20TH NATIONAL RESEARCH SCHOLARS MEET

By The Students, For The Students

11th- 12th December, 2024

Million Eyes

Biology Beyond Boundaries

ADVANCED CENTRE FOR TREATMENT, RESEARCH & EDUCATION IN CANCER
TATA MEMORIAL CENTRE

PREFACE

The National Research Scholars Meet (NRSM) in Life Sciences, formerly known as the Graduate Students Meet (GSM), is an annual event organized by the graduate student community of the Advanced Centre for Treatment, Research & Education in Cancer (ACTREC) under the motto, "*By the students, for the students*". First conceptualized in 2005, this unique meeting has since gained significant recognition and prestige among students from diverse fields of biological and clinical sciences.

NRSM provides a collaborative platform for scientists and research scholars from various areas of life sciences to discuss and brainstorm innovative ideas aligned with their scientific interests. Over the years, it has been graced by esteemed speakers whose work has left a lasting impact, including Shri Nilesh Desai (Director, SAC-ISRO, Ahmedabad), Prof. P. Balaram (former Director, IISc), Prof. S. C. Lakhotia (BHU), Prof. Satyajit Mayor (Director, NCBS), Dr. Bharat Vatwani (Ramon Magsaysay awardee), Prof. M. G. Deo (Moving Academy of Medicine and Biomedicine), Dr. Pranoti Mandrekar (University of Massachusetts, USA), and many others. Their contributions have provided insights into diverse areas such as immunology, developmental biology, protein chemistry, virology, cancer biology, epigenetics, psychology, ecology, evolutionary biology, and astrophysics.

NRSM offers a unique opportunity for young research scholars and students from across India to showcase their work through oral and poster presentations. It brings together intellectual minds from academia and industry on a shared platform, fostering the exchange of innovative scientific ideas. Participants from premier national institutes such as IITs, IISc, IISERs, NCBS, CCMB, IGIB, JNCASR, CDFD, and PGIMER, as well as representatives from leading industries like Xcelris Labs, Reliance Life Sciences, Merck Millipore, Leica Microsystems, AstraZeneca, and Zydus, have enriched this event with their contributions. Additionally, the conference receives support and funding from esteemed government agencies like Welcome-DBT, BRNS, ICMR, LTMT, HBNI, and CSIR.

This year marks a momentous occasion as NRSM celebrates its 20th annual conference under the theme, "**Million Eyes: Biology Beyond Boundaries"**. The event aims to explore life sciences from a multidisciplinary perspective, integrating insights from physics, mathematics, computational biology, artificial intelligence, and other pioneering disciplines. The 2024 NRSM will serve as a vibrant hub where young researchers, scientists, clinicians, and industry leaders come together to delve into these interdisciplinary intersections.

Beyond scientific discourse, NRSM also fosters creativity by hosting the "Creative Corner", an event that showcases participants' talents in photography, painting, and poetry. As in previous years, this milestone conference aspires to inspire collaboration among researchers, industry professionals, and students, contributing to the advancement of the scientific community.

Message from Director, Tata Memorial Centre

Dr Sudeep Gupta

Director, TMC, Mumbai

It gives me immense pleasure to connect with the faculty and delegates of the 20th National Research Scholars Meet (NRSM) 2024, a celebration of innovation and frontiers of biological research.

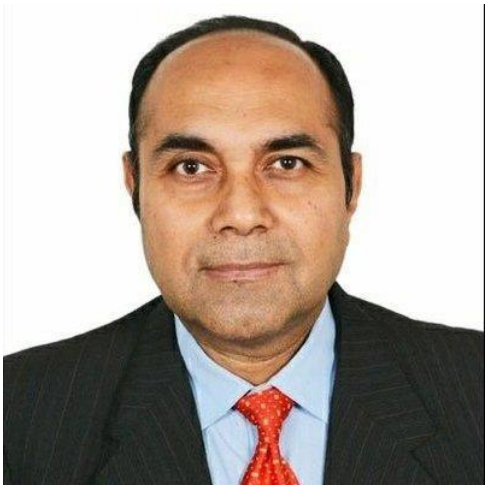
The theme, *"Million Eyes: Biology Beyond Boundaries,"* beautifully encapsulates the spirit of exploration and collaboration. In a world where biology increasingly intersects with fields like AI, engineering, and medicine, such a platform exemplifies the power of collective intellect in solving complex challenges and unveiling new horizons in science. Research, by its very nature, thrives not only within but also at the edges of disciplines. I am certain that the exchange of ideas at NRSM 2024 will inspire transformative thinking, spark novel collaborations, and lay the groundwork for impactful discoveries.

At Tata Memorial Centre (TMC), we are steadfast in our commitment to advancing research and delivering impactful solutions, particularly in the field of cancer. As a premier institution leading cutting-edge work in oncology, TMC strongly believes that the convergence of biology and medicine holds the key to unraveling the complexities of diseases like cancer.

To the talented scholars and professionals gathered here, I urge you to view your work not just through the lens of scientific inquiry, but as a means to profoundly impact human lives. It is your unwavering curiosity, innovative ideas, and dedication that will chart the course for a brighter, healthier future.

I commend the organizers for curating this inspiring forum and wish NRSM 2024 success. May this meet spark meaningful discussions, forge valuable partnerships, and ignite the transformative power of interdisciplinary science.

Message from Director, ACTREC



Dr Pankaj Chaturvedi
Director
ACTREC

It is an honor and a privilege to welcome you all to National Research Scholars Meet 2024: Million Eyes - Biology Beyond Boundaries. This conference is more than just an academic gathering—it is a celebration of diverse perspectives, an acknowledgment of the limitless ways we can explore, understand, and contribute to the vast field of biology.

As researchers, we often find ourselves delving deeply into our niches, but it is the intersections—where biology meets mathematics, engineering, artificial intelligence, and medicine—that spark innovation. NRSM 2024 is built on this spirit of collaboration and the belief that every unique perspective adds a valuable piece to the puzzle of life sciences.

Through your participation, this event becomes a vibrant mosaic of ideas, experiments, and experiences. I encourage each of you to engage deeply with the discussions, challenge established norms, and forge connections that could lead to breakthroughs.

Let this platform inspire you to not only push the boundaries of science but also to look beyond the horizon, embracing new approaches to solving the challenges of our time. Together, we embody the "Million Eyes" that will shape the future of biology and redefine its impact on the world.

I extend my heartfelt appreciation to the organizing team, whose tireless efforts and unwavering commitment have made NRSM 2024 a reality, creating a platform that celebrates innovation and collaboration in science.

Message from Deputy Director, CRI

Dr Prasanna Venkatraman
Deputy Director, CRI
ACTREC

'A million eyes- biology beyond boundaries'- this is how the title of the National Research Scholar Meet 2024 reads!

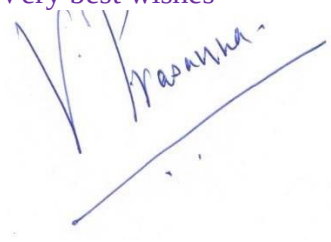
This remind me of Ayn Rand's Fountain head – Several decades ago, I was instantly drawn to the book which started as 'Howard Rock Laughed'! I wondered how anyone could start a story like that? It had that element of mystery, a glimpse of the flair for the authors style of writing, and beyond everything it gave a hint about the personality of the character that the author wanted to convey. I finished the book end to end in 3 days and it remains one of my favorites!

NRSM has the history of enchanting the audience with a captivating title that embodies the theme of the meeting. They spend several days thinking about the concept of the meeting and the teaser is released at the closing ceremony of each NRSM. As the baton is transferred from the previous NRSM organizers to the next, there is a nostalgia and a deep sense of responsibility that is transferred along. True to this year's theme the program is orchestrated by speakers from various branches of science who have composed many a symphony and the grand master would be the strokes from technological innovations that is shaping biology! This year, NRSM has introduced star student speakers, rightfully a cherry on top! There are several other interesting oral (10) and poster (47) presentations lined up with whooping prize money to be won, a delightful creative corner and an engaging panel discussion. If you have not seen the NRSM Instagram, you should visit immediately – a thriller is in store and ask for those Goggles!!

I also take this opportunity to congratulate the students of ACTREC and organizers of the NRSM for completing highly decorated two decades of this annual event! You make us proud.

It is my pleasure to welcome all the distinguished speakers, delegates, students from all over India to ACTREC and I wish you a pleasant stay here. Sit back, relax and enjoy the science, the food and take-home new knowledge and warm memories!

Very best wishes



Prasanna

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PROGRAMME

NRSM Day 1: Wednesday, December 11, 2024		
Time	**Title**	**Speaker**
8:30-9:30 am	**Registration (K.S. Entrance) and Breakfast (K.S. Audi Lawn)**	
9:30-10:00 am	**Welcome Address and Inauguration (R.R.U Audi, 7th Floor)**	
10:00-10:30 am	**Chief Guest talk**	**Dr. L.S. Shashidhara** (Director, National Centre for Biological Sciences, Bengaluru, India)
10:30-11:00 am	**Guest of Honour talk**	**Dr. C.S. Pramesh** (Director, Tata Memorial Hospital, Parel, Mumbai, India)
11:00-11:20 am	**Tea Break (outside Audi)**	
Session 1 (R.R.U Audi, 7th Floor)		
11:25-11:55 am	**Keynote address 1**: Understanding the chemical origins of life through the lens of Astrobiology	**Dr. Sudha Rajamani** (Professor, IISER Pune)
12:00-12:30 pm	**Keynote address 2**: Pathogen growth and virulence dynamics drive the host evolution against coinfections	**Dr. Imroze khan** (Assistant Dean, Research and Associate Professor of Biology, Ashoka University)
12:35-1:00 pm	**Student Talk 1**: The untold story of the DNA ladder: Base-Stacking and its Applications	**Mr. Abhinav Banerjee** (Research Scholar, Dr Mahipal Ganji Lab, IISc Bangalore)
1:05-1:15 pm	**Company Presentation-1: BGI**	
1:15-1:25 pm	**Company Presentation-2: Allianz Bio**	
1:25-2:25 pm	**Lunch break (K.S. Audi Lawn)**	
Session 2 (R.R.U Audi, 7th Floor)		
2:30-3:00 pm	**Keynote address 3:** Why, how and when are membrane-bound compartments cut?	**Dr. Thomas Pucadyil** (Rahul Bajaj Chair Professor, IISER Pune)
3:05-3:35 pm	**Keynote address 4**: In situ alternatives for adoptive cell immunotherapy using biomaterial systems	**Dr. Prakriti Tayalia** (Professor, IIT Bombay)
3:40-4:10 pm	**Keynote address 5:** Optoelectronic Materials for Applications in Neuroscience	**Dr. Vini Gautam** (Assistant Professor, Centre for Nano Science and Engineering (CeNSE), IISc)
4:15-5:45 pm	**Poster Presentations (Foyer Area, opposite to Raaga) and Evaluation + Tea Break**	
6:00-6:30 pm	**Scientifia (K.S. Audi Lawn)**	
6:30-7:30 pm	**Cultural programme (K.S. Audi Lawn)**	
7:30-9:00 pm	**Dinner (K.S. Audi Lawn)**	

NRSM Day 2: Thursday, December 12, 2024		
Time	**Title**	**Speaker**
8:30-9:30 am	**Breakfast (K.S. Audi Lawn)**	
9:35-10:20 am	**Offbeat Talk (R.R.U Audi 7th Floor):** Research for equitable healthcare	**Dr. Ravi Kannan** [Recipient of Awards: Padma Shri 2020 and Ramon Magsaysay 2023] (Surgical Oncologist and Director, CCHRC, Assam)
Session 3 (R.R.U Audi, 7th Floor)		
10:40-11:10 am	**Keynote address 6**: What determines the large-scale structure of the cell nucleus?	**Dr. Gautam Menon** (Dean, Research and Professor of Physics and Biology, Ashoka University)
11:15-11:45 am	**Keynote address 7**: Scaling Biology for Fun and Profit	**Dr. Shishir Kumar** (Assistant Professor, IIT Hyderabad)
11:50-1:30 pm	**Oral Presentations (R.R.U Audi, 7th Floor)**	
1:30-2:30 pm	**Lunch break (K.S. Audi Lawn)**	
Session 4 (R.R.U Audi, 7th Floor)		
2:35-3:35 pm	**Panel Discussion (R.R.U Audi, 7th Floor)**	
3:40-4:10 pm	**Keynote address 8**: Digital Pathology & AI: Enabling and Transforming Medical Research	**Dr. Swapnil Rane** (Professor, Computational Pathology & AI Laboratory, Tata Memorial Centre)
4:15-3:40 pm	**Student Talk 2**: Understanding the structure-function relationship of enzymes and biological macromolecules	**Mr. Parijat Das** (Research Scholar, Dr Prasenjit Bhaumik's Lab, IIT Bombay)
4:45-5:30 pm	**Prize Distribution and Valedictory Ceremony (R.R.U Audi, 7th Floor)**	
5:30-6:00 pm	**High Tea (K.S. Audi Lawn)**	

INVITED TALK ABSTRACTS

SPECIAL GUEST

Dr. Ravi Kannan
Recpient of Awards: Padma Shri 2020 and
Ramon Magsaysay 2023
Surgical Oncologist and Director, CCHRC,
Assam

Research for equitable healthcare

Access to quality healthcare is a basic human right, yet significant disparities persist across socioeconomic, geographic, and demographic dimensions, intensifying global health inequities. This talk delves into the complex facets of equitable healthcare, focusing on the integration of policy reform, technological innovation, and community-driven strategies to address these challenges.

Cancer care disparities persist across the globe, disproportionately affecting underserved populations due to socioeconomic, geographic, and systemic barriers. Achieving equity in cancer care is essential for improving patient outcomes and reducing global health inequities. Research for equitable healthcare is a pertinent domain that focuses on identifying, understanding, and addressing the multifaceted factors contributing to disparities in cancer prevention, diagnosis, treatment, and survivorship.

Despite advancements in cancer diagnosis and treatment, affordability remains a critical barrier, exacerbating health inequities. This talk also focuses on the primary roadblocks to making cancer care accessible and affordable for economically disadvantaged groups.

Dr Sudha Rajamani

Professor, IISER Pune

Understanding the chemical origins of life through the lens of Astrobiology

A central aspect of Astrobiology research concerns the delineation of life's origin and its early evolution on our planet. This intriguing and complex story that started several billions of years ago, continues to be a very intriguing and fascinating scientific mystery. Specifically, it involves characterising how the transition from chemistry to biology would have occurred on the early Earth to result in minimal life, which is vastly different from the living organisms that we know of as extant life. In this talk, I will give an overview of the current understanding prevalent in the field, while also sharing some of the contributions that we at the COoL lab@IISER Pune have made towards these attempts. Discerning the aforementioned phenomenon involves the use of a very interdisciplinary approach and a diverse set of tools. I will try to give a flavour of this while also highlighting how the fundamental understanding of the transition from non-life to life, also has important implications for figuring out if there is life elsewhere in the universe.

