#ICGA2024

5th ICGA Meeting 2024

Scan Me

Unlocking Insights:

Data-Driven Discovery in the Indian Cancer Landscape

BRIC National Institute Of Immunology, New Delhi

20-22 September 2024

ICGA FOUNDATION | Indian Cancer Genome Atlas

BRIC a DBT Organization

NII National Institute of Immunology

Centre for Chronic Disease Control
A World Health Organization (WHO) & Indian Council of Medical Research (ICMR) Collaborating Centre

ASHOKA UNIVERSITY

Persistent
See Beyond, Rise Above

AMITY UNIVERSITY HARYANA

CHIP
Center for Health Innovation & Policy Foundation

Book of Abstracts

#ICGA2024

5th Indian Cancer Genome Atlas (ICGA) Annual Meeting

WELCOME TO 5th ICGA ANNUAL MEETING (2024)

Dear Colleagues,

It is our distinct pleasure to extend a warm welcome to you in the vibrant city of New Delhi for the highly anticipated 5th Indian Cancer Genome Atlas (ICGA) Annual Meeting, ICGA2024.

About ICGA

The Indian Cancer Genome Atlas (ICGA) is a pioneering national mission dedicated to the multi-omics profiling of cancers across India's diverse landscape. The ICGA Foundation, a not-for-profit, public-private-philanthropic partnership registered as a Section 8 Company, stands as a testament to unwavering commitment. The Foundation aims to augment clinical diagnosis for Indian cancer patients and seeks to contribute to the Global Cancer Knowledge Base. Our inaugural project, focusing on the multi-omics profiling of breast cancer in Indian patients, is already making strides, driven by dedication and purpose.

About ICGA Meetings

The ICGA meetings provide an excellent platform to facilitate interactions among the rapidly growing scientific community interested in cancer research, omics, and precision oncology. India boasts a vast pool of talented graduate students who should also be exposed to a brainstorming meeting of this nature. The meetings bring together speakers of international repute, clinicians, researchers, omics experts, data scientists, and technology providers, along with students, to share the latest advancements in the field and updates on progress made by the Indian Cancer Genome Atlas.

The inaugural meeting took place in September 2019 as a TCGA India meeting, focusing on garnering wisdom from The Cancer Genome Atlas (TCGA). The second edition, held in December 2020, delved into the collaborative spirit of team science for multi-omics profiling of cancers relevant in South Asia. The third conference unfolded in January 2022 as a virtual meeting, dedicated to global insights on biobanking and omics. The fourth conference in October 2023 focused on "Advancing Towards Integrated Precision Oncology in India" and was held at the Indian Institute of Science Education and Research (IISER) Pune, Maharashtra.

5th ICGA Annual Meeting (2024)

This year, we are proud to host the 5th annual meeting focused on "*Unlocking Insights: Data-Driven Discovery in the Indian Cancer Landscape*". This landmark event will be held at the BRIC-National Institute of Immunology, New Delhi from 20 to 22 September 2024.

The primary objective of the 5th Annual meeting is to foster a comprehensive understanding of the cancer landscape in India through data-driven discoveries. Our mission extends beyond exploration, emphasizing practical applications in precision oncology and translational research. We aspire to foster networking and collaboration among a diverse assembly, including students, researchers, clinicians, data scientists, technology visionaries, and policymakers. The ICGA2024's distinguished roster of speakers and panelists hails from leading national and international institutions, and it also provides a platform for participants to present their research through poster presentations and lightning talks, spanning a rich array of topics related to cancer omics.

ICGA2024's Book of Abstracts

This compilation presents abstracts highlighting groundbreaking research from our participants, showcasing their unwavering dedication to advancing the field and inspiring us all.

All this has been possible thanks to your participation, support from our supporters, sponsors, and the commitment of our esteemed partners.

We do hope that you enjoy your attendance at the #ICGA2024!

With best wishes,
#ICGA2024 Organizing Team

PREFACE

Dear Colleagues,

It is my pleasure to warmly welcome you to the 5th Indian Cancer Genome Atlas (ICGA) Annual Meeting, #ICGA2024. This event presents a remarkable opportunity to learn from and engage with leading experts and pioneers in the fields of cancer research and omics. The theme for this year, "*Unlocking Insights: Data-Driven Discovery in the Indian Cancer Landscape*," will guide several thought-provoking lectures, panel discussions, poster presentations, and networking sessions, centered on cancer omics and precision oncology. The meeting will also highlight the progress made by the Indian Cancer Genome Atlas (ICGA) project, aimed at building a comprehensive molecular profile database for cancers prevalent across Indian populations.

I extend my heartfelt congratulations to the entire organizing team for their dedication and hard work in orchestrating this outstanding event. I thank the speakers and presenters for making time and sharing their invaluable knowledge and expertise on this platform. Lastly, my sincere thanks go out to the sponsors, partners, and collaborators for their generous support

I again welcome all of you to the National Institute of Immunology. We are happy to be part of the ICGA Annual Meeting, in the role of a co-organiser, as it promises to be a catalyst for cancer research in India. I am confident that the meeting will provide a rich exchange of insights and knowledge, and I hope it leads to new collaborations that will propel your research and professional growth. I eagerly look forward to engaging with you all at ICGA2024 and fostering meaningful discussions.

Here's to the grand success of #ICGA2024—I wish you a memorable and rewarding experience.

Best regards,

Dr. Debasisa Mohanty
Director, National Institute of Immunology (NII)

COMMITTEES

ADVISORY COMMITTEE

Dr. Anand Deshpande, Persistent Systems, India
Prof. Anguraj Sadanandam, Institute of Cancer Research (ICR), UK
Prof. Bushra Ateeq, IIT, Kanpur
Dr. CB Koppiker, Prashanti Cancer Care, Mission (PCCM), Pune
Prof. Chinta Mani, Sir Ganga Ram Hospital, Delhi
Dr. Debasisa Mohanty, BRIC-NII, Delhi
Prof. LS Shashidhara, TIFR-NCBS, Bengaluru
Prof. Ravi Mehrotra, ICGA Foundation
Prof. Ritu Gupta, AIIMS, Delhi
Prof. Sharmila Bapat, BRIC-NCCS, Pune
Prof. Shekhar Mande, SPPU, Pune
Prof. Sudeep Gupta, Tata Memorial Centre, Mumbai
Prof. Sunil Badve, Emory University, USA

ORGANIZING COMMITTEE

Dr. Debasisa Mohanty, BRIC-NII, New Delhi
Dr. Aastha Aggarwal, CCDC India
Mr. Akshay Chitlangia, Persistent Systems, Pune
Dr. Aneeshkumar AG, BRIC-NII, Delhi
Dr. Ankita Singh, ICGA Foundation
Ms. Anshika Chandra, CHIP Foundation
Dr. Aradhita Baral, Ashoka University, Sonipat
Dr. Banya Kar, BRIC-NII, Delhi
Dr. Krithiga Shridhar, CCDC India
Mr. Kunal Singla, CHIP Foundation
Prof. Ritu Kulshrestha, IIT Delhi
Dr. Suveera Dhup, ICGA Foundation
Dr. Ujjaini Dasgupta, Amity University
Dr. Shekhar Grover, CHIP Foundation

PARTNERS AND SPONSORS

PARTNERS

Media Partner

Outreach Partner

SPONSORS

Map of BRIC-NII

https://maps.app.goo.gl/iRWZHVJ55Jkz4x699

Schedule

Friday, 20 September 2024			
12:30	14:00	Registration *(auditorium)*	
13:00	14:00	Lunch *(NII grounds)*	
14:00	14:05	Welcome Address: Dr. Debasisa Mohanty, BRIC-NII *(auditorium)*	
Session 1:		Advancements in Cancer Research: From Molecular Insights to Clinical Applications	
14:05	14:30	*Understanding Breast Cancer in young premenopausal women from Indian cohorts- Exploration of cross talks between steroid hormones and nuclear receptors.* Prof. Jyothi S. Prabhu, SJRI, Bengaluru	
14:30	14:55	*Biomolecular research: the real test is when it reaches the last person on the ladder* Prof. Sunil Kumar, AIIMS, Delhi	
14:55	15:20	*Bridging Clinic, Epidemiology, and Biobanking: Lessons to Oncology from Precision Cardiology* Prof. D. Prabhakaran, CCDC, India	
15:20	15:45	*Breast cancer in young- is triple negative an Indian stereotype* Prof. Chintamani, Sir Ganga Ram Hospital (SGRH), Delhi	
15:45	15:55	*Non-invasive early detection of multiple cancers (Sponsored Talk)* Dr. Vamsi Veeramachaneni, Strand Life Science	
15:55	16:25	Tea/Coffee break *(Rock Garden)*	
16:25	18:15	Poster session *(NII Grounds)*	
Session 2:		Omics Innovations in Cancer Research *(auditorium)*	
18:15	18:40	*The Genomic Jigsaw Puzzle: Unraveling Head and Neck Cancer Through Integrative Approaches* Prof. Amit Dutt, University of Delhi, South Campus, Delhi	
18:40	19:05	*RNA-omics: knight in shining armour to decode the complex transcriptome of glioma patients* Prof. Ritu Kulshrestha, IIT, Delhi	

19:05	19:30	*PHALCON: Scalable variant calling from single-cell panel sequencing dataset from cancer patients* Dr. Hamim Zafar, IIT, Kanpur	
19:30	21:00	Networking Dinner *(NII Grounds)*	

Saturday, 21 September 2024			
Session 3:		Integrating Omics in Cancer Research *(auditorium)*	
9:15	9:40	*Targeting the Hidden: Discovery of Dark Neoantigens and Vaccine Targets in Pancreatic Cancer* Prof. Anguraj Sadanandam, ICR, London, UK	
9:40	10:05	*Multi-allelic Mutations of Tumor Suppressor Genes in Cancer Evolution* Dr. Sabarinathan Radhakrishnan, TIFR-NCBS, Bengaluru	
10:05	10:30	*Atlas of Blood Cancer Genomes: Our 10,000-patient odyssey to translating genomics* Prof. Sandeep Dave, Dukes University, USA	
10:30	10:55	*A Targeted Panel of 295 Genes for Multiple Myeloma* Prof. Anubha Gupta, IIIT Delhi	
10:55	11:05	*Revolutionize Life Sciences Research with AI on AWS cloud (Sponsored Talk)* Mr. Mainak Chakraborty, AWS, India	
11:05	11:35	Tea/Coffee Break	
11:35	12:00	*Keynote: Technology in Medicine and Healthcare* Prof. Abhay Karandikar, Secretary to the Government of India, Department of Science & Technology	
Session 4:		Panel Discussion	
12:00	13:00	Career Options: Inspiring Trajectories	
		Panelists: Dr. Banya Kar (BRIC-NII), Dr. Madhuri Dutta (The George Institute of Global Health), Dr. Nitya Nand Sharma (Premas Life Sciences), Dr. Amitavo Mitra (Saikrishna & Associates), Dr. Narendra Kumar (BRIC-NII)	

13:00	14:00	Lunch	
Session 5:		Panel Discussion	
14:00	15:00	Generative AI in Healthcare: Role in Onco-genomics	
		Panelists: Dr. Anamika Gambhir (DBT, GoI), Dr. Anand Deshpande (Persistent Systems), Prof. Anurag Agrawal (Ashoka University), Dr. Krithika Rangarajan (AIIMS New Delhi), Prof. Sharmila Bapat (BRIC-NCCS)	
Session 6:		Lightning Talks	
15:00	15:10	*Enhancing Cancer Patient Care: Integrating Palliative Approaches and LLM(Large Language Model)s* Mr. Ashish Makani, Ashoka University, Sonipat	
15:10	15:20	*Integrated Multi Omics Analysis of Young Onset Breast Cancer – An In-Silico Approach, Using Public Datasets* Mr. Hari PS, SSCHRC, Bengaluru	
15:20	15:30	*Multi-ensemble machine learning framework for omics data integration: A case study using breast cancer samples* Dr. Sunitha M Kasibhatla, C-DAC, Pune	
15:30	15:40	*Designing a Data-driven Discovery Framework for Oncology: Opportunities and Challenges* Dr. Urmila Kulkarni Kale, Citadel Precision Medicine, India	
15:40	15:50	QnA	
15:50	16:20	Tea/Coffee Break	
Session 7:		Innovative Approaches in Cancer Research: From Microbiome to Omics	
16:20	16:45	*Gut Microbiome and Metastatic Breast Cancer Control: A New Frontier* Dr. Nagarajan Kannan, Mayo Clinic, USA	
16:45	17:10	*Transcriptome Informed Discovery and Immuno-therapeutic Targeting of Tumor Specific Antigens in AML - and Solid Malignancies* Prof. Soheil Meshinchi, Fred Hutchinson Cancer Center, USA	
17:10	17:35	*Dissection of FOXA1 mutations in breast cancer* Dr. Dimple Notani, TIFR-NCBS, Bengaluru	
17:35	18:00	*Unlocking the utility of genomics in drug development and routine oncology practice* Dr Philip Beer, Step Pharma, UK	

Session 8:		ICGA Session	
18:00	18:25	Keynote: Dr. Rajesh S. Gokhale Secretary, Department of Biotechnology, Government of India	
18:25	18:45	*Revolutionizing Cancer Diagnostics: Advances and Implications in the Genomic Era* Prof. Ravi Mehrotra, ICGA Foundation, CHIP Foundation	
18:45	19:05	ICGA Journey So Far: Introduction to ICGA Platform	
19:05	19:15	QnA	
19:15	21:00	Gala Dinner	

Sunday, 22 September 2024			
Session 9		Precision Oncology: A Way Forward	
9:30	9:55	*Engineered 3-D ex vivo tumor models: Game changers in drug discovery and precision medicine* Dr. Neha Arya, AIIMS, Bhopal	
9:55	10:20	*Unraveling the Tapestry of Gastrointestinal Cancers: A Single-Cell and Spatial Transcriptomic Approach* Dr. Ashiq Masood, Indiana University, USA	
10:20	10:45	*Molecular Subtyping and prediction of risk of recurrence for early-stage receptor positive breast cancer using NanoString nCounter Flex from India* Prof. Arvind Krishnamurthy, Cancer Institute, WIA, Adyar	
10:45	10:55	*Democratizing Genomics: IDT's Role in a Changing World (Sponsored Talk)* Mr. Onkar Rahatkar, Integrated DNA Technologies (IDT)	
10:55	11:25	Tea/Coffee Break	
Session 10		Genomics and Oncology: Bridging Practice and Innovation	
11:25	11:50	*Integration of Genetics in routine oncology practice- A way forward* Dr. Ashutosh Mishra, AIIMS, New Delhi	
11:50	12:15	*Tumor-intrinsic and Tumor Microenvironment Signaling and Therapeutics* Dr. Manash Paul, Manipal University, Manipal	
Session 11		Panel Discussion	

12:15	13:15	Unified Front: Integrating Survivor Perspectives for Effective Cancer Research and Translation	
		Panelists: Dr. Aastha Aggarwal (Moderator), Prof. AC Kataki, Dr. Aruna Korlimarla Mrs. Jyotsna Govil, Dr. Siuli Mitra, Ms. Soumya Rajesh	
13:15	14:45	Lunch	
Session 12		Advancing Oncology through Genomics: Integration, Collaboration and Data Sharing	
14:45	15:10	*Data Sharing, Essential Component of Large-scale Genomics Projects* Dr. JC Zenklusen, TCGA, NIH-USA	
15:10	15:35	*Next Steps for ICGA* Prof. Sunil Badve, Emory University, Atlanta, USA	
15:35	16:05	Award function Closing remarks	
16:05	16:50	High tea	
17:30	19:00	Annual General Meeting (ICGA AGM2024)	

Poster list

Poster	Title	First Name	Last Name	Title of the abstract
P1	Dr.	BHAVANA	TIWARI	p53 mediated regulation of LINE1 retrotransposition derived R-loops
P2	Mr.	Sameer	Joshi	IRC20 modulates LOH frequency and distribution in S. cerevisiae
P3	Ms.	Archita	Dey	Meta-Analysis of epigenomics data including immune surveillance checkpoint molecules can be used as the blood based biomarkers of leukemia
P4	Ms.	Ankita Subhadarsani	Parida	LINE-1 transposon activation drives the genetic and epigenetic evolution of Triple- negative breast cancer persistors
P5	Ms.	SRINIDHI NARAYANI	S	Tumour microbial diversity: Association with metastasis in breast cancer
P9	Ms.	DIYA	CHATTOPADHYAY	p53-dependent autophagic degradation facilitates de novo silencing of LINE-1 transposons
P10	Mr.	ASTIK KUMAR	DE	Investigating the role of LINE-1 associated R-loops in Genomic instability and Cancer
P14	Ms.	Soundharya	R	Multi-modal transcriptomic analysis reveals association among partial EMT, anoikis resistance and hypoxia
P15	Mr.	Mustaffa	Hussain	Generating Digital Stains Via Neural Schrödinger Bridge in Pathology Images
P16	Ms.	JYOTI	SHEKHAWAT	TET3 promoter hypermethylation in head and neck carcinoma patients
P17	Mr.	Prateek	Paul	Integration of Knowledge Graphs and Machine Learning-Based Approach for Identifying Potential Synthetic Lethal Gene Pairs
P18	Ms.	DIPANWITA	NATH	Linking Targeted Pancreatic Cancer Genes with Metabolic Disorders: A Cross-species Translational Pathway
P19	Mr.	Himanshu	Bhardwaj	Establishment of a molecular genomics laboratory to revolutionize cancer care in rural areas of Bihar.
P20	Mr.	Abhishek	Bardhan	HAGLR, A Long Non-coding RNA of Potential Tumor Suppressive Function in Clear Cell Renal Cell Carcinoma: Diagnostic and Prognostic Implications
P21	Ms.	Shreya	Srivastava	Investigating The Transcriptome For Tumor Microenvironment Of Gastric Adenocarcinoma: Searching For Allies And Adversaries
P22	Mr.	Guruguhan	S	Comprehensive pan-cancer multi-omics analysis of the KEAP1-NFE2L2-CUL3 gene axis as a potential immunological and prognostic biomarker
P23	Mr.	Somesh Kumar	Jha	Phosphocholine-derived Lithocholic Acid-Gemcitabine Conjugate Mitigates Hepatocellular Carcinoma Progression via Modulation of Lipid and Immune Landscape

P24	Dr.	Shilpa	Patil	OncoConnect: An AI-driven approach for holistic interpretation of genomic data in the context of clinical characteristics of cancer patients
P25	Mrs.	Faseela	E E	Replication stress underlies genomic instability at CTCF/cohesin binding sites in cancer
P26	Ms.	Trishna	Pani	Alternative Splicing of UGCG Inhibits Tumor Progression in Breast Cancer
P27	Mr.	Sandipan	Das	Investigating the diagnostic and prognostic importance of lncRNA LINC01409 along with its mechanistic role in Prostate Cancer
P28	Ms.	SAMRIDDHI	ARORA	Orai3 oncochannel is a critical regulator of chemoresistance in pancreatic cancer
P29	Mr.	Prashant	Bhavar	Pre-clinical Evaluation of IND126, a KRASG12C Inhibitor in Non-Small Cell Lung Cancer
P30	Mr.	Agneesh Pratim	Das	Development of a method for protein structure selection that yield true active compounds early during virtual screening
P31	Ms.	Diya	Mallik	Comprehensive analysis of Long Non-Coding RNA ACTA2-ASA1 in Prostate Cancer: Diagnostic Implications
P32	Mr.	Shirshanya	Roy	Investigating the role of Super-Enhancer-transcribed long-noncoding RNA in Glioblastoma
P33	Mr.	Sharon	Raju	The NFAT2 Paradox: NFAT2 regulates both mRNA transcription and protein degradation of oncogenic calcium channel Orai3
P34	Mr.	Ajaikumar	S	Development and analytical performance study of cartridge based chemiluminescence immunoassay reagent for prostate specific antigen
P35	Mr.	Sarath	K V	Screening and identification of potential salivary microRNA biomarkers for oral squamous cell carcinoma: preliminary findings
P36	Ms.	Priyanka	Thareja	Phase Separation related gene signatures in Indian Breast Cancer patients
P37	Ms.	RESHU	CHAUHAN	Exploring the role of Hepatitis C virus in modulating the AFP protein expression to lead to Hepatocellular Carcinoma.
P38	Ms.	Neetu	Tyagi	lncRNACNVIntegrateR: A Novel Framework for Correlating lncRNAs Expression with CNV Abnormalities and Disease Progression
P39	Ms.	Ramita	Sharma	Recurrent NT5C2 Mutations Drive Drug Resistance in Relapsed Acute Lymphoblastic Leukemia: A System Biology based approach
P40	Ms.	Pragya	Kashyap	A novel machine learning approach for stratification of major non-small-lung cancer subtypes based on microbiome profiling of lung tissue
P41	Ms.	Pratiti	Bakshi	Investigating the underlying basis of the interaction between two large GTPases – hGBP2 and Drp1

P42	Dr.	Masum	Saini	Does Meningioma 1 gene bear prophecy for glioma patient survival?
P43	Dr.	Garima	Jain	Machine Learning-Based Analysis of Blood and Urine Exosomal miRNAs for Accurate Differentiation of Prostate Cancer and BPH
P44	Ms.	RITANKSHA	JOSHI	Identification of long non-coding RNA (lncRNA) signatures in meningioma: path to discovery of potential biomarkers and therapeutic targets?
P45	Dr.	Amruta	Chavhan	Bifunctional fusion proteins in cancer therapy
P46	Ms.	Juwayria	Juwayria	Deep Phenotyping of a Rare, Mixed Histology Non-small Cell Lung Cancer using Spatial Transcriptomics
P47	Dr.	Mallikarjuna	Thippana	Uncovering key genes and pathways associated with lung adenocarcinoma progression through systems biology approach
P48	Mr.	Abhilash	Dasari	Exploring the Dual Landscape of Gene Expression and Splicing in Non-Small Cell Lung Cancer (NSCLC)
P49	Mr.	Satya Prakash	Khuntia	Tumor Mutational Burden Disparities: A Critical Comparison Between Indian Cancer Patients and The Cancer Genome Atlas across cancer types
P50	Ms.	BARNALI	DOLUI	Is Anti-TIM3 Mediated Cancer Immunotherapy a Misguided Approach in Clinical Trials? Insights From the Mouse Breast Tumor Model
P52	Professor	Saran	Kumar	Glioblastoma Stemness: The Active Role of Tumor Vasculature
P53	Mr.	Deepak	Kumar	Empowering Biobanking Research through Effective Data Management: Glimpses from A Decade Old Biorepository at RGCIRC

Power Genomics Innovations with AWS

AWS offers purpose-built services, tools, and solutions to help you migrate securely and store data in the cloud, accelerate secondary and tertiary analysis, and integrate genomic data into multi-modal datasets.

Accelerate Time to Discovery

Process more samples, run more complex analyses, and effectively query at scale

Keep Costs Low & Performance High

Continuously optimize spend on compute and storage to build scalable applications

Collaborate on a Global Scale

Discover tools and services to move and collaborate while remaining secure and compliant

Collaborate with AWS to explore scalable, secure, and cost-effective solutions and technologies that accelerate genomic discoveries.

Scan the code to learn more

Advancements in Cancer Research: From Molecular Insights to Clinical Applications

Understanding Breast Cancer in young premenopausal women from Indian cohorts- Exploration of cross talks between steroid hormones and nuclear receptors

Prof. Jyothi Prabhu

St. John's Research Institute (SJRI), Bengaluru
https://sjri.res.in/molecular/keypersonnel/Dr.%20Jyothi%20S%20Prabhu

Abstract

The incidence of breast cancer in India is rising, particularly in urban centres and among younger adults. Younger women with breast cancer often have a higher proportion of aggressive subtypes associated with poor outcomes. A key difference between breast cancer in young and older women is the circulating levels of sex steroid hormones, which act as ligands for nuclear receptors such as estrogen and progesterone receptors. These nuclear receptors are known to cross-talk with each other, often substituting the action of one another, leading to therapeutic resistance and tumor progression. Exploring the cross-talk between various nuclear receptors and their interaction with circulating hormones is essential to understanding the mechanisms of resistance and devising effective therapies for younger women with breast cancer. I would present an overview of breast cancer in young premenopausal women from Indian cohorts, highlighting specific subtypes, the cross-talk between nuclear receptors, and its effects on the tumor microenvironment.

