts were found to contain nearly four times higher arecoline levels than raw or dried forms. These findings suggest that microbial and enzymatic processes during fermentation significantly increase arecoline concentration. Variations observed across regions further indicate that local environmental conditions, including soil characteristics, may influence alkaloid levels.To understand clinical relevance, a dietary and lifestyle survey was conducted among 187 cancer patients (81 women and 106 men). Multivariate linear regression analysis revealed a strong association between habitual areca nut consumption, particularly fermented forms and certain localized cancers. Among women, raw areca nut use was linked with cervical and ovarian cancers, while in men, combined use with tobacco and alcohol was strongly associated with oral and esophageal cancers. These findings highlight the need for culturally sensitive public health strategies and deeper molecular research to clarify how arecoline exposure contributes to cancer risk in this high-consumption region.

Key words: Agro-Climatic Variation; Cancer; Arecoline; Fermentation; Betel Nut; NER; HPLC

IACR - 778 **POSTER**

Neonatal Diabetes Mellitus

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Neonatal diabetes mellitus (NDM) is a rare but serious form of diabetes that presents within the first 6 months of life. The global incidence of NDM is relatively small, estimated to be between 1 in 90,000 to 1 in 160,000 live births. In contrast to the more prevalent autoimmune-mediated Type 1 diabetes mellitus, NDM is nonautoimmune, caused by monogenic mutations. **Case presentation:** A 28-day-old term male infant (37 weeks, 2600 g) admitted for acute bronchiolitis was incidentally found to have persistent hyperglycemia (>350 mg/dL). There was no history of gestational diabetes, parenteral nutrition, or sepsis. He had no dysmorphism, metabolic acidosis or ketonuria. Investigations showed low C-peptide (0.34 ng/mL), normal HbA1c for age, negative type 1 diabetes autoantibodies, and normal thyroid/adrenal evaluation. Family history was negative. The baby was put on appropriate dose subcutaneous insulin. Despite initiation of subcutaneous insulin, hyperglycemia persisted. Subsequently diagnosis of

neonatal diabetes mellitus was considered, given the early onset persistent hyperglycemia with low endogenous insulin and absence of autoimmunity. Whole exome sequencing revealed a heterozygous missense variant in the ABCC8 gene (c.4567G>A; p.Val1523Met), consistent with sulfonylurea responsive neonatal diabetes mellitus. Following initiation of oral glibenclamide, blood glucose levels normalized. Insulin was gradually tapered and stopped. The excellent response to sulfonylurea strongly supports KATP-channel related neonatal diabetes, most likely ABCC8-related neonatal diabetes mellitus.

Key words: Neonatal Diabetes Mellitus, ABCC8 Mutation, KATP Channel, Sulfonylurea Therapy, Glibenclamide, Monogenic Diabetes

IACR - 779 **POSTER**

Neonatal Craniosynostosis and Choanal Atresia: A Severe Presentation of Crouzon Syndrome

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Crouzon syndrome is a rare autosomal dominant craniosynostosis caused by mutations in fibroblast growth factor receptor genes, most commonly FGFR2 and occasionally FGFR3. It is characterized by premature cranial suture fusion, midface hypoplasia, and ocular proptosis. Neonatal airway compromise is uncommon but may be life-threatening, particularly when associated with choanal atresia. We highlight the importance of early recognition of craniofacial dysmorphism in neonates presenting with respiratory distress. Prompt imaging, including CT with 3D reconstruction, aids in identifying suture involvement and airway anomalies. Genetic confirmation through FGFR mutation analysis establishes the diagnosis and facilitates prognostication and family counseling. Early multidisciplinary management involving neonatology, otolaryngology, and craniofacial surgery is crucial for airway stabilization and planning definitive interventions. This case underscores that, although rare, neonatal presentation of Crouzon syndrome with airway obstruction requires a high index of suspicion and timely coordinated care to reduce morbidity and improve outcomes.

Key words: Crouzon Syndrome, Craniosynostosis, FGFR2 Mutation, autosomal Dominant, choanal Atresia

IACR - 780 **POSTER**

Molecular and Cellular Characterization of Translin and its Clinically Relevant Mutations

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Translin is a conserved nucleic acid–binding protein involved in RNA regulation, genome stability, and cellular stress responses; however, the structural consequences of cancer-associated mutations and the temporal dynamics of wild-type Translin localization remain

incompletely defined. In this study, we integrated in silico structural analysis with in vivo cellular investigations to examine mutation-induced perturbations and stress-dependent translocation behavior. Computational evaluation of selected cancer-associated variants reported in the COSMIC database revealed alterations within the OB-fold domain, predicting changes in protein stability, conformational flexibility, and structural integrity. These findings suggest that previously unclassified mutations may affect nucleic acid binding interfaces and potentially impair functional activity. To investigate physiological responses to genotoxic stress (2 Gy radiation), we assessed time-dependent expression and subcellular localization of wild-type Translin in A549, HEK293, HCT116, and U2OS cell lines using immunofluorescence microscopy and western blotting. Our results demonstrate that Translin translocation is strongly time-dependent and markedly cell type–specific, with distinct and in some cases opposing patterns of nuclear–cytoplasmic redistribution and expression dynamics. Collectively, this study highlights how structural variability and cellular context modulate Translin function, advancing understanding of its role in DNA/RNA-associated pathways and cancer-related cellular processes.