Dr Imroze Khan

Assistant Dean, Research and Associate Professor of Biology, Ashoka University

:

Pathogen Growth and virulence dynamics drive the host evolution against coinfections.

Coinfections, or the simultaneous infection of hosts by multiple pathogens, are widespread in nature with significant negative impacts on global health. Can hosts evolve against such coinfections as effectively as they would against individual pathogens? Also, what roles do individual pathogens play during such evolution? Here, we combined theoretical models and experiments with *Tribolium castaneum* populations evolving against two coinfecting bacterial pathogens, with contrasting growth and virulence dynamics, to reveal that fast-growing pathogens inflicting rapid mortality surges (i.e., fast-acting) restrict adaptive success against coinfections. While hosts rapidly evolved better survival against slow-growing bacteria causing long-lasting infections, evolution against coinfection was significantly delayed and resembled slow adaptation against fast-acting pathogens. Moreover, limited scopes of immunomodulation against fast-acting pathogens during coinfections can drive the observed adaptive patterns. Overall, we provide new insights into how adaptive dynamics and mechanistic bases against coinfections are critically regulated by individual pathogens' growth and virulence dynamics.

Dr Thomas Pucadyil

Rahul Bajaj Chair Professor, IISER Pune

Why, how and when are membrane-bound compartments cut?

Membranes are formed by the non-covalent assembly of lipids and are highly resilient to breakage or rupture. This feature likely explains why lipids were selected over the course of evolution to form membranes that encapsulate all living entities. But living membranes are constantly cut and sealed. This is apparent during cell and organelle division and vesicular transport. Over the course of many years of work from several labs, we have come to realize that the cutting processes display incredible diversity, both in terms of their kinetics and regulation. My talk will describe recent developments in our efforts at understanding the mechanistic basis of this diversity.

Dr Prakriti Tayalia

Professor, IIT Bombay

In situ alternatives for adoptive cell immunotherapy using biomaterial systems

In cancer treatment, immunotherapy is favored over chemotherapy and radiotherapy because it harnesses the immune system to selectively target cancer cells, thereby reducing collateral damage to healthy tissues. Targeted T-cell immunotherapy has shown remarkable success and has FDA approval in treating hematological malignancies, but has shown limited success in treating solid tumors, which are localized and hidden from circulating T-cells. Furthermore, the ex vivo protocols for this treatment strategy make it expensive and difficult to generate large number of T-cells. To overcome these limitations, we have illustrated the use of a 3D scaffold to serve as a platform for programming T-cells in vivo, thereby, doing away with ex vivo manipulation and need for removing them from the body. It is also known that the microenvironment of solid tumor recruits myeloid lineage cells from peripheral blood and bone marrow into the tumor with immunosuppressive macrophages forming 50% of the solid tumor. Given their ability to penetrate solid tumors more effectively than T-cells, preclinical studies with chimeric antigen receptor (CAR) expressing macrophages have shown to perform antigen specific phagocytosis, eliciting T-cell mediated adaptive anti-tumor response. Again, to overcome ex vivo manipulation, we have demonstrated another strategy as a proof of concept to perform in situ modification of peritoneal macrophages and circulating monocytes with CAR against solid tumor antigen, using a non-viral biomaterial-based system. We have also demonstrated localised use of an adjuvant that improves efficacy by providing spatial control over modification of macrophages and developing a prominent anti-tumor response.

Dr Vini Gautam

Assistant Professor, Centre for Nano Science and Engineering (CeNSE), IISc

Optoelectronic Materials for Applications in Neuroscience

Interfacing optoelectronic materials with neuronal cells provides a platform for understanding the formation and function of neuronal circuits in the brain. Here I will present two examples from my research where I have utilised optoelectronic materials to engineer the growth of neuronal circuits and stimulate their activity.

I will first highlight the use of organic semiconductors as artificial photoreceptors for interfacing with the visual system. In these studies, I utilised the optoelectronic signals from organic semiconductor/electrolyte interface to stimulate neuronal cells and thereby elicit neuronal activity in a blind retinal tissue [1]. These results have implications for the development of all-organic retinal prosthetic devices. Next, I will give an overview of my current project, where I design nanoscale surface topography on biocompatible scaffolds to mimic the biophysical features in the brain's extracellular matrix [2]. I use these scaffolds to guide the growth of neurons, understand the formation of neuronal circuits and evaluate the neuronal network activity in response to the biophysical properties of their surrounding environment. These results have implications for developing biocompatible scaffolds to better understand the functioning of the brain.

[1] V. Gautam *et al.* A Polymer Optoelectronic Interface Provides Visual Cues to a Blind Retina. 2014. *Adv. Mater.* 26, 1751-1756.

[2] V. Gautam *et al.* Engineering highly interconnected neuronal networks on nanowire scaffolds, 2017. *Nano Lett*. 17, 3369–3375.

Dr Gautam Menon

Dean, Research and Professor of Physics and Biology,
Ashoka University

What determines the large-scale structure of the cell nucleus?

Good models in biophysics help us make quantitative sense of diverse observations. I will use our work on how chromosomes are positioned in human cells in interface to illustrate what models in biology are useful for. This line of investigation draws on an emerging viewpoint in biophysics, the idea that living systems are out of equilibrium in specific ways that lend themselves to being modeled. This approach lies at the core of a new field, called active matter, that is now increasingly used to describe biological systems across scales, from schools of fish to the acto-myosin cortex to molecular motors. I will explain what active matter is all about and illustrate how active matter descriptions can be applied to the problem of large-scale nuclear organization.

Dr Shishir Kumar

Assistant Professor, IIT Hyderabad

Scaling Biology for Fun and Profit.

Data is the soil on which the trees of comprehension of complex systems grow (the social network, the brain). Especially for the biological entities, deciphering the mechanisms and interconnection of the processes they host, requires a huge amount of good quality data. Automation of experiments in biology using robots has been pursued by many to attack this problem. However, for the extraction of the mind-boggling amount of data that we need, there is only one suitable strategy: the miniaturisation and integration of the experimental processes in the form of microfluidics. In this talk, I will discuss the microfluidic technology we are developing to collect massive amounts of cellular level data. Large scale integration (LSI) of microelectronics serves as our main supply of ideas and techniques. I describe our work on miniature microscopy, microfluidic flow automation and advanced materials for building the microfluidic chips. I compare advantages and pitfalls and show examples of use in biological experiments. Finally, I discuss the steps we are taking to miniaturise the on-chip fluidic switches, which will yield truly scalable microfluidic systems.

Dr Swapnil Rane

Professor, Computational Pathology & AI Laboratory,
Tata Memorial Centre

Digital Pathology & AI: Enabling and Transforming Medical Research

Digital pathology and Computational Pathology are interdisciplinary fields, focusing on the use of computational tools to transform pathology as a branch. It is fueled by the availability of large scale multi-dimensional datasets primarily in the form of whole slide images linked to clinical information including treatment data, outcomes, genomic data and others. Computational pathology is driving medical research using machine learning and deep learning algorithms to look at patterns that may not be visible to the human eye. Accurate prediction of genomic mutations1,2,3 from histology and the ability to predict response/benefit4 to therapy not only promises personalized medicine, but also guides further research into the molecular mechanisms of response to therapy. Patients can be risk stratified into those likely to recur early following a particular therapy and those likely to have long term response/disease free status5. Further, efforts to make AI more interpretable, is driving hypothesis generation at previously never imagined scales.

AI/ML/DL algorithms are affected by several pre-analytical variables, such as slide quality, image quality, processing artefacts, staining variations, interlaboratory variations in addition to true biological variables such as ethnic differences and tumor heterogeneity. Several tools are being built to detect, segment, and quantify artefacts on the digitized slide6,7,8 which are important supporting tools for introducing AI/ML/DL algorithms for clinical use. Cautious AI9 tools are also essential for making the AI algorithms more robust and reliable for use in the clinics as well as in trials, to test their generalizability.

It is well known that AI algorithms trained on one population may not work equally well on another population due to several variables related to ethnic, epidemiological, laboratory, biological and other factors. To test any new algorithm and to train algorithms which work on your populations, data representative of your population is essential. Cancer Imaging Biobank (CAIB)10 is one such project which is aggregating pathology WSI and radiology images along with their linked clinical, treatment and outcome information from 4 organizations from India.

Mr Abhinav Banerjee

Research Scholar, Dr Mahipal Ganji Lab, IISc Bangalore

The untold story of the DNA ladder: Base-Stacking and its Applications.

DNA physical properties at short length scales dictate virtually every DNA related process. However, we lack a comprehensive understanding of the energetics involved in stabilizing DNA duplexes. Our recent single-molecule investigations into DNA base-stacking interactions have revealed that the DNA mechanical properties at short scales are determined by the sequence of the molecule. Our study has shed light on the sequence-specific variation in these interactions, with each di-nucleotide exhibiting a distinct behavior. For these measurements, we employed a multiplexed super-resolution-based imaging technique in conjunction with DNA nanotechnology. Additionally, we demonstrate the application of DNA stacking energetics in designing predictable multimeric DNA origami cage nanostructures and novel imaging probes capable of detecting biomolecular proximity at high resolution.

Mr Parijat Das

Research Scholar, Dr Prasenjit Bhaumik's Lab, IIT Bombay

Understanding the structure-function relationship of enzymes and biological macromolecules

Proteins are chains of amino acids that fold into three-dimensional structures stabilized by non-covalent interactions such as hydrogen bonds, hydrophobic effects, and van der Waals forces. These three dimensional structures are dynamic and exist as ensembles of conformations balanced by their energy landscape, meaning the native state includes multiple coexisting conformations. These dynamics range from subtle, localized movements like side-chain rotations to large-scale domain rearrangements. Such flexibility allows proteins to interact with ligands, substrates, or other macromolecules, modulating their function in a highly precise manner. One of the most compelling illustrations of the importance of protein dynamics in function is observed in enzymes. Enzymes, known for their remarkable catalytic efficiency, rely not just on their active site structure but also on their ability to undergo conformational changes that facilitate substrate binding and product release. Snapshots of these structural states can be captured by advanced biophysical techniques like X-Ray crystallography and cryo electron microscopy (cryo-EM) which allow us to understand the structure-function relationship of enzymes.

To illustrate the dynamics in proteins, we shall look into the crystal and cryo-EM structures of i) bacterial ω-transaminases, which undergo major conformational change on cofactor binding leading to subtle structural changes in the enzyme that allows the subsequent catalysis steps to take place, ii) fungal glutamate dehydrogenase, where prominent domain movements control enzyme catalysis, and the iii) pore forming toxin, a large ~2.5 MDa multimeric complex.

ORAL PRESENTATION ABSTRACTS

Understanding Sperm Chemotaxis with a Novel Microfluidics Device Authors:

Durva Panchal[1] and Priyanka Parte [1]*

1Department of Gamete Immunobiology, ICMR-National Institute for Research in Reproductive and Child Health, Mumbai, Maharashtra, India

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Background: In natural conception, chemotaxis selectively attracts capacitating sperm with the highest fertilization potential and guides them towards the egg, enhancing fertilization success. In infertile individuals undergoing IVF/ICSI, conventional sperm selection methods lack this mechanism, potentially reducing success rates. Identifying chemotactic compounds for assisted reproduction remains challenging due to limited tools.

Materials and Methods: Hydrophilic and hydrophobic metabolites extracted from ovulatory phase oviductal fluid were identified by LC-MS/MS and analyzed using XCMS. The chemotactic potential of some selected metabolites was evaluated by exposing capacitating sperm to metabolite gradients in a microfluidics device developed in our lab. Sperm response was analyzed by assessing directionality and straight-line-velocity.

Results: The first compound evaluated, N-formyl-L-aspartate, exhibited a bell-shaped curve, with maximum chemotactic response observed at 0.01M gradients for rat and human sperm. The second compound, X (name withheld), induced a strong chemotactic response at nanomolar concentrations in both rat and human sperm. The third compound, cinnamyl isovalerate, did not show chemotactic activity but promoted capacitation-like characteristics in sperm, suggesting its potential role in sperm capacitation. Both the fourth compound, tulobuterol, and the fifth compound, ferulic acid, failed to induce chemotaxis, indicating they do not act as chemoattractants.

Conclusion: Our study identified several promising metabolites, with N-formyl-L-aspartate and Compound X showing chemotactic responses in both rat and human sperm. These findings suggest the potential of chemoattractants in sperm sorting to selectively isolate good-quality sperm with maximal fertilization potential, thereby improving IVF/ICSI outcomes and ultimately increasing 'take-home baby' rates.

Keywords: Metabolomics, Chemotaxis, Microfluidics Sperm selection, IVF/ICSI

Phytochemical screening, evaluation of antioxidant potential and cytotoxic effects on NIH3T3 mouse embryonic fibroblast cell line of *Dalbergia latifolia* Roxb. leaves.

AUTHOR INFORMATION: Ms. Zoofishan Shaukat Kazi, MSc Botany, Department of Botany, St. Xavier's College (Empowered Autonomous Institute), Mumbai, Maharashtra, India.

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Background: Phytoconstituents with potent antioxidant and cytotoxic properties offer promising leads for developing anti-cancer therapies. *Dalbergia latifolia*, an underutilized tree with diverse ethnomedicinal uses, was investigated for its phytoconstituents, antioxidant activity, and cytotoxicity against NIH 3T3 mouse embryonic fibroblasts. The study explores its potential inmanaging oxidative stress and fibroblast-associated tumor microenvironments.

Materials and Methods: Aqueous and ethanolic extracts of leaves were screened for major phytochemicals. Ethanolicextract was further evaluated for total phenolic and flavonoid content and antioxidant assays(RPA, TAC, DPPH, ABTS). Cytotoxicity assessment at 10 to 200ug/mL was performed via MTT assay on NIH 3T3 cells.

Results: The ethanolic extract of leaves contained major phytochemicals like alkaloids, phenols, flavonoids, glycosides, quinones, and sterols along with high phenolic (8.1 ± 0.11 mg GAE/g)and flavonoid (3.6 ± 0.05 mg QE/g) content. It exhibited strong total antioxidant capacity (426.3 ± 12 mg AAE/g), reducing power activity (495 ± 6.22 mg BHT equivalent/g), and radical scavenging activity with IC50 values of 18.174 µg/mL for DPPH and 4.63 µg/mL for ABTS radicals. Significant cytotoxicity was observed against NIH 3T3 cells with IC50 of 37.75± 2.63 µg/mL.

Conclusion: These findings highlight the potential of *Dalbergia latifolia* leaf extracts in developing therapies targeting cancer-associated fibroblasts, key players in tumor progression as well as mitigation of oxidative stress. Further research on site-specific cancer cell lines, such as breastand pancreatic cancers, where fibroblast-driven tumor microenvironments are critical, is recommended to establish its therapeutic potential.

Keywords: *Dalbergia latifolia*, antioxidant, cytotoxic, cancer-associated fibroblast, NIH 3T3.