Biosketch

Dr Jyothi Prabhu is Professor and Head of Division of Molecular Medicine, St. John's Research Institute at Bangalore, Trained as Pathologist, her focus area of research is breast cancer. She has initiated cohort-based studies at multiple centres in collaboration with treating surgical and medical oncologists, pathologists with long term follow up. She has also been part of multiple industry collaborative research to answer specific questions of interest on drug development and resistance. Her current focus is on premenopausal breast cancer specifically to decipher the interaction between multiple nuclear receptors and the circulating hormones.

Prof. Sunil Kumar

AIIMS New Delhi
https://www.aiims.edu/index.php?option=com_content&view=article&id=12810&catid=222&lang=en

Abstract

As the increasing incidence and prevalence of cancer become a significant healthcare burden in India, it is also being realized that a majority of the patients present to the healthcare system with advanced-stage cancer. The financial cost of cancer management is prohibitive and all the more so in advanced-stage cancers.

Our NGO's ground-level experiences with patients and primary healthcare workers suggest that there is a growing need to make cancer care more accessible and affordable. Early detection of cancer is crucial to this and bio-molecular research which can be translated into point-of-care portable methods can play an important role in early detection of cancer. Development of on-site kit-based early detection methods can be used to screen common cancers (like oral, breast & cervical cancers) even at the primary health center level. It can mitigate the aftermath of cancer being detected at an advanced stage.

Our experience also shows that methods which are user-friendly to primary healthcare workers are adopted very well and can help in changing health-seeking behaviours, particularly in rural ladies. Voluntary and Non-Governmental organizations play a crucial role in connecting the needy population in remote and rural areas with the tertiary healthcare system and its delivery of translational research.

Biosketch

Dr Sunil Kumar is Professor and Head of the Department of Surgical Oncology at the ALL INDIA INSTITUTE OF MEDICAL SCIENCES, New Delhi.

As a clinician, his primary areas of interest are tumors of the thoracic cavity (like lungs, esophagus and mediastinum) and malignancies of the pancreas and biliary tract. His team has been working on cell-free and tumor DNAs in blood circulation and their prognostic implications.

Apart from his clinical work, he is also working for underprivileged cancer patients in rural and semi-urban areas of Bihar and Jharkhand through his NGO "Chandrakanti Devi Cancer Foundation". The primary focus of their work is on affordable cancer care and early detection of cancer in rural population.

Bridging Clinic, Epidemiology and Biobanking: Lessons to Oncology from Precision Cardiology

Prof. D. Prabhakaran

CCDC, India
https://ccdcindia.org/prof-d-prabhakaran/

Abstract

Epidemiology is the study of the distribution and determinants of health-related states in specified populations, and the application of this study to the prevention and control of health problems. Epidemiology is the basis of Public Health that can identify the right subgroups of populations at the right place and time to help intervene precisely with primary preventive strategies or early detection. Combining epidemiological data, biomarkers, and clinical information will help in: (1) precise disease prediction, prevention and early detection in general population, and (2) personalized treatment strategies for patients. The Cardiometabolic Risk Reduction in South Asia (CARRS)) is a population-based cohort study of Urban South Asians to address existing and emerging questions related to cardio-metabolic disease. CARRS involves questionnaires, anthropometric measurements and biospecimen collection. A new iteration 'Precision-CARRS', estimates the prevalence, and occurrence of subclinical and clinical vascular and myocardial disease, investigates the behavioural, environmental, and social factors, and profiles integrative multi-omics with specialized cardiac imaging including echocardiography, electrocardiogram and CT scans in Indian populations residing in New Delhi and Chennai. Indians are at high cardiovascular disease (CVD) and diabetes risk at young ages, despite thin body phenotype. 'Precision-CARRS' aims to unravel the natural history, pathophysiology, and causal factors to pave way for precision CVD diagnostics, prevention, and care for Indians. It can serve as a model for bridging clinics, epidemiology, and biobanking to deliver personalized cancer prevention for the population and equitable cancer treatment for Indian patients.

Biosketch

Professor Dorairaj Prabhakaran, educated at Bangalore Medical College, the All-India Institute of Medical Sciences, New Delhi and McMaster University, Canada, is an eminent cardiologist, and epidemiologist of global repute. He is currently Executive Director, Centre for Chronic Disease Control, a WHO and an ICMR Collaborating Centre of Excellence. In addition, he holds professorships/visiting positions at multiple national and international institutions.

He leads several projects in precision medicine, environmental and digital health to address the high burden of chronic diseases in India. He has over 650 publications with an H-Index of 114. He is a fellow of the Indian National Science Academy and received Doctor of Science (Honoris Causa) from the University of Glasgow.

Prof. Chintamani

Sir Ganga Ram Hospital (SGRM), Delhi

https://sgrh.com/doctor-details/surgical_oncology/prof-chinta-mani

Biosketch

Prof. Chintamani is a highly distinguished oncoplastic surgeon and Chairperson of Surgical Oncology at Sir Ganga Ram Hospital, New Delhi. He holds prestigious positions such as President and Governor-at-large of the American College of Surgeons (India Chapter), Fellow –Royal Society of Medicine-UK, and is an International Surgical Advisor to the Royal College of Surgeons of Edinburgh. Prof. Chintamani specializes in breast and endocrine cancers and is a founding member of Breast Global. He is deeply involved in surgical education, having trained numerous postgraduate students and authored several publications and textbooks.

Dr. Vamsi Veeramachaneni

Strand Life Science

https://strandls.com/

Abstract

Cancer incidence rates in India are growing rapidly by all accounts. In Western countries, different screening methods like mammograms, colonoscopies, low-dose CT, and pap smears have been adopted for different cancers. However, adoption of these technologies has been limited in India and repeated image-based screening carries risk of radiation exposure. Because of an absence of regular screening, most cancers in India are diagnosed at late stages and the five-year survival rates are low. To address this dire need, Strand has worked over the last 3 years to develop a blood-based multi-cancer detection test.

As part of the test development, we analyzed 7000 publicly available samples and curated ~500 papers to identify epigenetic signals associated with cancer. Most of the available information is from tissue samples and data on methylation patterns in cell free DNA (cfDNA) is very limited. We, therefore, collected blood samples from ~5000 treatment-naive cancer patients from 40 hospitals across the country. Samples from ~250 control subjects were also collected. Methylation sequencing of cfDNA extracted from ~1000 samples was carried out and methylation scores for 550,000 regions across the genome were computed using a custom scoring method. A rigorous machine learning approach was used to build a model for distinguishing cancer from control for 10 common cancers. The assay shows >75% early-stage sensitivity at >90% specificity. Strand is currently refining the tissue-of-origin prediction part of the assay so that appropriate follow-up actions can be suggested in case a positive cancer signal is detected. We are also working with multiple hospital partners and thought leaders to see how the test can be positioned alongside established cancer screening programs.

Biosketch

Dr. Vamsi Veeramachaneni received a PhD in computer science from Penn State for his work on genome assembly algorithms. After working for two years on computational evolutionary genomics, he joined Strand Life Sciences in 2004.

At Strand, Dr.Vamsi was part of the text-mining team that developed technologies to process all published bio-medical literature and guide researchers to create pathways. He has worked with pharma on projects involving data-mining of large toxicogenomics datasets, knowledge representation and visualization.

Dr. Vamsi has guided the development of the Strand-NGS product for the analysis of sequencing data and was involved in the development of the StrandOmics platform for clinical variant interpretation and reporting.

At present, Dr.Vamsi oversees R&D activities at Strand including the development of new genomics tests.

Omics Innovations in Cancer Research

The Genomic Jigsaw Puzzle: Unraveling Head and Neck Cancer Through Integrative Approaches

Prof. Amit Dutt

University of Delhi South Campus, Delhi

https://www.amitduttlab.com/

Abstract

Tongue cancer is the most predominant form of oral cancer in developed countries, with a varying incidence in developing countries. We set to address a critical issue of occult lymph nodal metastases in tongue cancer that plays a decisive role in the choice of treatment, wherein about 70% of patients can be spared from surgery with an accurate prediction of negative pathological lymph node status. We identified MMP10 as a potential prognostic biomarker that could help spare early-stage tongue cancer patients from mandatory elective neck dissection. We also found that miR-944 negatively regulates MMP10 and that overexpression of MMP10 induces tumor growth and nodal metastasis through the AXL signaling pathway. Additionally, we described the first comprehensive landscape of infectious pathogens in various types of cancer in Indian patients and found a significant prevalence of Fusobacterium nucleatum in tongue tumors, which is associated with poor survival and nodal metastases, defining a distinct subgroup of head and neck cancer.

Blosketch

Dr. Amit Dutt, a Professor at the Department of Genetics, University of Delhi South Campus, and a Principal Investigator at the Advanced Centre for Treatment, Research, and Education in Cancer (ACTREC), Tata Memorial Centre, Mumbai, spearheads a pioneering research team revolutionizing cancer treatment through the lens of genomic intricacies. With a postdoctoral tenure at the Broad Institute of MIT and Harvard, and a Ph.D. in Developmental Biology from the University of Zurich, Dr. Dutt's expertise is sought-after in the realms of lung, breast, and head and neck cancers. His multifaceted interests extend to devising innovative computational methodologies for analyzing expansive cancer genome datasets and investigating the microbial agents implicated in human carcinogenesis. Well known for his publications in esteemed scientific journals, Dr. Dutt has garnered numerous accolades and distinctions for his impactful contributions to the field of cancer research, including the most coveted, Shanti Swarup Bhatnagar Award in Medicine.

RNA-omics: knight in shining armour to decode the complex transcriptome of glioma patients

Prof. Ritu Kulshrestha

IIT Delhi

https://beb.iitd.ac.in/ritu.html

Abstract

GBM is the most aggressive and fatal form of malignancy among the central nervous system (CNS) tumors. Patients suffering from this insidious disease have a median overall survival (OS) of 15 months, and only 5% of patients survive beyond five years of diagnosis. The standard care of treatment is maximum safe surgical resection, followed by concomitant chemo- and radiotherapy. However, the tumor almost invariably recurs leading to dismal prognosis. There is a unanimous consensus among researchers that an in-depth understanding of the molecular pathogenesis of GBM progression is required to design more effective therapy. Our group has been trying to elucidate the ncRNA profiles of GBM and other glioma types using RNA sequencing approach and have been able to identify ncRNAs (miRNAs and lncRNAs) of prognostic or therapeutic significance. My talk today walks you through our journey of working on hypoxia regulated ncRNAs in GBM. Through analyses of microRNA/lncRNA signature of hypoxia in GBM we identified miRNA, miR-210 and its host gene lncRNA- miR-210HG to be significantly regulated by hypoxia in GBM. miR-210HG/miR-210 are induced by transcription factor- HIF1A under hypoxia. miR-210HG/miR-210 are also significantly correlated with poor prognosis in GBM. Functional analyses of miR-210HG/miR-210 show that they play oncogenic role by promoting cellular proliferation, migration and inhibit apoptosis. miR-210 is also shown to promote glycolysis and inhibit mitochondrial oxidative phosphorylation in GBM. A detailed mechanistic study identified novel target genes (NeuroD2, ALDH5A1) of miR-210 in GBM and their clinical relevance. Overall, this study highlights the importance of miR-210 in GBM progression and offers an interesting therapeutic approach of delivering anti-miR-210 either alone or in combination using a novel miRNA nanocarrier.

Biosketch

Dr. Ritu Kulshreshtha, is a Professor and Head of the Department of Biochemical Engineering and Biotechnology, Indian Institute of Technology Delhi. Her present areas of research include understanding the role of non-coding RNAs in the development and progression of various cancers (glioblastoma, meningioma and breast cancer), identification of novel prognostic biomarkers, cancer heterogeneity, hypoxia-tumor biology, development of novel nanoparticles for miRNA delivery and exploring the potential of miRNA-based therapeutic strategies for the treatment of cancer patients. She is a recipient of the Outstanding Young Faculty Fellowship Award (Kusuma Trust) and Prof. P.C. P. Bhatt Faculty Research Award (Basic Research) at IIT Delhi. She has several publications in International Journals of repute and her research work is highly cited. She is currently serving on the Editorial Board of various International Journals.

PHALCON: Scalable variant calling from single-cell panel sequencing dataset from cancer patients

Dr. Hamim Zafar

IIT Kanpur

https://www.iitk.ac.in/bsbe/hamim-zafar

Abstract:
Single-cell sequencing (SCS) technologies bring cellular resolution in resolving intra-tumor heterogeneity, which can cause drug resistance and relapse in cancer. Nonetheless, SCS methods pose several technical challenges, such as uneven coverage, allelic dropout (ADO), or artifacts subjected to erroneous amplification. Single-cell variant callers have been developed to distinguish the true variants from technical artifacts. However, recently emerging parallel sequencing methods can now sequence up to thousands of cells by targeting only disease-specific genes. Current variant callers are not scalable for such high-throughput datasets and do not effectively address the amplification biases in panel-based sequencing protocols.
To address these, we present a statistical variant caller, PHALCON, which enables scalable mutation detection from large-scale single-cell panel sequencing data by modeling their evolutionary history under a finite-sites model along a clonal phylogeny. PHALCON infers the underlying cellular sub-populations based on genotype likelihoods of candidate sites and reconstructs a clonal phylogeny and the most likely mutation history (loss and recurrence included) using a probabilistic framework that maximizes the likelihood of the observed read counts given the genotypes. In this talk, we will discuss how PHALCON outperforms existing state-of-the-art methods in terms of variant calling accuracy (7.29-51.67% improvement), accuracy in inferring the tumor phylogeny (410.43-32931.8% improvement) and runtime (60-70 times faster). Furthermore, we will illustrate PHALCON's application on real tumor single-cell panel sequencing datasets from triple negative breast cancer and AML patients where PHALCON detected novel somatic mutations in important oncogenes and tumor suppressor genes with high functional impact and orthogonal support in bulk datasets.

Biosketch:
Dr. Hamim Zafar completed his Ph.D. in 2018 from the Department of Computer Science at Rice University, USA in the field of Computational Biology. He joined IIT Kanpur as a joint faculty in CSE and BSBE in 2018. He took a year-long break for pursuing Lane Fellowship in the Computational Biology Department at Carnegie Mellon University, USA, and resumed his position at IIT Kanpur in 2019. His research interests include computational biology, probabilistic models, and single-cell omics. In addition, he also works on elucidating the role of cellular heterogeneity in oral and cervical cancer. He is currently the recipient of Har Gobind Khorana-Innovative Young Biotechnologist Award from DBT and the Wellcome Trust/DBT India Alliance Early Career Fellowship.

Integrating Omics in Cancer Research

Targeting the Hidden: Discovery of Dark Neoantigens and Vaccine Targets in Pancreatic Cancer

Prof. Anguraj Sadanandam

ICR, UK

https://www.icr.ac.uk/our-research/researchers-and-groups/dr-anguraj-sadanandam

Abstract

Pancreatic neuroendocrine tumours (PanNENs) are rare and highly heterogeneous cancers, often resistant to standard treatments such as surgery and chemotherapy, especially in aggressive grade 3 forms. This project focuses on identifying and validating "dark" neoantigens—unique protein markers derived from non-canonical regions of the genome, specifically splice variants. These neoantigens are specific to cancer cells and hold promise as targets for personalised vaccines. We aim to develop tailored vaccine-based treatments, potentially improving patient outcomes with these difficult-to-treat tumours.

Biosketch

Dr. Sadanandam is a Director of the Centre for Global Oncology and a Group Leader in Stratified and Precision Medicine at the Institute of Cancer Research (ICR), London. He is currently applying his multidisciplinary skills and AI/ML to the integrated science of stratified medicine to understand cell-of-origin, inter- and intra-tumoral/immune/stromal heterogeneity, and test precise therapies for different subtypes of GI cancers. Dr. Sadanandam led/co-led the research to define transcriptome/multi-omics subtypes of pancreatic, colorectal and gastroesophageal cancers associated with prognosis and potential personalised therapies (multiple high-impact publications).

Dr. Sabarinathan Radhakrishnan

TIFR-NCBS, Bengaluru

https://www.ncbs.res.in/faculty/sabari

Abstract

Tumour development mirrors Darwinian evolution, where natural selection fosters cells with advantageous or 'driver' genetic alterations. This selection pressure is evaluated from the recurrence of these alterations in cancer patient cohorts. Identified driver alterations typically include mutations in Oncogenes (ONGs) and Tumour Suppressor Genes (TSGs). Unlike ONGs, TSGs are negative regulators of cell proliferation and require mutations in both alleles ('two-hits') for tumorigenesis (Knudson, 1971). However, two-hit frequencies vary widely across TSGs, questioning the universality of this hypothesis. To investigate factors underlying this variability, we leveraged data from The Cancer Genome Atlas and defined 'two-hit' as the cooccurrence of a protein-affecting point mutation in one allele with deletion of the other. Our findings show that two-hit frequencies of TSGs are higher for truncating mutations than missense mutations. Additionally, deletions involved in TSG two-hits often span large regions on certain chromosome arms, possibly reflecting a balance between positive and negative selection for the codeletion of linked TSGs and essential genes, respectively. We also examined the impact of whole genome doubling (WGD), by extending the definition of a 'two-hit' to that of an 'all-hit'. Despite higher deletion rates in WGD samples, we see that all-hit frequencies of TSGs remain consistent. Further evidence suggests that this arises because point mutations and deletions in TSGs tend to precede WGD in the course of tumour evolution. By elucidating how TSG mutations shape tumour evolution and vice-versa, these findings can aid TSG identification and functional impact prediction of TSG point mutations.

Biosketch

Sabarinathan Radhakrishnan is a faculty at the National Centre for Biological Sciences (NCBS), Bangalore; and his lab is interested in the application of computational and functional genomics approaches to study the cancer evolution. He obtained his PhD in Bioinformatics from the University of Copenhagen, Denmark and then did his post-doctoral training (with Prof. Nuria Lopez-Bigas) in the area of computational cancer genomics at the Institute for Research in Biomedicine (IRB), Barcelona.

Prof. Sandeep Dave

Dukes University, USA

https://medicine.duke.edu/profile/sandeep-s-dave

Sandeep Dave is the Wellcome Distinguished Professor of Medicine at Duke University. Dr. Dave received his engineering and medical degrees from Northwestern University. He completed his clinical and post-doctoral training at Northwestern (internal medicine) and the National Institutes of Health (hematology-oncology) in Bethesda, Maryland. With a background in computing and medicine, his research develops genomic approaches to better understand the biology of blood cancers and to clinically translate the application of genomic technologies.

Dr Dave's work has been published in many peer-reviewed journals including *Cell, Nature Genetics*, *Blood*, and the *New England Journal of Medicine*. In addition to institutional awards for his teaching and research, he has also been the recipient of many honors and awards including the Research Scholar Award from the American Cancer Society and a career award from the Doris Duke Foundation. He was elected to the American Society of Clinical Investigation, the honor society of physician scientists and the Scientific Advisory Board of the Lymphoma Research Foundation. He is a standing member of the NIH Cancer Genetics Study Section and editor of the WHO ("blue book) for blood cancers.

Since 2018, Dr. Dave has led the spinoff ddb.bio to clinically translate genomics through the development of Duoseq, a complete solution for DNA and RNA sequencing in blood cancers.

A Targeted Panel of 295 Genes for Multiple Myeloma

Prof. Anubha Gupta

IIIT Delhi

https://www.iiitd.ac.in/anubha

Abstract

Abstract: Multiple myeloma (MM), a hematological cancer, evolves from a benign premalignant stage of monoclonal gammopathy of undetermined significance (MGUS) at a low and variable rate. MM shares genomic features with MGUS. Identifying distinctive features of these two entities is vital to understanding myeloma pathogenesis. We present a clinically-oriented targeted panel of 295 genes that potentially cause MGUS-to-MM transition and influence survival outcome in MM. Additionally, we introduce the concepts of transformative genes that are significantly altered in the malignant stage (MM) but not in the premalignant stage (MGUS). This is achieved by designing an attention-based graph neural network, namely BIO-DGI, that extracts gene-gene interactions utilizing a-priori information from nine protein-protein interaction (PPI) databases. BIO-DGI analyzes the whole-exome sequencing data of 1154 MM and 61 MGUS samples collected from a diverse population of American, European, and Indian subcontinents. This 295-gene panel can provide critical insights into disease progression.

Biosketch

Anubha Gupta received her PhD. from IIT Delhi, India in 2006 in Electrical Engineering. She did her second Master's from the University of Maryland, College Park, USA from 2008-2010 in Education. She worked as Assistant Director with the Ministry of I&B, Govt. of India from 1993 to 1999 and, as faculty at NSUT-Delhi (2000-2008) and IIIT-Hyderabad (2011-2013), India. Currently, she is working as a Professor at IIIT-Delhi. Prof. Gupta has authored/co-authored more than 100 technical papers, has two US and two Indian patents. She is a recipient of SERB POWER Fellowship, 2021 and IETE PROF SVC AIYA MEMORIAL AWARD-2022. Her recent work on "Explainable AI Model for Cardiac Disorder Detection" won the 2023 "Lab2market" challenge of IndiaAI, Govt. of India. Her research interests include applications of machine learning in cardiovascular disease diagnosis, cancer genomics, cancer imaging, biomedical signal and image processing including fMRI, MRI, EEG, and ECG signal processing.

Mr. Mainak Chakraborty

AWS, India

https://aws.amazon.com/government-education/worldwide/india/

Abstract

Viewing biological sequences as the 'language of life' opens up exciting possibilities for applying generative AI to the field of protein engineering and design. Just as large language models can be trained on vast text datasets to become helpful assistants exhibiting language understanding, generative biology models can learn the "language" of proteins by training on extensive protein sequence data. By understanding the patterns and relationships within these sequences, these models are capable of generating novel, functional protein sequences tailored for applications like drug design, enzyme engineering, or synthetic biology. While proteins are different from text due to their three-dimensional structures, this highlights the potential for leveraging the power of generative AI to accelerate discoveries and innovations in fields revolving around the building blocks of life. This technology is at the heart of transformation that ties together evolution, molecular biology, artificial intelligence, medicine, and health.

AWS is at the forefront of accelerating generative AI innovation, enabling organizations to harness the power of large language models (LLMs) and foundation models (FMs). By providing easy access to the broadest set of high-performing generative AI models, AWS simplifies the process of building and scaling generative AI applications. We are seeing tremendous excitement and momentum around generative AI in the life sciences space from small scale process automation to fundamentally changing research and discovery. For example, AstraZeneca is accelerating the transformation of drug discovery and precision medicine using genomics, so that researchers can turn insights into science faster. Gilead is generating insights from key datasets that accelerate the analysis of large quantities of unstructured information from a variety of sources across their enterprise. Pfizer has deployed AI solutions to create medical/scientific content and patent applications, enabling breakthroughs to reach patients faster. Do join me in this session to understand how you can harness AI to revolutionize your genomics and life sciences research using AWS.

Biosketch

Mainak Chakraborty is a Senior Solutions Architect at AWS cloud specialising in the field of Bio-Medical Research. He has been working with both national and international research organizations to help them innovate and accelerate their research using the power of AWS services. His expertise lies in helping researchers and scientists design and run analysis of clinical, genomics and imaging data at scale, generate new insights, build machine learning models and use generative AI to solve complex problems in life sciences and precision medicine.

Keynote Address

Prof. Abhay Karandikar

Secretary to the Government of India, Department of Science & Technology

https://dst.gov.in/

Biosketch

Prof. Abhay Karandikar is currently Secretary, Department of Science of Technology (DST). Before joining DST in October 2023, he served as the Director, IIT Kanpur from April 18th, 2018 to September 25th, 2023 (on lien from IIT Bombay). He also served as Dean (Faculty Affairs) and Head of the Electrical Engineering Department at IIT Bombay. He spearheaded a national effort in setting up Telecom Standards Development Society of India (TSDSI), India's standards body for telecom with participation of all stakeholders. Prof Karandikar was the founding member and former Chairman of TSDSI. He was also Member (Part-Time) of Telecom Regulatory Authority of India (TRAI) from January 2018- January 2021. Prof Karandikar has several patents issued and pending, contributions to IEEE, 3GPP standards,contributed chapters in books and large number of papers in international journals and conferences to his credit. Prof Karandikar was awarded with IEEE SA's Standards Medallion in December 2016 in New Jersey. His team also won Mozilla Open Innovation challenge prize in March 2017 for his work on rural broadband and digital empowerment in rural India.