Key words: Translin; Cancer-Associated Mutations; Cosmic Database; OB-Fold Domain; Protein Stability; Genotoxic Stress; Nuclear Cytoplasmic Translocation; Cell Type Specific Regulation

IACR - 781 **POSTER**

Development of a Tumor-Activatable Chrysin-Cisplatin Pt(IV) Prodrug for Enhanced DNA Damage, Inhibition of DNA Damage Tolerance, and Targeting of Ovarian Cancer Stem Cells

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Cisplatin is a frontline chemotherapeutic for ovarian cancer, but its clinical efficacy is limited by chemoresistance driven by cancer stem-like cells (CSCs) and translesion DNA synthesis mediated by DNA polymerase eta (Pol η). To address this, we developed rationally designed chrysin–cisplatin conjugates in Pt(II) and Pt(IV) forms to combine DNA damage induction with inhibition of DNA damage tolerance. The Pt-IV conjugate exhibited enhanced stability under physiological conditions and preferential activation under reductive and acidic environments, enabling controlled release of chrysin in tumor-like conditions. Functional studies demonstrated strong cytotoxicity in both cisplatin-sensitive and resistant ovarian cancer cell lines, associated with downregulation of Pol η, increased DNA damage, and apoptosis induction. Notably, Pt-IV significantly reduced CSC populations, evidenced by decreased $CD44^{+}/CD117^{+}$ fractions and disruption of CSC-enriched spheroids. In vitro 3D microtumor models confirmed its ability to penetrate tumor-like structures, induce DNA damage, and inhibit proliferation. In vivo xenograft studies further demonstrated superior antitumor efficacy compared to cisplatin, along with effective CSC depletion and minimal systemic toxicity. Collectively, these findings establish the chrysin-cisplatin Pt-IV conjugate as a promising dual-action prodrug capable of enhancing platinum efficacy by inducing DNA damage and suppressing repair pathways, thereby overcoming chemoresistance in ovarian cancer.

Key words: Platinum Prodrug, Chrysin, Cisplatin Resistance, Ovarian Cancer, Cancer Stem Cells, DNA Polymerase Eta, Translesion DNA Synthesis, Pt(IV) Prodrug, DNA Damage, Chemoresistance, Tumor Xenograft, 3D Microtumor Model

IACR - 782 **POSTER**

Clinical Presentation of Wilsons Disease -A Case Report

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Introduction: Wilson's disease is a rare Autosomal recessive disease causes by mutation in ATP7B gene. The disease is characterized by defective copper excretion leading to deposition in Liver, Kidneys, Brain, and Corneas.
Case Presentation: A 16 year old female presented with behavioral changes and difficulty in walking. On examination patient had shuffling gait, mask like face, dysarthria and presence of Keyser-Fleischer rings. Lab investigations revealed Low serum Ceruloplasmin levels (<9.58 mg/dl) and high 24 hour urinary copper (169mcg/day). Liver showed coarse nodular echotexture on USG and MRI Brain revealed T2/FLAIR hyperintensities in bilateral Thalami showing diffusion restriction and blooming foci in bilateral Putamen and Globus Pallidus.
Conclusion: There should be high suspicion of Wilson's disease when a patient presents with symptoms like ataxia, Dysarthria, behavioral changes etc. Early diagnosis and treatment can reverse symptoms and prevent disease progression.

Key words: Wilsons Disease an Autosomal Recessive Disease with ATP7B Generate Mutation which Leads to Decreased Excretion of Copper and its Accumulation in Liver Kidneys, Brain and Cornea. Early Diagnosis and Treatment can Reverse Symptoms and Prevent Disease Progress

IACR - 783 **POSTER**

CARMIL-2 Associated Immunodeficiency Presenting with Recurrent Oesophageal Candidiasis and Strictures in a Paediatric Patient

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Background: CARMIL-2 (RLTPR) deficiency is a rare autosomal recessive combined immunodeficiency caused by impaired CD28-mediated T-cell co-stimulation, leading to defective cellular immunity and susceptibility to recurrent infections, particularly chronic mucocutaneous candidiasis. **Case Presentation:** We describe a pediatric patient presenting with recurrent dysphagia and failure to thrive due to persistent esophageal candidiasis complicated by progressive esophageal strictures requiring repeated endoscopic dilatations. The child had a history of recurrent mucocutaneous fungal infections and intermittent respiratory illnesses since early childhood. Immunological evaluation revealed T-cell dysfunction with impaired activation. Genetic testing confirmed a pathogenic variant consistent with CARMIL-2 deficiency. Secondary causes of immunosuppression were excluded. **Management and Conclusion:** The patient required prolonged systemic antifungal therapy, nutritional rehabilitation, and endoscopic management of strictures, along with

institution of infection prophylaxis and immunologic follow-up. This case highlights the importance of considering primary immunodeficiency in children with refractory or recurrent esophageal candidiasis and structural complications. Early diagnosis of CARMIL-2 deficiency enables appropriate immunologic management and genetic counseling, reducing long-term morbidity.