Screening for antimicrobial resistance in Mumbai locality and developing phage therapy against multi-drug resistant Pseudomonas sp. - a pilot study

Ketki Kabir[1] and Dr. Jacinta Teresa George[1,*]

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Background: The overuse of antibiotics in healthcare, agriculture, and animal husbandry has led to Multidrug Resistant (MDR) strains. As antibiotics lose efficacy, bacteriophage therapy is emerging as a promising alternative. A pilot study in Mumbai was conducted to assess localresistance levels using two sampling sources and to isolate bacteriophages against pathogenic MDR strains obtained.

Materials and Methods: All isolates, including *Pseudomonas syringae*, were tested for resistance using 3-4 antibiotics via disc diffusion. Potential MDR isolates were further screened with a broader antibiotic set, followed by 16S rRNA sequencing for identification. Environmental samples were also usedto isolate bacteriophages targeting MDR strains.

Results: The resistance levels for different antibiotics were seen to be ranging between 28.57%- 37.5% of total isolates, excluding gentamicin, that had 0% resistant isolates. Five potentiallyMDR isolates were found during preliminary screening and secondary screening. The one exhibiting the highest MDR profile (eight of ten antibiotics tested) was identified to be *Pseudomonas aeruginosa* (via 16s rRNA amplicon sequencing method). *P. syringae* showed resistance to tetracycline; however, still showed sensitivity towards gentamicin, vancomycin and amoxicillin. Further, two bacteriophages each against *P. aeruginosa* and *P. syringae* wereisolated from different water bodies showing clear zones of lysis.

Conclusion: The lytic activity of the bacteriophages against their specific host organisms *in vitro* could prove to be a promising candidate for their application into therapy for the treatment of plantand animal infections caused due to these bacteria.

Keywords: antimicrobial resistance, bacteriophage therapy, biocontrol, multidrug resistant, *Pseudomonas aeruginosa, Pseudomonas syringae*

Development of a Cost-Effective *Bacillus*-Based Biofertilizer and Biocontrol Agent forWheat

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Background: Chemical fertilizers and pesticides, used for agriculture, disrupt ecosystems by damaging soil quality and reducing crop nutritional value. This study aims to isolate, characterize,and optimize a potent plant growth-promoting bacterium for biocontrol and biofertilizer applications.

Material and Methods: JPP strain (*Bacillus subtilis*), isolated from mangrove soil, exhibited several beneficial traits, including indole-3-acetic acid (IAA) production, biofilm formation, highsalt tolerance, and promising biocontrol capabilities. Current efforts focus on developing a cost- effective medium for large-scale production of this organism. Blackstrap molasses was used as aninexpensive carbon source, ten different nitrogen sources were tested, including glutamic acid, aspartic acid, proline, beef extract, glycine, yeast extract, sodium nitrate, ammonium sulphate, andammonium chloride.

Results: Several antimicrobial compounds such as derivatives of palmitic acid, fatty acid amides,pyridine, were detected in the cell-free supernatant by LC-MS analysis. In soil-pot experiments, this strain significantly increased shoot and root length in saline soil when bio-primed, comparedto control conditions. Optimal growth conditions were identified at pH 7 and 25°C, with 0.1% molasses (approx. 1.35 mg glucose equivalent /L) and 0.5% yeast extract providing the best carbonand nitrogen sources, respectively, for maximizing cell growth and bioactive metabolite synthesis.The resulting medium yielded high cell density comparable to conventional media, and the CFS exhibited antimicrobial activity in well diffusion assays.

Conclusion: The study highlights the JPP strain's potential as a biocontrol agent as well as a cost-effective biofertilizer and for large-scale production and future field trials.

Keywords: Biofertilizer, Biocontrol, *Bacillus*, antimicrobial, CFS, cheap media

Integrative Approaches for Biomarker Discovery and Drug Repurposing in Gastric Cancer

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Background: Gastric cancer is a leading global health concern, with high morbidity and mortality rates. Early diagnosis and targeted therapies are crucial for improving outcomes. Thisstudy focuses on identifying reliable biomarkers and therapeutic targets through innovative strategies, contributing to early detection and advancing therapeutic approaches in gastric cancer research.

Materials and Methods: This study integrated network biology, gene enrichment, pathway enrichment analyses, molecular docking, virtual screening, molecular dynamics simulations, and MM-PBSA energy calculations. Gastric cancer genes were identified through public databases and text mining. Network analysis pinpointed hub genes, while docking simulationsvalidated drug-target interactions. Combinatorial scaffold synthesis generated virtualcompounds.

Results: Network analysis highlighted key therapeutic targets with ACTB identified as potential drug target. Pathway enrichment analysis revealed the critical roles of these genes incarcinogenic pathways. Screening 626 FDA-approved drugs highlighted Norgestimate and Nimesulide as promising candidates for repurposing in gastric cancer therapy. Further, 56,160virtual compounds derived from scaffold libraries were screened, with 76 compounds prioritized based on favorable interactions with hotspot residues such as GLU214 and LYS18.MM-PBSA energy calculations validated the binding stability and suggested the therapeutic potential of these compounds.

Conclusion: This study highlights the importance of computational approaches in gastric cancer research. The identified hub genes, drug candidates, and novel compounds lay the groundwork for future experimental validation and clinical application. It underscores the potential of repurposing existing drugs and developing therapies for gastric cancer treatment.

Keywords: Gastric Cancer, Biomarkers, Therapeutic Targets, Drug Repurposing, Network Biology, Molecular Docking, Virtual library

Augmenting Solid Tumor Immunotherapy via CAF Reprogramming using Injectable Hydrogel

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Background: Adoptive cell therapies have shown great potential against blood cancers, but challenges such as dense extracellular matrix (ECM) secretion by cancer-associated fibroblasts (CAFs) in the tumor microenvironment prevent the penetration of genetically modified T-cells into the tumor. Directly targeting CAFs may promote tumor metastasis and the targeting agents may also affect normal fibroblasts, necessitating alternative strategies.

Materials and Methods: To address this challenge, we have developed a novel injectable hybrid polymeric hydrogel composed of Pluronic F-127 and crosslinked-gelatin for localized reprogramming of CAFs, aiming to reduce systemic toxicity and enhance T-cell penetration in solid tumors. The hydrogel was subjected to physical and biological characterization, and biocompatibility was assessed in vivo in immunocompetent mice.

Results: The hydrogels have excellent shear thinning properties and are injectable through a 21G needle which eliminates the use of surgical implantation. Porosity tests by scanning electron microscopy (SEM) imaging and rhodamine B isothiocyanate (RITC)-dextran penetration via confocal microscopy revealed that the hydrogels are porous. Biocompatibility assays with splenocytes indicated high cell viability (~80%), and hemocompatibility tests showed no RBC lysis on coculture with blood. Additionally, these hydrogels allowed uniform loading of splenocytes. In vivo studies proved that the hydrogel is biocompatible and can be used for in vivo cell delivery.

Conclusion: In conclusion, we have developed a biocompatible and injectable biopolymeric hydrogel which can facilitate localized delivery of CAF reprogramming agent and genetically modified T cells, offering a promising potential for enhancing solid tumor immunotherapy.

Keywords: Cancer-associated fibroblasts (CAFs), Hydrogel, Solid tumor, Immunotherapy

Pharmacological activation of GPER1 (G protein-coupled estrogen receptor) inhibits prostate cancer progression

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Introduction: Prostate cancer (PCa) offers opportunities for chemoprevention due to its long latency period. GPER1 is being explored for its therapeutic potential in various cancers. In PCa cells, GPER1 activation by its agonist-G1, leads to inhibition of proliferation *in vitro* and *in vivo*. However, its role as a chemopreventive target in PCa is unexplored.

Methods: Prostatic GPER1 (pGPER1) expression was assessed in human datasets and PCa and Benign Prostatic Hyperplasia (BPH) tissues. TRAMP (Transgenic Adenocarcinoma of Mouse Prostate) mice prostates were assessed for GPER1 expression using qRT-PCR and flow- cytometry. Stable GPER1-silenced clones were generated using shRNA in RWPE-1, LNCaP and PC3 cell lines. Proliferation, migration, invasion, RT2 profiler and zymography assays were carried out. TRAMP mice subcutaneously administered with different doses of G1 were assessed for their tumor progression.

Results: A decreased frequency of GPER1-positive cells in high-grade PCa compared to BPH tissues was observed. A similar observation was found in the public expression datasets. In TRAMP mice, the frequency of pGPER1-positive cells and expression was found significantly increased at the HGPIN (High-Grade Intraepithelial Neoplasia) stage and decreased at the poorly-differentiated carcinoma (PDC) stage compared to respective age-matched controls. GPER1-silencing led to an increase in migration and invasion while proliferation remained unchanged *in vitro*. Further, GPER1 regulated epithelial to mesenchymal transition through miR200a-ZEB2-E-Cadherin loop and other metastasis-associated genes. GPER1 activation with G1 in TRAMP mice prevented progression of HGPIN to PDC.

Conclusion: GPER1 signaling offers a protective advantage by preventing PCa progression.

Keywords: GPER1, Chemoprevention, Prostate Cancer, TRAMP mice

Novel Design Strategy and Evaluation of Inhibitors that Target Global PPI network of Gankyrin

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Background: PSMD10/Gankyrin is a proteasomal assembly chaperone and oncoprotein implicated in several cancers, including hepatocellular carcinoma. Gankyrin, through mediating protein-protein interactions (PPIs), influences key cancer-associated pathways like pRb inactivation, p53 degradation, Ras-dependent tumorigenesis. Peptide inhibitors are promising agents against proteins that function through PPI. In this study, Gankyrin has been screened against potential peptide inhibitors with core motif EEVD that inhibits its interaction with one of its binders, Clic1.

Methods: Gankyrin was expressed and purified by affinity and gel filtration chromatography. Eight 10- mer peptides containing EEVD core motif were derived from proteins that bind Gankyrin (based on docking or direct binding studies). Limited trypsinolysis and SDS-PAGE was done to confirm binding of the peptides. Affinity of best-binding peptides was determined through Protein-peptide ELISA. Highest affinity peptide was modified to increase affinity to Gankyrin and used to compete Gankyrin-Clic1 interaction.

Results: Limited trypsinolysis followed by SDS-PAGE showed that the peptides bound to Gankyrin, probably with varying affinities, and were divided based on the binding potential for each peptide. Two best binding peptides were identified, with binding affinities (kd) 58 μM and 200 μM. The strongest binder was modified, which increased binding affinity to 1 uM. This peptide also showed inhibition of Gankyrin-Clic1 interaction.

Conclusion: Peptide with the highest affinity will be optimized (sequence and structure) to develop a peptide inhibitor. Designing peptide inhibitors whose sequences are derived from known interactors of oncoprotein Gankyrin to inhibit these same interactions is a promising method for targeting cancer.

Keywords: Cancer, Peptide, Inhibitor, PSMD10

Assessing the Comparative Bioactivity of Trastuzumab Biosimilars Using a Cell-Based Inhibition of Proliferation Assay

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Background: Trastuzumab is instrumental for the treatment of HER2-positive breast cancers, and growing global demand has led to the emergence of its biosimilars. It's essential to ensure these biosimilars are as safe and effective as the original drug. This studyfocuses on developing a cell-based bioassay to compare the efficacies of trastuzumab biosimilars with the reference product.

Methods: To assess the bioactivity of biosimilars, a comprehensive characterization of several HER2-positive breast cancer cell lines was done using western blotting, RT-PCR, and flow cytometry to select an appropriate cell line for the bioassay. Further, to evaluate the bioactivity of trastuzumab biosimilars an anti-proliferation bioassay was performed using Alamar Blue.

Results: The molecular characterization of various HER2-positive breast cancer cell linesof SKBR3, BT-474, MDA-MB-453, MDA-MB-175, MDA-MB-231, and MCF-7—explored HER2 receptor expression using western blotting, RT-PCR, and flow cytometry to identify a suitable cell line for a bioassay. The SKBR3 cell line, which abundantly expressed HER2 receptor, was selected for this purpose. An inhibition of proliferation bioassay using Alamar Blue assessed the activity of trastuzumab biosimilars against a reference standard of trastuzumab. Four biosimilars were evaluated and their relative potencies were determined using 4PL non-linear sigmoid curve analysis. The trastuzumab biosimilars were found to function similarly to the reference standard of trastuzumab basedon their relative potencies.

Conclusion: The efficacies of different trastuzumab biosimilars are found to be similar tothe reference standard of trastuzumab in terms of potency, thus establishing a robust cell- based bioassay method for trastuzumab biosimilars.

Keywords: Trastuzumab, Biosimilars, Biological activity, Bioassay

Ets21c governs blood cell homeostasis and innate immune response in *Drosophila.*

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Background: A harmonious interplay of signalling mechanisms sustains tissue homeostasis. Unravelling the regulators of tissue homeostasis during development and upon stress response remains a significant challenge. Ets21c is a stress-inducibletranscription factor implicated in various physiological processes. This study aims toelucidate the role of Ets21c in hematopoiesis and immune homeostasis.

Materials and Methods: We use whole animal mutants of ets21c, Ets21c knockdownor over-expression lines for spatial modulation of Ets21c using the UAS-Gal4 systemin Drosophila. We have analyzed the hematopoietic parameters with antibodymarkers using immunofluorescence and confocal-imaging based approaches. Inorder to look at anti-microbial peptide levels, qRT PCR based approach was used inthe presence or absence of bacterial infection.

Results: Ets21c over-expression in the lymph gland (LG) progenitors resulted in a significant increase in plasmatocyte and lamellocyte differentiation, accompanied bydecreased crystal cell differentiation. Differentiated hemocytes respond to stressors,such as bacterial infections and wasp infestation. Perturbing Ets21c levels in the LGaffected number of niche cells and extent of differentiation underscoring its essentialrole in hematopoiesis.

Consistent with existing literature, LG-specific Ets21c expression was significantly elevated upon bacterial infection. Our investigation upon exposure of ets21c loss-of-function mutant larvae to Gram-negative bacteria (P. rettgeri) revealed that Ets21c is an important regulator of infection induced emergency hematopoiesis and immune response.

Conclusion: Our study highlights the critical role of Ets21c in developmental hematopoiesis. Furthermore, Ets21c is pivotal in mounting immune responses by promoting blood cell differentiation and regulating AMP expression during cellular and humoral immune responses.

Keywords: Ets21c, Hematopoiesis, AMP (Anti- microbial peptides), Stress-induced hematopoiesis

POSTER PRESENTATION ABSTRACTS

Title: Flow cytometric evaluation of normal ranges of surface immunoglobulin B-cell subsets in healthy controls and its clinicalsignificance

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Introduction: Common variable immunodeficiency (CVID) is a rare inborn errors of immunity (IEI) characterised by significantly reduced immunoglobulinlevels. Euroflow demonstrated the utility of B-cell subset levels expressing different surface heavy-chain immunoglobulins (sIg) in the diagnosis of IEI. Data on the normal range of sIg+B-subsets in healthy controls is limited and there is no data from Indian population. Hence, we are using flow cytometer to evaluate normal ranges of sIg subsets in healthy controls.