Panel Discussion

Panelists:

Dr. Banya Kar (BRIC-NII) [Moderator]
Dr. Madhuri Dutta, (The George Institute of Global Health)
Dr. Nitya Nand Sharma (Premas Life Sciences)
Dr. Amitavo Mitra (Saikrishna & Associates)
Dr. Narendra Kumar, Scientist (BRIC-NII)

Biosketch

Banya is a biologist-turned-science communication and engagement practitioner. She currently leads science communication and public relations at the National Institute of Immunology (NII) in New Delhi. With a PhD in Life Sciences from Utkal University, Dr. Kar has over six years of experience in ideation, strategy, and execution of organizational communications and science engagement. She has facilitated national and international partnerships and orchestrated multi-stakeholder programs. Dr. Kar is passionate about building an evidence base for effective science engagement practices in India and has a strong understanding of the national science and health research ecosystem.

Madhuri is the Head - Centre for Operational Research Excellence at George Institute for Global Health India and leads research management and capacity building initiatives. She is an India Research Management Initiative (IRMI) Fellow, supported by the DBT/Wellcome Trust India Alliance. Madhuri is part of the global CORE unit and works with colleagues from other regional offices of the institute.
She has a PhD in life science and a decade of research management experience from her previous positions at the DBT/Wellcome Trust India Alliance, Public Health Foundation of India and Indian Institute of Health Management Research. She has contributed to several courses, workshops and training programmes in research skills, for early career researchers. Madhuri is interested in creating institutional processes that facilitate quality research and an enabling research environment.

Nitya Nand Sharma is Strategic Business Unit Head – Applied Genomics at Premas Life Sciences Pvt Ltd. He pursued Ph D degree in Biotechnology from Himachal Pradesh University, Shimla. Further, he worked as a Research Associate at Central Potato Research Institute, Shimla, to develop transgenic potato against late blight - a highly devastating disease.
In 2012, explored the genomics service forefronts while working as a Jr Scientist – Genomics in Xcelris Genomics based in Ahemdabad responsible for successful execution of various genomics and transcriptomics projects. In 2013, started sales career with Premas Life Sciences as Territory Sales Manager, and gained techno commercial expertise in the genomics space, gaining insights of genomics technologies of Illumina, Fluidigm, 10x Genomics, Covaris, etc.

Amitavo is currently Partner at Saikrishna & Associates. He is a patent law expert with particular focus in the biotech, biomedical device(s), and pharma domain. He holds a PhD in Cellular and Molecular Biology from Dartmouth College and postdoc from Tufts Medical Centre. He transitioned to India in 2013, working at the National Institute of Immunology before

pursuing an LLB from Delhi University. Dr. Mitra has extensive experience in drafting and prosecuting patent applications. His expertise bridges the gap between advanced scientific research and intellectual property law.

Narendra did his PhD in Computational Biology from National Institute of Immunology and was a Postdoctoral Research Scientist at Georgia Institute of Technology and later Postdoctoral Computational Biologist (chromatin epigenetics) at the University of Glasgow. He changed tracks and worked as a Professional Freelancer (NGS Data Analysis) for a year before joining Jaypee University of Information Technology as an assistant professor, where he continued his research career along with teaching responsibilities. He moved to industry as a Sr. Bioinformatics Scientist at Elucidata and later worked as a Business Portfolio Partner, Dr. Reddy's Laboratories. His love for research brought him back into academic research and is currently working as a Scientist, Computational Biology at NII.

Panel Discussion

Panelists:
Dr. Anamika Gambhir (Department of Biotechnology, Government of India)
Dr. Anand Deshpande (Persistent Systems Ltd.)
Prof. Anurag Agrawal (Ashoka University) – Lead Discussant
Dr. Krithika Rangarajan (AIIMS New Delhi)
Prof. Sharmila Bapat (BRIC-NCCS)

Biosketch
Dr. Anamika Gambhir is currently Scientist G at Department of Biotechnology, Government of India.

Dr. Anand Deshpande is the Founder, Chairman, and Managing Director of Persistent Systems. With a B.Tech from IIT Kharagpur and a Ph.D. in Computer Science from Indiana University, he has been a visionary leader since 1990. Under his guidance, Persistent Systems has grown into a global company with over 23,000 employees. Dr. Deshpande has received numerous accolades, including the EY Entrepreneur of The Year™ Award in 2023. He is also actively involved in various educational and non-profit initiatives, focusing on data, higher education, and entrepreneurship.
He is a part-time member of the Unique Identification Authority of India (UIDAI), a trustee of the VLDB Foundation, and is actively working on projects to create a data platform for Indian patients suffering from cancer (founder member of Indian Cancer genome Atlas) and diabetes. He is an honorary Adjunct Professor of Practice at the Desai Sethi School of Entrepreneurship at IIT Bombay, Chairman of the Board of Governors of IIT Patna, and the interim Chairman of the Board of Governors at IIIT Allahabad. In addition, he is on the governing board of the College of Engineering, Pune, and on the board of Gokhale Institute of Politics and Economics, Pune. Currently, he is member and co-Chairperson Governing Body, Biotechnology Research and Innovation Council (BRIC).

Professor Anurag Agrawal is Dean, BioSciences and Health Research, Trivedi School of Biosciences, Ashoka University, India, and former director of the Institute of Genomics and Integrative Biology, a national laboratory of CSIR, India. After completing graduate medical education at the All India Institute of Medical Sciences, Delhi, he further trained in Internal Medicine, Pulmonary Disease and Critical Care at Baylor College of Medicine, Houston, USA, followed by a PhD in Physiology from Delhi University. His primary research is in respiratory biology and broader interests are in a new vision of health and healthcare seen through the lenses of emerging technologies. He serves on numerous national and global advisory groups, most recently chairing the World Health Organization technical advisory group for viral evolution. He received the Shanti Swaroop Bhatnagar Prize in 2014, the Sun Pharma Foundation award in 2020, and is a fellow of the Indian national science academies.

As a radiologist and a pioneering researcher in data science, Dr. Krithika Rangarajan's mission centres on harnessing the potential of data science to infuse a more compassionate approach into medical practice. Her extensive research focuses on two critical aspects:

leveraging AI to extend healthcare to underserved regions and reinstating the human element in doctor-patient interactions for a more holistic healing experience.
Currently holding positions as an Oncoradiologist and an Assistant Professor at the esteemed All India Institute of Medical Sciences, New Delhi, she brings a wealth of experience to the table. Her prior role as a postdoctoral fellow at the Indian Institute of Technology, Delhi, further augmented her expertise.
With an MD from AIIMS and being a fellow of the Royal College of Radiology, her credentials underscore her profound knowledge and accomplishments in the field. At Ashoka University, she will impart her insights and expertise through a dedicated course on precision health. Her commitment to merging technology with compassion in healthcare aligns perfectly with Ashoka's ethos of holistic education and impactful learning.

Dr. Sharmila Bapat, Director BRIC-NCCS, Pune heads the ovarian cancer biology group at the National Centre for Cell Science, Pune. Her research involving the identification of quiescent, regenerative ovarian cancer stem cells, their transcriptional regulation, neo-angiogenesis, drug resistance and tumor dormancy are considered pioneering. Over the last several years her group has integrated basic biology approaches with computation to interpret ovarian cancer intra-tumor heterogeneity and cellular plasticity, besides identification of systems-based gene signatures and transcriptional networks. Dr. Bapat has received several awards including ICMR-Prem Nath Wahi Award, DBT-National Woman Bioscientist Award, R.M. Tiwari Research Oration Award, TATA Innovation Award, Fulbright Fellowlowship (USIEF)etc. besides recognition as Fellow of the Indian Academy of Sciences (Bangalore), National Academy of Sciences (Allahabad) and Maharashtra Academy of Sciences (Pune). She currently serves on the Council of the Indian Academy of Sciences, Bangalore, and is Secretary of the Pune Chapter of the NASI. Dr. Bapat holds professional memberships of American Association of Cancer Research (AACR), Indian Association of Cancer Research (IACR), Indian Society of Cell Biology (ISCB), International Epigenetics Society and Indian Women Scientists Association.

Lightning Talks

Enhancing Cancer Patient Care: Integrating Palliative Approaches and LLM(Large Language Model)s

Presenting Author: Ashish Makani
Ashish Makani, Dr Anurag Agrawal
KCDH-A, Ashoka University, Sonepat, Haryana

Abstract
Cancer remains a leading cause of mortality worldwide, with complex factors contributing to patient deaths. This presentation synthesizes insights from two critical areas of research: the underlying causes of cancer mortality and the potential of Large Language Models (LLMs) in palliative care. Recent studies have elucidated that cancer patients often succumb not just to the primary disease, but to a cascade of secondary complications. These include organ failure, infections, and the physical and emotional toll of aggressive treatments. Importantly, research indicates that early and consistent palliative care can significantly improve both quality of life and survival rates among cancer patients. In light of these findings, there is a pressing need for innovative approaches to deliver comprehensive, patient-centered palliative care, particularly for patients recovering at home. Large Language Models (LLMs) emerge as a promising tool in this context. These advanced AI systems can potentially revolutionize home-based care for cancer patients in several ways:
1. Personalized Information: LLMs can provide patients with tailored, easily understandable information about their condition, treatment options, and palliative care strategies.
2. Symptom Monitoring: Through natural language interactions, LLMs can help track and analyze patient-reported symptoms, alerting healthcare providers to concerning changes.
3. Emotional Support: LLMs can offer 24/7 conversational support, addressing the psychological aspects of cancer care that are crucial in palliative approaches.
4. Treatment Adherence: These models can send reminders and educate patients about the importance of adhering to their treatment and palliative care plans.
5. Care Coordination: LLMs can assist in coordinating complex care schedules and facilitating communication between patients, caregivers, and healthcare providers.
By integrating LLMs into palliative care strategies, we have the potential to address many of the factors contributing to cancer mortality, especially for patients recovering at home. This approach promises to enhance the continuity of care, improve patient engagement, and potentially increase survival rates through better management of symptoms and complications. This presentation will explore the intersection of these two critical areas, discussing both the challenges in current cancer care and the innovative solutions that LLMs offer in the realm of palliative care. By bridging these concepts, we aim to outline a future where technology-enhanced palliative care becomes an integral part of comprehensive cancer treatment, ultimately improving outcomes for patients worldwide.

Integrated Multi Omics Analysis of Young Onset Breast Cancer – An In-Silico Approach, Using Public Datasets

Presenting Author: Hari P S
Email: hari.ps@ssnccpr.org
Hari PS[1], Guruguhan S[1], Aruna Korlimarla[1]

[1]Department of Research, Sri Shankara Cancer Hospital and Research Center, Bangalore

Background

Breast cancer (BC) incidence is rising among young women, with aggressive features and high metastatic rates. Young onset Breast Cancer (YBC), defined by ESMO as ≤40 years of age, has a worse prognosis and may represent a distinct pathological entity compared to breast cancer in those >60 years (OBC). YBC often requires intensive treatment wherein, not all patients respond similarly, underscoring the need for personalized therapies. We aimed to understand the aggressive nature of YBC and identify potential drivers using multi-omic profiling of age-separated publicly available datasets.

Patients and Methods

We analysed gene expression from RNA sequencing data, DNA alterations, proteomic profiles along with clinical information from the TCGA and METABRIC cohorts. Initially, using a machine learning model on batch-corrected RNA-Seq data from a combined YBC cohort (n=218), we identified potential prognostic clusters. These clusters were functionally annotated and clinically correlated. Further analysis with additional data validated pathway markers and consistency.

Results

These analyses identified 6 prognostic clusters, enriched with pathways related to ERBB2 signaling, cell cycle, immune system, ECM organization, and metabolism. Multi-omics integration confirmed the robustness of these processes in YBC, revealing intricate regulatory networks and key protein interactions.

Conclusions

This integrative multi-omics analysis offers a strong prognosis-based classifier for understanding young-onset breast cancer. By identifying key biomarkers and targets, the study supports the development of personalized treatments to improve patient outcomes.

Multi-ensemble machine learning framework for omics data integration: A case study using breast cancer samples

Presenting Author: Sunitha M Kasibhatla

Email (presenting authors): sunithak@cdac.in and archanasa@cdac.in

Kunal Tembhare, Tina Sharma, Sunitha M. Kasibhatla, Archana Achalere, Rajendra Joshi

HPC-Medical and Bioinformatics Applications Group, Centre for Development of Advanced Computing, Innovation Park, Panchavati, Pashan, Pune, 411008, Maharashtra, India

Abstract

Multi-omics data in conjunction with clinical information has enabled customisation of prognosis, diagnosis and predictive accuracy of various disease phenotypes. Machine learning approaches provide insightful techniques for systematic multi-omics data integration. In this study, survival prediction of breast cancer patients was undertaken using omics data of 302 female patients from The Cancer Genome Atlas (TCGA). The data included gene expression, miRNA expression, DNA methylation and copy number variation. Three computational multi-ensemble ML pipelines were tested using Support Vector Machine (SVM), Random Forest (RF) and Partial Least Squares-Discriminant Analysis (PLS-DA) algorithms. Analysis of the results obtained revealed that SVM with PLS-DA method (integrated with gene expression, DNA methylation, and miRNA expression modalities) was the best-performing model with an Area Under Curve (AUC) of 89% and an accuracy of 83% for survival prediction (Figure 1). Predicted biomarkers include hub-genes like *PELO*, *HSPA8*, *PIK3CA* and *APOBEC3F* from gene-expression data; ITGA5, ZNF135, ZSCAN16, VRK3, AFF3, CASP14, PCSK6,EDA, FGF22, BZW2, KCNC3, EDC4, TAC1, NDUFB9, DCLK1, SPOCK1 from DNA methylation data; mir-625, mir-144, mir-31, mir-1305, mir-26b, mir-425, mir-130a, mir-30a, mir-511, mir-342 from miRNA expression data. Nonsense-mediated decay (NMD) a nuclear-transcribed mRNA catabolic process important for maintaining the quality of the transcriptome and that averts generation of putative truncated or potentially harmful proteins was found to be enriched.

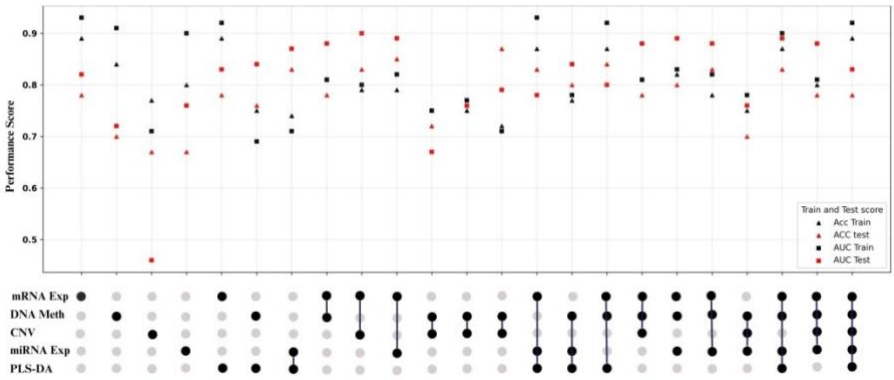


Figure 1: Performance metrics of individual and combined data modalities for SVM and SVM+PLS-DA models

Reference:

- Tembhare K, Sharma T, Kasibhatla SM, Achalere A, Joshi R, Multi-ensemble machine learning framework for omics data integration: A case study using breast cancer samples, Informatics in Medicine Unlocked, 47, 2024, 101507, ISSN 2352-9148, https://doi.org/10.1016/j.imu.2024.101507.

Designing a Data-driven Discovery Framework for Oncology: Opportunities and Challenges

Presenting Author: Dr. Urmila Kulkarni Kale
Email (presenting author): urmila@citadelpm.io
Anant Shelke, Meenal Kinikar, Nithin Rao, Rishikesh Parulekar, Supriya Hakeem, Subhash Ajmani, Jimmy Ye & Urmila Kulkarni Kale
Citadel Precision Medicine India Pvt. Ltd, Hyderabad, India.

Abstract

The premise of precision medicine in oncology recognizes that all cancer patients are unique, as are their disease progression trajectories and treatment responses. The Cancer Genome Atlas (TCGA) provides access to patient (and cohort) records across various modalities, such as clinical, radiological imaging, genomics, transcriptomics, proteomics, and many others. An attempt has been made to develop statistical and AL/ML-based algorithms to analyze breast cancer data to facilitate the discovery of diagnostics and prognostic biomarkers and signatures. The cohort-based analytics provides in-depth analysis, including stratification based on overall survival. The patient-based analytical models enable BRCA subtype prediction using MRI image data, tumor immune microenvironment characterization using transcriptome, and precision prescription prioritization (PPP) simulation using multi-modal multi-omics data. The algorithms for PPP are modular and allow users to carry out analytics using an individual modality and a combination of multi-modal and multi-omics data. These outcomes aid in diagnosis, prognosis, and prioritization of therapy and will be presented using breast cancer as a case study. The framework is, however, open and modular to ingest and analyze data from other solid tumors. To realize the potential of precision medicine and data analytics across therapy areas, it is imperative to establish a partnership with national and international stakeholders. One of the significant bottlenecks that need to be addressed is the limited availability of patient data, an essential prerequisite for training and validating AI/ML algorithms. This calls for developing robust data sharing and access frameworks adhering to patient data privacy and various regulatory practices.

Innovative Approaches in Cancer Research: From Microbiome to Omics

Nagarajan (Raj) Kannan, Ph.D.
Mayo Clinic, Rochester, MN, USA
https://www.mayo.edu/research/faculty/kannan-nagarajan-ph-d-m-s/bio-20233074

Biosketch

Nagarajan Kannan, Ph.D., is combining cutting-edge technologies to study single cells, genetic approaches to track clones, and functional assays to quantify stem and progenitor cell numbers and their differentiation programs. Through his research in his Stem Cell and Cancer Biology Laboratory, Dr. Kannan hopes to identify cellular and molecular mechanisms that prevent or promote development of faulty progenitors in healthy epithelial tissues and their evolution into malignancies such as breast cancer.

In addition to being principal investigator of the Stem Cell and Cancer Biology Lab and conducting clinical studies, Dr. Kannan is an assistant professor of laboratory medicine and pathology at Mayo Clinic College of Medicine and Science in Rochester, Minnesota. One of Dr. Kannan's main missions is to discover rare, cancer-prone faulty progenitor cells hidden in healthy breast tissues. This research may lead to improved early detection of cancer and to preventive therapies for people at a higher risk of developing breast cancer.

Transcriptome Informed Discovery and Immuno-therapeutic Targeting of Tumor Specific Antigens in AML - and Solid Malignancies

Soheil Meshinchi, MD., Ph.D.

Fred Hutchinson Cancer Center, Seattle, WA

https://www.fredhutch.org/en/faculty-lab-directory/meshinchi-soheil.html

Abstract

Acute myeloid leukemia (AML) has remained a therapeutic challenge with minimal advances in treatment options over the past three decades. This stagnation is partly due to the lack of appropriate targets and targeted therapies. Current targeted therapies focus on AML-associated antigens, such as CD33 and CD123, which are also expressed in normal hematopoiesis. This overlap limits the utility of these therapies, as effective targeting of these antigens could lead to severe myelosuppression or myeloablation.

Our goal was to identify AML-specific targets for therapeutic development—antigens that are expressed exclusively in AML and are completely absent in normal hematopoiesis. Targeting these AML-specific antigens could potentially eradicate the disease without causing hematopoietic toxicity.

We have completed transcriptome sequencing of 300 normal hematopoietic specimens, as well as diagnostic specimens from over 3,000 children and young adults with AML. By comparing the transcriptomes of normal hematopoiesis and AML, we identified a list of AML-specific genes. These genes were further classified into transmembrane and intracellular targets based on the presence or absence of a transmembrane domain sequence motif.

We have advanced three targets through our pre-clinical, IND-enabling pipeline: FOLR1 CAR-T, currently in a clinical trial for infant AML; Mesothelin CAR-T, in clinical development for KMT2A-r AML; and PRAME TCR mimic CAR-T, which has completed all IND-enabling studies and is preparing to enter a clinical trial for high-risk AML. Several other AML-specific targets are in various stages of development. Additionally, to optimize the use of these assets, we are evaluating the expression of these targets in other malignancies.

Given the high expression of FOLR1 in solid tumors, FOLR1 CAR-T is advancing into clinical trials for osteosarcoma, ovarian, uterine, and pancreatic cancers, with similar plans for Mesothelin and PRAME. We propose that data driven, sequence informed identification of tumor-specific targets is a viable path toward effective therapeutic development for malignancies.

Biosketch

Dr. Soheil Meshinchi is a Full Professor at the Fred Hutchinson Cancer Center in Seattle. With over 25 years of experience in AML biology, he chairs the NCI designated Integrated Translational Science Center (ITSC) and NCI TARGET AML initiative. As part of TARGET AML initiative, they have sequenced over 3000 AML cases where the data from this sequencing effort is being used to discover AML-specific targets for therapeutic development.

A library of validated AML-specific targets has been transitioned into clinical development as Chimeric Antigen Receptor (CAR) T cell therapies, Antibody-Drug Conjugates (ADC), or Bispecific T cell Engagers (BiTE). Shared targets between AML and solid tumors are also under study as potential therapeutic options in high-risk solid malignancies.

Dr. Dimple Notani
Associate Professor & EMBO Global Investigator
National Centre for Biological Sciences-TIFR, Bengaluru
https://www.ncbs.res.in/notanilab

Dr Notani's lab is interested in understanding the features of functional enhancers and how they regulate the transcription. They use genomics, single cell perturbations, molecular biology and microscopy approaches to delineate the enhancer functions.

The goal of their research is to extend the understanding of these molecular mechanisms underlying the linkages between chromatin domains, distal regulatory elements and associated non-coding RNAs (the enhancer RNAs) in gene regulation. The gained knowledge will help develop strategies to target enhancer to amend the mis-expression of disease related causal genes as "enhancer therapy." The group uses combination of approaches such as Genetic perturbations, molecular biology, biochemistry, genome sequencing and live cell imaging to functionally tie the enhancers, transcription and genome folding.

Dr. Philip Beer
Step Pharma, UK
https://step-ph.com/portfolio/philip-beer/

Abstract
The genomics revolution is fundamentally changing the way cancer is diagnosed and treated. Genomics is powering the discovery of a new generation of anti-cancer drugs, as well as the development of biomarkers to select patients who are most likely to derive benefit. Genomics is increasingly informing cancer diagnosis, stratification and prognostication. As cancer is essentially a disease of the genome, genomics also underpins many biological insights into the genesis of malignant transformation and the evolution of drug resistant disease.
Despite recent advances, barriers exist at all stages of this pathway that prevent the full utility of genomic data being realised. The large datasets currently underpinning research are largely populated with cancers from patients in Europe and North America, and are biased, therefore, both in terms of the constitutional genetics of the subjects and the likely environmental exposures that caused their cancers. When genomically targeted therapies do reach the market, access is often hindered by difficulties accessing appropriate testing, even in countries with well-funded healthcare systems. Related to this, genomic testing is often perceived to be too expensive for routine use, and confusion remains around the best assay to use at different stages of the patient journey.
This talk will explore how genomics is powering modern drug development and patient treatment, whilst highlighting current barriers and suggesting potential solutions. Key bottlenecks and learnings will be illustrated, where appropriate, by research vignettes and clinical case histories.

Biosketch
Philip is a physician scientist and cancer biologist. He is currently Chief Scientific Officer at Step Pharma, a small French biopharma with a first in class anti-cancer drug in phase 1 clinical development. Alongside drug development, Philip works extensively in the cancer genomics space, through research projects, including the International Cancer Genome Consortium, and clinical molecular tumour board work. Philip is a board certified haematologist trained at Imperial College, London; he undertook a PhD at the University of Cambridge, UK, and post-doctoral studies at the BC Cancer Agency, Vancouver, Canada.

Keynote Address

Dr. Rajesh S. Gokhale
Secretary, Department of Biotechnology,
Government of India

Dr. Rajesh Sudhir Gokhale is a Professor of Biology at Indian Institute of Science Education and Research, Pune on lien. Currently, serving as Secretary for Department of Biotechnology (DBT) Government of India from October 2021 onwards. He joined as a faculty in National Institute of Immunology, India after conducting his postdoctoral training at Stanford University, He was the Director of Institute of Genomics and Integrative Biology from 2009 to 2016. Dr. Gokhale is known for his studies on the metabolic diversity of pathogens. He is credited with the discovery of a family of Long-chain Fatty acyl-AMP ligases (FAAL) and his studies assisted in the elucidation of biochemical crosstalk between fatty acid synthases and polyketide synthases in Mycobacterium tuberculosis. He holds US and Indian patents for his invention of Method to Modulate Pigmentation Process in the Melanocytes of Skin. An alumnus of the Indian Institute of Science, he is an elected fellow of the Indian Academy of Sciences (2007)[5] and the Indian National Science Academy (2014). The Council of Scientific and Industrial Research, the apex agency of the Government of India for scientific research, awarded him the Shanti Swarup Bhatnagar Prize for Science and Technology, one of the highest Indian science awards, in 2006, for his contributions to biological sciences. He received the National Bioscience Award for Career Development of the Department of Biotechnology in 2009.