Key words: CARMIL-2 Deficiency, RLTPR, Immunodeficiency, Recurrent Esophageal Candidiasis, Failure to Thrive, Esophageal Strictures

IACR - 784 **POSTER**

Pharmacogenetic Profiling of ARID5B Intronic Variant and Methotrexate Response in Acute Lymphoblastic Leukemia Patients

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High-dose methotrexate (HD-MTX) is a key component of acute lymphoblastic leukemia (ALL) therapy but shows marked inter-patient variability in pharmacokinetics, toxicity, and treatment response. Genetic variants in *ARID5B*, a transcriptional regulator implicated in ALL susceptibility and methotrexate sensitivity, may contribute to this heterogeneity, though data from Indian populations remains limited. A pilot cohort of 44 ALL patients and 26 age matched healthy controls was recruited following institutional ethical approval. Genomic DNA was isolated from peripheral blood, and the *ARID5B* rs10821936 (C>T) intronic variant was genotyped using PCR-RFLP and validated by Sanger sequencing. Plasma methotrexate concentrations were measured at 24, 48, and 72 hours post-HD-MTX using competitive ELISA in a subset of patients. Clinical parameters, Treatment-related toxicities and early outcomes were documented. Genotype distribution among ALL patients was CC 36.4%, CT 50%, and TT 13.6%, with 100% concordance between RFLP and sequencing results. Mean plasma MTX levels declined from 1.8 ± 0.4 µmol/L at 24 h to <0.1 µmol/L at 72 h in most patients. Clinically significant toxicities included hepatotoxicity (11.3%), grade ≥3 myelosuppression (6.8%), and transient nephrotoxicity (4.5%). A higher proportion of relapse/refractory cases was observed among patients carrying the heterozygous CT genotype, though statistical association analysis is ongoing. This preliminary study demonstrates the feasibility of *ARID5B* pharmacogenetic profiling and methotrexate pharmacokinetic monitoring in ALL cohort. Early trends suggest a potential role of rs10821936 in treatment response variability, warranting expanded analyses incorporating additional ARID5B variants, isoform-specific expression, and epigenetic profiling.

Key words: Acute Lymphoblastic Leukemia, Pharmacogenomics, Genetic Variants, Hematological Malignancies

IACR - 785 **POSTER**

Integrated Network Analysis Identifies PBK Overexpression Increases the Risk of Crohn's Disease to Colorectal Cancer

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Chronic intestinal inflammation is one of the established risk factors for colorectal cancer. Inflammatory bowel diseases and Serrated polyps increase CRC risk; however, the key molecular drivers linking these conditions to tumor progression remain poorly understood.
RNA-sequencing datasets were obtained from the Gene Expression Omnibus, GSE67250 (Crohn's disease), GSE102746 (Ulcerative Colitis), and GSE76987 (Sessile Serrated Polyps). Differential expression analysis was performed in GEO2R using a DESeq2-based pipeline with padj <0.05 and log2FC ≥ 1 as the threshold value. Top 500 significant DEGs from each dataset were integrated and analyzed through STRING and Cytoscape hub gene analysis, with pathway enrichment using ShinyGO and biological validation via web-based tools. The PBK gene was identified as a top-ranked hub gene enriched in inflammatory and proliferative pathways and was significantly upregulated in Crohn's Disease (log2FC 4.09). Validation in TCGA and GEPIA databases showed elevated PBK expression in CRC, with relative hypomethylated promoter. High PBK expression was significantly associated with reduced overall survival in the KM plot. Network analysis showed interaction with ZBTB26 and TP53, suggesting its involvement in tumorigenesis. PBK has emerged as a link that may contribute to the progression of Crohn's disease to CRC and may serve as a potential candidate biomarker.

Key words: Inflammatory Bowel Disease, Crohn's Disease, CRC, PBK, Network Analysis

IACR - 786 **POSTER**

Glutamine as a Metabolic Marker for Predicting Cisplatin Response in Cervical Cancer Cohorts

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Reprogrammed one-carbon and amino acid metabolism is essential for cancer sustenance. Glutamine metabolism has emerged as a key oncogenic hallmark, supplying carbon for TCA cycle anapleurosis and nitrogen for amino acid and nucleotide biosynthesis. Cisplatin-treated cancer cells become metabolically vulnerable and increasingly glutamine-dependent. Enhanced intracellular glutamine metabolism elevates glutathione (GSH) levels, mitigating cisplatin-induced mitochondrial ROS and contributing to chemoresistance. This study evaluated the correlation between glutamine/glutamate and GSH levels in blood, cervico-vaginal fluid (CVF), and tumor tissues across clinically annotated stages of invasive cervical cancer, and assessed the association between tissue GSH–cisplatin binding efficiency and systemic glutamine/glutamate levels.
Quantification of glutamine and glutamate in blood and CVF before and after concurrent chemoradiotherapy (CCRT), measurement of tissue GSH, platinum accumulation, cisplatin–GSH conjugates, and cisplatin–DNA adducts, correlated with systemic glutamine/glutamate

level, analysis of glutamine transporter (SLC1A5, SLC7A5) expression by immunofluorescence and flow cytometry.
Plasma glutamine levels were significantly higher than CVF levels. Stage-specific increases in GSH were observed in both plasma and CVF, while glutamine levels peaked at stage IIB compared to stages III and IV. Expression of glutamine transporters SLC1A5 and SLC7A5 was markedly elevated in advanced stages relative to Stage 0.
This proof-of-concept study suggests that glutamine metabolism and its regulatory components may critically influence cisplatin response in cervical cancer. Targeting glutamine metabolism warrants further investigation as a potential therapeutic strategy. Glutamine metabolism thus represents a promising therapeutic target in cancer management.