Methods: We studied sIg+B-subsets in peripheral blood of 36 healthy volunteers.11-color FCM assay with antibodies against IgG1 (clone SAG1), IgG2 (clone SAG2), IgG3 (clone SAG3), IgG4 (clone SAG4) IgA1 (clone SAA1), IgA2 (clone SAA2), IgM (clone, G0-127), IgD (clone IA6-2) along withbackbone B -cell. Data was acquired on LSR Fortessa (BD Biosciences).

Results: The median percentage of B-lymphocytes was 4.95% (range 1.89- 18.62). Median (range) of naive and memory B-cells were 70.65% (43.67- 86.14) and 25.19% (5.02-53.09) respectively. The median percentage of IgG1+B was 5.78% (range 0.76-15.33), IgG2+B 2.16% (range 0.35-5.63), IgG3+B 1.35% (range 0.10-8.36), IgG4+B 0.31% (range 0.02-1.17), IgA1+B 3.44% (range 0.29-7.73), IgA2+B 1.65% (range 0.20-6.13), IgM+B 84.20% (range 64.32-93.99) and IgD+B 79.18% (range 56.66-96.30). We have diagnosed CVID case which shows 97.30% of all B-cells expressing IgD and 94.05% B-cells expressing IgM. IgG+/IgA+ memory-B-cells were markedly reduced. B-cells also showed moderate positivity for CD21 but CD81 and CD23were negative.

Conclusion: We have established a normal range of various surface immunoglobulin expressing B-cell subsets in healthy volunteers and demonstrated its clinical utility.

Keywords: CVID, IEI , B subsets

Designing Exo-miRNA complexes using milk exosomes: A novel approach for dealing withinflammation.

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Background: Milk-derived exosomes can be harnessed as effective nanocarriers for drug and miRNA delivery dueto their small size, biocompatibility, and ability to cross biological barriers, including the blood-brain barrier. This study investigates their potential to deliver anti-inflammatory microRNAs (miRNAs) for therapeutic applications.

Materials and Methods: Exosomes were isolated from *Bubalus bubalis* milk using differential and ultracentrifugation techniques. Dynamic light scattering experiments were performed to measure zeta potential,
hydrodynamic size, and stability. Protein concentration was estimated, and purified samples were probed for exosomal markers TSG101 and HSP70. The effects of milk exosomes on cell viability wereassessed through an MTT assay using the HCT116 colorectal cancer cell line.

Results: Isolated milk exosomes demonstrated a size distribution of <200 nm, stability confirmed via zeta potential, and the presence of HSP70 and TSG101 markers. Protein concentration was estimated at
4.6 µg/µl per 50 ml of milk, indicating scalable production compared to alternatives like Au/Ag nanoparticles or exosomes from mesenchymal stem cells (1–5 µg per 1 million MSCs). The MTT assayrevealed significant inhibition of cell viability in treated cells. These results underscore their capacity to carry anti-inflammatory miRNAs, such as miR-146a and miR-21, which inhibit inflammasome
formation and modulate inflammation through NF-κB or TLR signalling pathways.

Conclusion: Milk exosomes represent scalable, cost-effective, and biocompatible carriers for delivering bioactivemiRNAs to reduce inflammation and suppress cancer progression. Surface-modified Exo-miRNA complexes targeting inflammatory pathways hold promise for novel therapeutic strategies against cancer and inflammatory conditions.

Keywords: milk exosomes, nanocarriers, miRNA delivery, inflammation

Screening and Characterization of Bacteriophages for developing targeted therapeuticcocktails against three phytopathogens

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Background: Plant pathogens like *Pseudomonas syringae*, *Pantoea agglomerans*, and *Xanthomonas oryzae* pose significant challenges to agrarian economies, especially in India. *P. syringae* and *P. agglomerans* infect economically important species, while *X. oryzae* threatens rice crops. This research focused on isolating and characterizing phages against these phytopathogens.

Materials and Methods: Different environmental samples - sewage samples and marine sample - were collected from locations all over suburban Mumbai and used as potential sources for phage isolation. After co-incubation with the host, spot assay was performed and the plates were inspected for plaques. These plaques were further excised, purified and enumerated.

Results: Two distinct bacteriophages targeting *Pseudomonas syringae* were identified, named PS1 and PS2, based on plaque morphology. Using the double agar overlay method, PS1 produced small, turbid plaques with an average diameter of 0.5 cm, while PS2 formed larger, clearer plaques with an average diameter of 0.8 cm. The phage titers were 5.60×10^{18} PFU/ml for PS1 and 9.66×10^{19}PFU/ml for PS2. The clear plaques of PS2 indicate effective lytic activity, suggesting its potential for therapeutic applications, while the turbid plaques of PS1 are characteristic oflysogenic phages, offering insight into their different modes of action.

Conclusion: Future work will focus on characterizing the phages' physical, chemical, and biological properties through electron microscopy and genome sequencing. *In vitro* and *in vivo* assays will evaluate their lytic activities, individually and in combination. The goal is to develop a safe, effective phage cocktail to combat bacterial pathogens and prevent resistance.

Keywords: Bacteriophage, Bacteriophage therapy, Biocontrol, *Pantoea agglomerans*, Phage, cocktail, Phage resistance, Phytopathogens, *Pseudomonas syringae*, *Xanthomonas oryzae*

The role of BRD4 in acquiring Drug-Tolerant Persister (DTP) phenotype in different subtypes of TNBC

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Background – TNBC is the most aggressive and heterogeneous type of breast malignancy and its clinical management relies mainly on chemotherapy. But a large number of patients develop therapy resistance with residual disease which harbours DTP cells. Recent molecularstudies have shown that chemoresistance in TNBC tumours is largely driven by epigenetic
mechanisms.

Materials and methods - We have longitudinally modelled cellular state transitions from dormant DTP into proliferating drug-tolerant persister (PDTP) cells representing different
TNBC subtypes. To elucidate the role of Bromodomain-containing protein 4 (BRD4) we havecharacterized the DTP population using genetic and pharmacological approaches.

Results - BRD4 is an important epigenetic reader protein and is shown to play key role in themetastasis and development of drug resistance in solid as well as liquid tumours. Here we have shown that BRD4 mRNA is selectively overexpressed in TNBC tumors and cell lines ascompared to other members of BET family, BRD2 and BRD3. By immunohistochemistry analysis we also found that BRD4 protein is overexpressed in the tumour tissues of TNBC patient compared to non-TNBC ones and has a strong nuclear localization. We found that DTP and PDTP derived from TNBC subtypes shows differential expression of BRD4.

Conclusions - As several BRD4 inhibitors are in clinical trials, these findings can havepotential therapeutic implications for TNBC chemoresistant patients.

Key words – TNBC, Chemoresistance, DTP, BRD4.

Elucidating the therapeutic potential and effects of Mitocurcumin on the *Drosophila Yorkie* inducedgut tumor overgrowth model.

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Background: Normal cells balance ROS production and scavenging to maintain redox homeostasis. Disrupting this balance induces oxidative stress and apoptosis, a potential cancer treatment strategy. Mitocurcumin, a stable, mitochondria-targeted curcumin derivative, may enhance therapeutic effects. This study examines Mitocurcumin's molecular impact on a *Drosophila* Yorkie-induced gut tumor model.

Materials and Methods: A *Drosophila* larval gut tumor model was created using the Yki3SA transgene driven by *escargot-Gal4* in ISCs and EBs. Larvae were starved, treated with 25 µM Mitocurcumin for 12-14hours, dissected, and prepared for immunofluorescence or RNA isolation. Mitotic activity and apoptosis were analyzed with H3P and DCP1 antibodies, respectively. Gene expression was assessed via qPCR.

Results: Mitocurcumin treatment reduces mitotic activity and induces apoptosis in ISC-EBs in both control and Yorkie backgrounds. We observe a volumetric reduction in Escargot-positive ISC-EB clusters, which are typically large and deformed in the tumor background. Given the altered metabolic demands of cancer cells, we analyzed the metabolic profile of Yki tumors. Our results show no change in glycolysis, but a significant reduction in TCA and ETC complex genes, along with an increase in Pentose Phosphate Pathway(PPP) genes in Yki tumors. Additionally, mitochondrial content decreases in these tumors. We aim to explore if mitocurcumin can alter this metabolic profile.

Conclusion: Mitocurcumin induces stress even in wild-type larval gut by disrupting expression of ETC complex molecules, reduces mitotic activity, and results in increased apoptosis. In tumor-induced larvae, it further downregulates mitotic activity, significantly increases apoptosis thereby, reducing Yki-induced Esg-positive tumor cell load.

Keywords: ROS, Redox homeostasis, Oxidative stress, Apoptosis, Mitocurcumin, ISC (Intestinal Stem Cells), EB (Enteroblasts), Yki3SA, escargot-Gal4, Glycolysis, TCA cycle, ETC complex, Pentose PhosphatePathway (PPP), Mitochondrial content.

Synthesis of a biomimetic nanomaterial using ghost membrane forcancer theranostic application

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Background: Photothermal therapy (PTT) is an emerging cancer nanomedicine. Our group focuses on developing tumour-targeted theranostic photothermal agents (PTAs) using organic near-infrared fluorescent (NIRF) imaging-compatible FF-BSC and IR820 dyes. Integrating biomimetic principles into PTAs facilitates enhanced homing through active nanomaterial uptake within tumours. We aim to design a biomimetic PTA nanomaterial that enables homotypic binding interactions for cancer theranostic applications.

Materials and Methods: The synthesis of cancer cell ghost membranes (CCGMs) was optimised for EpCAM-overexpressing radioresistant breast cancer cells, with encapsulation of PTAs achieved via electroporation. Physical characterisation of CCGMs was performed using dynamic light scattering (DLS), transmission electron microscopy (TEM), and zeta potential analysis to evaluate hydrodynamic size, morphology, and surface charge, respectively. Immunoblotting confirmed cancer cell-specific markers on CCGM-NIR dye nanoconjugates,and *in vitro* efficacy was assessed using the MTT assay.

Results: The optimised CCGM protocol produced an enriched membrane fraction with retained membrane-anchored proteins (EpCAM, Cadherin) while depleting significant mitochondrialand cytoplasmic components. DLS and TEM analyses revealed a biconcave cup-shaped structure with a mean diameter of 120 ± 20 nm, while zeta potential measurements indicated a surface charge of -13.1 ± 3 mV. PTA uptake was assessed via fluorescence confocal microscopy, and *in vitro* PTT efficacy was evaluated using both EpCAM-positive and -negative cancer cells.

Conclusion: The NIRF PTA dye-encapsulated biomimetic nanoformulation enables active tumour targeting via homotypic binding to the EpCAM moiety on cell surfaces, potentially broadening the application of PTT therapy for deep-seated tumours.

Keywords: Biomimetic nanoformulation, photothermal agents, homotypic interaction

Redefining Platinum Chemotherapy: A Shift Towards Kinetically InertAgents

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Background: Despite spectacular clinical success, the efficiency of Pt drugs is masked by intrinsic and acquired resistance and toxic side effects like nephrotoxicity. Finding a strong correlation between the kinetic lability, therapeutic effect, and the deficiencies of Pt drugs, we aimed to designa kinetically inert yet efficacious Pt drug candidate to address the issues of Pt chemotherapy.

Materials and Methods: Compound characterization was done using MALDI-TOF Mass Spectrometry, High-Performance Liquid Chromatography, and Inductively coupled Plasma-MassSpectrometry. *In vitro* studies were carried out using MTT assay. *In vivo* studies were done ethically using mice xenograft models. Docking studies were implemented using AMDock v.1.5.2with Autodock 4.2. Confocal Laser Scanning Microscopy was utilized for imaging purposes.

Results: A kinetically inert Pt drug candidate compound 4 was synthesized and characterized. Thecompound showed promising *in vitro* anti-cancer activities in a panel of different cell lines, betterthan cisplatin. Owing to its kinetic inertness, compound 4 was able to overcome multi-factorial Ptresistance and possessed notable plasma stability. Noteworthy, compound 4 demonstrated promising anti-tumor efficacy *in vivo* both in Pt-sensitive and resistant models and alleviated nephrotoxicity which is the major dose-limiting side effect of cisplatin. Mechanistic investigationsindicated the multi-targeting ability of compound 4, targeting nuclear DNA including QDNA, andcausing oxidative stress in cancer cells through mitochondrial dysfunction.

Conclusion: Our results suggested that the development of kinetically inert yet efficacious and multi-targeted Pt drug candidates is feasible. This will offer the prospects of overcoming the deficiencies of clinical Pt drugs like resistance and toxic side effects like nephrotoxicity.

Keywords: Pt drugs, Kinetic Inertness, Plasma Stability, *in vivo* efficacy, nephrotoxicity.

Target.AI – Drug sensitivity prediction for targeted cancer therapy

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Background: The aberrant alteration in genes, such as EGFR, resulting from somatic mutations, is associated with driverphenotype, making them a critical target in cancer therapy. This study aims to predict the response of Tyrosine Kinase Inhibitors (TKI) in cancer patients through an easy-to-use web server utilizing artificial intelligence (AI) techniques.

Methods: We developed an automated and scalable server, including modeling, molecular docking, and molecular dynamics (MD) simulations to elucidate the interactions of EGFR mutants (N ~ 750) with TKIs. These EGFR mutation models, molecular docking scores, and MD simulation reveal an interesting correlation between in-silico observations and clinical TKI sensitivity. We developed a machine learning (ML) model utilizing features of protein sequence, structure, and dynamics.

Results: The ML model achieves a clinical grade accuracy for the TKI-sensitivity prediction for mutations occurringin the kinase domain of EGFR. Using this model, we characterize the sensitivity of novel EGFR kinase domain mutations previously considered variants of unknown significance (VUS).

Conclusion: We present a new AI model capable of non-linear interpretation from complex data, allowing us to predictthe sensitivity of novel EGFR VUS observed during clinical follow-up of cancer patients. Further refinement and clinical validation of this model may provide valuable solutions to predetermine the drug sensitivity of patients in clinics.

Keywords: Target.AI, Cancer targeted therapy, Artificial Intelligence

Effect of Bromelain on Transgenerational *C. elegans* on High Glucose Diet

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Background: High-glucose diets induce hyperglycemia-associated oxidative stress, inflammation, and neuropathy, exhibiting transgenerational effects. Phytocompounds have recently been shown to modulate glucose-induced stress at epigenetic and metabolic levels. This study aims to elucidate bromelain's ameliorative potential in mitigating glucose-induced physiological and oxidative stress alterations in *Caenorhabditis elegans.*

Materials and Methods: *C. elegans*, with fully annotated genome and short generation time, served as the model organism. F1 and F2 generations were exposed to high-glucose (0–500 mM) and bromelain (0, 0.05, 0.1 mg/ml) diets. Assays included glucose and bromelain toxicity, pharyngeal pumping, thrashing, and antioxidant estimation (DPPH) assay.