Prof. Ravi Mehrotra

Founder, Centre for Health Innovation and Policy (CHIP) Foundation
Director, Indian Cancer Genome Atlas (ICGA) Foundation

https://www.ravimehrotra.co.in/

Abstract

Cancer screening and diagnosis are rapidly advancing through genomic technologies, revolutionizing early detection and precision medicine. Genomic tools, including next-generation sequencing (NGS) and liquid biopsies, enable comprehensive analysis of tumor DNA and RNA, uncovering genetic mutations and molecular signatures that inform diagnosis. These innovations facilitate earlier detection of cancers, including those difficult to diagnose with traditional methods, and guide personalized treatment approaches. However, integrating genomic data into clinical practice raises challenges such as data interpretation, cost, and ethical considerations. Despite these hurdles, genomic advancements hold great promise for enhancing cancer screening, improving diagnostic accuracy, and tailoring patient care.

Biosketch

Professor Ravi Mehrotra's expertise covers the gamut of cancer prevention, state of the art diagnostics and treatment. He is currently Founder of Centre for Health Innovation and Policy Foundation and Director of India Cancer genome Atlas. He was till recently the Founder- CEO of the ICMR-India Cancer Research Consortium and directed the ICMR-National Institute of Cancer Prevention and Research (NICPR) at Noida. He completed his medical training followed by MD and D.Phil. and Fellowship of the Royal College. His research includes cancer prevention and tobacco control. Editorial board member of 10 international medical journals, Mehrotra has published >200 scientific articles. He is cited more than 17,000 times and has an H-index of >50. He won the prestigious Dr.P.N.Wahi and Dr. Lachman awards in Cancer Prevention and the Ernest Fernandes Award of the Indian Academy of Cytologists, in addition to being its past President. Dr Mehrotra's research has helped shape the national cancer services in India. He has raised the profile of cancers among the general public and politicians and the subsequent political support has paved the way for many new cancer screening services now widely available in India e.g, cervical cancer screening programme. He established the WHO Knowledge Hub on Smokeless Tobacco during his tenure as the director of NICPR. This acts as a global beacon of knowledge on smokeless tobacco. His impact on health at an international level has also been phenomenal. By working as committee members at the International Agency for Cancer Research (IARC) he has contributed to several key global policy and technical documents on cancers.

Launch of ICGA Data Portal

At the ICGA2024 Annual Meeting, the Indian Cancer Genome Atlas will launch its highly anticipated data portal, a customized version of cBioPortal. This cutting-edge platform is designed to facilitate data sharing within the scientific and medical communities, offering an invaluable resource for oncogenomics research. With enhanced capabilities tailored to analyze a wide range of cancer-related data, from biomarkers to proteomics, the ICGA data portal promises to accelerate data-driven discoveries and foster collaboration across the field of cancer research in India and beyond

Precision Oncology: A Way Forward

Engineered 3-D ex vivo tumor models: Game changers in drug discovery and precision medicine

Dr. Neha Arya

Department of Translational Medicine, All India Institute of Medical Sciences, Bhopal

https://aiimsbhopal.edu.in/index_controller/facultyDetails?sid=218&id=

Abstract

Two-dimensional (2-D) culture of cancer cells and xenograR models are the gold standards for preclinical testing of candidate molecules. While the 2-D flat culture offers simple and inexpensive culture practices, the cells grown on 2-D substrates do not completely recapitulate the traits of solid tumors. As a result, 2-D cultures demonstrate a poor co-relation with the in vivo tumor drug sensitivity. On the other hand, in vivo models are associated with enhanced cost, increased incubation time along with difficulty in visualizing dynamics of metastasis. Therefore, there has been a paradigm shift toward the development of 3-D ex vivo tumor models that can mimic the properties of solid tumors in vivo and can be utilized for understanding disease pathophysiology as well as in drug discovery. In my talk, I will discuss about various 3-D ex vivo tumor models engineered in our laboratory and their applications in pre-clinical research.

Biosketch

Dr. Neha Arya is currently working as an Assistant Professor at the Department of Translational Medicine, All India Institute of Medical Sciences (AIIMS), Bhopal. She received her Bachelor's and Post-Graduate Degree in Microbiology from the University of Delhi. She earned her Ph.D. degree from Indian Institute of Technology Kanpur, Department of Biological Sciences and Bioengineering following which she went to the University of Freiburg, Germany as a Post Doctoral Researcher. Thereafter, she worked as a DST-INSPIRE Faculty Fellow at AIIMS Bhopal and as an Assistant Professor in Medical Devices National Institute of Pharmaceutical Education and Research (NIPER)-Ahmedabad. The overarching interests of her research group include design and fabrication of biomaterials for tissue engineering (with a focus on in vitro tumor models) and point-of-care cancer diagnostics.

Unraveling the Tapestry of Gastrointestinal Cancers: A Single-Cell and Spatial Transcriptomic Approach

Dr. Ashiq Masood
Indiana University, Indianapolis, USA

https://cancer.iu.edu/about/members/bio/30117

Abstract
Gastrointestinal (GI) cancers encompass a diverse array of solid tumor malignancies characterized by complex molecular landscapes and significant cellular heterogeneity. Traditional approaches such often whole genome sequencing and bulk transcriptomics fail to capture the intricate details of these complex tumors. My presentation focuses on how integrating single-cell RNA sequencing and spatial transcriptomics provides unprecedented insights into the biology of GI cancers. Our work, along with findings from other studies, uncovers remarkable insights in GI Cancer biology. Single-cell transcriptomics has enabled the identification of distinct cellular subpopulations, including rare and previously uncharacterized cell types, uncovering key differences in gene expression patterns that drive tumorigenesis, progression, and metastasis.
Spatial transcriptomics complements this by mapping cellular entities within their tissue context, offering insights into spatially resolved gene expression gradients and cellular ecocritical to tumor development and therapeutic response. The findings deepen our understanding of the molecular underpinnings of GI cancers and identify promising therapeutic targets and diagnostic markers, ultimately advancing the field of personalized medicine.

Biosketch
Dr. Ashiq Masood is a physician-scientist serving as the GI Oncology Program Leader and Associate Professor of Medicine at Indiana University School of Medicine. With extensive training in computational biology and cancer genomics, Dr. Masood's research focuses on leveraging single-cell RNA sequencing and spatial transcriptomics to unravel therapeutic resistance mechanisms in gastrointestinal tumors. His expertise spans both laboratory research and clinical practice, as he actively treats patients with GI cancers and has significant experience in clinical trials. Dr. Masood's work at the intersection of advanced genomic technologies and clinical oncology positions him as a leader in the field, contributing to the development of innovative approaches in GI cancer treatment and research

Molecular Subtyping and prediction of risk of recurrence for early stage receptor positive breast cancer using NanoString nCounter Flex from India

Prof. Arvind Krishnamurthy

Arvind Krishnamurthy, Vijayalakshmi Ramshankar, Aravinda Lochan, Srinidhi R, V. Radhakrishnan, Cancer Institute, Chennai

https://cancerinstitutewia.in/surgical-oncology

Abstract:

The management of breast cancers depend on several clinico-pathological factors such as age, performance status, tumor size nodal status, metastasis, grade, hormone receptor status, HER2 neu status, patient preference among others. In the era of precision medicine and personalised medicine, many Gene Expression Assays provide predictive and prognostic information beyond that obtained from the classical clinicopathologic factors. In routine, clinical practice, the gene expression assays are primarily used to identify high genomic risk early-staged breast cancer patients (mainly Stages I and II, hormone receptor positive, HER2-neu negative) who are more likely to benefit from the addition of chemotherapy to adjuvant endocrine therapy. Additionally, these assays can potentially help prognosticate selected patients of breast cancers

The commercially available assays include Oncotype DX, MammaPrint, Prosigna, EndoPredict, and Breast Cancer Index. These assays are typically performed following surgery (from formalin fixed paraffin-embedded tissue). However, the penetration of the above-mentioned gene expression assays in routine clinical practice in the Indian subcontinent is low and this has largely been attributed to its higher costs and the increased turnaround times.

The prediction analysis microarray (PAM50) gene expression assay using Nano String nCounter Flex measures mRNA expression of 50 cancer-related genes; the assay classifies the tumors by breast cancer intrinsic subtype and generates its risk of recurrence (ROR) score. We have been offering this molecular service for our patients and for patients operated at other centers as well. We intend to present our results of its clinical utility in 180 patients.

Considering the results of (PAM50) gene expression assay using Nano String nCounter Flex as gold standard, we observed the discordance rates on the clinical decision made by oncologists blinded to the results of the assay to be as high as 45 % with the vast majority of the clinicians over estimating the clinical risk of recurrence and advising chemotherapy for their patients. Our study thus reiterates the clinical utility of genomic risk over and above clinical risk, which will potentially aid help oncologists in making better informed decisions with regards to the management and prognostication of early-stage breast cancers.

Biosketch

Dr. Arvind Krishnamurthy is a Professor and Head of Surgical Oncology at the Cancer Institute (WIA) Adyar, Chennai. He did his Super Specialty Oncology training from the prestigious Tata Memorial Center, Mumbai. His areas of clinical interest are Thoracic, Head/Neck and Breast Oncology. He has authored more than 215 publications (Including 6 book chapters) in reputed national and international peer reviewed journals. He has won several awards including the Dr. KS Sanjivi Award in 2011, Best Doctors Award from the Tamil Nadu Dr. MGR Medical University (2012) and the Iyan Valluvar award. (2010) and the Sushruta Award in Medicine (2019)

Dr. Ashutosh Mishra
AIIMS New Delhi

https://www.aiims.edu/index.php?option=com_content&view=article&id=12806&catid=222&lang=en

Abstract
As we understand more about cancers, we are able to iden3fy hereditary and environmental risk factors which affect cancer causa3on. These risk factors are an important target for interven3ons, as these interven3ons can prevent cancers. Hereditary cancers cons3tute about 16% of total cancer burden. As we have iden3fied these genes causing cancers, we have also iden3fied ways to target these and reduce cancer risk. The world s3ll lags far behind in cancer gene3cs, more so, in the low- and middle-income countries. The burden of hereditary cancers is s3ll not well documented in these countries. There is a need to iden3fy the popula3ons at risk so that we can reduce it and prolong survival by using targeted therapies where feasible. Here in India and in much of the developing world, cancer gene3cs is s3ll in its infancy facing innumerable challenges like lack of educa3on and awareness, non-affordability, nonavailability, social s3gma, and a lack of gene3c specialists. At AIIMS New Delhi, In our surgical Oncology prac3ce, we found 592 breast cancer pa3ents eligible for Gene3c counselling and tes3ng as per NCCN guidelines. Out of these, 27.9 % (165) underwent gene3c tes3ng and 89 (15%) tested posi3ve for pathogenic muta3ons. Out of these 89 pa3ents, 50 pa3ents had given consent for Risk reducing surgery. But finally, only 31 (5.2%) pa3ents underwent risk reducing surgery. These results are mo3va3ng, and we can do much beWer by Integra3ng cancer gene3cs in rou3ne oncology clinics, as that is the first point of contact for the pa3ent. Gene3c counselling and tes3ng need to be made a part of rou3ne cancer treatment and to be available to the masses, as now we have prophylac3c and therapeu3c management strategies for hereditary cancers.

Biosketch
Dr. Ashutosh Mishra is an Associate Professor at Department of Surgical Oncology at AIIMS, new Delhi. His area of interest is Breast, Gynae & GI Oncology. He has 17 years of experience in surgical oncology. Dr. Mishra has achieved many fellowships like: FACS, FSSO, F-ESSO, F-UICC, FAIS, FMAS, FIAGES, MBA etc. He is also a visiting fellow at the UHNM-UK. His surgical expertise are in Breast Oncoplasty and Minimally Invasive Gynaec and GI Surgery, HIPEC & PIPAC. Dr. Mishra has been honoured with many awards BSI-New Delhi Young Scientist Award 2021, SSO (USA) –IASO Fellowship 2021 & 2024, BSI Award by International Society of Surgery (ISS/ SIC), Vienna 2022, He is PI & Co-PI in more than 30 national and international projects funded by Cancer Research UK, NIHR UK, DBT, DST, DHT, CSIR, ICMR, NCDIR, Bayer's India etc. He has More than 50 publications in indexed Journals. Dr. Mishra is an Editorial Secretary IASO - Indian Association of Surgical Oncology [2023-2025], National Representative- European Society of Surgical Oncology [2024-2026] Scientific Committee Member- Society of Surgical Oncolgy, USA [2024-2026], Director of Education- Association of Breast Surgeons of India [2024-2026], Executive Member- Delhi Oncology Forum [2021-2024] and an Associate Editor- Annals of Breast Diseases.

Dr. Manash Paul

Manipal University

https://researcher.manipal.edu/en/persons/manash-kumar-paul

Abstract

Type I interferon (IFN-I) and IFN-gamma promote the body's immune response against tumors by helping T cells to react. Paradoxically, the activation of immunological checkpoints by IFNs may contribute to the development of T-cell fatigue. The mechanisms that control these different reactions are not well understood. We have recently elucidated the role of interferon regulatory factor 1 (IRF1) in coordinating the contrasting impacts of interferons (IFNs). The expression of IRF1 in tumor cells hinders the host's antitumor immunity by obstructing the Toll-like receptor and IFN-I-dependent pathways. This is achieved by inhibiting the interferon-stimulated gene (ISG) and effector programs in immune cells. Conversely, the presence of IRF1 in the host is necessary for the development of immune responses against tumors. From a mechanistic standpoint, IRF1 has the ability to bind either alone or in conjunction with STAT1 at the promoters of immunosuppressive, but not immunostimulatory, ISGs in tumor cells. Therefore, we may conclude that the production of IRF1 in tumor cells acts against the immune response mediated by host IFN-I and IRF1, which is necessary for suppressing tumor development and promoting immune evasion. Thus, IRF1 selectively regulates the effects of IFNs on tumor cells and the tumor microenvironment and may be targeted to boost anti-tumor immunity.

Biosketch

Dr. Paul is an expert in the field of stem cells and cancer and just joined as an Associate Professor with the Manipal School of Life Sciences, Manipal Academy of Higher Education (MAHE), Manipal, India. Before returning to India, he had an association with the University of California, Los Angeles, USA, for approximately 14 years, working as a Postdoc, a Scientist, and a Scientist Faculty (Group ID: Faculty). He has contributed significantly to stem cell biology, regenerative medicine, drug discovery, immune-oncology, and lung cancer. Dr. Paul is the recipient of many awards, including the prestigious AAISCR-R Vijayalaxmi Award for Innovative Cancer Research, UCLA Vice Chancellor's Award, Editor's Choice Award: Annuals of Biomedical Engineering, and the BSCRC Travel Award. Dr. Paul has authored more than 75 research articles and is a senior member of the IEEE, a member of many scientific societies, and an editorial member of many international journals.

Panel Discussion

Panelists:
Dr. Aastha Aggarwal (Moderator), CCDC India
Prof. AC Kataki, Former Director, Dr. Bhubaneswar Borooah Cancer Institute, Guwahati
Dr. Aruna Korlimarla, Sri Shankara Cancer Hospital and Research Center, Bengaluru
Mrs. Jyotsna Govil, Indian Cancer Society, Delhi
Dr. Siuli Mitra, CMC Vellore and DBT-Wellcome Trust India Alliance
Ms. Soumya Rajesh (Cancer Survivor)

Biosketch
Dr Aastha Aggrawal
Public health researcher with focus on chronic disease epidemiology, I have contributed to studies centered on bringing insights into risk factors and biological underpinnings of cardio metabolic conditions, cancers and beyond. Equipped with a PhD in Physical Anthropology with specialization in molecular anthropology, from the University of Delhi, India, I bring a unique interdisciplinary perspective to my work. With over a decade of experience, I've been an integral force in the entire lifecycle of research studies — from conceptualization to publishing. I am passionate about teaching and capacity building, and have trained diverse cohorts at various levels, imparting crucial knowledge in data collection, laboratory analysis, research ethics, and more technical subjects such as data linkages, genetic epidemiology - driving the growth of future public health professionals. As the Member Secretary of the Institutional Ethics Committee (IEC), I have played a pivotal role in strengthening the research ethics ecosystem at my institution thereby upholding the highest ethical standards in our endeavors. I have received various fellowships at different points in my career fueling my dedication to making a meaningful impact on global health.

Prof AC Kataki
Prof. Amal Chandra Kataki, MBBS, MD (Distinction), UICC Fellow (Geneva), is the former Director of Dr. B. Borooah Cancer Institute, Guwahati. He trained in Gynaecologic Oncology at prestigious institutions like Mayo Clinic, MD Anderson Cancer Center, and Memorial Sloan Kettering Cancer Center. With 217 research publications and 35 research projects, he is a member of RAB at AIIMS Guwahati and SAC at RMRC (ICMR) Dibrugarh. Dr. Kataki has edited several oncology books and guides PhD students at multiple universities. He has served on various expert groups for ICMR, DBT, and the Ministry of Health & Family Welfare, Government of India.

Mrs. Jyotsna Govil
Mrs. Jyotsna Govil has been a dedicated volunteer with the Indian Cancer Society since 1985 and currently serves as the Chairperson of its Delhi Branch. She has held various key positions, including Hony. Secretary (2012-2016) and Vice Chairman of the Indraprastha Cancer Society. Mrs. Govil has also been a member of the Review Board and Ethics Committee at Rajiv Gandhi Cancer Institute for 12 years. She is a founder member of the APAC HPV Consultation and represents India on its Board. Her contributions to cancer control have been recognized with numerous awards, including the Lifetime Achievement Award in 2014.

Dr Siuli Mitra

Siuli Mitra is a science communicator working to make science accessible to the public. She is currently a consultant with DBT/Wellcome Trust India Alliance, CMC Vellore, and also serves as a Consultant (Fellowship Affairs) with the Indian National Science Academy, Delhi. Trained as an anthropologist, Siuli transitioned from research to science communication, beginning her journey at BRIC-THSTI in Faridabad. She later worked as a Communications Specialist in the Office of the Principal Scientific Adviser to the Government of India, where she developed and implemented effective communication strategies. Siuli now collaborates with scientists and clinicians to build the capacity of individuals and institutions in public communication of science, technology and health.

Aruna Korlimarla

• My experience in the current position also involves development of Research and molecular diagnostics to offer a comprehensive test menu in cancer molecular diagnostics, molecular pathology and cancer genomics in an NABL certified laboratory environment. I have developed and established interpretation and reporting clinical cases in cytogenetics (such as PCR, Next Generation Sequencing, karyotype, FISH, and microarray), providing consultation to healthcare professionals and clients, assay development, and troubleshooting technical issues. • Lead a team of researchers focused on translational oncology and molecular research • Spearhead biomarker discovery projects, identifying novel targets for personalized therapies

Advancing Oncology through Genomics: Integration, Collaboration and Data Sharing

Dr JC Zenklusen

TCGA, NIH-USA

https://gdc.cancer.gov/about-gdc/gdc-team/jean-claude-zenklusen-phd

Abstract

A vital part of large-scale science must be the propagation of the data beyond publications. It is essential to provide the scientific community with the totality of the data generated to allow not only for use, but also for verification of the findings published. The Cancer Genome Atlas (TCGA) is probably the clearest example of open, full, disclosure of all the data. This talk will focus on the process and tools used for dissemination of the data to the wider sc(and lay) community.

Biosketch

Jean-Claude ZenKlusen, Ph.D., was born in 1964 in Visp, Switzerland. He earned a Master in Sciences (Biochemistry) from the University of Buenos Aires in 1990. He received his Ph.D. in Cancer Biology & Genetics from The University of Texas MD Anderson Cancer Center UTHealth Houston Graduate School of Biomedical Sciences (formerly known as The University of Texas Graduate School of Biomedical Sciences at Houston) in 1995. In 1996, he took a postdoctoral position at the National Genome Research Institute, where, while participating in the Human Genome Project, he cloned two novel tumor suppressor genes. In 2003, he joined the National Cancer Institute as the senior staff scientist at the Neuro-Oncology Branch, directing the Glioma Molecular Diagnostic Initiative and its companion data portal, Rembrandt. In 2009, he became the scientific program director of the Office of Cancer Genomics, where he oversaw a variety of large-scale projects.

In August 2013, ZenKlusen was named director of The Cancer Genome Atlas (TCGA), the largest-scale cancer genomics project to date. Under his leadership, the TCGA collaborated with more than 700 scientists across the country to develop the "TCGA PanCanAtlas," which was published in a series of papers in Cell and its sister journals in 2018. His team earned the 2015 Samuel J. Heyman Service to America Medal, a People's Choice Award, and the 2020 American Association for Cancer Research Team Science Award. In addition to TCGA, he also provided outstanding leadership for the International Genome Cancer Consortium Pan-Cancer Analysis of Whole Genomes project, leading to the publication of a series of papers in Nature and its sister journals in February 2020. Internationally recognized as an expert in genomic research and genomic technologies, ZenKlusen has more than 156 peer-reviewed publications, including dozens featured in Cell, Cancer Cell, and Nature

.

Prof. Sunil Badve

Emory University, Atlanta, USA

https://winshipcancer.emory.edu/bios/faculty/badve-sunil.html

Biosketch

Dr. Sunil S. Badve, MD, FRCPath, is Vice Chair for Pathology Cancer Programs and a Professor in the Department of Pathology and Laboratory Medicine at Emory University School of Medicine. A surgical pathologist and translational researcher, he specializes in breast cancer and thymic pathology. Dr. Badve has made significant contributions to understanding tumor infiltrating lymphocytes in triple-negative breast cancer and reclassification of thymic tumors. His research focuses on novel prognostic markers and gene signatures for thymomas and ER+ breast cancer. Dr. Badve has over 260 peer-reviewed publications and serves on several editorial boards

Poster Session

p53 mediated regulation of LINE1 retrotransposition derived R-loops

Presenting Author: Bhavana Tiwari

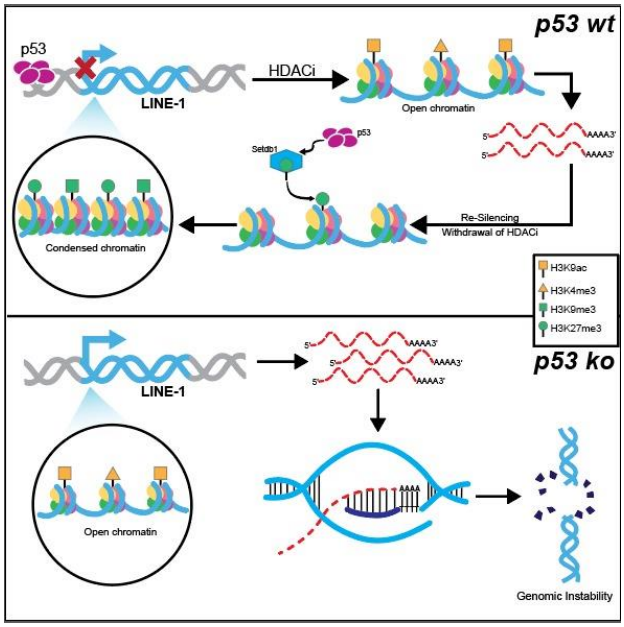
Pratyashaa Paul[1], Arun Kumar[1], Astik Kumar De[1], Ankita Subhadarsani Parida,[1], Gauri Bhadke Satyajeet Khatua[1] and Bhavana Tiwari[1]

[1]Department of Biological Sciences, Indian Institute of Science Education and Research Berhampur, India

Email (presenting author): btiwari@iiserbpr.ac.in

Abstract

Long Interspersed Nuclear Element 1 (LINE1/L1) retrotransposons, comprising around 17% of the human genome, typically remain quiescent in healthy somatic cells but become activated in various cancer types. Recently we demonstrated that p53 silences L1 transposons in human somatic cells, potentially constituting a tumor-suppressive pathway. Here, we report that loss of p53 results in a marked elevation of both L1 mRNA-gDNA (cis L1 R-loops) and L1 cDNA hybrids (trans L1 R-loops), pivotal intermediate components of retrotransposition. Furthermore, induction of L1 by HDAC inhibitors (HDACi) led to the accumulation of these cis and trans L1 R-loops in $p53^{-/-}$ cells, which were mitigated by treatment with a reverse transcriptase inhibitor. The p53-mediated restoration of hyperactivated L1 transposon silencing was accompanied by recruiting histone repressive marks specifically H3K9me3 and H3K27me3 and inhibiting the deposition of H3K4me3 and H3K9ac marks at the L1 promoter. This study elucidates a novel role of p53 in regulating the formation of RNA-DNA hybrids and initiating the suppression of hyperactivated L1 elements. These findings underscore the mechanistic underpinnings of p53 in preserving genome stability through the regulation of L1-derived R-loops.