Key words: Cervical Cancer, Glutamine Transporter, Cisplatin Resistance

IACR - 787 **POSTER**

Mechanistic Insights into the Perioperative Cortisol-glucocorticoid-Receptor-AURKA Axis in Breast Cancer Progression

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Breast cancer (BC) incidence is rising globally, necessitating novel therapeutic targets, particularly for non-luminal subtypes refractory to ER/PR-directed therapies. Cortisol dysregulation in BC implicates the glucocorticoid receptor (GR) as a key signalling mediator through its crosstalk with prognostically relevant kinases. A reported association between GR and Aurora Kinase A (AURKA) prompted evaluation of this axis in BC. The perioperative period represents a brief yet critical window with potential long-term impact on disease progression. This study therefore investigated the functional relevance of the cortisol/GR/AURKA axis in breast cancer during the perioperative period.
Perioperative plasma cortisol levels in BC patients and healthy volunteers were quantified using ELISA and LC–MS, alongside histopathological characterization and GR expression analysis. Cortisol-induced effects on tumor aggressiveness were assessed using *in vitro* sphere formation, migration, and cell-viability assays. AURKA expression was evaluated *ex vivo* and *in vitro* using flow cytometry, immunoblotting, and immunofluorescence. GR–AURKA co-localization and interaction were examined by immunofluorescence and co-immunoprecipitation. GR occupancy at the AURKA promoter was assessed by chromatin immunoprecipitation, and functional interaction was validated using *in vitro* kinase assays.
GR transcriptionally regulated AURKA and physically interacted with its active phosphorylated form. Perioperative plasma cortisol levels were significantly elevated in breast carcinoma patients compared with healthy controls, indicating cortisol-mediated GR activation. This activation was associated with increased AURKA expression, supporting the functional relevance of the cortisol/GR/AURKA axis in BC. Cortisol-driven GR/AURKA axis contributes to breast cancer progression and is preferentially activated during the perioperative

period, identifying this pathway as a potential perioperative therapeutic target to improve clinical outcomes.

Key words: Breast Cancer, Glucocorticoid Receptor (GR), AURKA, Stress

IACR - 788 **POSTER**

Mitochondrial TERT Accumulation as a Prognostic Marker in HER^{2+}/EGFR-Driven Breast Cancer

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HER2-enriched, EGFR-positive breast cancer represents a distinct and aggressive molecular subtype of HER2-positive disease, accounting for roughly 15–20% of all breast cancers, and is defined by the concurrent overexpression of HER2 and EGFR, which contributes to an elevated propensity for metastatic progression. Therefore, exploring the underlying mechanisms of resistance in HER2-targeted therapy is a need of the hour. The present study focuses on the impact of altered mitochondrial dynamics due to TERT localization among HER2/EGFR overexpressed patients on aggressiveness of the disease.

HER2 enriched breast cancer patients were recruited in the study (n=35) after signing proper informed consent form. Paraffin-embedded tissue blocks were sectioned for H&E staining, immunofluorescence (IF), immunohistochemistry study (IHC) and real-time qPCR. Corresponding biochemical parameters were assessed. Lymph node status of each patient was recorded. Expression of TERT, AURKA, EGFR, mTOR were checked in mitochondrial, cytosol as well as nuclear fraction. EMT and metastatic markers were observed. Fusion and fission markers were checked to determine mitochondrial dynamics. HER2 enriched chemo-immunotherapy resistance patients tissue transcriptome analysis was done to identify relevant markers.

TERT predominantly localized in HER2/EGFR-positive tumors compared to those with low EGFR expression. In EGFR-overexpressing cases, elevated levels of mTOR, AURKA, and markers of metastasis and EMT were observed. High EGFR expression also correlated with increased mitochondrial fission. Results from IF, Western blot, qPCR, and IHC analyses further indicated a positive association with lymph node involvement and therapeutic response, though treatment is still ongoing.

HER2-positive, EGFR-overexpressing patients exhibited elevated mitochondrial TERT, a feature associated with poor prognosis.

Key words: HER2 Positive Breast Cancer, EGFR, mTOR, AURKA, EMT, Mitochondrial TERT, Mitochondrial Dynamics

IACR - 789 **POSTER**

Lipin-1 Plays a Role in Mitotic Progression and is regulated by DBC1-SIRT1 Axis during Adipogenesis

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Lipins are conserved proteins that plays a significant role in various cellular processes like lipid metabolism, nerve functions, lipolysis and insulin resistance. In mammals, lipin family includes 3 members: lipin-1, lipin-2 and lipin-3. Among these lipin-1 is the most well studied member because of its versatile functions. The most prominent functions of lipin-1 are: i) its role in the regulation of triglycerides and phospholipid biosynthesis through its phosphatidic acid phosphatase (PAP) activity and ii) as a transcriptional co-activator by regulating the expression of several genes involved in lipid metabolism. Our recent studies have shown that lipin-1 is phosphorylated and regulated by the mitotic kinase, PLK1. Interestingly, our results revealed that lipin-1 undergoes phosphorylation changes during the mitosis and is localized to the centrosomes. In addition, lipin-1 is known to play a major role in the differentiation of 3T3-L1 preadipocytes into adipocytes. DBC-1, an inhibitor of SIRT1 deacetylase, also plays a crucial role in adipogenesis. Our results also showed that expression of DBC1 leads to the elevated acetylation levels of lipin-1and hence its stabilization by inhibiting SIRT1. In summary, our study reveal a novel role of lipin-1 in mitosis and the regulation of its adipogenic activity by DBC1/SIRT1.