Results: Glucose toxicity assay revealed that *C. elegans* exhibited stress at 500 mM glucose in the subsequent F2 generation. Behavioral assays, including pharyngeal pumping and thrashing, showed a decreased pumping rate and an increased thrashing rate over a one-minute observation, correlating with rising glucose concentrations. DPPH assay demonstrated a color shift from purple to light yellow, indicating enhanced antioxidant activity at higher bromelain concentrations due to DPPH radical neutralization. Nitric oxide assay showed yellow coloration, indicative of oxidative stress. Notably, increased bromelain concentrations reduced NO levels, suggesting bromelain mitigates glycemic stress by modulating inflammation and inhibiting iNOS activity.

Conclusion: Bromelain ameliorates the transgenerational effects of a high-glucose diet in *C. elegans*, mitigating metabolic disturbances in the F2 generation. Enhancements in glucose homeostasis and regenerative health suggest its potential as a dietary intervention to reduce metabolic stress, underscoring its therapeutic significance in managing heritable dietary impacts.

Keywords: Bromelain, High glucose diet, Transgenerational effects, *Caenorhabditis elegans*

CanInsight: Insights into cancer biology through transcriptome

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Background: Transcriptomics offers a dynamic snapshot of gene activity, bridging the genomic blueprint andfunctional outcomes. RNA-seq analysis often involves isolated interpretations, such as cancer subtype prediction or tumor immune profiling. We developed an AI-based model to deliver quick, integrative insights into tumor biology through transcriptomics. Using well-annotated datasets, our model refines cancer classification and predictive features like MSI and TMB, addressing high-dimensional data challenges and enabling personalized oncology applications.

Material and Methods: Our framework leverages transcriptomic data from TCGA RNA-Seq experiments across 28 cancer cohorts. Machine learning models classify tissues of origin, detect malignancies, and stratify samples by cancer type, histology, and molecular traits such as HPV status, metastasis,MSI, and TMB. Model accuracy and precision are systematically evaluated using statistical methods.

Result: The AI system achieves an average classification accuracy of 90%, outperforming traditional methods in scalability and accessibility. It excels in analyzing Cancers of Unknown Primary (CUP), a clinical challenge, by identifying tissue origins and molecular characteristics. A user-friendly web server provides real-time predictions and visualizations, making the framework accessible for biological and clinical use without requiring programming skills.

Conclusion: This study integrates transcriptomics and machine learning to address high-dimensional data challenges in pan-cancer diagnostics. It bridges molecular profiling and clinical applications, providing a cost-effective, scalable solution. The framework is particularly impactful for CUP,enabling precise tissue and molecular feature inference.

Keywords: Transcriptomics, Artificial Intelligence, Cancer Classification, Cancers of Unknown Origin

Investigating the Role of transcription factor Ets21c in the Drosophila hematopoietic niche

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Background: Human ERG oncoprotein, mammalian counterpart of the *Drosophila* Ets21c has been previously shown to be upregulated during Acute Myeloid Leukemia (AML). The molecular function of Ets21c, a stress inducible transcription factor in regulating developmental hematopoiesis remains unknown. Here, we delineate Ets21c function in the hematopoietic niche in the lymph gland.

Materials and Methods: We employ *ets21c* whole animal mutants, Ets21c knockdown or over-expression lines to spatially modulate Ets21c expression using the UAS-Gal4 system. We analyze the hematopoietic parameters using various antibody markers employing immunofluorescence and confocal imaging-based approach. The imaging data is then analyzed using ImageJ software.

Results: Ets21c loss of function mutants display a smaller niche as compared to wildtype and their bloodcell differentiation was affected. This intrigued us to explore the role of ets21c in the niche. Upon ets21c overexpression we observed a significant increase in the niche size as well as lamellocyte differentiation, which have been shown to be associated with hyperactivation of Insulin signalling. When recombinant human ERG was expressed in the niche specifically, similar results were obtained. We further aim to delineate the role of Ets21c during development focussing on niche and unravel new conserved mechanisms with its mammaliancounterpart, ERG.

Conclusion: We have investigated the role of Ets21c in the niche during development. Our results suggest that ERG and Ets21c act similarly in regulating the niche cell proliferation as well as expansion.This study will shed insights on unmasking novel mechanism regulated by ERG and its role during development via Ets21c its fly counterpart.

Keywords: Ets21c, ERG, Hematopoiesis, Drosophila

Systematic Molecular Profiling of Thyroid Cancer Identifies TherapeuticTargets in Indian Cohort

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Background: Thyroid cancer (TC) is the most common endocrine malignancy originating from parafollicular C cells or follicular cells of thyroid gland. The incidence rate has steadily increased by 30% in India in past decade, raising an interest to study the molecular alterations underlying the genome of Indian patients for therapeutically relevant biomarkers in TC.

Materials and Methods: We performed integrative whole-exome and whole transcriptome sequencing of fresh frozen and FFPE tissue samples for genomic characterization of TC. Using computational tools we characterized the mutational profile of different subtypes of TC followed by molecular pathway analysis andunderstanding the tumor immune-microenvironment. Also, we structurally characterized few novel mutations.

Results: The mutational landscape of TC revealed that somatic *RET* mutation (50%) was predominantly observed in MTC subtype, alongside low frequency of mutations in *RAS* and *BRAF*. Notably, we reported a novel *RET* kinase domain mutation Y900S showing affinity to *RET* inhibitors accessed via docking and MD simulation. TheATC subtype revealed somatic alterations in major hallmark genes like *TP53* (~42%), *BRAF* (~10%) and *RAS* (~27%), along with novel pathogenic mutation in *THRA* (11%). In the PTC cohort we identified somatic hallmark alterations in *BRAF* (38.6%)and *RAS* (26.3%) along with non-hallmark alterations driven molecular subtype and a germline *DUOX2* (8.8%) mutation associated with poor prognosis.

Conclusion: Overall, our study provides a comphrehensive molecular profiling of Indian thyroid cancer patients underlying MTC, PTC and ATC subtypes for underscoring potential therapeutic therapies.

Keywords: Thyroid Cancer, integrative sequencing, *RET*, *DUOX2*, *THRA*, mutation profile, actionable biomarkers

Comprehensive genomic profiling of 1,000 Indian cancer genomes identify opportunity of precision medicine: a retrospective cohort study

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Background: Cancer patients with targetable biomarkers show much better responses to molecularly guided therapy. Global genomic profiling has catalogued novel biomarkers and driver genes indeveloped nations, enabling tailored therapeutic strategies. However, Indian ethnic diversity ispoorly represented in such global genomic studies. This study aims to determine the landscapeof molecularly targeted therapeutics using comprehensive genomic profiling to identify noveltherapeutic opportunities.

Materials and Methods: We attempted genomic characterization of 1000 Indian patient samples across 27 cancer typesusing whole exome and whole transcriptome sequencing. We developed an integrated genomics analysis computational pipeline and a clinical inference tool ClinOme to identify molecularly guided therapeutics.

Results: We identify recurrent high tumor mutation burden (TMB), microsatellite instability, and high PD-L1 expression in multiple cancers. Furthermore, we observe cancer hallmark genes such as*TP53* (40 %), *PIK3CA* (13 %), *CDKN2A* (12 %), *KRAS* (8 %), *EGFR* (7 %), *BRAF*, *RET*, *ERBB2*, *MET*, *ALK*, *FGFR3*, *KIT*, *STK11*, *FGFR2*, *ERBB3* at below 5 % frequency in Indian cohort. Altogether, about 42 % of Indian patients harbor therapeutically relevant alteration. However, we observe that only 8 % of Indian patients have access to all therapeutic options based on DCGI approvals.

Conclusion: Our study provides strong evidence for disproportional somatic molecular biology associated with ethnic descent, further underscoring novel therapeutic opportunities in one of the world'slargest ethnic populations.

Keywords: Pan-cancer, Indian ethnicity, genomic profiling, clinical and therapeutic markers, computational tools.

Developing Novel Polymeric Biomaterials as Non-Viral Gene Delivery Vectors for Enhancing Transfection in Immune Cells

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Background: Gene delivery to immune cells boost immune system's ability to combat diseaseslike cancer or autoimmune disorders. Viral vectors are effective, but have high immunogenicity,manufacturing issues, costly, and safety issues. Non-viral vectors are promising alternative, but struggle with transfection efficiency, heterogeneity, and immune activation risks.

Methods: To address this challenge, we have developed a novel polymeric biomaterial-based non-viral gene delivery system and assessed its gene delivery efficiency in hard-to-transfect immune cells (T-cells and macrophages). We have synthesized a library of novel β-aminoestercopolymers which self-assembled into nanoparticles upon complexing with genetic material (GFP-pDNA).

Results: This novel β-aminoester copolymers were successfully synthesized via Michael addition of functionalized acrylates, amino-alcohols and hydrophobic amines (lipids) in different molar ratios and with subsequent capping using different end groups (1º, 2º, 3º, heterocyclic amines). Higher molar ratio of amino-alcohols w.r.t lipids (1:0.5) in polymer (endgroup heterocyclic amine) enhances the transfection efficiency of GFP-pDNA in J774A.1 macrophage cells by four-fold. In contrast, altering the end cap group to amine chemical moieties (1º, 3º and heterocyclic) in β-aminoester polymer improved the transfection efficiencyof GFP-pDNA in primary murine splenocytes and human T lymphocytes (Jurkat cells).

Conclusion: We systematically varied polymer backbone hydrophobicity and end-cap structure to probe structure-function relationships that enhance the transfection efficiency. We screened them in a high-throughput manner in various immune cells for enhanced gene delivery. We willuse the selected non-viral formulation that shows high transfection efficiency for application in cancer immunotherapy.

Keywords: Non-viral gene delivery, Transfection, hard-to-transfect immune cells, β-aminoestercopolymers, nanoparticles

UNDERSTANDING THE ROLE OF LCN2 IN THERAPY RESISTANCE ANDTUMOR PROGRESSION

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Background: Therapy resistance is a major challenge in colorectal cancer (CRC) treatment, leading to low survival rates. Lipocalin 2 (LCN2) is a secreted glycoprotein, which is upregulated in CRC. One of the mechanisms through which LCN2 imparts therapy resistance in CRC is by promoting the expression of ETS1 transcription factor, resulting in an inhibition of ferroptosis. The focus of this project is to understand the mechanisms by which LCN2 induces ETS1 expression. Further, we aim to generate a genetic mouse model for *KRAS* mutated colorectal cancer expressing high LCN2 levels.

Materials and Methods: LCN2 over-expressing and LCN2 knockdown cells were generated from HCT116 and DLD1 cells respectively. Protein levels were assessed by western blot analysis and localization was checked by immunofluorescence assay. In order to generate tumors in mice, intraperitoneal injection of tamoxifen was given and mice were monitored for 10-12 months.

Results: LCN2 over-expressing CRC cells show an increase in colony formation and tumor growth upon 5-Fluorouracil (5-FU) treatment, indicating the role of LCN2 in 5-FU resistance. LCN2 over-expressing cells exhibit increased EGFR activation and enhanced EGFR membrane localization upon 5-FU treatment. Moreover, inhibiting EGFR in LCN2 over-expressing cells leads to a decrease in cell survival. In the genetic mouse model, the tumor tissue was confirmed by H&E staining and further characterized by staining for epithelial markers.

Conclusions: The study aims to understand the role of LCN2 in therapy resistance and tumor progression, potentially aiding in the development of effective CRC treatment.

Key words: LCN2, therapy resistance in CRC, EGFR recycling, genetic mouse model of CRC

Deciphering the Unexplored Mechanisms of Venetoclax- Azacitidine Combination Therapy Resistance in Acute Myeloid Leukemia (aml)

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Background: AML, being an aggressive blood cancer, requires immediate diagnosis and treatment. The combination therapy of venetoclax-azacitidine (Ven-Aza), although highly effective in newly diagnosed (ND) patients, has grim response in relapsed-refractory (RR) patients. In this study, we have delineated the unexplored intricacies of the acquired resistance to Ven-Aza combination therapy.

Materials and methods:

- Cytotoxicity and apoptosis assays
- Cell proliferation and cell cycle assays
- Cellular ROS, Mitochondrial ROS and JC-1 staining assays
- Immunoblotting
- BH3 profiling assay
- Phase contrast microscopy, electron microscopy, live cell imaging and confocal microscopy

Results and conclusions: All VAR AML cells had higher IC50 values for Ven-Aza compared to VAS cells. They were smaller in size than VAS cells, had high levels of cellular ROS, mitochondrial ROS and hyperpolarized mitochondria. They also expressed low levels of BCL2, DNMT1 and mitochondrial fusion proteins; and increased levels of BFL1, MCL1 and mitochondrial fission proteins. BH3 profiling assay demonstrated an enhanced apoptotic dependency on BFL1 and MCL1 in VAR cells. Electron micrographs showed that VAR cells had more mitochondria per cell and decreased mitochondrial length, area and perimeter compared to VAS cells. Mitocurcumin elevated mitochondrial ROS, collapsed mitochondrial membrane potential, triggered oxidative stress signaling thereby activating intrinsic apoptotic pathway in all VAR cells. Our study unravels the contribution of mitochondria in Ven-Aza resistance. We also propose use of mitocurcumin as a leading molecule for the treatment of Ven-Aza resistant AMLs.

Keywords: Acute myeloid leukemia, Venetoclax-Azacitidine, Mitocurcumin

Aggregation-Induced Emission (AIE)-Based Fluorescence Probe for Dual Sensing of Protamine and Trypsin

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Background: Protamine and trypsin play critical roles in clinical and biological processes, such as neutralizing heparin and regulating enzyme activity, respectively. Nevertheless, current detection strategies face the challenges of having low sensitivity, high costs, and time-intensive procedures.

Materials and Methods: A sensing system based on fluorescence was developed utilizing a cationic derivative of allyl pyridinium tetraphenylethylene (ALPTPE) in conjunction with anionic dextran sulfate sodium (DSS) to detect protamine and trypsin by aggregation-induced emission (AIE) mechanism. The evaluation of the system's sensitivity and selectivity was conducted across diverse environmental conditions and confirmed through the use of actual human urine samples.

Results: The results showed that ALPTPE formed aggregates with DSS due to charge neutralization, leading to enhanced fluorescence emission. Upon adding protamine, significant decrease in fluorescence intensity is observed due to disruption of the ALPTPE-DSS complex, leading to its disassembly and causing the observed "turn-off" in fluorescence. A notable increase in fluorescence emission is observed upon the addition of trypsin which can be attributed to the progressive disassembly of the DSS-PrS complex, driven by the enzymatic cleavage of protamine by trypsin. The sensor system showed a linear response range from 0.1 to 10 µg/mL for protamine and from 0.01 to 1 µg/mL for trypsin. The method demonstrated high selectivity towards other proteins and enzymes, exhibiting minimal interference.

Conclusion: This fluorescence-based sensing platform provides a rapid, precise, and highly sensitive approach for the detection of protamine and trypsin, offering an efficient alternative to conventional methods.