IRC20 modulates LOH frequency and distribution in *S. cerevisiae*

Presenting Author: Sameer Joshi
Email: sameerjoshi21@iisertvm.ac.in

Sameer Joshi[1*], Suman Dash[1*], Nikilesh Vijayan[1] and Koodali T. Nishant[1,2].
[1]School of Biology, Indian Institute of Science Education and Research Thiruvananthapuram, Trivandrum 695551, India
[2]Center for High-Performance Computing, Indian Institute of Science Education and Research Thiruvananthapuram, Trivandrum 695551, India
*Equal contribution

Loss of Heterozygosity (LOH) due to mitotic recombination is frequently associated with the development of various cancers (e.g., retinoblastoma). LOH is also an important source of genetic diversity, especially in organisms where meiosis is infrequent. Irc20 is a putative helicase, and E3 ubiquitin ligase involved in DNA double-strand break repair pathway. We analyzed genome-wide LOH events, gross chromosomal changes, small insertion-deletions and single nucleotide mutations in eleven *S. cerevisiae* mutation accumulation lines of *irc20Δ*, which underwent 50 mitotic bottlenecks. LOH enhancement in *irc20Δ* was small (1.6 fold), but statistically significant compared to the wild type. Short (≤ 1 kb) and long (> 10 kb) LOH tracts were significantly enhanced in *irc20Δ*. Both interstitial and terminal LOH events were also significantly enhanced in *irc20Δ* compared to the wild type. LOH events in *irc20Δ* were more telomere proximal and away from centromeres compared to the wild type. Most of the LOH events occurred due to interhomolog mitotic recombination rather than deletions. Gross chromosomal changes, single nucleotide mutations and in-dels were comparable between *irc20Δ* and wild type. Locus-based and genome-wide analysis of meiotic recombination showed that meiotic crossover frequencies are not altered in *irc20Δ*. These results suggest IRC20 primarily regulates mitotic recombination and does not affect meiotic crossovers. Our results suggest that the IRC20 gene is important for regulating LOH frequency and distribution.

Meta-Analysis of epigenomics data including immune surveillance checkpoint molecules can be used as the blood based biomarkers of leukemia

Archita Dey[1], Salini Das[2]
[1]Department of Biotechnology, Swami Vivekananda Institute of Modern Science, West Bengal, India.
[2]Department of Environmental Carcinogenesis & Toxicology, Chittaranjan National Cancer Institute, Kolkata, India
email of the presenting author: architadey1609@gmail.com

Detection of blood based biomarkers is an non-invasive mode of early detection of cancer that helps to predict disease risk and prevent its progression.In India, the incidences of Leukemia is frequently getting increased in all forms. Epigenetic modification of genes can often alter the expressions of several essential proteins which participate in the surveillance of immune checkpoint to suppress the occurrence of early onset of cancer. Therefore such epigenetic markers such as DNA methylation status can be an important clue to decipher the chances of cancer. A meta data of around 2000 patients have been taken from the big data repositories like GEO (Gene Expression Omnibus), NCBI. The data of patients detected with various stages of leukemia were compared with the non cancerous groups. Analysis performed in GEO2R clearly reflected the epigenetic alterations of DNMT3A, TET2, IDH1, IDH2, EZH2, ASXL1 and others were found to be highly correlated with both the incidences of leukemia and their immune related effects. Prior identification of such markers would help the physicians to design novel therapeutic strategies to combat leukemia. Moreover the impact of conventional treatment modalities over such epigenetic markers is another arena of research.

LINE-1 transposon activation drives the genetic and epigenetic evolution of Triple- negative breast cancer persistors

Presenting Author: Ankita Subhadarsani Parida

Email (presenting author): ankitap@iiserbpr.ac.in

Ankita Subhadarsani Parida, Arun Kumar, Pramod Kumar Yadav and Bhavana Tiwari*

Department of Biological Sciences, Indian Institute of Science Education and Research Berhampur, Odisha 760010

Abstract

Triple-negative breast cancer (TNBC) poses a significant challenge due to its worst prognosis and capacity to resist treatment. Despite extensive genomic analyses of protein-coding regions, effective treatments remain elusive, making TNBC a major ongoing problem. Recent advances in next-generation sequencing suggest that activation of LINE-1/L1 transposons is linked to poor prognosis and drug resistance in cancer patients. In this study, we examined the role of de-repressed L1 transposons in the genetic and epigenetic evolution of TNBC persisters. Utilizing single-cell RNA sequencing (scRNA-seq) data analyses, we monitored the dynamics of young L1 elements over multiple days of chemotherapy drug exposure in a persister cell line model.

Our findings show that young L1 elements undergo dynamic changes in expression and methylation, indicating their role in TNBC persisters' adaptive response to drug-induced stress. Initially, L1 elements exhibited increased transcriptional activity in response to chemotherapy, resulting in heightened genomic instability and the development of drug resistance mechanisms. Over time, shifts in L1 methylation patterns indicated their role in the epigenetic regulation of drug response pathways.

Further integrative analyses, combining scRNA-seq and epigenetic profiling, identified distinct cellular subpopulations within the persister cell line, each displaying unique L1 dynamics correlated with varying degrees of drug resistance and persistence. These insights highlight the importance of L1 retrotransposition in the genetic and epigenetic evolution of TNBC persisters under therapeutic pressure. Our study reveals young L1 retrotransposons' role in TNBC persisters' adaptive evolution, highlighting potential therapeutic targets for combating drug-resistant breast cancer.

Tumour microbial diversity: Association with metastasis in breast cancer

Presenting Author: Srinidhi Narayani Seenivasan

Email (presenting author): srinithinarayanis@gmail.com

Srinidhi Narayani Seenivasan[1#], Samrat Ashok Vasudevan[1], Avinash Kumar Raghupathy[1], Gowdham Manivel[1],Firoz Rajan[2], Ezhir Selvan[2], Sangita Mehta[3], Rajeswari K Muthusamy[3], Shobanaa Pechimuthubabu Seethalakshmi[3], Sharmila Yogeswaran[3], Lavanya Paramasivam[3], Ganesan Velmurugan[1*#]

[1]Chemomicrobiomics Laboratory, Department of Biochemistry & Microbiology, KMCH Research Foundation, Coimbatore, Tamil Nadu, India.

[2]Department of Surgical Oncology, Kovai Medical Center & Hospital, Coimbatore, Tamil Nadu, India.

[3]Department of Pathology, Kovai Medical Center & Hospital, Coimbatore, Tamil Nadu, India.

#Correspondence: srinithinarayanis@gmail.com, vel@kmchrf.org

Abstract

Breast cancer is the most prevalent malignancy amongst women worldwide. It exhibits remarkable heterogeneity at both the molecular and cellular levels, contributing to variations in metastatic potential among different subtypes. It is well known that the gut microbiota plays a key role in etiology and pathogenesis of cancer including breast cancer. The micro ecology of the breast tissue and the tumour microenvironment plays an important role in tumourigenesis. Recent microbiome studies have revealed the abundant presence of metabolically active microbes in breast tumour tissues. But the functional role of the tissue microbiota on metastasis and its implications on tumourigenesis of breast cancer is unexplored.

The objective of the study is to determine the microbial diversity in tissues of breast cancer patients and also to correlate it with metastasis. Briefly 93 pair of tumour and tumour adjacent tissues were collected from breast cancer patients undergoing surgery with informed consent. Upon longitudinal follow up, 10 patients developed metastasis to distant organs. 16S rDNA sequencing revealed significant changes in tumour microbiota and its association with disease progression and metastasis. Further differentially expressed microbial signatures were identified which can serve as a prognostic marker for metastasis. The output of the study generates knowledge on tissue microbiota and its implications on tumour progression. Thus, understanding the interplay between microbiome and metastatic progression would enable novel management strategies and enhances better patient outcomes.

Mutation driven mechanistic understanding of response vs resistance against EGFR-TKI treatment in lung cancer cell lines

Presenting Author: Anupama Goyal

Email (presenting author): anupama.goyal@tcgcrest.org

Nivedita Dharwar[1], Tulika Mitra[1], Snigdha Patel[1], Sonali Das[1,2], Anupama Goyal[1,2]*

[1] *Department of Data Science, TCG Lifesciences Pvt. Ltd., Block-BN, Plot-7, Sector-5, Salt Lake, Kolkata 70 0 091, India*

[2] *First Floor, Tower 1, Bengal Eco Intelligent Park (Techna), Block EM, Plot No 3, Sector V, Salt Lake, Kolkata 700091, West Bengal, India*

*Corresponding Author: anupama.goyal@tcgcrest.org

Abstract

Lung cancer, the second most prevalent cancer, accounts majorly for cancer-related mortality worldwide (GLOBOCAN 2022). NSCLC, comprising both adenocarcinoma (LUAD) and squamous cell carcinoma (SCC), is known to be the most frequently observed histological subtype, accounting for ~85% of all cases. Molecular studies suggest EGFR mutations are occurring in 40-60% South-East Asian patients as opposed to only 10-20% of Caucasian patients contributing to LUAD. Owing to efficacy and tolerability, the global success of EGFR-TKIs influence treatment guidelines and is SOC in EGFR-mutated NSCLC. The advent of 1st generation EGFR-TKI 20 years ago, launched the era of targeted therapy in EGFR-mutated patients. However, development of resistance called for evolution of subsequent generations; 4th generation EGFR-TKI started to progress to early clinical phase in 2023. In the present study, we compared mutational profiles of EGFR-TKI resistant vs responsive colonies derived from cell lines, PC-9 and HCC4006. We aimed to unravel common pathways and protein families that may contribute to resistance onset. We have obtained whole genome/exome sequencing data from >10 studies available in public domain & analysed employing our *in-house* pipeline. Our analysis suggests that members of olfactory receptors that regulate cancer cell proliferation, apoptosis, metastasis & senescence and Preferentially expressed antigen in melanoma (PRAME) family, a target for immune therapy across cancers, may contribute to EGFR-TKI resistance. We hypothesize that validation wrt mutation of these key players in patient-derived ctDNA, PDX and organoids may reveal biomarker identification and efficacy prediction.

p53-dependent autophagic degradation facilitates *de novo* silencing of LINE-1 transposons

Presenting Author: DIYA CHATTOPADHYAY

Email (presenting author): diyac23@iiserbpr.ac.in

Diya Chattopadhyay[1], M Sai Kirti Krishnan,[1] Arun Kumar Narayan[1] and Dr. Bhavana Tiwari[1 *]
[1] Indian Institute of Science Education and Research, Berhampur, Odisha:760010
Correspondence: btiwari@iiserbpr.ac.in

Abstract

A recent pan-cancer study utilizing whole-genome sequencing data from various human cancer genomes revealed that LINE-1/L1 retrotransposons are active exclusively in cancer cells, contributing to genomic rearrangements and amplifications within cancer genomes. Consistent with these findings, our study has linked the tumor suppressor gene p53, which is mutated in over half of human cancers, to the transcriptional regulation of L1 transposons. Specifically, we demonstrated that wild-type p53 directly represses these mobile genetic elements by recruiting epigenetic repressive marks to their promoter regions, whereas p53 hotspot mutant alleles fail to do so.

In this study, we demonstrate that p53 initiates *de novo* silencing of LINE-1 transposons when activated by HDAC inhibitors. We used HDAC inhibitors to induce the de-repression of the LINE-1-encoded ORF1 protein. However, upon drug withdrawal, p53 wild-type cells re-silence activated L1 transposons, unlike p53 knockout cells, suggesting that p53 might regulate the degradation of L1-ORF1p for its early clearance from the cells.

Furthermore, through transcriptomic and proteomic analyses on p53 wild-type and knockout cells, we identified several downregulated autophagic pathway genes in p53 knockout cells, implying that p53 is involved in the autophagic degradation of L1-encoded proteins. Using immunoprecipitation experiments, we elucidated the mechanism by which L1-ORF1p interacts with E3 ubiquitin ligases, a process regulated by p53 to facilitate the clearance of L1-ORF1p, which possesses cellular transformation potential. Our findings suggest that p53 functions to degrade L1-ORF1p, highlighting its repressive role in preventing cellular transformation.

Investigating the role of LINE-1 associated R-loops in Genomic instability and Cancer

Presenting Author: ASTIK KUMAR DE

Email (presenting author): astikd23@iiserbpr.ac.in

*Astik Kumar De[1], Pratyashaa Paul[1], Satyajeet Khatua[1], Ankita Subhadarsani Parida[1], Fizalin Pattanayak[1], Arun Kumar[1], Gauri Vittal Bhadke[1] and Dr. Bhavana Tiwari[1]**

[1] Indian Institute of Science Education and Research Berhampur, Odisha-760010

Correspondence: btiwari@iiserbpr.ac.in

Background: Retrotransposons, accounting for about 35% of the human genome, are dynamic DNA sequences that relocate within the genome via RNA intermediate. Normally, these mobile genetic elements remain silenced under the control of host-encoded repressors such as p53. However, in cancer and cellular stress conditions, LINE-1 retrotransposon expression levels surge. This reactivation leads to the formation of numerous L1RNA:cDNA hybrids during retrotransposition, which, under the influence of limited RNA:DNA hybrid-resolving factors, stabilize into R-loops. These R-loops are three-stranded structures with an RNA:DNA hybrid and displaced single-stranded DNA, are associated with LINE-1 and have the potential to induce cancer. Despite their significant role in cancer development, there is a scarcity of tools and reagents for detecting and visualizing R-loops.

Research study: This study established a platform for investigating R-loops induced by LINE-1 retrotransposons. Mutated versions of the catalytic domain of RNaseH (D210N/SM) were cloned and expressed, specifically binding to RNA:DNA hybrids. Techniques like immunofluorescence, western blot, slot blot were performed to identify presence of R-loops.

In cells treated with LINE-1 enhancer drugs, we observed co-localization of LINE-1 proteins and R-loops in stable cells. A follow-up treatment with reverse transcriptase inhibitors was administered to distinguish LINE-1-associated trans-R-loops from other R-loops. DRIP-qPCR experiments confirmed the abundant presence of LINE-1-associated R-loops in p53 knock out cells compared to wild-type cells. The increased frequency of L1-associated R-loops was associated with genomic instability and inflammation.Conclusion: This study unveils a novel role of LINE-1-associated R-loops in contributing to genomic instability and cancer.

Spatial Distribution of Immune Infiltrates in Matched Pre- and Post-NACT Samples of BRCA-Mutated and Wildtype Breast Cancer patients: Retrospective Case Studies

Presenting Author: Jisha John

Email (presenting author): jishajohn@prashanticancercare.org

Jisha John[b,c],Sakshi Deepak Durge[a] ,Pooja Vaid[b,d] ,Dr. Rupa Mishra[b,c] ,Dr. C.B. Koppiker[b,c],Dr. Madhura Kulkarni[b,c]

[a] Indian Institute of Science Education and Research (IISER), Pune; [b] Center for Translational Cancer Research: A Joint Initiative of Indian Institute of Science Education and Research (IISER), Pune and Prashanti Cancer Care Mission (PCCM), Pune; [c] Prashanti cancer care mission (PCCM), Pune, [d] Ashoka University, Sonipat, Haryana

Abstract

Germline BRCA mutations associated with hereditary breast and ovarian cancers are characterized by high recurrence and chemoresistance. Studies have shown differential TiME (Tumor immune microenvironment) in BRCA-mutated breast cancers compared to that of BRCA wild-type tumors. (Leonora de Boo et al, European Journal of Cancer, 2020). Studies have also shown that TNBC subtype has high immune infiltration that's prognostic (Leonora de Boo et al, European Journal of Cancer, 2020). We have identified unique patients with multiple tumours at presentation with distinct molecular subtype, yet, all originating within germline-BRCA1 mutant background. These patients provide a unique opportunity to investigate the influence of subtype specific tumour biology and/or BRCA1 mutation status on TiME. Our study aims to examine the tumor immune microenvironment in pre- and post-NACT treated tumor samples of distinct subtypes with differential response, for the same patient (Table 1).

All 5 patients mentioned in the table underwent germline genetic testing by next-generation sequencing of genes associated with hereditary breast and ovarian cancer. All pre-treatment biopsy samples and post-NACT surgery tumor samples were stained using multiplex fluorescence immunohistochemistry. Further, density of different immune cell types, namely, T-cells (CD3, CD4, CD8), B -cells (CD19), and Macrophages (CD68) in pre- and post-treatment tissues will be analysed and presented during the conference.

Prognostic Association of Immunoproteasome Expression and its Correlation with Tumor-Infiltrating Lymphocytes in Breast Cancer

Presenting Author: Sampada Ghute

Email: sampada.ghute@students.iiserpune.ac.in

Sampada Ghute [a], Disha Kshirsagar [d], Dr. Sabarinathan Radhakrishnan [d], Dr. C. B. Koppiker [b, c], Dr. Madhura Kulkarni [b, c]

[a] Indian Institute of Science Education and Research (IISER), Pune; [b] Center for Translational Cancer Research: A Joint Initiative of Indian Institute of Science Education and Research (IISER), Pune and Prashanti Cancer Care Mission (PCCM), Pune; [c] Prashanti cancer care mission (PCCM), Pune, [d] National Centre for Biological Sciences (NCBS), Bengaluru

Abstract

The proteasome system is crucial for maintaining protein homeostasis by degrading misfolded or unwanted proteins into smaller peptides. Proteasomes exist mainly in two forms: Constitutive Proteasome (CP) and Immunoproteasome (IP). While CP is ubiquitously expressed, IP is predominantly found in immune cells and can be induced in non-immune cells by IFN-γ and TNF-α. The immunoproteasome is involved in the modulation of chronic inflammatory environments, as well as in optimal antigen presentation of tumor epitopes to tumor-infiltrating CD8+ T cells.

This study aims to investigate the association of IP catalytic subunit expression in the tumor cells with tumor-infiltrating lymphocytes (TILs) in the tumor microenvironment, and survival outcomes in breast cancer patients. Using immunohistochemistry, we want to investigate if IP expression is associated with and can potentially predict immune cell infiltration.

Our findings are expected to provide significant insights into the prognostic value of immunoproteasome expression in breast cancer, potentially offering a predictive marker for patient outcomes and therapeutic responses.

Multi-modal transcriptomic analysis reveals association among partial EMT, anoikis resistance and hypoxia

Presenting Author: Soundharya R

Email (presenting author): soundharyar@iisc.ac.in

Soundharya R [1,2], Tanishk Patodi [3], Snehal Vijay Khairnar [4], Roshini Sundararajan [5], Vidula Sonawane [3], Mohit Kumar Jolly [1,*]

[1] Department of BioEngineering, Indian Institute of Science, Bangalore, 560012, India

[2] IISc Mathematics Initiative, Indian Institute of Science, Bangalore, 560012, India

[3]Dr. D. Y. Patil Biotechnology and Bioinformatics Institute, Dr. D. Y. Patil Vidhyapeeth, Pune 411033, India

[4] Institute of bioinformatics and biotechnology, Savitribai Phule Pune University , Pune 411005, India.

[5]Anna University, Guindy, Chennai, Tamil Nadu 600025, India

* Author to whom correspondence should be addressed: mkjolly@iisc.ac.in

Abstract

The presence of hypoxia in the tumor microenvironment is often correlated with an increase in metastatic events and collective migration of tumor cells. Collective cell migration is usually driven by a partial epithelial-mesenchymal transition (pEMT). Besides, the disseminating cancer cells need to resist anoikis (cell death upon detachment) in order to successfully metastasize. This study integrates multi-modal transcriptomic data to investigate the association between hypoxia, pEMT, and anoikis resistance across various cancer types, using publicly available datasets on NCBI GEO and patient data from TCGA. Our findings reveal a consistent upregulation of hypoxia-responsive genes and anoikis-resistance signature, concomitant with pEMT markers in multiple cancers. Furthermore, the spatial distribution of activity scores of hypoxia, pEMT and anoikis resistance pathways within tumor micro-environments using spatial transcriptomic analysis reveals interconnection among these processes specifically in triple negative breast cancer (TNBC). The clinical relevance of our findings is underscored by survival analyses, which show that patients exhibiting simultaneous enrichment of hypoxia, anoikis, or pEMT signatures have significantly worse survival. Our work thus offers insights into associations among multiple inter-connected axes governing cellular plasticity driving metastasis.

Integration of Knowledge Graphs and Machine Learning-Based Approach for Identifying Potential Synthetic Lethal Gene Pairs

Prateek Paul* and Jaspreet Kaur Dhanjal,
Department of Computational Biology,

Indraprastha Institute of Information Technology Delhi,
Okhla Industrial Estate, Phase III, New Delhi, India, 110020.

* Presenting author, correspondence: prateekp@iiitd.ac.in

Abstract:

Synthetic lethality (SL) a phenomenon where the disruption of two genes simultaneously leads to cell death while disrupting either gene alone does not. Our project focuses on discovering novel SL-pairs by integrating and analyzing existing SL knowledge graphs (KG) with bioinformatics techniques. These existing KG contain comprehensive datasets on gene interactions, pathways, and disease-associations, which are crucial for understanding the complex networks of gene relationships. By integrating data from multiple sources, we aim to construct a unified and enriched KG that encapsulates a broad spectrum of SL-interactions.

Further, graph-based algorithms will be used to analyze the integrated-KG. Techniques such as DeepWalk and node2vec will be used to generate embeddings that capture the underlying structure and relationships within the graph. These embeddings will help in identifying patterns and clusters indicative of potential SL pairs.

Feature extraction from the KG will involve deriving topological properties, gene expression profiles, and mutation statuses. These features will serve as inputs for machine learning models. We will train ML-models, including RF, SVM, and neural-networks, to predict novel SL-pairs. To validate the predicted SL pairs, we will perform a thorough literature review and compare our findings with experimental data from resources. This dual validation approach ensures that our predictions are both scientifically grounded and experimentally supported. By identifying druggable targets within the validated SL-pairs, we will perform virtual screenings of compound libraries. This project synergizes KG-analysis, ML, and drug discovery to accelerate the identification of new SL-pairs and potential cancer therapies, paving the way for innovative treatments.

Keywords:
Knowledge Graphs, Synthetic lethality, Machine Learning, Drug discovery

Linking Targeted Pancreatic Cancer Genes with Metabolic Disorders: A Cross-species Translational Pathway

Presenting Author: Dipanwita Nath

Email: nath.dipanwita231@gmail.com

Authors: Dipanwita Nath[1], Animesh Acharjee[1,2,3,4*]

1. Institute of Cancer and Genomic Sciences, University of Birmingham, B15 2TT, Birmingham, UK[Text Wrapping Break]*2. Institute of Translational Medicine, University Hospitals Birmingham NHS Foundation Trust, B15 2TT, Birmingham,UK*[Text Wrapping Break]*3. MRC Health Data Research UK (HDR), Midlands Site, UK*[Text Wrapping Break]*4. Centre for Health Data Research, University of Birmingham, B15 2TT, UK*
** Correspondence: a.acharjee@bham.ac.uk*

Abstract

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is one of the most aggressive cancers, with late-stage diagnosis often leading to fatal outcomes, as surgical resection remains the only treatment. Multiple investigations have indicated a link between PDAC and metabolic disorders such as obesity, inflammation, and diabetes. In this research, we have delved into the intricate relationships between targeted PDAC genes and their roles in metabolic disorders.

Methods: We utilised bulk RNA-Seq data from the Gene Expression Omnibus (GEO) for mouse and human adipose tissues, alongside single-cell RNA-Seq data from advanced PDAC. We compared expression levels of targeted genes—ITGAM, PECAM1, CCL5, STAT1, STAT2, CD44—across a pan-transcriptomic profile. Cell clusters were identified from single-cell data, followed by pathway enrichment analysis using KEGG and protein-protein interaction network analysis using STRING database to validate the connections between PDAC recurrence genes and metabolic disorders.