Key words: Lipin, DBC1, SIRT1, Adipogenesis, Mitosis

IACR - 790 **POSTER**

Sustainable Utilization of Soy Whey in Pineapple Juice Formulation for Enhancement in Antioxidant, Antidiabetic, and Antiproliferative Potential

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The current investigation assessed the antiproliferative, antioxidant, and antidiabetic properties of soy whey-fortified pineapple juice beverages fabricated as a value-added nutraceutical rich drink. The soy whey was incorporated at 10%, 20%, and 30% (v/v) levels into freshly extracted pineapple juice. Soy whey fortification considerably enhanced the total phenolic content (TPC) from 49.4 ± 1.2 to 55.7 ± 2.6 mg GAE/100 mL and total flavonoid content (TFC) from 27.8 ± 0.9 to 38.3 ± 1.4 mg QE/100 mL at 30% soy whey incorporation. Antioxidant activity improved significantly, with DPPH activity increased from 30.6 ± 1.8% (control) to 49.9 ± 1.5% for fortified samples, while as ABTS inhibition improved from 29.3 ± 2.1% to 45.4 ± 1.7% respectively. The fortified beverages represented significant α-amylase and α-glucosidase inhibition activities, reaching 29.5 ± 1.6% and 30.2 ± 1.9% inhibition, respectively, compared to 18.7 ± 1.3% and 20.5 ± 1.5% for control samples. In vitro antiproliferative potential against MCF-7 breast cancer cells showed dose-dependent inhibition, with the 30% fortified beverage sample exhibited 28.6 ± 2.4% inhibition at 200 µg/mL concentration as compared to 19.3 ± 1.8% in control sample. The present investigation demonstrate that soy whey fortification considerably enhanced the nutraceutical potential of pineapple juice and offers a sustainable

approach for emerging nutraceutical beverages targeting oxidative stress, diabetes, and cancer risk reduction.

Key words: Beverages; Soy Whey; Sustainability; Antidiabetic Potential; Antioxidant Activity, Anti-Cancerous

IACR - 791 **POSTER**

SProgel, a Versatile Protein Biopolymer Supporting 3D Cell Growth: Potential Implications in Tumor Microenvironment Studies

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The tumor microenvironment (TME) plays a critical role in cancer progression. Tumor cells alone are not solely responsible for metastasis; rather, dynamic interactions between tumor cells and surrounding stromal and immune components significantly influence tumor initiation, progression, and metastatic spread. Among the key cellular constituents of the TME are macrophages, commonly referred to as tumor-associated macrophages (TAMs). Extensive research has identified TAMs as major promoters of metastasis, orchestrating multiple processes that facilitate tumor progression. A comprehensive understanding of these interactions requires experimental models that closely replicate *in-vivo* conditions. Three-dimensional (3D) cell culture systems have emerged as a transformative approach, offering enhanced physiological relevance and improved representation of native tissue architecture compared to conventional 2D cultures. However, existing 3D culture techniques are often complex, labour-intensive, and time-consuming, which can hinder rapid biomedical investigations. To address these limitations, we propose SProgel, a protein-based biopolymer that functions as a stable and versatile substrate for 3D cell growth. SProgel maintains physiological stability over extended durations and supports diverse applications in medical and biotechnological research. In the present study, SProgel is utilized to establish a 3D co-culture system of cancer cells and macrophages to effectively mimic the tumor microenvironment. Furthermore, the expression of specific TAM markers is being investigated to understand the factors and stimuli that drive TAM polarization and formation. This platform offers a novel and promising strategy for studying tumor–immune interactions and may contribute to the development of targeted immunotherapeutic approaches.

Key words: 3d Cell Culture, Protein Biopolymer, Tumor Microenvironment, Tumour Associated Macrophages (TAMs)

IACR - 792 **POSTER**

MicroRNA Cluster–Mediated Control of PDK3 Drives Metabolic Plasticity and EMT in Cervical Cancer

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Cervical cancer is a major health burden worldwide, and its pathogenesis is closely associated with changes in molecular and metabolic pathways. The coordinated impact of large miRNA clusters has not been thoroughly studied, even though several studies have examined individual miRNAs for the treatment of cervical cancer. Our previous study revealed that the expression of the chromosome 14 microRNA cluster (C14MC), one of the largest imprinted miRNA clusters in humans, was significantly decreased in patients with cervical cancer. PDK3, a metabolic kinase whose expression is increased in cervical cancer tissues and cell lines, was strongly inversely correlated with C14MC expression. Studies have shown that PDK3 overexpression drives EMT in many other cancers via ERK/STAT signaling. Hence, the current study is designed to elucidate the role of the C14MC–PDK3 axis in metabolic reprogramming and EMT-associated progression in cervical cancer. CRISPR-based activation was used to restore C14MC expression in cervical cancer cell lines. To assess tumorigenic qualities, biological assays were conducted. Downstream targets were identified by transcriptomic profiling. Luciferase reporter assays and protein analysis were used to evaluate the interaction between PDK3 and these proteins. Metabolic alterations were checked using fluorescence dye-based confocal microscopy. EGF-induced EMT was validated by cytoskeleton staining and EMT marker analysis. C14MC activation repressed PDK3 expression and dramatically reduced proliferation and invasion. Metabolic investigations revealed improved mitochondrial efficiency, reflecting improvements in morphology, membrane potential, cellular stress, and other properties. EMT induction in the cells resulted in cytoskeletal remodeling and mesenchymal marker alteration, indicating a connection between metabolic and phenotypic changes. The C14MC-PDK3 regulatory axis is essential for controlling metabolic plasticity and EMT-driven aggressiveness in cervical cancer and is a potential target for therapeutic intervention.