Keywords: Protamine, Trypsin, Aggregation-Induced Emission, Fluorescence sensor

Deciphering Drug-Resistance Mechanisms in Fluoroquinolone (FQ)-Resistant DNA Gyrase Mutants in *Mycobacterium tuberculosis*: Paving the Path to the Design of Better Drugs to Combat Drug-Resistance (DR)

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Background: The complexes of FQs moxifloxacin (MFX) and levofloxacin (LFX) (used in India) with *M. tb.* DNA gyrase mutants- GyrA subunit mutants A90V, S91P, D94A, D94G, D94H, D94N, and D94Y - were simulated through MDS to analyse the mechanisms of drug-resistance, to possibly facilitate DR-resistant drug-design.

Methods: Plain and steered (SMD) all-atom MDS facilitated the analysis of DNA Gyrase-DNA-drug complexes of the wild type (WT) and the drug-resistant mutants. Plain MDS yielded occupancies of drug-enzyme non-covalent interactions (NCIs), while SMD simulated the drug's persistence in the binding site, via NCIs.

Results: MFX and LFX require an Mg^{2+} ion bound near the carboxylate group of the drug to bind D94 via a strong electrostatic interaction. The mutants are located at or near this electrostatic interaction and either directly (D94 position mutants) abrogate this bond or create misalignments in orientation that abrogate other NCIs nearby. D94 mutants attract the carboxylate group (via Mg^{2+}) towards D89, altering the drug's orientation in its binding pocket, breaking NCIs, and facilitating the drug's earlier egress from the pocket, compared to the WT. An MFX-derivative was similarly tested, to attempt tighter DNA gyrase-binding, as seen with SMD.

Conclusion: The D94 mutants directly abrogate the key drug-D94 electrostatic attraction, while A90V and S91P disrupt neighbouring and auxiliary NCIs. An alternative binding mode for D94-binding that retains the orientations of the drug as seen in the WT, along with contacts to immutable residues, might be beneficial.

Keywords: Fluoroquinolones, Moxifloxacin, Levofloxacin, drug-resistance, molecular dynamics (MD) simulations (MDS)

Deciphering the role of Dab2 in skin tumour initiation and stem cells in Squamous cell carcinoma

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Background: Dab2 is an endocytic adapter protein widely expressed across mammalian tissues. It is involved in endocytosis of receptors of key signalling pathways. Dab2 is upregulated in human and mouse hair follicle stem cells. However, loss of Dab2 has been reported in several cancer types. The role of Dab2 in tumorigenesis and CSCs regulation is still obscure.

Materials and methods: We have used a chemically induced murine skin SCC model harbouring an inducible K14 bound Cre-LoxP system for the conditional knockout of Dab2 in the skin. Further, we isolated stem-like cells from DMBA/TPA treated WT and Dab2 cKO mouse skin at various time points. Moreover, we performed total RNA sequencing on the sorted stem-like cells.

Results: No significant difference was observed in the percentage of stem-like cells isolated from WT and Dab2cKO mouse skin treated with DMBA/TPA. However, expression profiling revealed positive enrichment of proliferative and metabolic pathways in the WT stem-like cells. Moreover, positive enrichment of epigenetic pathways and DNA damage repair pathways and negative enrichment of proliferative and metabolic pathways was observed in the Dab2 cKO stem-like cells.

Conclusion: Loss of Dab2 has been reported in several cancer types, suggesting its role as a putative tumour suppressor. Hitherto, our data showed that loss of Dab2 delays tumour initiation and progression in mouse SCC. Loss of Dab2 alters the expression profile of stem- like cells isolated from DMBA/TPA WT and Dab2cKO skin, suggesting its role in CSCs regulation during tumorigenesis.

Keywords: Disabled-2, Squamous Cell Carcinoma, Tumorigenesis, Gene Set Enrichment Analysis

Raman Spectroscopy based Detection of Chronic Myelogenous Leukemia: Insights from India

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Background: Chronic Myelogenous Leukemia (CML) is a myeloproliferative disorder marked by the Philadelphia chromosome, a shortened chromosome 22 formed by reciprocal chromosomal translocation. Diagnostic tools for CML include increased myeloid cell count, immature myeloid cells in peripheral blood, and detection of the transgene from translocation. Initially, the disease is managed with tyrosine kinase inhibitors (TKIs), but resistance to TKIs can lead to disease progression. Resistance detection methods are varied and complex, posing challenges for resource-poor countries with limited healthcare facilities. A universal resistance detection method, regardless of mechanism, would be beneficial.

Materials and Methods: Raman Spectroscopy, requiring minimal sample preparation, captures the biochemical profile of a sample and has shown potential for cancer detection. It can also differentiate between TKI- resistant and sensitive cell lines. In this study, a Raman microscope (Witec alpha300R, Ulm, Germany) was used to identify biochemical changes in CML by analyzing spectral data (λ = 532 nm, 8 mW, 1200 grooves/mm, 10 s acquisition, 10 integrations, cm−1) of cells, serum, and plasma from CML patients, compared with healthy volunteers.

Results: Multivariate analysis techniques such as Principal Component Analysis (PCA) and Principal Component based Linear Discriminant Analysis (PC-LDA), were employed for analysis of the spectral data. PC-LDA showed 95-100% classification efficiency, depending on the type of sample.

Conclusion: Our findings demonstrate the utility of Raman Spectroscopy in the detection of CML. Future directions will focus on checking its potential to segregate TKI sensitive and resistant patients in a larger patient cohort.

Keywords: CML, Raman Spectroscopy, PCA, LDA, Patients, Healthy Volunteers

Exosomes as conduits of Radiation-induced Bystander effects

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Background: Radiation-induced bystander effects describe effects observed in non-targeted cells due to signals released from irradiated cells. Exosomes are secretory nano-vesicles and are key mediators of intercellular communication. Radiation alters the release and cargo of exosomes however, their precise function in bystander signalling and the underlying molecularmechanisms remains obscure.

Materials and Methods: Here we have employed various techniques like Immunoblotting, TEM, NTA , acetylcholine esterase activity and zeta potential to qualitatively and quantitativelycharacterize the exosomes isolated from non-irradiated and X-ray irradiated cells. Exogenous addition of radiation altered exosomes was also done to observe changes in bystander cell phenotype.

Results: The cup shaped morphology and purity of the isolated exosomes were validated by TEM examination and immunoblotting respectively. Radiation increased exosome release in adose-dependent manner, as demonstrated by acetylcholine esterase activity and NTA-based quantification. Interestingly, NTA data also revealed that radiation altered the size of exosomes.Furthermore, Zeta potential measurements indicated enhanced colloidal stability of radiation- altered exosomes. Notably, the exogenous addition of these exosomes resulted in a range of alterations in the phenotype of bystander cells, including enhanced migration, invasion, and reduced proliferation, as well as an enhanced uptake by the non-irradiated cells.

Conclusion: These findings hint towards the role of ionizing radiation in modifying the releaseof exosomes as well as in altering the exosomal profile. These radiation-altered exosomes alsoplay a crucial role in transmitting radiation effects to the non-targeted bystander cells resultingin changed phenotype.

Keywords: Bystander effect, Exosomes, Radiation

Identification of mechanisms by which LCN2 promotes autophagy and tumor progression in colorectal cancer.

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Background: Previous studies of our laboratory have demonstrated that loss of PKP3 led to an LCN2-dependent tumor-formation; LCN2 inhibition using monoclonal-antibody led to CRC-tumor regression and increased 5-FU sensitivity. It was observed that LCN2-associated increased autophagy led to radio-resistance. LCN2 & autophagy can be potential targets in CRC treatment.

Materials & Methods: Autophagy flux is evaluated in LCN2 overexpressing and knockdown cell lines using Western blotting, immunofluorescence staining, live-cell imaging, and electron microscopy. Validation experiments are performed in the KPC:APC mice model. Wound-healing assays for cell- migration, transwell assays for cell invasion, and clonogenic assays for therapy-resistance are performed.

Results: Upon IC_{50} treatment of 5-Fluorouracil, increased LC3-puncta was observed using confocal and electron microscopy. Real time autophagy flux was studied; cells were transfected with mCherry- EGFP-LC3 probe and autophagy flux was found to be more in 5-FU treated cells. Using western blotting, levels of autophagic proteins were found to be increased upon 5-FU treatment in LCN2 high cells. Using purified recombinant wildtype LCN2 pulldown, it was determined that LCN2 interacts with autophagic proteins like ATG4B. Elevated LC3 levels are observed in colon tumors of KPC:APC mice. Autophagy inhibition using chloroquine significantly reduces the migrative and invasive potential of the cells.

Conclusion: Increased autophagy is observed in LCN2 high cells upon drug treatment. Autophagy is required for LCN2-associated increased cell migration and invasion implying that there might be feedback loop mechanism. Increased LC3 in KPC:APC mice tumor indicates autophagy as potential target in CRC. LCN2 interacts with autophagic proteins suggesting its direct role in regulating autophagy.

Keywords: Lipocalin2 (LCN2), Autophagy, Colorectal cancer (CRC), Tumor progression & therapy resistance.

Early Diagnosis and Stratification of Oral Sequential Carcinogenic Changes in Hamster Buccal Pouch Model – A Serum Raman Spectroscopy approach

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Background – Oral cancer, a prevalent malignancy with high mortality due to late diagnosis, often complicates treatment and worsens prognosis. Early detection is crucial, and RS offers insights into biochemical changes preceding morphological alterations. Due to limitations in studying early oral malignancy stages in humans, the HBP model was used.

Materials and Methods – Forty-five female Syrian Golden hamsters were divided into three groups, consisting of 15 hamsters: treated group with 0.5% DMBA, vehicle control, and untreated control for 14 weeks. Weekly retro-orbital blood collection and serum separation
were done. Raman spectra were acquired, preprocessed, and analyzed using PCA and PC- LDA for classification.

Results –Visual changes recorded show changes in the pouch due to treatment. No significant changes in weight were observed between the different groups. Stratification of the treated group was observed as early as the 4th week (~70%), with classification efficiency increasing to 80% in Week 7 and 87% in the 10th week using a 3-model approach. A 2-model approach showed similar trends: 80% in week 4, 87% in week 7, and 93% and 87% in week 10 when compared to control and vehicle-control groups, respectively.

Conclusion – The stratification at distinct stages might be correlated with histopathological changes in the buccal pouch of hamsters. These findings suggest that serum RS can detect biochemical alterations during carcinogen treatment, while also highlighting its potential as an early diagnostic tool for oral cancer detection.

Keywords: Raman Spectroscopy (RS), hamster buccal pouch (HBP), Principal Component Analysis (PCA), PC - Linear Discriminant Analysis (PC-LDA)

Exploring the Anticancer Potential of *Pterospermum acerifolium* and *Dalbergia sisso*

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Background: Breast cancer is second leading cause of mortality, necessitating exploration of potential targeted therapies. Indian medicinal plants exhibit anticancer potential with minimalside effects, and hence, present promising avenues for drug discovery. *Pterospermum acerifolium* and *Dalbergia sisso* are recognized for their pharmacological attributes, although their anti-cancer benefits are underexplored in breast cancer.
Methods: Anticancer efficacy of crude leaf extracts of *P. acerifolium* and *D. sisso* was evaluated using Gene Ontology, KEGG pathway analysis, protein–protein interaction networks, and compound-target-pathway analysis. Comprehensive systems pharmacologyframework was established that linked *P. acerifolium* and *D. sisso* with breast cancer and breast cancer bone metastasis. *In vitro* anticancer activity of crude leaf extracts of *P. acerifolium* and *D. sisso* was accessed on T47D and MDA-MB-231 breast cancer cell lines.
Results: *In silico* analysis identified 3 compounds and 12 targets for *P. acerifolium*; whereas

4 compounds and 25 target genes for *D. sisso* demonstrating multiple-targets, and involvement of multiple pathway networks in breast cancer metastasis. *In vitro* studies revealed dose-dependent inhibition of proliferation of T47D and MDA-MB-231 cells. Comparative analysis indicated that *P. acerifolium* exhibited superior anticancer activity than that of *D. sisso*.
Conclusion: The study highlights anticancer potential of *P. acerifolium* and *D. sisso* extracts,paving the way for discovery of novel compounds and development of alternative therapeuticstrategies for breast cancer treatment. Further, we will be identifying active ingredients of phytochemical extracts, and evaluate their molecular and cellular effects on breast cancer.

Keywords: Breast cancer, network pharmacology, cancer therapeutics, phytochemicals

Elucidating the cross-talk between epithelial tumours and the hematopoietic organ, lymph gland in *Drosophila*

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Background: The hallmarks of cancer include tumour-promoting inflammation. Many epithelial tumors cause systemic effects in distant organs by secreting factors in circulation resulting in severe syndromes like cancer cachexia. These secreted factors could have an impact on the stem cell homeostasis and hematopoiesis thereby contributing to systemic inflammation which is fairly under characterised.

Materials and methods: We use *Drosophila* as a model organism to understand *in-vivo* inter-organ communication between the tumor and the lymph gland. The *UAS-Gal4* system has been employed to model Yki^{3SA}-induced gut tumors using the stem-progenitor specific *esg-Gal4*. We use antibody- based markers to ascertain various hematopoietic phenotypes using immunofluorescence and confocal-imaging based approach.

Results: Our results demonstrate that the lymph gland of the larvae bearing gut tumor has a smaller HSC niche as compared to the control and also higher differentiation of three blood cell types. Transcriptomic analysis of circulating hemocytes suggests the blood cells have a higher gene expression of tumor secreted factor ImpL2, an antagonist of insulin signalling that bind to *Drosophila* Insulin (dILP2). Our data shows that systemic upregulation ImpL2 results in a smaller lymph gland niche due to abrogation of insulin signalling causing an imbalance in blood cell homeostasis.

Conclusion: This study provides evidence that there is active crosstalk between the tumor cells and the lymph gland wherein there is hematopoietic remodelling characterized by smaller niche and increased differentiation leading to systemic inflammation.

Keywords: Crosstalk, *Drosophila*, Gut tumor, Hematopoiesis, ImpL-2, Lymph gland.

Mechanics of extracellular matrix dictates radiation response of breast cancer cells

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Background: Extracellular matrix (ECM) stiffening is a peculiar feature of breast tumor microenvironment that facilitates cancer progression. Stiff ECM is instrumental in potentiating survival, proliferation, contractility, invasion and stemness of cancer cells. However, the role of ECM rigidity in regulating radio-response of cancer cells remains largely intangible and needs in-depth investigation.

Methods: To recapitulate the stiffness of normal breast stroma (0.5kPa) and metastatic breast tumor (5kPa), stiffness-tunable hydrogels were fabricated. To elucidate the impact of ECM- stiffness on radio-response, various functional and molecular assays including cell survival, apoptosis, migration, immunofluorescence, cell cycle profiling immunoblotting and RNA sequencing were performed.