Results: Our analyses revealed significantly high expression of PDAC-associated genes in obese mice and human samples. Single-cell analysis linked specific cell clusters to metabolic markers in PDAC. Pathway and protein interaction analyses further indicated that signaling pathways involved in diabetic complications and Inflammatory Bowel Diseases are enhanced by activity of PDAC recurrence genes.

Conclusion: Our findings highlight a strong association between the upregulation of PDAC recurrence genes and activation of metabolic pathways linked to obesity, diabetes, and inflammation. The consistent expression patterns across species suggest potential for developing targeted therapies to inhibit these metabolic pathways post-pancreatic cancer resection, potentially reducing fatality.

Keywords: Pancreatic ductal adenocarcinoma (PDAC), Single-cell RNA-Seq Analysis, Inflammatory Bowel Disease (IBD

Establishment of a molecular genomics laboratory to revolutionize cancer care in rural areas of Bihar

*Presenting author: Himanshu Bharadwaj[1]

*Email: h.bhardwajn1999@gmail.com

Moitri Basu[1], Ravikant Singh[1], Kumar Prabhash[2], Amit Dutt[3], Anuradha Choughule[2], Vanita Noronha[2], Pratik Chandrani[2], Vidya Veldore[4]

1- *Homi Bhabha Cancer Hospital & Research Centre, Muzaffarpur, Bihar, India*
2- *Tata Memorial Hospital, Mumbai, India*
3- *University of Delhi, South Campus, India*
4- *4baseCare, Bangalore, India*

Introduction:

Genomic profiling is now integral to the routine diagnosis and treatment of certain cancers, but these services remain scarce in rural India. This article highlights the establishment of a molecular genomics laboratory at Homi Bhabha Cancer Hospital and Research Centre, Muzaffarpur, to implement these advanced benefits to cancer patients in rural Bihar.

Objective:

To highlight challenges in establishing next-generation sequencing (NGS) facility for genomic profiling of cancer patients in resource-limited settings and glimpse of our molecular findings.

Material and methods:

Biopsy samples in formalin-fixed paraffin embedded (FFPE) blocks were used for macrodissection-based DNA extraction, library preparation, and sequencing on MiniSeq (Illumina) followed by variant calling. A targeted 72-gene panel with clinical relevance was used, ensuring quality metrics at each step.

Result:

Despite challenges of being in tier 3 city of Bihar, 103 cancer patient samples were sequenced in its first year since November 2022. Lung cancer was 71% (73 out of 103) while remaining were of other cancer types. The genomic landscape highlighted the presence of actionable alterations in well-known driver genes including *EGFR* (34%), *KRAS* (10%), *ALK* (6%), *BRAF* (4%) in lung cancer. Zooming in on 7 lung cancer cases (all smoker) with *KRAS* alterations, 5 cases harboured substitutions at 12th codon of exon 2- G12C or G12D. These observations corroborate with the incidence of specific alterations already reported in literature.

Conclusion:

Operating such high-end technology in a peripheral centre encountered unique challenges, requiring innovation and resourcefulness. This highlights the laboratory's potential in unlocking genomic landscape of Bihar and in supporting quality cancer care in rural India.

HAGLR, A Long Non-coding RNA of Potential Tumor Suppressive Function in Clear Cell Renal Cell Carcinoma: Diagnostic and Prognostic Implications

Presenting Author: Abhishek Bardhan

Email (presenting author): abhishekbiology1998@gmail.com

Abhishek Bardhan[a], Anwesha Banerjee[a], Dilip Kumar Pal[b], Amlan Ghosh[a]
[a]*Genetics of Non-communicable Diseases, Department of Life Sciences, Presidency University, 86/1 College Street, Kolkata, West Bengal 700073, India*; [b] *Department of Urology, IPGME&R, Kolkata, West Bengal, India*

Abstract

Research works suggested the role of long non-coding RNAs (lncRNAs) in pathogenesis of clear cell renal cell carcinoma (ccRCC). lncRNA *HAGLR* is studied in several malignancies, but not in ccRCC. From The Cancer Genome Atlas Kidney Renal Clear Cell Carcinoma (TCGA-KIRC) dataset, we analyzed molecular alterations of *HAGLR* and constructed a competitive endogenous RNA (ceRNA) network with related miRNAs and mRNAs. Gene Ontology analysis was done to identify important pathways enriched with *HAGLR* recovered mRNAs. Clinical importance of *HAGLR* and related mRNAs was assessed and, the impact of selected mRNA-encoding genes on tumor immune infiltration was studied using TIMER. *HAGLR* expression was reduced in ccRCC than in normal kidneys, and correlated significantly with gene promoter methylation. Low *HAGLR* level in tumors showed diagnostic potency, and was associated with clinicopathological parameters (stage/grade/metastasis) and poor patient survival. The *HAGLR*-associated ceRNA network constituted 13 miRNAs and 23 mRNAs differentially expressed in the TCGA-KIRC dataset. From *HAGLR* recovered mRNA-encoding genes, we developed a 5-gene (*PAQR5*, *ARHGAP24*, *HABP4*, *PDLIM5*, and *RPS6KA2*) prognostic signature in the training dataset and validated it in testing as well as entire datasets. The expression level of signature genes showed negative correlation with tumor infiltration of immune cells having adverse impact on ccRCC prognosis and also with tumor derived chemokines facilitating the infiltration. In conclusion, *HAGLR* seemed to play a tumor suppressive role in ccRCC. *HAGLR* and associated gene signature may have implementation in improving existing prognostic measure and developing effective immunotherapeutic strategies for ccRCC.

Investigating The Transcriptome For Tumor Microenvironment Of Gastric Adenocarcinoma: Searching For Allies And Adversaries

Presenting Author: Shreya Srivastava

Email (presenting author): shreyasrivastava769@gmail.com

Shreya Srivastava[a], Dr. Raghavendra Lingaiah[a] , Dr. Shalini Singh[b], Dr. Shagun Misra[b], Dr. Rajneesh Kumar Singh[c],
Dr. Niraj Kumari[d],
[a] *Department of Pathology, SGPGIMS*; [b] *Department of Radiotherapy, SGPGIMS;* [c]*Department of Surgical Gastroenterology, SGPGIMS;* [d]*Department of Pathology and Lab Medicine, AIIMS Raebareli*

Abstract

Objective: The tumor microenvironment's (TME) influence on Gastric Adenocarcinoma tumor behavior and prognosis is substantial, despite valuable information from molecular classification about driver mutations and biomarkers. The study's objective was an in-depth exploration of the transcriptome for differentially expressed genes (DEG) and immune cell infiltration in TME.

Materials and methods: Five GAC cases were recruited, and their resected specimens (tumor + normal tissue) were collected for histopathological review and transcriptome profiling (IonTorrent). RNA-seq data filtering, normalization, and differential gene expression (DGE) analysis were performed in RStudio (R4.1.2) using DESeq2 followed by validation through qPCR. Functional pathway analysis was performed using Gene Ontology and KEGG. Gene signatures of immune and stromal cells were analyzed using xCell and TIMER2.0 in RPKM normalized expression data to categorize patients based on their immune and stromal scores.

Results: DGE revealed 488 differentially expressed genes of which 386 were upregulated and 102 were downregulated. Gene Ontology and KEGG pathway analysis indicated that the most upregulated genes were associated with the ECM receptor interaction pathway. In TME analysis, 2 of 5 cases exhibited high immune but low stromal scores (group 1), while 3 had low immune but high stromal scores (group 2). On co-expression analysis, 20 genes upregulated in group 1 were not found in group 2, with 16 downregulated genes shared between both groups. Furthermore, Group 1 demonstrated higher infiltration of CD8+, CD4+, macrophages, NK cells, and B cells than Group 2. This strongly correlates with literature suggesting a link between higher T-cell infiltration in tumors and poor prognosis.

Conclusion: The observed DEG and immune infiltration variances in the two groups strongly indicate their potential prognostic value.

Comprehensive pan-cancer multi-omics analysis of the *KEAP1-NFE2L2-CUL3* gene axis as a potential immunological and prognostic biomarker

Presenting Author: Guruguhan S

Email (presenting author): guruguhan23@gmail.com

Guruguhan S[a], Tapas Patra[a], Aruna Korlimarla[a], Durgadevi Veeraiyan[a], Akhileshwar Namani[a] *

[a] *Department of Molecular Research, Sri Shankara Cancer Hospital and Research Centre, Sri Shankara National Centre for Cancer Prevention and Research, Sri Shankara Cancer Foundation, Bangalore 560004, India.*

**Corresponding author: akileshwarnamani@ssnccpr.org*

Abstract

NRF2 signaling pathway dysregulation is caused by mutations in the *KEAP1-NFE2L2-CUL3* (K-N-C) genes in human cancers. A thorough pan-cancer investigation is necessary to completely comprehend the oncogenic role of the NRF2 signaling pathway, despite the fact that multiple studies have shown its dual role in cancer. Thus, we conducted a series of multi-omics analyses in the context of K-N-C mutant pan-cancer patients using the TCGA and CPTAC datasets. Our analysis includes mutational landscape, co-mutations and co-copy number alterations, differential gene expression from TCGA transcriptomics data, differential protein expression from proteomics CPTAC data, immunomics, and overall survival analysis. In addition, functional annotations, pathway-based gene signature survival analysis, and in silico analysis of NRF2 transcription factor binding sites were also performed to identify known and putative NRF2-regulated genes and biomarkers. We found that patients with K-N-C mutants had a poor prognosis. These patients have a high tumor mutation burden (TMB), low immune cell infiltration, and a modulated immune microenvironment. Functional annotations revealed that the upregulated genes associated with the K-N-C mutations were enriched in various metabolic pathways, and high expression of genes involved in these pathways predicted poor prognosis in the pan-cancer cohort. Our results provided new insights into the role of the NRF2 signaling pathway in human cancers and expanded our understanding of the downstream targets underlying its oncogenesis. Our study paves the way for early diagnosis and the development of precision therapy for cancer patients.

Phosphocholine-derived Lithocholic Acid-Gemcitabine Conjugate Mitigates Hepatocellular Carcinoma Progression via Modulation of Lipid and Immune Landscape

Somesh K. Jha1 , Nishant Pandey1 , Dolly Jain1 , Kajal Rana1 , Jasleen Kaur2 , Ali Khan3 , Ruchira Chakroborty1 ,
Arnab Mukhopadhyay,2 Avinash Bajaj1, *, and Ujjaini Dasgupta3, *
1. Laboratory of Nanotechnology and Chemical Biology, Regional Centre for Biotechnology, 3rd Milestone
Faridabad-Gurgaon Expressway, Faridabad-121001, Haryana, India.
2. Molecular Ageing Lab, National Institute of Immunology, Aruna Asif Ali Marg, New Delhi-110067.
3. Laboratory of Sphingolipid Biology, Amity Institute
of Integrative Sciences and Health & Amity Institute of Biotechnology, Amity University, Manesar, Gurgaon-122413, Haryana.
Email: ujjainidu@gmail.com, bajaj@rcb.res.in

Hepatocellular carcinoma (HCC), ranked as the fifth most commonly diagnosed cancer, has the highest mortality rate, with over 90% of patients succumbing to the disease. The situation is worsened due to late diagnoses, limited therapeutic options, systemic toxicities of chemotherapeutics, the emergence of drug resistance, and a lack of understanding of how various metabolic and immune regulators interact within the tumour microenvironment (TME). Therefore, to target the HCC, we developed an oral formulation of gemcitabine (GEM) upon its conjugation with phosphocholine-derived lithocholic acid (LCA-GEM-PC) and tested it against a chemically-induced liver cancer model. Our studies demonstrated that oral delivery of LCA-GEM-PC is more effective in inhibiting tumor growth and restoring liver function to healthy levels. Bulk RNA sequencing of healthy, untreated liver cancer and treated liver cancer tissues revealed significant alterations in lipid metabolic and immunoregulatory genes in untreated cancer tissues that get normalized on LCA-GEM-PC treatment. LC-MS/MS analysis showed dysregulation of lipid metabolites from the Kennedy and sphingolipid pathways that get normalized upon LCA-GEM-PC treatment. TCGA data in the liver hepatocellular carcinoma (LIHC) cohort corroborated these findings, showing similar dysregulation in cancer patients. Immune profiling revealed an inflammatory milieu in the untreated TME with an elevated M1/M2 macrophage ratio compared to the healthy liver. LCA-GEM-PC treatment reduced this inflammatory state to healthy levels. TCGA analysis showed that HCC patients had more iNOS+ (inflammatory) macrophages than ARG1+ macrophages, with ARG1+ expression negatively correlated with lipid biosynthesis genes. My poster will present these observations, prompting us to investigate the potential crosstalk between lipid mediators and immune cells in HCC for future therapeutics.

OncoConnect: An AI-driven approach for holistic interpretation of genomic data in the context of clinical characteristics of cancer patients

Presenting Author: Shilpa Shantinath Patil
Email (Shilpa Patil): shilpa@omdisha.com

Shilpa S Patil[a], Sucharitha MV[a], Sandhya Krishnan[a], Athira Mathew[a], Iris Thomas[a], Nimisha Gupta[a], Vaijayanti Gupta[a]

[a] *G-KnowMe, OmDisha Healthcare Technologies Pvt Ltd, B201, Godrej Woodsman Estate, Bellary Road, Hebbal, Bangalore 560024*

Holistic interpretation of genomic data in the context of diagnostic specifications and other clinical attributes of a cancer patient needs deep understanding of molecular biology and the judgments of trained scientists that help physicians make therapeutic decisions. Comprehension of current clinical literature, various databases, and country specific guidelines to identify truly actionable genomic markers is currently lacking in the field. Due to these complexities, the cost and time needed for generating a comprehensive genomic report is really high.

OncoConnect is an AI-powered tool with intuitive workflows and a user-friendly interface that helps clinical interpreters construct a meaningful and comprehensive genomic report by looking up information from multiple sources and providing inputs to make guideline-driven decisions within a short period of time (Schematic 1). OncoConnect workflow follows the up-to-date SOPs for scoring annotations and predicting the oncogenicity of known and novel variants. Developed by skilled scientists and augmented with AI and NLP, the tool efficiently matches clinical trials considering patient's diagnosis, genomic profile and several other clinical parameters including treatment history and comorbidities. The tool amalgamates oncogenicity predictions with associated therapies and prognostic data and further prioritizes variants according to the country specific guidelines.

OncoConnect is highly customizable and designed to consume input VCFs from various platforms, configure lab-specific interpretation pipelines, and integrate multiple external and in-house databases. Additionally, report formats can be tailored and seamlessly exported from the workflow. In summary, OncoConnect facilitates efficient and cost-effective generation of highly actionable and up to date genomic reports.

Replication stress underlies genomic instability at CTCF/cohesin binding sites in cancer

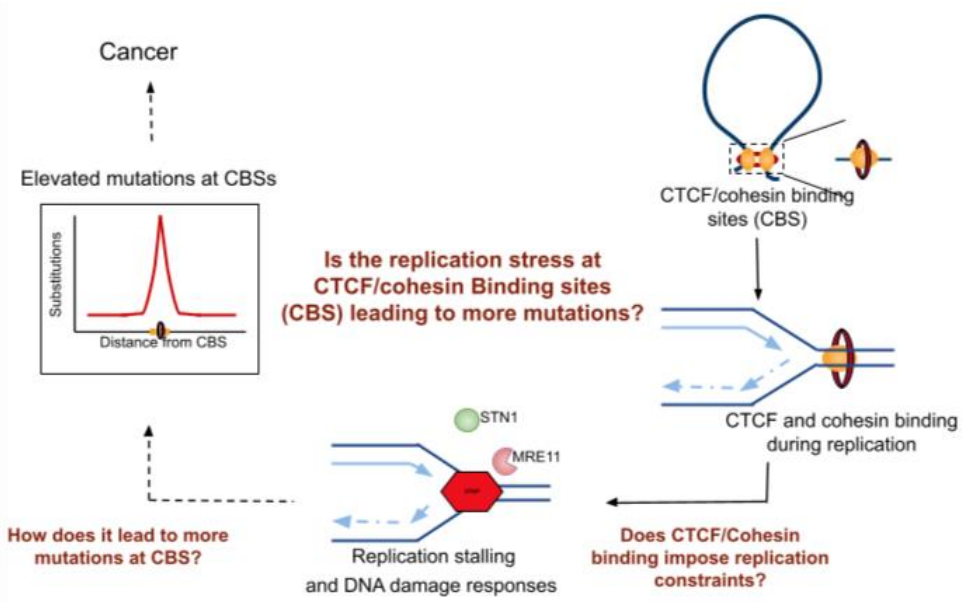
Presenting Author: Faseela E E

Email (presenting author): faseelaee@ncbs.res.in

Faseela E E[a], Dimple Notani[a], Sabarinathan Radhakrishnan[a]

[a] *National Centre for Biological Sciences-*
Tata Institute of Fundamental Research (NCBS-TIFR),
GKVK, Kodigehalli, Bangalore, Karnataka, 560065

Abstract



CCCTC-binding factor (CTCF) and cohesin play a major role in the formation of chromatin loops and topologically associating domains (TADs) that control gene expression and DNA replication. CTCF/cohesin binding sites (CBS), which are present at the loop anchors and TAD boundaries are frequently mutated in cancers. However, the molecular mechanisms underlying this remain unclear. In this study, we propose that the increased somatic mutations observed at CBS could result from replication constraints imposed by the CTCF/cohesin complex on the DNA, and the consequent activation of error-prone repair. We find that CTCF and cohesin are bound to DNA during replication and they colocalize with proteins associated with replication stalling and DNA breaks. Further, with ChIP-sequencing we assessed the DNA occupancy of above proteins in S phase and found that they are highly enriched at CBS as compared to control sites. Moreover, analysis of somatic mutations from cancer genomes supports that the enrichment of mutations at CBS sites is higher in samples having somatic alterations in replication stress-associated proteins. Taken together, these results suggest that the binding of CTCF/cohesin on the DNA during replication causes stress and genome instability, and this can lead to mutations.

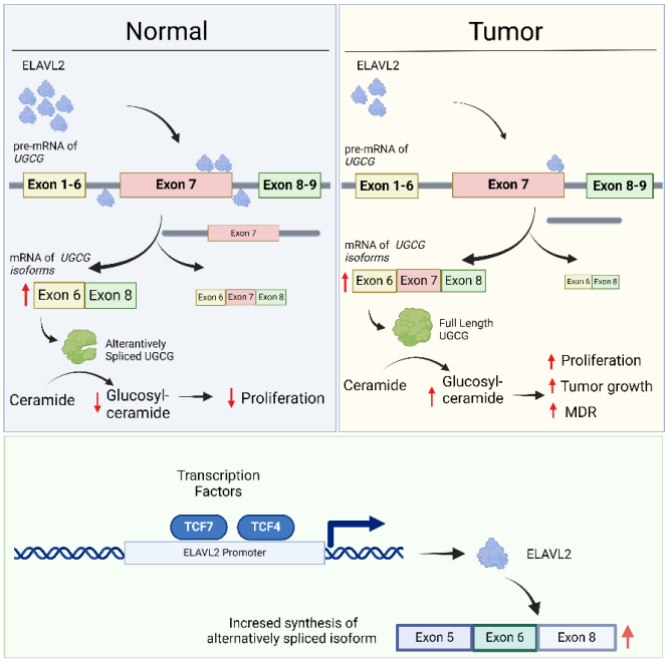
Alternative Splicing of UGCG Inhibits Tumor Progression in Breast Cancer

Trishna Pani

tina.trishna@gmail.com

Trishna Pani[a], Rajeswari Tripathi[a], Nishant Pandey[b], Soundharya R[c], Nafees Ansari[a], Dr. Mohit K Jolly[c], Dr. Arnab Mukhopadhyay[d], Dr. Avinash Bajaj[2], Dr. Ujjaini Dasgupta[1*]

[a]Amity Institute of Integrative Sciences and Health, Amity University Haryana, Panchgaon, Manesar, Gurgaon, 122413 Haryana, India. [b]Regional Centre for Biotechnology, NCR Biotech Science Cluster, 3rd Milestone Faridabad-Gurgaon, Expressway, Faridabad, 121001 Haryana, India. [c]Department of Bioengineering, Indian Institute of Science, C V Raman Avenue, Bangalore-560012, Karnataka, India, [d]National Institute of Immunology, Aruna Asaf Ali Marg, New Delhi- 110067.



Aberrant alternative splicing (AS) has been recognized as one of the hallmarks of cancer. Using bioinformatically analysed RNA seq data from TCGA BRCA cohort we identified a cassette exon (CE) event of UDP-glucosylceramide (UGCG) in Luminal A subtype which was further validated in patient-derived tumor tissue of all breast cancer subtypes. This CE event in UGCG turns out unique as the spliced transcript is more in adjacent normal breast tissue in comparison to the full-length transcript that predominates in the tumor tissue where it regulates uncontrolled cell proliferation. The AS form of UGCG is devoid of exon 7 that covers a catalytic motif for the enzyme. Loss of the exon 7 results in loss of catalytic activity of UGCG as shown by reduced glucosylceramides levels. Further investigation revealed that the splicing factor, ELAVL2, regulates this AS event. RNA immunoprecipitation demonstrated ELAVL2's binding to UGCG, and alteration of ELAVL2 levels confirmed its regulatory role. Using Transfac-based analysis we next identified potential transcription factors that might be regulating the synthesis of ELAVL2. Thus, this study elucidates a specific UGCG, AS event that regulates breast tumor progression and highlights the regulatory mechanisms involving the splicing event.

Scheme 1: Illustrating the role of UGCG AS in regulating tumor progression.

Investigating the diagnostic and prognostic importance of lncRNA LINC01409 along with its mechanistic role in Prostate Cancer

Presenting Author: Sandipan Das
Email (presenting author): sandipandas635@gmail.com
Sandipan Dasa , Pramit Kumar Ghosha , Abhishek Bardhana , Amlan Ghosh a
A Genetics of Non-Communicable Diseases Lab, Department of Life Sciences, Presidency University,
86/1 College Street, Kolkata-700073, West Bengal, India

Abstract

Exploration of the mechanistic factors involved in alternative splicing of Androgen Receptor (AR) to its transcript variant, ARv7 can provide insights into Prostate Cancer (PCa) tumorigenesis and possibly improve current diagnostic and prognostic protocols. Long non-coding RNAs (lncRNAs) affect several cellular processes and thus have oncogenic/tumor suppressive roles. In this study, we have studied the role of a lncRNA, LINC01409 in PCa. Bioinformatics analysis of available data on LINC01409 from GDC TCGA PRAD dataset using UCSC XENA Browser and GEPIA2 webtool revealed its possible role in PCa oncogenesis and progression. U2AF2, a splicing factor involved in alternative splicing of AR was discovered as a potential interacting RNA binding protein of LINC01409. Docking and MD simulation studies on LINC01409-U2AF2 interaction showed that binding of LINC01409 increases the stability of U2AF2. qRT-PCR analysis on an independent human sample pool showed LINC01409 to be overexpressed in tumor samples with respect to control samples ($p<0.05$). In silico correlation analysis of LINC01409 expression with AR, ARv7-specific exon and the exon not present in ARv7 expression, showed that LINC01409 expression is significantly correlated with AR and ARv7-specific exon expression ($p<0.05$) but not with the exon not present in ARv7 ($p>0.05$). LINC01409 expression association with clinicopathological parameters of PCa patients was also analyzed. Finally, potential 4- gene diagnostic and prognostic signatures (LINC01409, AR, U2AF2, and PRKAG2-AS1, another lncRNA involved in alternative splicing of AR) were developed. Thus, the oncogenic role of LINC01409 in PCa warrants further analysis of the generated signatures for possible implementation to improve current measures.