Keywords: Cervical cancer, MicroRNA, CRISPR, Mitochondria, EMT

IACR - 793 **POSTER**

Comparative analysis to identify key genes in invasive ductal carcinoma using dimensionality reduction approach

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Invasive Ductal Carcinoma (IDC), the most prevalent histological subtype, arises in the lactiferous ducts and penetrates the surrounding mammary parenchyma. Consequently, it remains a leading cause of oncological mortality globally, characterized by profound biological diversity that dictates clinical progression. For molecular diagnostics, high-throughput microarray and transcriptomic profiling are utilized but these are characterized by high dimensionality. Therefore, employing dimensionality reduction (DR) methods such as PCA, LASSO and RFE becomes essential for retaining the significant features (genes) while mitigating the noise. PCA is used for feature extraction and involves transformation of correlated variables into a smaller set of uncorrelated variables called principal components

while preserving maximum variance. LASSO method which employs L1 regularization which shrinks the magnitude of non-contributing coefficients to zero retaining only the significant features. The TCGA dataset used in the analysis has 1231 samples (37 normal vs 1194 Invasive ductal carcinoma) that contain expression 60660 genes. PCA analysis shows 58% of total cumulative variance in the dataset. Top 50 variable genes were identified from 1231 samples. Among the top variable genes, carboxypeptidase B1 (CPB1), collagen 1A1 and collagen 1A2 were identified. As collagen is a major structural component of extracellular matrix (ECM) that is an important part of the tumor microenvironment and plays critical roles in cancer development and metastasis. This study helped to identify key genes playing a role in progression of invasive ductal carcinoma using dimensionality reduction approach.

Key Words: Invasive Ductal Carcinoma (IDC), Extracellular matrix (ECM), Dimensionality reduction (DR)

IACR – 794 **POSTER**

Landscaping of Rare Genetic Disorders in a highly consanguineous and endogamous Population of Kashmir

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Background: Genetic screening remains conclusive and confirmative diagnosis for more than 5000 rare genetic disorders (RGDs). Home to a large customarily consanguineous inbred population, our region has resulted in a melting pot of conservative genetic pool to build up pathogenic genetic variations. The diagnostic ambiguity is typically related to patients with multifaceted phenotypes therefore, prompt diagnosis in RGD patients creates a probable clinical impression for guiding personalized treatments. We at our genetic centre SKIMS have created a diagnostic and counselling facility for most of the prevalent RGDs. **Methods:** Uncharacterized RGDs are identified for common genetic variants through a range of cytogenetic and molecular techniques. Karyotyping involving cell culturing and GTG banding is done for identification of various chromosomal aberrations and FISH technique for various micro-deletions and cancer related genes. Different PCR variants for the detection of mutations in different RGDs. Besides complex RGDs are being evaluated through Next generation sequencing. **Results:** Overall, 18500 RGD patients of 18 major disease groups were evaluated for different genetic alterations and 4869 (57.3%) were identified positive in the cohort. Among the chromosomal aberrations, Down's syndrome predominated (15%) followed by11% in recurrent pregnancy losses. Among monogenic RGDS, Cystic Fibrosis was seen in majority of cases (n=240). Neuromuscular and neurodevelopmental group including DMD was found in 30% (99/330), Spinal muscular Atrophy in 61% (305/500), Huntington disease in 75% (150/200) cases while as Spinal cerebellar atrophy in 10% cases (35/350). Chromosomal micro-deletions were detected in 9.5% and Her-2 gene over amplification in 26% in cancers of breast, stomach and ovary through FISH technique. Inherited cardiomyopathies had absolute genetic variants present with different phenotypic features. Prenatal genetic testing through amniocentesis-a new initiative identified 26% cases (40/150) harbouring either a chromosomal or molecular variants that warranted for the medical termination of the pregnancy. Overall >60% and 40% cases had a consanguinity in autosomal recessive and dominant RGDs respectively. **Conclusion:** The current retrospective diagnosis for RGDS offers clinically

meaningful diagnostic information that significantly influences management and counselling. The population specific genetic variants in RGDS elucidate new gene -disease associations and demonstrate parental screening and prenatal genetic testing to enable informed reproductive choices. The data aids to establish in-house, diagnostic facility for prevalent RGDs for translation into societal benefits through advocacy programs, genetic counselling, and therapeutic options.