Results: Breast cancer cells cultured on stiff scaffold (5kPa) when irradiated, showed significantly decreased apoptosis with concomitantly higher clonogenic survival elevated proliferation and migration compared to that of on soft scaffold (0.5kPa). Furthermore, immunofluoresece and immunoblotting confirmed low levels of γH2AX in irradiated cells under stiff-ECM conditions than soft ECM, suggesting attenuated DNA damage. Collectively, these findings confirm poor radiation response in cells experiencing stiff ECM. To delineate the molecular mechanisms underlying observed ECM stiffness-induced radio-resistance cells were subjected to transcriptomics, which revealed differential regulation of genes involved in cells cycle regulation, cell death, organelle assembly and biogenesis.

Conclusion: We demonstrate that breast cancer cells acquire radio-resistance when exposed to stiff ECM, which is reflected from mechano-transduction-driven survival advantages post- irradiation. We further show that these changes are associated with differential transcriptional
regulation of the canonical and non-canonical pathways which warrants further investigation; opening new avenues for mechano-targeting.

Keywords: Stiff ECM, Mechano-transduction, Radio-resistance

The impact of physical activity on childhood and adolescent cognitive growth and its link to obesity

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Background: The impact of physical activity and obesity on human brain has long been a debatable matter. There are several studies that either accept or refute the relation. It is influenced by several factors like age, gender and socio-economic status. This research aims to dwell on these topics.

Material and methods: An observational analytical study was conducted. A questionnaire was circulated amongst parents of children between 3 to 18 years of age. Incomplete forms and children suffering from previous diseases were excluded. The variables were compared, analyzed and interpreted by using SPSS software.

Results: Considering the exclusion criteria a total of 292 responses were considered. A bivariate cross tabulation was made comparing variables such as age group, gender and socioeconomic status with engagement in physical activity. It was found that kindergarten children (81.8% of the kindergarten children) participated more in physical activity as compared to higher age groups.

More boys (79.4%) participated in physical activity as compared to girls (60.7%). A weak correlation of -0.111 was found between engagement in physical activity and time taken to complete a topic. Children with higher than normal BMI took more time to finish a topic. Conclusion: The findings implied that younger children engaged more in physical activity. Males were found to be more physically active as compared to females. Children with sedentary lifestyle and higher BMI were found to take longer time to understand a concept.

Keywords: physical activity, obesity, cognitive development, age group, gender

Proteomics-Based Identification and Validation of Potential Biomarkers in Head and Neck Squamous Cell Carcinoma

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Background: HNSCC (Head and neck squamous cell carcinoma) accounts for 1.5 million cases globally in 2020 and has poor survival rates in advanced stages. Early detection is critical for better outcomes. Proteomics provides a powerful tool for identifying biomarkers, enabling early diagnosis, prognosis, and targeted therapeutic strategies to combat resistance and metastasis.

Materials and Methods: Serum samples from oral cavity cancer patients at different time points of treatment will be enriched with acetonitrile. Mass spectrometry-based proteomics will be utilized for discovery and validation of proteins. Final biomarker verification using ELISA will be performed, and the data will be correlated with survival analysis to assess prognostic relevance and clinical applicability.

Results: Serum enrichment was successfully optimized to ensure high abundant protein depletion, preparing the samples for advanced proteomic analysis. Preliminary evaluations confirm their suitability for iTRAQ and SWATH workflows. These complementary approaches will enable the identification and quantification of differentially expressed proteins. Selected candidate proteins from this analysis will undergo targeted quantification using MRM or PRM. Subsequently, ELISA assays will validate these findings, correlating protein expression levels with patient survival outcomes to uncover clinically significant biomarkers.

Conclusion: This study aims to identify and validate robust serum biomarkers for oral cavity cancer using advanced proteomic approaches. The integration of proteomic findings with survival analysis has the potential to enhance early diagnosis, improve prognostic assessment, and contribute to the development of personalized therapeutic strategies.

Keywords: ELISA, HNSCC, iTRAQ, MRM, PRM, SWATH

Spargel (Drosophila PGC1-α) regulates blood cell homeostasis in the *Drosophila* lymph gland

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Background: Tissue homeostasis relies on a balance between stem cell maintenance and differentiation, with disruptions potentially causing cancer or tissue degeneration. Here, we aim to elucidate the role of Spargel, a target of the histone acetyltransferase GCN5. Spargel regulates mitochondrial biogenesis and here we investigate its role in regulating lymph gland hematopoiesis.

Material and Methods: We have employed whole animal mutants of Spargel, Spargel knockdown and over-expression lines wherein we can spatio-temporally modulate Spargel expression using UAS-Gal4 system. We use various hematopoietic antibody markers for immunofluorescence and acquisition with confocal imaging for determining hematopoietic phenotypes that are analyzed using ImageJ software.

Results: Our study shows that whole-animal mutants for Spargel showed abnormalities in blood cell homeostasis, indicating its role in hematopoietic regulation. Targeted manipulation of Spargel expression revealed that its depletion in specific lymph gland cells led to an increase in crystal cell differentiation, while overexpression suppressed crystal cell lineage. Furthermore, Spargel overexpression caused a notable reduction in niche size, which may disrupt overall homeostasis within the lymph gland. We are currently characterizing the hematopoietic phenotypes caused upon perturbation of Spargel in different cell subsets along with studying how mitochondrial structure and dynamics change in the lymph gland upon Spargel perturbation.

Conclusions: Our study suggests that Spargel plays a crucial role in maintaining blood cell homeostasis wherein its levels determine niche size and extent of blood cell differentiation. Our future aim would be to determine its impact on mitochondrial dynamics in the lymph gland.

Keywords: Drosophila, Stem Cells, Hematopoiesis, Spargel, Mitochondria

Role of Transforming Growth Factor Beta-Induced (TGFBI) in Cancer-Associated Fibroblast and its influence on TME.

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Background: Non-small cell lung carcinoma has poor survival due to genetic alterations and heterogeneous tumor microenvironment (TME). Cancer-associated fibroblasts (CAFs)represent predominant cells in TME. Preliminary RNA sequence analysis has shown TGFBI/BigH3 to be up-regulated in Lung cancer patient-derived CAFs. Hence, it is importantto study influence of TGFBI in TME.

Methods: To understand the role of TGFBI in CAFs, we used siRNA targeting TGFBI. Phenotypic changes were observed with respect to migration and contraction properties of CAFs employing transwell migration and collagen contraction assays. Analysis of RNA sequencing was performed to understand genes, and pathways regulated by TGFBI at molecular level.

Results: Higher expression of TGFBI was observed in CAFs compared to NF (Normal fibroblasts) at both the cellular and secretory levels. Upon TGFBI knockdown, CAF showed reduced migration in the trans-well migration assay. Also reduced contractile property of CAF upon TGFBI knockdown. From the transcriptomics analysis, we observed that immune-relatedpathways were up-regulated while cell cycle-related pathways were down-regulated upon knockdown of TGFBI in CAFs. Validation of differential gene expression was confirmed by quantitative real-time PCR.

Conclusion: Our study suggests that TGFBI may play a vital role in maintaining CAF phenotype and modulating immune response in TME. This study can highlight the understanding of CAF's expressed TGFBI role in TME and overall outcome on tumor growth.

Keywords: NSCLC: Non-small cell lung carcinoma, NF: Normal Fibroblast, CAF: Cancer-associated fibroblasts, TGFBI: Transforming Growth Factor Beta-Induced

The role of cancer cell driver mutations in Tumor microenvironment

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Background: Tumor Microenvironment (TME) is a complex ecosystem surrounding tumour cells with extracellular matrix and stromal cells including fibroblast, immune cells andendothelial cells. Non-small cell Lung Cancer (NSCLC) harbors diverse genetic alterations andheterogeneous TME. We want to understand the role of driver mutations in shaping the TME in NSCLC.

Material and Methods: We performed CIBERSORTx deconvolution analysis to plot the abundance of stromal cell signatures with patient groups mutated with different oncogenes. Wegenerated doxycycline-inducible KRAS Knockdown Calu1 and A549 cells to perform differentfunctional assays with Normal Fibroblast (NF) to understand the impact of KRAS mutations on Fibroblast modulation.

Results: The in-silico deconvolution analysis using CIBERSORTx for TCGA Pan-Cancer Atlas data showed that the KRAS mutant patient group are associated with the most abundantCAF gene signature. The collagen contraction assay showed that the mutant KRAS tumour cells grown with NFs can modulate the contractility of fibroblast when compared to KRAS knockdown tumour cells co-cultured with NFs.

Conclusion: Oncogenic KRAS in NSCLC plays an important role in the modulation offibroblast behaviour in the Tumour microenvironment.

Keywords: Cancer-Associated Fibroblast, Tumour Microenvironment, KRAS

Can RT-PCR serve as alternate gold standard for validation of ER/PR results?

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Background: ER/PR are critical for patient management, but no molecular standard exists for result confirmation besides NGS. This study aimed to use an alternate approach for evaluation of ER/PR status in breast cancer cases using mRNA-based RT-PCR testing as a point-of-care tool to serve as an adjunct to conventional IHC.

Materials and Methods: The study included 60 histologically confirmed breast cancer samples stored at Pathology Department of Tata Memorial Hospital. FFPE blocks with IHC data confirming the expression of ER/PR were analyzed. Concordance analysis, sensitivity, and specificity were calculated for each marker. Kappa statistics was employed to assess the overall agreement.

Results: Sixty breast cancer samples were examined, all providing conclusive outcomes for ER and PR status. Standardization involved using 10 confirmed negative samples in IHC, establishinga cycle threshold of 34; cycles exceeding 34 were deemed negative, while those below 34 were deemed positive. Moderate concordance rates were observed, with ER achieving 81.67% and PR achieving 73.34%. Sensitivity for ER was 91.66% and PR was 73.91% and specificity for ER was 91.66% and PR was 86.48% indicating robust accuracy for ER. Kappa statistics demonstrated perfect agreement for ER and substantial agreement for PR between the two systems.

Conclusions: The study demonstrates that RT-PCR based system exhibits moderate concordance with IHC for ER and PR, possibly due to number of low positive cases seen in IHC. Further understanding and testing are necessary to establish this assay as an independent tool for conducting transcript based biomarker detection instead of IHC.

Keywords: ER/PR, RT-PCR, breast cancer, IHC

Investigating the impact of Curcumin on Transgenerational *Caenorhabditis elegans* exposed to High Glucose Diet

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Background: High-glucose diet has been linked to metabolic conditions and neurodegenerative diseases. *Caenorhabditis elegans i*s considered a model organism due to its well-characterized genetics, short lifespan. This study examines the transgenerational effects of elevated glucose levels on *C. elegans* and evaluates curcumin's potential to ameliorate these neurodegenerative effects.

Materials and Methods: *C. elegans* (WT) were exposed to high glucose (0,50, 100, 400 mM) and treated with curcumin (0,25, 50, 100 μM) to evaluate the behavioral and antioxidant effects on the F1 and F2 generations. L4-stage worms from each generation were examined to evaluate the effect of glucose and curcumin's possible protective benefits.

Result: The study observed that a high-glucose diet had effects on *C. elegans.* Behavioral assay like pharyngeal pumping and thrashing were performed, and the results showed that with increased glucose concentrations (0 - 400 mM). the worms showed decreased pumping rate and thrashes. Interestingly, curcumin (0,25, 50, 100 μM) treatment had reversed some of these effects. Curcumin showed increased pumping and thrashing rate similar to control, indicating its ability in preventing high-glucose-induced damage. Enzymatic assay like DPPH had observable color change from purple to yellow indicating a shift in antioxidant activity.

Conclusion: A high glucose diet affects *C. elegans,* resulting in negative transgenerational effects. Curcumin appears to have potential benefits through lowering oxidative stress and increasing worm health. This reveals that curcumin may be beneficial for mitigating the effects of increased glucose levels.

Keywords: High-glucose diet, *Caenorhabditis elegans*, Neurodegenerative diseases, Transgenerational effects, Curcumin

Positive Feedback Regulation as a Driver Mechanism Behind Drug Resistance in HER2 positive Breast Cancer

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Background: HER2 positive breast cancer (BC) accounts for 20-25% BC cases worldwide. The personalized treatment strategy has improved disease outcomes significantly but the clinical challenge of drug resistance continues. In this context of drug resistance, our study focuses on regulatory roles of downstream signalling molecules driven by HER family receptors.

Material and Methods: Trastuzumab (R.I.-80) and neratinib (R.I.-10) drug-resistant HER2+ve BC cell models were established. Immunoblot and immunofluorescence was performed to check differentially expressed proteins of HER2-STAT3 signalling axis. TRIM-ing of candidate proteins led us to validation of preliminary observations. Bioinformatics analyses were performed to delineate role of STAT3, driving HER2 drug resistance.

Results: In resistant cell models, Heregulin- β1 ligand driven phospho-STAT3 activation and HER2 TRIM-ing mediated p-ERK, p-Akt, p-STAT3 inhibition suggested STAT3 as a downstream target of HER2-HER3 signalling axis. STAT3 TRIM-ing showed significant ($p<0.05$) abrogation of upstream kinases, indicating STAT3 driven positive feedback loop. Bioinformatic analysis of STAT3 interaction network revealed Enhancer of Zeste Homologue2(EZH2) as a lead interactor, which was overexpressed and constitutively activated in resistantcell model. EZH2's relevance in HER2-STAT3 axis was verified by inhibiting Akt. Also, STAT3 binding motifs in EZH2 & HER2 promoter region suggested their transcriptional regulation by STAT3, imparting the positive feedback loop.

Conclusion- Our results underscores STAT3 mediated HER family receptor regulation, where EZH2's significant role was also realized. Thereby, the study highlights a STAT3 driven positive feedback loop, impacting HER2 drug resistance.

Keywords- Drug resistance, EZH2, Feedback regulation, HER2, STAT3, TRIM-ing

Influence Of Tp53 Mutations on Tumor Stromal Interactions In PDAC

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Background- Pancreatic ductal adenocarcinoma (PDAC) is characterized by highly desmoplastic stroma and cancer cell mutations like TP53, the major causes for metastasis andchemoresistance. PDAC is a highly heterogenous cancer, it is important to understand how different TP53 hotspot mutations might play role in cell and non-cell autonomous mediated tumour progression.

Material and methods- To study impact of TP53 hotspot mutations on cancer associated fibroblasts (CAFs), the major stromal population, TP53 KO pancreatic cancer cell was generated by CRISPR/Cas9 technology and transduced with recombinant lentiviruses to re- express different mutant p53 proteins. Subcutaneous and orthotopic injections were standardised in NOD SCID and C57/BL/6J mice respectively.

Results- Migration assay showed higher migration rates in p53 re-expressed pancreatic cancercells compared to p53 KO cancer cells. Also, migration of CAFs was seen to be more towardsmutant p53 re-expressing cancer cells than p53 KO cells. Increased mRNA expression of CAFactivation markers was observed when cocultured in a contact dependent manner with p53 re-expressed cancer cells as compared to p53 KO cells. For *in vivo* studies, successful tumours were obtained within a justifiable period of time from subcutaneous injection in NOD-SCID mice as well as orthotopic injection in pancreas of C57/BL/6J mice.