Orai3 oncochannel is a critical regulator of chemoresistance in pancreatic cancer

Presenting Author: Samriddhi Arora

Email (presenting author): samriddhi.arora@rcb.res.in

Samriddhi Arora [a], Gyan Ranjan [a] and Rajender K. Motiani [a]

[a] *Laboratory of Calciomics and Systemic Pathophysiology, Regional Center for Biotechnology Faridabad- 121001*

Abstract

Pancreatic cancer (PC) is one of the most aggressive and chemoresistant cancers, leading to cancer-associated deaths. Calcium dysregulation is a critical player in tumor advancement and resistance to chemotherapy. Our earlier findings have unveiled a novel calcium influx oncochannel, Orai3 as a crucial player in pancreatic cancer progression and metastasis. Through *in vitro* assays, we have shown that Orai3 plays a pivotal role in regulating the cell cycle, apoptosis, and migration of pancreatic cancer cells. Furthermore, our *in vivo* data have underscored the critical involvement of Orai3 in growth and metastasis of pancreatic cancer tumors. Further, we show that Orai3 plays an important role in pancreatic cancer chemoresistance. Our data highlights upregulation of Orai3 and STIM1 in gemcitabine-resistant pancreatic cancer cells. Subsequent inhibition of Orai3 in these cells leads to a significant decrease in proliferation, cell cycle arrest in the G1/S phase, resistance to apoptosis, and enhanced stemness characteristics. From a mechanistic perspective, our unbiased transcriptomics analysis identified SLIT3 as a potential gene that functions downstream of Orai3 in inducing gemcitabine-resistance. SLIT3 exhibits a marked upregulation in gemcitabine-resistant cells but shows an inverse pattern upon Orai3 inhibition in these cells. Our *in vivo* study in zebrafish reveals a heightened metastatic potential of cells resistant to gemcitabine. These results suggest that Orai3 is a critical regulator of gemcitabine resistance in PC cells. It is a promising target for a synergistic therapeutic approach to combat chemoresistance.

Pre-clinical Evaluation of IND126, a KRASG12C Inhibitor in Non-Small Cell Lung Cancer

Presenting Author: Prashant Bhavar

Email: prashantb@vegen.in

Prashant Bhavar[1], Appaji Mandhare[1] , Partha Pratim Sarma[1], Anuj Ramesh Kshirsagar[1]
[1] *VeGen Labs LLP, ASPIRE-BioNEST, University of Hyderabad, Hyderabad, Telangana, India,*

Abstract

$KRAS^{G12C}$ mutation occurs in ~13% of NSCLC, 4% of colorectal and ~2% of patients with other solid tumors. Treatment with KRASG12C inhibitors as single agent (e.g. Lumakras and Adagrasib) have shown to have a transient effect on overall KRAS signalling because such initial oncoprotein signalling inhibition is accompanied by re-accumulation of active KRAS and/or reactivation of alternative pathways including MAPK pathway such as RAF and/or ERK. One approach towards overcoming the acquired resistance towards G12C inhibitors, is combining them with other inhibitors involved in Ras/Raf/MEK/TKI pathway. IND126 is a novel, potent and highly selective inhibitor of KRASG12C.

IND126 was evaluated in a panel of KRAS G12C mutant and wild type cell lines both as single agent and in combination with MAPK pathway inhibitors using cell viability assay and in-vivo efficacy of IND126 either as single agent or in combination with others was evaluated in a KRAS G12C mutated NSCLC tumour model.

IND126 exhibited nM potency in a panel of NSCLC and colon cancer cell lines and demonstrated selectivity over KRAS wild type or non KRAS G12C mutant cell lines. IND126 in combination with other pathway inhibitors demonstrated significant in vitro synergy. Similarly, in H358-G12C xenograft model, IND126 exhibited tumor growth inhibition (>75%) at therapeutically relevant doses both as single agent and in combination.

Combination of IND126 with inhibitors of Ras/Raf/MEK/TKI pathways could be an effective approach to overcome the acquired resistance and/or reactivation of alternative pathways with single agent use of KRASG12C inhibitors 2.

Development of a method for protein structure selection that yield true active compounds early during virtual screening

Presenting Author: Mr. Agneesh Pratim Das
Email (presenting author): pratimagneesh.apd@gmail.com

Agneesh Pratim Das[1,2], Prajwal Nandekar[3], Puniti Mathur[2], Subhash M. Agarwal[1]

[1] *Bioinformatics Division, ICMR-National Institute of Cancer Prevention and Research, I-7, Sector-39, Noida - 201301, Uttar Pradesh, India*
[2] *Amity Institute of Biotechnology, Amity University Uttar Pradesh, Sector-125, Noida - 201313, Uttar Pradesh, India*
[3] *Schrödinger India Private Limited, Bengaluru - 560098, Karnataka, India,*

ABSTRACT

In the realm of in-silico drug discovery, selecting the optimal 3D structure for virtual screening (VS) is a known problem. This problem becomes an even more complicated if multiple crystal structures of the same protein have been resolved, which is often the case of therapeutically important proteins. Thus, the choice of crystal structure impacts the accuracy of identifying potential drug candidates during VS exercises, where only top hits proceed to experimental validation. Therefore, to enhance this selection process, a computational workflow has been developed. This workflow systematically evaluates protein crystal structures that are more likely to yield true active compounds early in the screening process. The workflow integrates several techniques like: cross-docking to assess binding affinity with non-native ligands, ligand similarity calculations, analysis of binding-site residue conformations, metadynamics for binding pose stability, and enrichment parameter evaluation. These steps collectively identify crystal structures that are capable of effectively docking diverse ligands, exhibiting stable co-crystal ligands, and distinguishing true actives. As a case study this approach has been used to identify inhibitors for EGFR mutants in lung cancer treatment, showcasing its clinical relevance. The proposed methodology is adaptable to other therapeutic targets with multiple crystal structures available, offering a systematic solution to the challenge of selecting the protein structure for virtual screening in drug discovery.

Comprehensive analysis of Long Non-Coding RNA *ACTA2-AS1* in Prostate Cancer: Diagnostic Implications

Presenting Author: Diya Mallik

Email (presenting author): dm2133342@gmail.com

Diya Mallik[a], Mayukh Chatterjee[a] , Abhishek Bardhan[a], Amlan Ghosh[a]

[a] *Genetics of Non-Communicable Diseases, Department of Life Sciences, Presidency University, 86/1 College Street, Kolkata, West Bengal 700073, India*

Abstract

The second most common malignant condition worldwide is prostate cancer (PCa), which lacks appropriate primary screening methods, disabling proper management of disease. Non-invasive plasma based detection of long non-coding RNAs (lncRNAs) marks them suitable for diagnosis in various malignancies. Increasing studies indicated the role of lncRNA *ACTA2-AS1* in different cancers. However, little is known regarding its expression and role in PCa. The chromosomal region where *ACTA2-AS1* resides is frequently deleted in PCa. Herein, assessment of copy number variation of *ACTA2-AS1* in PCa using the public dataset, GDC TCGA PRAD showed 20% deletion. Expression status of *ACTA2-AS1* was analyzed using the same dataset which revealed significant downregulation of *ACTA2-AS1* in PCa compared to normal. In-vivo validation of copy number variation and expression of *ACTA2-AS1* was carried out using multiplex PCR and qRT-PCR respectively. 44% and 20% deletion of *ACTA2-AS1* was respectively obtained in PCa and benign prostatic hyperplasia (BPH). Reduced expression of *ACTA2-AS1* obtained in PCa in comparison to BPH was shown to be associated with advanced tumor grade. Mechanistically, by using the GDC TCGA PRAD dataset, we demonstrated negative correlation of *ACTA2-AS1* with miR-4428 and AR whereas positive correlation with KLF9. Furthermore ROC curve revealed *ACTA2-AS1*, KLF9 and AR as fair, moderate and poor diagnostic markers respectively. Diagnostic potency of three gene diagnostic signature (*ACTA2-AS1*, KLF9 and AR) and two gene diagnostic signature (*ACTA2-AS1*, KLF9) were similar and a bit more than *ACTA2-AS1* individually. Collectively, this study provides insights into tumor suppressive role and diagnostic potency of *ACTA2-AS1* in PCa.

Investigating the role of Super-Enhancer-transcribed long-noncoding RNA in Glioblastoma

Presenting author: Shirshanya Roy
Email: 21lsph06@uohyd.ac.in

Shirshanya Roy[1], Manjari Kiran[1,*]

[1]*Department of Systems & Computational Biology, School of Life Sciences, University of Hyderabad, Hyderabad, Telangana - 500046, India*

Abstract

Glioblastoma, previously known as Glioblastoma Multiforme (GBM), is the deadliest of all gliomas due to its high malignancy, invasiveness, and resistance to therapy, and it has an abysmal 5-year survival rate of 6.9% and a median survival of 15 months post-diagnosis. Despite decades of research, the etiology of GBM is still incompletely known. An emerging avenue of research is superenhancer (SE) regions, which are clusters of putative enhancers with a much more potent regulatory effect compared to typical enhancers (TE), and which are responsible for determining cell-fate and establishing cell-type-specific expression patterns. Alterations in SE activity have been linked to various cancers, including gliomas. They are found at several key oncogenic drivers like RUNX1, BCL3, FOSL2, and one hypothesis is that they might regulate expression of their target gene through transcribed lncRNA. The objective of this study is to use RNA-seq data to find and identify these SE-transcribed lncRNAs (SE-lncRNA) and study their association with cancer progression. To do this, we obtained raw RNA-seq data from The Cancer Genome Atlas, and analyzed this data using an Allele-Specific Expression-analysis approach. We found 14 SE-lncRNA genes that showed allelic imbalance in their expression levels across the population. Only 3 of these genes, namely SBF2-AS1, TMEM44-AS1, and MALAT1, were annotated, and had been studied before in relation to glioma progression. The rest were unannotated, and represent genes of interest requiring further study and experimental validation to identify potential risk variants, which may help expand our understanding of the molecular mechanisms of GBM.

The NFAT2 Paradox: NFAT2 regulates both mRNA transcription and protein degradation of oncogenic calcium channel Orai3

Presenting Author: Sharon Raju

Email (presenting author): sharon.raju@rcb.res.in

Sharon Raju[a], Akshay Sharma[a], Gyan Ranjan[a], Rajender K Motiani[a]

[a] Laboratory of Calciomics and Systemic Pathophysiology (LCSP), Regional Centre for Biotechnology (RCB), Faridabad-121001, India

Abstract

Pancreatic cancer is one of the most lethal forms of cancers with limited therapeutic options. We recently identified a novel calcium channel, Orai3, which is transcriptionally upregulated in pancreatic cancer and is associated with poor prognosis. However, the molecular mechanisms driving Orai3 upregulation remain poorly understood. In this study, using extensive bioinformatic analysis, we found that NFAT2 transcription factor has potential binding sites on the Orai3 promoter. NFAT2 overexpression and NFAT inhibition studies revealed a dichotomy in the regulation of Orai3 by NFAT2 in non-metastatic v/s metastatic cells. Our data shows that NFAT2 regulates Orai3 transcription in non-metastatic cells, while NFAT2 acts as a bimodal regulator of Orai3 in metastatic cells. In metastatic cells, NFAT2 overexpression induces Orai3 protein degradation, while in non-metastatic cells, it does not. Further, we reveal that March8 E3 ubiquitin ligase physically interacts with Orai3 and stimulates Orai3 degradation via the lysosomal pathway. Mechanistically, NFAT2 can regulate March8 transcription in pancreatic cancer cells, but it depends on the DNA methylation status of the March8 promoter. In metastatic cells, the March8 promoter is hypomethylated compared to non-metastatic cells, and hence NFAT2 induces March8 mediated Orai3 protein degradation in metastatic cells. Zebrafish Xenograft injections show that stable knockdown of March8 increases metastatic events compared to its control. To summarize, this study, for the first time, has identified that the same transcription factor can drive mRNA transcription and protein degradation of the same target depending upon the epigenetic status of the degradation machinery.

Development and analytical performance study of cartridge based chemiluminescence immunoassay reagent for prostate specific antigen

Ajaikumar S
ajaikumar.s@agappe.in
Ajaikumar S[a], Amar Rao H T[b], Biby T Edwin[a]
[a]Agappe Diagnostics Limited, Cochin, Kerala;
[b]Yenepoya Medical College, Mangalore, Karnataka

Introduction

A cartridge based chemiluminescence immunoassay (CLIA) has been developed for the high sensitive detection of prostate specific antigen (PSA) in human serum. The assay development focused on indigenous affordable cartridge based CLIA platform for rapid quantification of PSA biomarker.

Aim

To develop cartridge based, highly sensitive, fast and accurate chemiluminescence immunoassay for the detection of prostate specific antigen.

Materials & Method

An immunoassay reagent system for PSA detection has been standardized based on the Sandwich immunoassay method. The Anti-PSA monoclonal capture antibody subjected to biotinylation using Biotinamide Caproate N-Hydroxy Succinimide ester crosslinking. The working concentration for the biotinylated antibody is 10µg/mL. The anti-PSA monoclonal detector antibody (200µg) is subjected for the ALP conjugation using Alkaline phosphatase labelling-SH kit and the working concentration is 1:200000 dilution. A calibration curve preparation have been done with the developed reagents in the MispaCube cartridge CLIA analyzer. The obtained RLUs were converted into concentration ng/mL using the Toshiba calibrator software application.

Result

Analytical performance report

- Calibration stability of 5 weeks is confirmed using external and internal controls of PSA.
- The accuracy in terms of trueness of PSA CLIA reagent kit is satisfactory in comparison with Maccura i1000 (R^2 = 0.9969) [Fig.1].
- The Linearity range of PSA CLIA assay is confirmed as ranges from 0.2 - 120 ng/mL.
- No hook effect even at 2053 ng/mL of PSA concentration.
- Satisfactory stability study report on accelerated stability, shipping stability and real time stability.

Screening and identification of potential salivary microRNA biomarkers for oral squamous cell carcinoma: preliminary findings

Presenting Author: Sarath K V

Email: sarathkvsatheesh95@gmail.com

Sarath K V[a,b], Nivedita L Rao[a], Biby T Edwin[b], Krishnakumar Thankappan[c]

[a] Department of Biochemistry, Yenepoya Medical College, Yenepoya (Deemed to be University), Mangaluru, India.

[b] R&D Reagents, Agappe Diagnostics LTD, Kochi, India.

[c] Head and Neck Oncology Department, Amritha Institute of Medical Sciences, Kochi, India.

Background and Aim

MicroRNAs (miRNAs) are small non-coding RNA molecules majorly involved in gene expression regulation. MicroRNA expression variations have been found in several types of carcinomas, including oral squamous cell carcinoma (OSCC), the sixth most common human cancer worldwide. Early detection of cancer is crucial to improving patient outcomes and survival. Saliva is a minimally invasive biofluid compared to blood, for biomarker identification. This study was aimed to screen for and identify potential salivary miRNA biomarkers for newly diagnosed OSCC and compare their expression profiles with those of healthy individuals.

Methods

Whole unstimulated saliva of newly diagnosed OSCC (n = 18) and healthy control (n = 13) individuals was collected from Amrita Institute of Medical Sciences, Kerala, India. The expressions of ten miRNAs, miR-31, miR-184, miR-145-5p, miR-125a-5p, miR-27b-3p, let-7a-5p, miR-345-3p, miR-200a-3p, miR-3928-5p, and miR-1307-5P, were quantified in all the samples by using quantitative PCR (qPCR). Independent sample t-test and Mann-Whitney U test were performed to identify the significantly different miRNAs between case and control groups.

Results

Five salivary miRNAs, miR-1307-5p, miR-145-5p, miR-345-5p, let-7a-5p, and miR-31, of the ten that were screened showed expression variations and were identified as potential biomarkers for OSCC in the preliminary biomarker-screening stage. Of these, miR-1307-5p showed statistically significant upregulation in OSCC patients compared to healthy controls ($p = 0.028$).

Conclusion

miR-1307-5p can become a potential biomarker for OSCC detection. Further larger study of the five identified salivary microRNAs and OSCC stage-wise comparison of their expressions can establish their clinical utility as biomarkers in OSCC.

Phase Separation related gene signatures in Indian Breast Cancer patients

Presenting Author: Priyanka Thareja

Email (presenting author): priyankathareja10@gmail.com

Priyanka Thareja[a], Bhudev C. Das[a], Priyanka Jain[a]*
Amity Institute of Molecular Medicine and Stem Cell Research (AIMMSCR), Amity University,
Noida, Uttar Pradesh, India

Abstract

Breast cancer is the leading cancer among women in India, representing 13.5% of all cancer diagnoses and 10.6% of cancer-related deaths as of 2020. It was estimated that India had 118,000 new cases of breast cancer, with a total number of living cases at over 525,000. Cancer progression is hallmarked by loss of genomic integrity leading to change in protein conformations. This study aimed to identify potential phase separation (PS) related gene signatures in breast cancer. In this study we identified transcriptional level changes in Indian breast cancer tumor vs normal tissue from three datasets (GSE89116, GSE15852 and PRJNA835602) available in public domains. Comparative analysis of the above dataset shows two significant (FC >1.5 &adjp-value <0.05) upregulated (PRC1 and SDC1) and three significant (FC < -1.5 &adjp-value <0.05) down-regulated genes (ACACB,SORBS1 andTIMP4) common among the three datasets. Further phase separation related gene signatures were explored among up & down regulated genes. Phase separation related eleven upregulated and four downregulated genes were commonly found in tumors of breast cancer patients (GSE89116 and PRJNA835602). Pathway analysis of phase separation related differentially expressed genes shows their involvement in cell cycle regulation. Upregulated PRC1 (Protein regulator of cytokinesis 1) and downregulated SORBS1 (Sorbin and SH3 domain-containing protein) were found to have 27.26% and 2 % disordered regions using the DisProt tool. This is the first study to identify phase Separation related gene signatures in Indian Breast Cancer patients that can be further studied to identify their role as potential biomarkers in disease progression.

Exploring the role of Hepatitis C virus in modulating the AFP protein expression to lead to Hepatocellular Carcinoma.

Presenting Author: Reshu Chauhan

*Email (Presenting author): 2023200202.reshu@dr.sharda.ac.in

Reshu Chauhan[1]*, Bennet Angel[1], Vinod Joshi[1], Annette Angel[1], Shareef BM[1], Aarya Chitransh[1]

[1]*Centre of Excellence in Virology and Immunology, Sharda University, Greater Noida, U.P, 201310, India*

Abstract

Alpha-fetoprotein, or AFP, is a glycoprotein secreted by liver cells and exists in two forms, native AFP and tumor AFP (tAFP). It functions in the cell cycle transition from the G1 to the S phase and promotes angiogenesis. tAFP plays a crucial role in the progression of hepatocellular carcinoma (HCC). However, its role in Hepatitis C virus (HCV) triggered HCC progression is unclear. We did in-silico analysis utilizing various bioinformatics tools, such as the RCSB Protein Data Bank, ClusPro 2.0 (protein-protein docking), and PyMOL 3.0 to find the cause for this. Our study firstly revealed that of the various HCV proteins; the Core, NS3, and NS5A have effective binding. Secondly, it was observed that of these proteins, NS5A exhibited the highest binding affinity with tAFP (-1116.8 kcal/mol). The binding affinity was also found to be maximum when interaction of AFP- NS5A along with host receptor CXCR4 (CXC motif chemokine receptor 4) (-1562.6 kcal/mol) was checked. This suggests that the presence of HCV protein NS5A may enhance the binding efficiency of tAFP thereby accelerating the progression of HCC. These interactions can thus be used for therapeutic designing of inhibitors or modulators to disrupt or prevent Hepatocellular Carcinoma.

Keywords: Alpha-fetoprotein, Hepatocellular carcinoma, HCV

Lnc RNACNV Integrate R: A Novel Framework for Correlating lncRNAs Expression with CNV Abnormalities and Disease Progression

Neetu Tyagi
ntyagi654@gmail.com

Authors: Neetu Tyagi[a, b], Shikha Roy[a], Dinesh Gupta[a*]

[a]*Translational Bioinformatics Group, International Centre for Genetic Engineering and Biotechnology (ICGEB), New Delhi, India.*

[b]*Regional Centre for Biotechnology (RCB), Faridabad, Haryana, India.*

Abstract

Recent technological advancements have made multi-omics datasets more accessible, providing new opportunities for understanding complex diseases. Integrating these datasets is crucial for a comprehensive view of biological systems, but challenges like matching samples and developing practical integration methods persist. We developed lncRNACNVIntegrateR, an R package designed to explore the association between long non-coding RNAs (lncRNAs) and copy number variations (CNVs). lncRNACNVIntegrateR takes transcriptome data and absolute CNV calls, combined with clinical data from the same samples, to perform pre-processing, lncRNA-CNV correlation, and identification of prognostic signatures linked to CNV alterations. The package also constructs a risk score model based on CNV-driven lncRNA signatures and provides functional enrichment analysis to explore the roles of targeted genes in disease progression. We validated lncRNACNVIntegrateR using TCGA datasets, specifically glioblastoma (GBM) and colorectal adenocarcinoma (COAD). The risk score model achieved AUC values of 0.79 for GBM and 0.70 for COAD, demonstrating robust accuracy. lncRNACNVIntegrateR thus emerges as a valuable tool for integrating transcriptome and CNV data, offering insights into the relationship between lncRNAs and CNVs, enhancing our understanding of disease mechanisms, and supporting personalized treatment strategies.

Recurrent NT5C2 Mutations Drive Drug Resistance in Relapsed Acute Lymphoblastic Leukemia: A System Biology based approach

Ramita Sharma[*1], Himanshu Singh[1], Sugunakar Vuree [3, 4#]

1. *School of Bioengineering and Biosciences, Lovely Professional University, Punjab, India.*
2. *Department of Biotechnology, Vignan's Foundation for Science, Technology, & Research (Deemed to be a university), Guntur 522 213, India.*
3. *Virchow Biotech Pvt Ltd, Manufacturing and R&D Facilities, Survey No.172 part, Gagillapur Hyderabad, India – 500 043.*

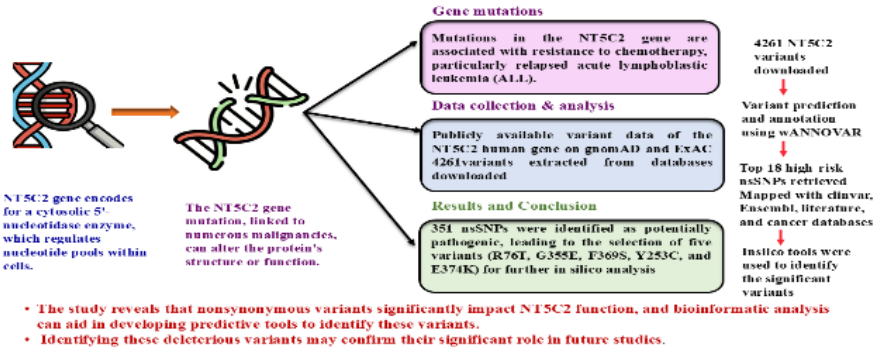
[*] Presenting Author ramita.bioinfo11@gmail.com

[#]Corresponding author: sugunakarvure@gmail.com

Abstract: The NT5C2 is a cytosolic II protein, a 5'-nucleotidase involved in purine metabolism, catalyzes the conversion of nucleotides into nucleosides. NT5C2 mutations drive thiopurine resistance in relapsed ALL by increasing nucleotidase activity through altered regulatory mechanisms. Recurrent mutations in NT5C2 have been identified as a common genomic lesion in relapsed ALL and linked to acquired thiopurine resistance. Mutant proteins showed elevated 5'-nucleotidase activity, preference for thiopurine metabolites, and reduced uptake. These mutations also influenced endogenous nucleotide homeostasis and thiopurine-induced metabolomic response, contributing to NT5C2-mediated drug resistance in ALL and suggesting potential therapeutic targeting in relapsed ALL. Our studies discovered and examined putative single nucleotide polymorphisms (SNPs) in the NT5C2 gene using a wide range of sequence- and structure-based bioinformatics techniques. A total of 351 nonsynonymous SNPs (nsSNPs) that are deleterious were found by applying seven predictive algorithms. Five nsSNPs—R76T, G355E, F369S, Y253C, and E374K—were filtered for further research because of their possible damaging effects. The structural and functional implications of these variants are assessed using a range of in silico techniques, such as meta-SNP, SNP&GO, I-Mutant 2.0, MutPred 2, HOPE, and ConSurf. Identifying these variations emphasizes the significance of the pathophysiology associated with the diseases and may confirm their important role in future studies.

Keywords: Relapse-Acute Lymphoblastic Leukemia, wANNOVAR, variants prediction and annotation.