Key Words: Rare genetic disorders (RGDs), Karyotyping, GTG banding, FISH

IACR – 795 **POSTER**

Metabolic and Autophagic Plasticity in Glioblastoma Chemoresistance

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Glioblastoma (GBM) remains a highly aggressive malignancy characterized by rapid recurrence and profound resistance to Temozolomide (TMZ). The present study identifies two critical molecular adaptations, metabolic remodeling and autophagic signaling, that drive TMZ evasion. Recent investigations reveal that GBM cells undergo a strategic "isoform switch" within the AMPK heterotrimer. This structural transition reduces the complex's sensitivity to ATP-mediated inhibition, allowing resistant cells to maintain mitochondrial homeostasis and spare respiratory capacity under chemo-induced stress. Concurrently, the GABARAP family displays differential expression patterns that modulate glial cell survival. Specifically, the knockdown of certain GABARAP members enhances proliferation and reduces TMZ sensitivity by suppressing p53 expression, highlighting a subtle regulatory link between autophagy and apoptosis. Together, these findings suggest that TMZ resistance is not a static trait but a dynamic adaptation involving AMPK-mediated metabolic flexibility and GABARAP-dependent autophagic tuning. Targeting the specific AMPK complex or leveraging GABARAP expression profiles offers a dual-pronged therapeutic strategy to overcome chemoresistance and improve the prognosis for GBM patients. While the AMPK subunit switch focuses on the bioenergetic "shield" that allows GBM cells to ignore the stress of chemotherapy, the GABARAP isoform preference highlights a signaling "bypass" where the loss of specific GABARAP proteins prevents the cell from triggering p53-mediated death.

Key Words: Glioblastoma (GBM), Temozolomide, chemotherapy, GABARAP

IACR – 796 **POSTER**

Exploiting Lipid Metabolism Dependencies to Overcome Therapy Resistance in Colorectal Cancer

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Colorectal cancer (CRC) remains a major cause of cancer-related mortality, largely due to therapy resistance and disease relapse. These clinical challenges are driven by a small subpopulation of cancer cells known as drug-tolerant persister cells (DTPs), which survive initial treatment and act as a reservoir for residual disease. Drug-tolerant persister cells (DTPs) undergo profound metabolic reprogramming that enables survival under therapeutic stress. Emerging evidence identifies this metabolic adaptation as a major driver of tumor progression, characterized by dysregulated lipid metabolism and lipid droplet (LD) accumulation in aggressive, therapy-resistant colorectal cancer (CRC). A key feature of this adaptation is enhanced de novo lipogenesis (DNL) and accumulation of lipid droplets (LDs), yet molecular drivers and therapeutic implications of this lipid remodeling remain poorly understood. In this study, we investigated the mechanisms underlying LD accumulation and evaluated whether disrupting LD formation leads to a metabolic vulnerability in therapy resistant CRC. Using CRC tissues, cell lines, DTP models, patient-derived organoids (PDOs), and in vivo xenograft and patient-derived xenograft (PDX) models, we performed biochemical, molecular, imaging and lipidomic analyses. In this study, we found that increased LDs contribute to tumor progression and demonstrated that CRC DTPs exhibit marked overexpression of Lipin1 (LPIN1), a key enzyme facilitating the sequestration of free fatty acids into LDs. LP1N1 upregulation is driven by the ETS1 - PTPN1-c-Src-CEBPβ signaling axis. Inhibition of lipid-droplet formation using statins or suppression of LPIN1 disrupts lipid homeostasis, resulting in lipotoxicity and ferroptotic cell death in DTPs and PDOs. This effect is accompanied by

increased lipid reactive oxygen species and is rescued by ferroptosis inhibitors or N-acetyl cysteine. Importantly, targeting LPIN1 significantly suppresses tumor growth in CRC DTP xenograft and PDX models. Collectively, our findings identify LPIN1 - driven lipid-droplet formation as a critical metabolic vulnerability in therapy-resistant CRC, offering a promising strategy to overcome resistance and prevent relapse.
KEYWORDS: Drug tolerant persister cells, Tumor progression, De novo lipogenesis, Non-responder, Lipin 1, Lipid droplet, Ferroptosis

IACR – 801 **POSTER**

In silico Screening and Molecular Dynamic Simulation Approach: A Drug Repurposing Strategy targeting a novel oncogene RPP25 against Triple-Negative Breast Cancer

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Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer that lacks the expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2), resulting in limited treatment options and poor clinical outcomes. It accounts for approximately 10–15% of all breast cancer cases worldwide. Although chemotherapy continues to be the main therapeutic approach, its success is often hindered by tumor heterogeneity, recurrence, and metastasis. Therefore, identifying novel molecular targets and developing effective therapeutic strategies are crucial for improving TNBC management. In this study, an in-silico analysis of multiple publicly available datasets (GSE167152, GSE171957, GSE38959, GSE96859, GSE203119, and GSE246824) was conducted to identify a novel gene target using differential gene expression patterns between TNBC tissues and normal breast tissues. These analyses revealed significantly increased levels of RPP25 (ribonuclease P and MRP subunit p25) in TNBC tissues, a pivotal oncogene that might potentially be involved in TNBC progression. Kaplan-Meier survival analysis showed poor survival outcomes in patients with elevated levels of RPP25, also suggesting its clinical relevance as a prognostic marker. RPP25, located on chromosome 15q24.2, is a key component of the RNase P and RNase MRP complexes that regulate RNA processing and protein synthesis. Dysregulation of RPP25 may promote abnormal cell proliferation, resistance to apoptosis, and genomic instability, contributing to cancer progression. Furthermore, virtual drug screening approaches, including molecular docking and network-based methods, were employed to identify potential therapeutic candidates targeting RPP25. These analyses identified glimepiride, an FDA-approved antidiabetic drug, as a promising small molecule with potential binding affinity toward RPP25. In future, we intend to investigate the oncogenic role of RPP25 and glimepiride-mediated targeted therapeutics against TNBC using in vitro and in vivo studies.