Figure 1:



A novel machine learning-based lung microbiome data analysis reveals important bacterial biomarkers for stratification of major non-small-cell-lung cancer subtypes

Pragya Kashyap[1], Kalbhavi Vadhi Raj[2], Naveen Dutt[3], Pankaj Yadav[1,4]

[1]Department of Bioscience & Bioengineering, Indian Institute of Technology, Jodhpur, Rajasthan, India
[2]Department of Electrical Engineering, Indian Institute of Technology, Jodhpur, Rajasthan, India
[3]Department of Pulmonary Medicine, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India
[4]School of Artificial Intelligence and Data Science, Indian Institute of Technology, Jodhpur, Rajasthan, India

Correspondence:
Pankaj Yadav
Department of Bioscience and Bioengineering
Indian Institute of Technology
Jodhpur, 342030 Rajasthan, India
Email: pyadav@iitj.ac.in
Tel: +91 0291 280-1211

Abstract

Accurate classification of adenocarcinoma (AC) and squamous cell carcinoma (SCC) is a major challenge to cytopathologists owing to their high heterogeneity and variance in cell populations. Several subsequent clinical tests are performed to distinguish between AC and SCC, which is time-consuming and costly approach. Here, we introduce a machine learning (ML) model trained using lung microbiome data along with key metadata features to accurately classify AC and SCC.

We studied microbiome data obtained from resected lung tissue samples of AC and SCC patients. We used linear discriminant analysis effect size (LEfSe) algorithm to identify significant differentially enriched taxa in AC and SCC. Moreover, linear discriminant analysis algorithm was applied to reduce the dimensionality of the dataset while also maximizing inter-class distances and minimizing intra-class distances between AC and SCC. Next, we compared six different supervised classification algorithms *viz.* logistic regression, naïve-bayes, random-forest, extreme-gradient-boost (XGB), k-nearest-neighbour, and deep-neural-network. Hyperparameters were trained using the Bayesian-optimization-algorithm.

Our LEfSe revealed 12 lung microbiota such as Proteobacteria, Deinococcota, Firmicutes and 4 metadata features that could potentially classify AC and SCC. Our analysis shows that XGB model outperforms other five classification models with an accuracy of 76.4%. Also, on the independent dataset, XGB has the highest AUC of 0.70. We found enrichment of citrate cycle and carbon fixation pathways in AC, while glutathione metabolism and oxidative phosphorylation pathways were enriched in SCC. This study for the first time classified NSCLC subtypes and revealed important bacteria and metadata features for their potential as predictive and diagnostic biomarkers.

Investigating the underlying basis of the interaction between two large GTPases – hGBP2 and Drp1

Presenting Author: Pratiti Bakshi

Email (presenting author): pratitibakshi@nii.ac.in

Author-Pratiti Bakshi[a], Sangita Dey[a], Monika Mittal[a], Apurba Kumar Sau[a*]

[a]*National Institute of Immunology, New Delhi - 110067*

Human guanylate-binding protein 2 (hGBP2) and Dynamin-related protein 1 (Drp1) are multi-domain proteins that belong to the dynamin superfamily of large GTPases. Unlike Drp1, which catalyzes the formation of GTP to only GDP, interferon gamma-inducible hGBP2 hydrolyzes GTP to GDP and further to GMP through successive phosphate cleavages. hGBP2 undergoes substrate binding- and hydrolysis-induced oligomerization and exhibits anti-cancer properties. By alternative splicing, Drp1 generates several isoforms which undergo post-translational modifications that regulate its biological functions. Upon GTP hydrolysis, Drp1 forms large oligomers and it acts as a major player in mitochondrial fission, and thus, important in cellular tumorigenesis. These two GTPases have an N-terminal globular domain where substrate binding and hydrolysis take place, which is followed by a C-terminal elongated helical or stalk domain. Drp1 is present in the cytoplasm and it migrates to the mitochondrial outer membrane during the fission activity. hGBP2 (a cytoplasmic protein) interacts with Drp1 and inhibits its translocation to the mitochondria and therefore helps suppressing Drp1-mediated breast cancer metastasis. It is therefore essential to understand the underlying basis of their interaction, which may have a therapeutic importance. Our study has been focused on elucidating the molecular mechanism of their interaction with respect to their 1) oligomeric forms, 2) effects of substrate binding and hydrolysis, and 3) post-translational modifications. Also, our goal is to investigate the differential expression of Drp1 isoforms in distinct cancer scenarios.

Does Meningioma 1 gene bear prophecy for glioma patient survival?

Presenting Author: Masum Saini

Email (presenting author): masum_genetics@hotmail.com, masum@rcb.res.in

Masum Saini[a b], Ajaya Nand Jha[c], Rajiv Tangri[c d], Md.Qudratullah[a] and Sher Ali[a e]

[a] *National Institute of Immunology, Aruna Asaf Ali Marg, New Delhi 110067, India*; [b] *Regional Centre for Biotechnology, NCR Biotech Science Cluster, 3rd Milestone, Faridabad-Gurgaon Expressway, Faridabad 121001*; [c] *Max Super Specialty Hospital, 1, Press Enclave Road, Saket, New Delhi 110017, India*; [d] *Dr. Lal PathLabs, National Reference Laboratory, Sector 18, Rohini, New Delhi 110085, India*; *and* [e] *Department of Life Sciences, SBSR, Sharda University, KP-III, Greater Noida 201310, India*

Abstract

Gliomas are a type of human brain tumors comprising <1.6% of all new cancer diagnoses worldwide. These tumors have a poor clinical prognosis, which is evident from the mortality to incidence rate ratio (MIR) of 0.74 as compared to say, breast (MIR 0.27) or prostate cancer (MIR 0.25), thus being far more fatal than the latter two that have significantly higher incidence rates. Therefore, newer molecular insights will improve Glioma diagnosis, prognosis and therapy. As a step in this direction, we investigated Meningioma 1 (*MN1*) gene -a transcriptional co-regulator, which is also implicated in other malignancies. Though, its significance in glioma pathology remains to be understood, MN1 and other regulatory molecules such as insulin growth factor 1 (IGF1) modulate expression of insulin-like growth factor binding protein 5 (IGFBP5), which is associated with higher glioma grade and shorter survival span of patients.

We quantified expression of MN1, IGFBP5 and IGF1 in 40 gliomas and examined their correlation. Copy number of MN1 gene and correlation between its mRNA-protein levels was evaluated. To validate our findings and ascertain the association of MN1 expression levels with patient survival, we used Publicly available TCGA datasets. *MN1* overexpression correlated with low-grade (LGGs) and not high-grade gliomas (HGGs) and was not determined by the copy number alteration of the gene. Notably, gliomas with upregulated *MN1* have better overall survival (OS) and progression-free survival (PFS). Our findings also suggested a grade-specific interplay between repressive and activating roles of MN1 and IGF1, respectively, in the regulation of *IGFBP5*. Thus, *MN1* overexpression, a promising predictor of OS and PFS in gliomas, may serve as a prognostic biomarker in clinical settings to categorize patients with survival advantage.

Machine Learning-Based Analysis of Blood and Urine Exosomal miRNAs for Accurate Differentiation of Prostate Cancer and BPH

Presenting Author: Garima Jain

Email (presenting author): garima.jain@bhu.ac.in

Shweta Singh5*, Abhay Kumar Pathak2*, Sukhad Kural3, Lalit Kumar3, Mahima Yadav4, Manjari Gupta2, Sameer Trivedi3, Parimal Das1, Garima Jain1,5#*

1Centre for Genetic Disorders, Institute of Science, Banaras Hindu University, India.
2 DST-CIMS, Institute of Science, Banaras Hindu University, Varanasi, India.
3 Department of Urology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.
4 Department of Pathology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.
5MIRNOW, BIONEST, Banaras Hindu University, India.

**Equal Contribution First Authors, # Correspondance - garima.jain@bhu.ac.in*

Abstract

Prostate cancer (PCa) is a leading cause of cancer-related deaths in men globally. Current diagnostic tools, such as prostate-specific antigen (PSA) testing, often lack the specificity and sensitivity needed to distinguish accurately between prostate cancer and benign prostatic hyperplasia (BPH), leading to false positives, unnecessary biopsies, and suboptimal treatments. Thus, identifying non-invasive biomarkers that can reliably differentiate between these conditions is crucial for improving diagnostic precision and patient care.

Exosomal miRNAs, known for their roles in carcinogenesis, have emerged as promising biomarkers for cancer detection. In this study, we analyzed the differential expression of selected miRNAs and lncRNA in urine-derived exosomes from 50 clinical samples. We also evaluated their expression in blood samples to explore potential correlations. Using logistic regression, we assessed the diagnostic performance of these miRNAs individually and in combination. A four-miRNA combination (miR-101, miR-21-5p, miR-19b-3p, and miR-375) achieved an accuracy of 0.77, precision of 0.81, recall of 0.86, F1 score of 0.83, and an AUC score of 0.82. The model yielded 3 false positives, 2 false negatives, and 13 true positives.

Testing whether combining blood and urine samples could enhance accuracy revealed that while overall model performance remained stable, wider variations in miRNA expression between blood and urine were observed in PCa patients compared to BPH patients. Additionally, miRNA target gene analysis highlighted the involvement of key cancer-related pathways, with a particular focus on ROR1, a target gene of miR-19b and miR-101. These findings underscore the potential of exosomal miRNAs and machine learning in improving non-invasive PCa and BPH diagnosis.

Identification of long non-coding RNA (lncRNA) signatures in meningioma: path to discovery of potential biomarkers and therapeutic targets?

Ritanksha Joshi
bez218444@dbeb.iitd.ac.in

Ritanksha Joshi [a], Jyotsna Singh [b], Vaishali Suri [b#], Ritu Kulshreshtha [a*]

[a] *Department of Biochemical Engineering and Biotechnology, IIT Delhi, New Delhi, India- 110016*
[b] *All India Institute of Medical Sciences, New Delhi, India-110029;*
[*]*Corresponding author* [#]*Co-corresponding author*

Abstract

Meningioma is one of the most common primary brain tumors, classified into 3 malignancy grades by WHO. Surgical resection and radiotherapy are the mainstays of treatment and often inadequate to tackle higher grade tumors. Complex histology coupled with lack of reliable genetic and epigenetic markers impacts accuracy of grading and prognosis. Distinct interactions between the coding (mRNAs) and noncoding (ncRNAs) transcriptomes have been shown to drive regulation of gene expression at multiple levels and impact disease development. There is little known about the dysregulated long non-coding RNA (lncRNA) signature in meningioma. In our study, through transcriptome profiling of Indian meningioma patient tumor samples (N = 75) inclusive of WHO grades (1, 2, and 3) and healthy controls (N = 4), we characterized lncRNA expression profiles associated with individual tumor grade and within-grades. Several lncRNAs such as H19, SOX2-OT among others showed significant dysregulation across meningioma grades, and was validated by RT-qPCR. The differentially expressed lncRNAs were predicted to impact key pathways such as mTOR signaling, cell cycle, focal adhesion, previously implicated in meningioma. Kaplan-Meier survival analysis revealed lncRNAs of prognostic significance. LncRNA-mRNA expression correlation networks identified functional roles of both well-characterized and novel unannotated lncRNAs. Through lncRNA-miRNA-mRNA ceRNA networks, key associations of lncRNAs with other commonly dysregulated miRNAs and mRNAs and their regulatory axes were identified. Overall, our comprehensive analysis of long noncoding RNA signatures in meningioma unveils important ncRNA-mRNA inter-relationships that may impact meningioma pathogenesis. Further functional validation of key lncRNAs may thus reveal potent biomarkers and therapeutic targets.

Bifunctional fusion proteins in cancer therapy

Presenting author: Amruta Chavhan

Email: chavhanamruta31@gmail.com
Author: Amruta Chavhan
*Medical Intern, Jawaharlal Nehru Medical College,Wardh*a.

Abstract

Bifunctional fusion proteins, which integrate two different biological roles into a single molecule, are an emerging class of medicines in the treatment of cancer. Comparing this dual functioning to standard monotherapies offers various advantages, including the ability to target cancer cells more precisely and effectively. These proteins are made to change the tumour microenvironment, help transport drugs more effectively, or strengthen the immune system's defences against malignancies.This abstract focuses on two notable examples: Bintrafusp alfa and Catumaxomab.

Bintrafusp alfa (M7824) is a bifunctional fusion protein that targets both programmed death-ligand 1 (PD-L1) and transforming growth factor-beta (TGF-β). PD-L1 inhibition reactivates T cells by blocking immune checkpoint pathways, while the TGF-β trap modulates the tumour microenvironment by reducing immunosuppression and fibrosis. This dual mechanism has shown promise in treating various solid tumours,including non-small cell lung cancer (NSCLC) and cervical cancer, by simultaneously enhancing anti-tumor immunity and altering the tumour stroma to inhibit cancer progression.Contrarily, catumaxomab is a bispecific antibody that targets CD3 on T cells and epithelial cell adhesion molecule (EpCAM) on tumour cells. T cells and tumour cells are brought close by this contact, which promotes immune-mediated killing.Catumaxomab also engages Fc receptors on other immune cells, amplifying the immune response. It is primarily used in treating malignant ascites associated with EpCAM-positive carcinomas, demonstrating the potential of bifunctional proteins in managing complex tumour environments.These examples highlight the potential of bifunctional fusion proteins to revolutionise cancer therapy by offering more targeted and effective treatments.

Microarray Integrated Spatial Transcriptomics (MIST) for Affordable, Robust, and Comprehensive Digital Pathology

JUWAYRIA
nkhh.juwayria@gmail.com Juwayria
a , Sunil Kumar b , Deepali Jain b , Prabhat Singh Malik b , Ishaan Gupta a*
1 Department of Biochemical Engineering and Biotechnology, Indian Institute of Technology, New Delhi, India
2 All India Institute of Medical Sciences, New Delhi, India

Abstract

Spatial transcriptomics allows positional mapping of cells and their gene expression in a tissue section at near single-cell resolution. We investigate a rare lung cancer case: lung adenocarcinoma (LUAD) carcinoma admixed with squamous cell carcinoma (LUSC). Using Visium based in-house developed microarray integrated spatial transcriptomics (MIST) approach, we have analyzed multiple regions of interest (ROIs) for both histologies (LUAD and LUSC) from distinct tumor areas: i) tumor core, ii) tumor periphery, iii) normal adjacent to tumor (NAT), iv) distant normal tissue and, v) reactive lymph node. We observed differential infiltration of immune cells in NAT of adeno and squamous component of the tumor, where the former was dominated by cancer-associated fibroblasts (CAFs), and the latter showed an assorted mixture of various immune cells such as CAFs, B cells, T helper cells, macrophages, etc. A similar trend was observed in LUAD and LUSC tumor periphery. Interestingly, the core of the tumor in both LUAD and LUSC was dominated by CAFs. In conclusion, research comparing different cancer types often focuses on single histologies in separate individuals. This approach inherently introduces bias, confounded by inter-individual variability. Investigating mixed histologies offers an internally controlled environment for more precise comparison of the two histologies.

Uncovering key genes and pathways associated with lung adenocarcinoma progression through systems biology approach

Presenting Author: Dr. Mallikarjuna Thippana

Email (presenting author): arjun.ins@uohyd.ac.in

Mallikarjuna Thippana [a], Lalitha Guruprasad [a]

[a] *School of Chemistry, University of Hyderabad, Hyderabad, India*

Abstract

Lung adenocarcinoma (LUAD), a prevalent form of lung cancer, is often found in non-smokers and has the potential to metastasize into lung squamous cell carcinoma. The development and progression of tumors are influenced by various factors including genetic factors, oncogenic viruses, exposure to carcinogens, and hormonal factors. To improve patient survival, new prognostic strategies that require understanding the molecular mechanisms integral to tumorigenesis are needed. Identification of these critical mechanisms is essential for effective disease management. We employed a systems biology approach using transcriptomic profiling data available in the public domain to uncover complex interactions and regulatory networks in patients with lung adenocarcinoma. By constructing and analyzing co-expression and protein-protein interaction networks of dysregulated genes obtained from statistical filtering, we identified key genes that play central roles in tumor progression. These genes often serve as hubs in the network with a high degree of connectivity with other genes, suggesting their importance in cellular processes. These genes interact with each other and other cellular components, such as transcription factors, providing insights into the regulatory pathways that are disrupted in lung cancer. Furthermore, we will investigate the prognostic significance of these genes in patients. This work not only highlights the most influential genes, but also offers a comprehensive view of the transcriptomic landscape of lung adenocarcinoma, opening new avenues for research and treatment.

Keywords: Lung cancer, Essential genes, Therapeutic targets, Interaction networks and Prognostic significance

Exploring the Dual Landscape of Gene Expression and Splicing in Non-Small Cell Lung Cancer (NSCLC)

DASARI ABHILASH

abhilashdasari.10@gmail.com

Dasari Abhilash[a], Ishaan Gupta[a]

[a] *Department of Biochemical Engineering and Biotechnology, Indian Institute of Technology, New Delhi, India*

Abstract

Most cancer analyses focus primarily on differential gene expression (DGE) to identify relevant molecular changes. However, to fully understand the drivers of these changes, it is essential to also study splicing mechanisms, which add complexity by generating multiple transcript variants from a single gene, potentially leading to diverse protein functions and oncogenic properties. In this study, we analyzed 20 samples (10 NSCLC and 10 controls) to map both DGE and splicing events. We uncovered a dual landscape: 664 genes were upregulated, 426 downregulated, and 407 exhibited significant splicing alterations, including exon skipping, intron retention, and changes in splice site usage. Interestingly, only 20 genes were both differentially expressed and spliced, suggesting that splicing often operates independently to diversify the functional output of genes without altering their expression levels. Enrichment analysis revealed that upregulated genes were primarily involved in epithelial differentiation and nuclear division, while downregulated genes were linked to pathways such as G-protein coupled receptor signaling and blood vessel morphogenesis. Spliced genes were associated with cadherin binding and actin binding—key for cell adhesion and motility, which are hallmarks of cancer invasion and metastasis. Our findings suggest that while gene expression changes set the stage for tumor progression, alternative splicing fine-tunes the molecular repertoire, enhancing NSCLC adaptability. This dual analysis opens new avenues for targeted therapies that disrupt these regulatory networks in NSCLC.

Tumor Mutational Burden Disparities: A Critical Comparison Between Indian Cancer Patients and The Cancer Genome Atlas across cancer types

Presenting Author: Satya Prakash Khuntia

Email (presenting author): satya@4basecare.com

Satya Prakash Khuntia[a], Nilesh Mukherjee[a], Vyomesh Javle[a], Giridharan Periyasamy[a], Kshitij Datta Rishi[a], Hitesh Madan Goswami[a], Vidya Harini Veldore[a]

[a] *4baseCare Precision Health Pvt. Ltd, Bangalore, India*

Background

Tumor Mutational Burden (TMB)/load has emerged as a pivotal biomarker in cancer immunotherapy. TMB exhibits considerable variability across different cancer types and populations. This study aims to elucidate these variations by comparing TMB values derived from an Indian PAN cancer cohort with those from TCGA, utilizing TarGT IndieGene panel (4.4 MB) derived from Indian cancer population, optimized for TMB estimation.

Methodology

The analysis involved two datasets: one from Indian pan-cancer patients(n=1000) and the other from TCGA(n=7905). For both datasets bootstrapping techniques were utilized to derive robust statistical estimates, including median, mean, and percentiles (>75th percentiles), which are indicative of high mutation loads. Comparative assessments between the Indian and TCGA cohorts were conducted using non-parametric statistical methods, specifically the Mann-Whitney U Test and bootstrap hypothesis testing, to evaluate differences in TMB across various percentiles and central tendencies.

Results

Significant differences (p-value < 0.05) in TMB distribution, were observed across specific cancer types, including breast, genitourinary, and pancreatic cancers, particularly at higher percentiles. For instance, a TMB score of 7 in bladder cancer, which is not considered eligible for immuno-oncology (IO) treatment based on the Pan-Cancer profile and is typically around the 50-60th percentile in TCGA data, was found to be at the 95th percentile in the bladder cancer cohort from India. These findings underscore the critical role of importance of population-specific/cancer specific TMB insights in patient selection and treatment decisions.

Is Anti-TIM3 Mediated Cancer Immunotherapy a Misguided Approach in Clinical Trials? Insights From the Mouse Breast Tumor Model

Presenting Author: Barnali Dolui
e-mail (Presenting Author): barnalidolui1990@gmail.com
Barnali Dolui[1a], Banani Majumdar [1b], Arunita Ghosh[1c], Kartiki Desai[2], Arghya Bandopadhay[3], Anupam Basu[1,2*]
[1] Department of Zoology, The University of Burdwan, Burdwan, India, [2] National Institute of Biomedical Genomics, Kalyani, [3] Nil Ratan Sircar Medical College and Hospital, Kolkata, India
*Corresponding / Supervisor author: e-mail: abasu@zoo.buruniv.ac.in

T cell immunoglobulin and mucin-domain containing-3 (TIM3), an immune checkpoint receptor, plays a crucial role in tumor immune evasion and cancer progression. Despite ongoing clinical trials targeting TIM3 with anti-TIM3-based immunotherapy, significant setbacks have been encountered, and the exact role of TIM3 remains unclear. This study aimed to investigate the effects of TIM3 blockade on breast cancer progression using a 4T1-induced breast tumor model in BALB/C mice. Intraperitoneal administration of TIM3 monoclonal antibody unexpectedly led to increased tumor volume and invasive growth, with a marked increase in liver metastasis observed through morphological and histopathological studies. Flow cytometry analysis revealed that anti-TIM3 treatment increased tumor-infiltrating CD4+ and CD8+ T cells while significantly reducing Foxp3+ cells. Elevated levels of TNF-α, IL-17A, IFN-γ, and IL-10 were observed in the serum following TIM3 blockade. Mass spectrometry-based proteomic analysis of tumor samples showed that TIM3 blockade upregulated the BAT3 adaptor molecule, along with increased expression of B2M, CDK4, and CD44, while downregulating S100-A8/A9 proteins. GSEA analysis further revealed enrichment of the mTORC/PI3K/AKT signalling pathways and epithelial-mesenchymal transition (EMT) genes. These findings suggest that TIM3 blockade may promote invasive tumor growth through B2M and CDK4-mediated cellular proliferation, and downregulation of S100-A8/A9, which could suppress autophagy-induced cell death and apoptosis. Additionally, TIM3 blockade may upregulate BAT3-mediated activation of mTORC, leading to suppression of FoxP3, which could induce metastasis through CD44-mediated EMT gene upregulation. This study is the first to demonstrate that TIM3 blockade can create an immunosuppressive environment, potentially promoting cancer aggressiveness-contrasting with other immune checkpoint receptors. These findings suggest that rather than blocking TIM3, enhancing it signalling might be a more effective strategy for tumor immunotherapy.

Glioblastoma Stemness: The Active Role of Tumor Vasculature

Shubhraneel Saha[1], Samiksha Kukal[1], Anjali Bhat[1] and Saran Kumar[1*]

[1] Kusuma School of Biological Sciences, Hauz Khas, IIT Delhi 110016

* ksaran@iitd.ac.in

Abstract:

Tumor vasculature, once thought of simply as a transport system for nutrients and oxygen, is now recognized as an active player in shaping the plasticity of cancer cells. Our research delves into the intricacies of glioblastoma stemness, focusing on the interplay between perfusion-dependent and perfusion-independent factors that contribute to this phenomenon. We developed a novel methodology to isolate potential cancer stem cells residing near blood vessels, utilizing marker-independent labeling of quiescent cells and perfusion-based strategies. Transcriptomic analysis of these isolated cells revealed a distinct set of genes associated with glioblastoma stemness, impacting cell cycle regulation and therapeutic resistance. Further investigation highlighted the significance of the metabolic microenvironment, mTOR signaling pathways, and Notch-mediated communication between glioblastoma stem cells and endothelial cells. These findings underscore the critical role of perfusion-influenced signalling pathways and endothelial cell interactions in driving glioblastoma stemness. This deeper understanding of the tumor microenvironment and its active role in glioblastoma stemness offers promising avenues for developing more effective therapies targeting this resilient cell population.

Selected References:

1. Identification of vascular cues contributing to cancer cell stemness and function. S Kumar et al., *Angiogenesis* 25 (3), 355-371. [I.F – 9.2]

2. Intra-tumoral metabolic zonation and resultant phenotypic diversification are dictated by blood vessel proximity. S Kumar et al., *Cell metabolism* 30 (1), 201-211. e6 [I.F – 27.7]

3. Cancer plasticity: investigating the causes for this agility. S Saha et al., *Seminars in Cancer Biology* 88, 138-156. [I.F – 12.1]