Keywords: Triple-negative breast cancer, RPP25, Drug Repurposing, Glimepiride.

PGE2–Galectin-9 axis driven three-way crosstalk between tumor- APC- NK Cell in the microenvironment

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Natural killer (NK) cells are key effectors of antitumor immunity but, their function is suppressed within the tumor microenvironment (TME). We investigated the role of antigen-presenting cells (APCs) in NK cell exhaustion in cancer and sought to identify the tumor-derived mediators responsible for this effect. Phenotypic and functional alterations in NK cells and APCs were evaluated following exposure to Lewis lung carcinoma (LLC) tumor-conditioned medium (TCM) using magnetic bead-based cell purification, flow cytometry, ELISA, and calcein release assays. NK cells from TCM-treated spleen cultures or tumor-bearing mice exhibited elevated TIM3 expression and reduced cytotoxicity, whereas purified NK cells exposed to TCM alone showed no changes. Depletion of APCs reversed TIM3 upregulation and restored NK function, highlighting a critical tumor-APC-NK crosstalk. LLC cells secreted prostaglandin E2 (PGE2), expressed high galectin-9 (Gal9), but lacked TIM3. TCM enhanced Gal9 expression in B cells and macrophages and increased TIM3 in dendritic cells, promoting an immunoregulatory phenotype. Prolonged TCM exposure also expanded myeloid-derived suppressor cells (MDSCs) with increase in surface and soluble Gal9. Tumor-derived PGE2 induced Gal9 in macrophages, while COX-2 inhibition (NS-398) or EP4 receptor antagonist (MK-2894) reduced $Gal9^+$ APCs, limited MDSC expansion, and restored NK proliferation and IFN-γ production. Recombinant Gal9 increased TIM3 on NK cells, whereas Gal9-neutralizing antibody abrogated TCM-induced exhaustion of NK cells. Overall, these findings reveal that NK cell dysfunction arises from tumor-APC-mediated signalling, predominantly driven by Gal9 induced by tumor-secreted PGE2, which upregulates TIM3 on NK cells. Targeting this tumor-microenvironment crosstalk may enhance NK-mediated antitumor immunity.

Key Words: Natural killer (NK) cells, Tumor microenvironment (TME), Lewis lung carcinoma (LLC)

Uncovering Hidden Drivers of Glioblastoma: A Bioinformatics Approach to Identify Novel Gene Targets and Drug Repurposing Strategies

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Glioblastoma (GBM) is a highly aggressive and therapy-resistant primary brain tumor associated with poor prognosis and limited treatment options. Persistent challenges such as

tumor heterogeneity, recurrence, and resistance to standard therapies necessitate the identification of novel molecular gene targets and effective therapeutic strategies. In this study, an integrative in-silico screening of multiple publicly available transcriptomic datasets (GSE50161, GSE109824, GSE31262, GSE145645, and GSE207821) was performed to identify gene drivers using differentially expressed genes (DEGs) between GBM and normal brain tissues. Genes were filtered using thresholds of log2 fold change ≥ 1.5 and $p < 0.005$, followed by functional enrichment and survival analyses. Subsequently, seven key candidate genes, including LMNB1, NEMP1, SPC25, GAS2L3, DBF4, TNFRSF10B, and C21orf62, were identified as significantly associated with GBM pathogenesis. Functional annotation using KEGG pathway analysis revealed their involvement in critical oncogenic processes, including cell cycle progression, mitotic regulation, DNA replication, apoptosis, and nuclear architecture maintenance. Notably, SPC25 and NEMP1 overexpression correlated with poor patient survival (KM survival analysis), highlighting their prognostic significance. Conversely, TNFRSF10B exhibited tumor-suppressive, pro-apoptotic activity in other cancers. Furthermore, virtual screening-based drug repurposing identified potential small-molecule candidates targeting NEMP1 and SPC25, including Meprednisone, MK-0773, Nemiralisib, Lumacaftor, and Orelabrutinib. These findings suggest a promising and cost-effective therapeutic avenue for GBM management. In conclusion, this study identifies a novel gene panel with diagnostic and prognostic relevance and highlights potential repurposable drugs, warranting further experimental validation for clinical translation.

Key Words: Glioblastoma, Drug repurposing, novel oncogenes, NEMP1 and SPC25

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The Department of Biochemistry is one of the oldest departments of the University and was established in 1983. It is supported by the DST-FIST grant that enabled us to procure several high quality equipments and upgrade our instrumentation facility. In addition, the faculty members have also obtained several generous extramural grants from various funding agencies like DBT, DST, ICMR etc., which has contributed towards building a decent research infrastructure. The major areas of research in the department are Biochemistry, Cancer Biology, Signal transduction, Medicinal plants, Epigenetics etc. The department has a rich history of producing high quality scientists, academicians, administrators (Vice Chancellors, Directors of institutes, Deans etc.). Our students and faculty members have gone for advanced studies and trainings (Ph.D, Post-doctorate) to internationally reputed institutes both at the national and international levels.

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