Conclusions- TP53 mutations in cancer are reported to have different transcriptional signature.Hence, it is expected that different p53 mutations in cancer cells might play differential role inre-wiring of stroma. Coculture studies followed by RNA sequencing might determine how TME is impacted based on the p53 status in cancer cells.

Keywords- PDAC, TME, TP53, CAFs

Investigation of Cancer Stem Cell-associated Drug Resistance Genes in Gastric Cancer cell lines”

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Background - Gastric cancer (GC) is challenging to treat due to acquired drug resistance andlack of alternate therapy. Cancer stem cells (CSCs) are major factors imparting resistance. Identifying gastric cancer stem cells (GCSCs) and specific genes involved in GCSCs mediateddrug resistance is crucial and may be targeted to combat the disease.

Materials and Methods - CSC-like cells were isolated from GC cell lines using side populationassay and pulse-chase label retention assay, validated using pluripotent stem cell markers by qPCR. 5-FU resistance genes were analyzed in AGS/AGS^{5FU} and KATO III/KATO III-SP. Theeffect of 5FU-resistance genes will be validated in GC orthotopic mice model.

Results - Using SP assay, KATO III showed 15-18% CSC-like cells with increased pluripotent stem cell genes. AGS^{5FU} showed higher percentage of PKH^{+} cells as compared to AGS. PKH^{+} cells exhibit increased expression of pluripotent stem cell markers as compared to PKH^{-} cells, indicating dye-retaining cells showing stem cell-like characters. Expression of Thymidine phosphorylase (TYMP) (responsible for the conversion of 5FU to its active form) and thymidylate synthase (TYMS) (inhibited by 5FU) were significantly altered between sensitive and resistant cell lines. AGS^{5FU} cells showed ~3.8-fold decreased TYMP and ~1.4-fold increasedTYMS as compared to AGS. GC orthotopic mice models are being developed to study 5FU resistance in tumor progression.

Conclusion - Our preliminary data suggested that TYMP and TYMS genes could be involved in causing 5FU resistance in AGS^{5FU} cell line. Deciphering the detailed mechanism by which CSCscan cause 5FU-resistance is under investigation.

Keywords- Gastric Cancer, Cancer Stem Cells, 5-FU, TYMP, TYMS

Exploring the role of 26S Proteasomal Chaperone PSMD9 in maintaining nucleolar architecture and homeostatic cellular physiology

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Background: PSMD9 is a proteasomal chaperone involved in the assembly of the 19S Regulatory Particle of 26S Proteasome. Overexpression of PSMD9 in breast cancer is correlated with radio-resistance. Additionally, PSMD9 is important in maintaining nucleolar architecture and wild type p53 levels. This study aims to understand the functional aspect of the same.

Materials and Methods: To assess the abundance of proteins of interest, immunoblotting was performed. To inspect direct physical interaction, co-immunoprecipitation assays were carried out. For visualization of cellular morphology and protein localization, immunofluorescence was carried out. For observing cellular dynamics, live cell imaging and FRAP were conducted. Cell cycle analyses were performed using FACS.

Results:

- PSMD9 knockouts grow slower, have larger nuclei and aberrant nucleolar morphology.
- The nucleolar morphology of the knockout cells is restored when rescued with PSMD9 overexpression.
- The abundance of a crucial nucleolar phosphoprotein, NPM1 is low in PSMD9 KO which, however, does not alter nucleolar dynamics.
- PSMD9 KOs have higher abundance of p53, exhibit higher protein synthesis and are sensitized to nucleolar stress response.

Conclusion: In conclusion, we can say that PSMD9 has a significant functional role in maintaining nucleolar architecture. In absence of PSMD9 cells are stressed which lead to slow growth and cellular morphological changes. These experiments pave the way for exploring novel non-canonical functions of PSMD9 in maintaining homeostasis and cellular physiology.

Keywords: PSMD9, nucleolar architecture, nucleolar stress, p53 levels, NPM1

Investigating the effect of mitocurcumin on metastatic potential of non-small cell lung cancer (NSCLC)

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Background- Despite only 0.01% of tumor cells successfully metastasizing, metastasis accounts for 90% of cancer deaths. Mitochondria have emerged as a promising therapeutic target, as mitochondrial dynamics are linked to key metastasis traits, including motility, invasion, microenvironment modulation, plasticity, and colonization. Mitocurcumin-1 (MiC), a curcumin derivative with two TPP moieties, selectively accumulates in cancer cell mitochondria. By inhibiting TrxR2 and modulating reactive oxygen species, MiC demonstrates potential anticancer activity. ROS inturn affects mt-Dynamics hence we aim to evaluate whether MiC modulates metastasis in lung cancer.

Materials and Methods-A549, H1299, and LLC-1 lung cancer cell lines were studied. IBIDI inserts facilitated wound healing assays, while Boyden Chamber assessed migration and invasion (matrigel coated). Confocal microscopy analyzed mitochondrial and lysosomal structures, and western blot evaluated protein levels. Frozen cell samples were sent to MedGenome for transcriptome analysis. NOS-SCID and C57BL/6 mice will be used for in vivo MiC evaluation.

Result-MiC treatment delayed gap closure in wound healing assays and reduced cell migration and invasion in Boyden chamber experiments. Mesenchymal markers such as N-Cadherin, Vimentin, and Twist were downregulated. Mitochondria exhibited a more rounded structure, with increased colocalization of mitochondria and lysosomes. Transcriptome analysis further revealed modulation of metastasis-related gene expression in MiC-treated cells compared to controls.

Conclusion-Lung cancer cells' ability to migrate and invade reduces upon MiC treatment. MiC downregulates the early metastatic markers. MiC treatment leads to degradation of mitochondria via mitophagy in human NSCLC cell lines (A549 and H1299). MiC treatment modulates migration related genes

Keywords-Metastasis, mitocurcumin, mitochondrial dynamics

Structural Elucidation of the SAM Domain of EphB4 Receptor Tyrosine kinase

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Background: Eph receptor tyrosine kinase intracellularly consists a juxtamembrane region, kinase domain, and SAM domain with the juxtamembrane and SAM-kinase linker regulating kinase activity. Since SAM domain forms the part of this allosteric regulation network thus mutations in the SAM domain can disrupt this allosteric regulation. Noting the importance of SAM domain, we have analyzed the cancer-associated EphB4-SAM mutations using biophysical techniques to study receptor activation.

Material and Methods: EphB4 mutations retrieved from CBioPortal were evaluated for pathogenicity by using *in silico* pathogenicity predictors. Mutation predicted to be pathogenic were further evaluated using stability predictors. Mutations predicted to pathogenic are introduced by site directed mutagenesis, and structural impacts were evaluated using circular dichroism, fluorescence, and X-ray crystallography.

Results: *In silico* analyses of SAM domain mutants E914K, A931T, and D946N revealed destabilizing effects, while S964T was stabilizing. Among these mutants, two D946N and S964T are in the conserved region. Thermal denaturation experiments showed all mutants were destabilizing when compared with the wild-type. Far-UV circular dichroism data showed strong negative ellipticity at 208 and 222 nm, indicating α-helix dominance in both WT and mutants, though helical content was decreased in mutants. Intrinsic fluorescence assays showed a 320 nm emission for WT and mutants, with a blue shift in S964T, indicating a more hydrophobic environment due to the serine-to-threonine substitution.

Conclusion: Thermal denaturation and circular dichroism data confirm mutant destabilization and loss of helical content. Intrinsic fluorescence shows that S964T increases hydrophobicity and affects protein structure and stability.

Keyword: EphB4, Circular Dichroism**,** Sterile Alpha Motif

Evaluation of phytochemical, antimicrobial and cytotoxic properties of Flower Extract of *C.ternatea* Linn

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Background: *Clitorea ternatea* is a plant of the Fabaceae family. Research and studies are being conducted on *C. ternatea* to ascertain its pharmacological properties. Pharmacological investigations on this plant have shown it has a variety of medicinal properties, including antibacterial, antioxidant and anti-asthmatic activities. There is limited research on detailed properties of the flower extract.

Materials and methods: Phytochemical qualitative evaluation of the flower extract was performed as per standard protocols. The antimicrobial activity of *C. ternatea* flower crude extracts was tested against *E.coli*, *S. aureus* and *P. aeruginosa.* Antioxidant activity of the extract was estimated by the DPPH Method. MTT assay was performed to assess cell viability against A549.

Results: The crude extract from the flower confirmed the presence of alkaloids, terpenoids, cardiac glycosides, fats and anthocyanins. Antimicrobial activity was tested in the range of (5mg/ml to 0.5mg/ml). *E.coli* and *S.aureus* showed sensitivity to growth at 0.5mg/ml whereas *P.aeruginosa* was resistant and displayed mild sensitivity at 5mg/ml. Antioxidant activity was studied using DPPH Method. The IC50 of the extract was estimated as 0.05ug/ml. The IC50 of *C.ternatea* flower extract was found to be 40.42mg/ml against A549.

Conclusions: The growing shift towards eco-friendly products highlights the potential of modern pharmaceuticals derived from traditional medicinal plants. Preliminary evidence suggests that Clitoria ternatea flowers possess significant medicinal properties, notably as a potent antioxidant, with additional antimicrobial and cytotoxic effects. These findings justify further research into its therapeutic applications.

Keywords: *C. ternatea*, antioxidant activity, cytotoxic activity, antimicrobial activity, anythocyanin

Identifying the genomic heterogeneity in Head and Neck Cancer subsites

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Background: Head and Neck Squamous Cell Carcinoma (HNSCC) is one of the most prevalent cancers globally, especially in Southeast Asia, with India contributing to 30% of global cases. Despite advancements in clinical diagnosis, the genetic variation among different HNSCC sub-sites in India remains underexplored.

Material and Methods: A meta-analysis of literature specific to Indian HNSCC patients was conducted. Genomic data from different HNSCC sub-sites were curated from 22 research articles comprising an Indian cohort. Data extraction involved identifying genes with their mutation frequencies across each sub-site, followed by pathway analysis to discover common molecular processes.

Results: Significant genes with the highest mutation frequencies were identified: THAP7 (94.11%) in Oral cancer, GSTM2 (95%) & NR4A3(95%) in Tongue, PTK2 (80%) in Sino-Nasal, WIF1 (40%) in Laryngeal/Pharyngeal cancer and GSTT1 (81.87%) in overall HNSCC. Pathway analysis revealed shared genes across multiple sub-sites further contributing to common pathways between them.

Conclusion: This study highlights the genomic heterogeneity within HNSCC sub-sites in India, despite their clinical similarities thereby offering new insights to precise, population targeted therapies. Furthermore, common genes found across various sites along with their common pathways, point to a shared genetic base that may contribute to cancer metastasis and progression via shared pathways.

Keywords: Head and neck squamous cell carcinoma (HNSCC), genomic heterogeneity, mutation frequency, sub-site variation, molecular pathways, Indian population, targeted therapy

Elucidating the mechanisms of resistance to spontaneous antitumor antibodies in epithelial malignancies.

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Background: In many cancers, TIL-Bs carry strong prognostic significance and are emerging as key predictors of response to immune checkpoint inhibitors. We hypothesize that the ineffectiveness of antitumor antibodies is partly due to the non-canonical expression of different Fc receptors by the cancer cells as part of their immune escape mechanism.

Materials and methods: We will correlate expression of FcRs some immune cells and epithelial cells where transcytosis of antibodies occurs, with 18S rRNA. An orthotropic mouse model will be established to validate the findings followed by FACS analysis of the processed tumors to check the prevalence of FcRs. In order to fulfil this objective, we will first transduce murine transplantable cancer cell lines with lentiviral constructs for expressing murine FcγR and Fcα/μR, individually.

Results: The status of various FcRs was analyzed from four different murine cancer cell lines. Here, we observed a consistent expression of all the receptors across the selected cell lines except in CT26 where there was a mild expression of Pigr and no expression of Fcrn.

Conclusion: To date, no comprehensive study has demonstrated the immunomodulatory functions of these Fc receptors when expressed by epithelial cancer cells. If our hypothesis is factual, then therapeutically, this could lead to something similar to checkpoint inhibitors, where cancers can be treated by monoclonal antibodies targeting these Fc receptors.

Keywords: Antitumor antibodies, Epithlial malignancies, cancer, FcRs, Checkpoint Inhibitors, non-canonical

Ancestral sequence reconstruction of the htra family of proteins and their functional implications

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Background: Ancestral Sequence Reconstruction, a computational method, is crucial in identifying the chronology of the mutations of macromolecules across evolutionary time. When the technique is applied to the heat-shock induced serine proteases, htras, present ubiquitously across almost all taxonomic forms, factors that led to the conservation can be elucidated.

Materials And Methods: Firstly, databases will be built to predict the ancestors. The latter shall then be subjected to biophysical and biochemical assays. Finally, structural comparisons of the extant and the ancestral proteins will be employed to unravel those residues that might be important for targeting.

Results: So far, ancestors have been predicted of mature htra2 and observed to have significant conservation of the key residues – those involved in trimerisation, active site triad and putative substrate binding sites. Apart from these, secondary structural elements do not differ much between the extant and the predicted extinct sequences. Additionally, generation of mutations in some substrate binding grooves in the serine protease domain and the PDZ domain are underway to decipher the subtle differences in the enzymatic activities between the human and the bacterial orthologues. Understanding the former shall be instrumental in analysing the course of evolution as well.

Conclusion: Despite the availability of structural and sequential information on htras, effective targeting has not been achieved. Thus, from synthesising the ancestral sequence to the cognate therapeutic intervention, the project aims to attempt to bridge a few gaps in the existing biology of these serine proteases.

Keywords: Evolution, Cancers, Neurodegenerative disorders, Autoimmune disorders, Mutations

CancerBiomeDB: a Knowledge Base on Microbiome Signatures for Pan-Cancer Immunotherapy

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Background: Gut Microflora influences efficacy of cancer immunotherapy. Studies indicate compositional deviations in gut flora leading to development of non-responsiveness to immunotherapy however, a clear understanding of gut microflora shifts associated with clinical benefit across cancer types is lacking. We present a comprehensive meta-analysis exploring the relationship between gut microbiota and cancer immunotherapy outcomes.

Materials and Methods: The data were organized into a knowledgebase, including taxa, cancer types, location, clinical outcomes, etc. Data curation, processing, and visualization were performed using R, Python libraries, and iTOL. We developed a database using XAMPP stack with HTML, CSS, and JavaScript for the front end and PHP, and MySQL for the back end.

Results: We analyzed 2595 articles and deposited extracted information in the database. Statistical analysis revealed that most commonly studied cancer types are gastrointestinal cancer, melanoma, and lung cancer. We identified a total of 279 candidate taxa reported in these studies. Further statistical evaluation revealed eubiotic bacteria, including *Faecalibacterium prausnitzii* and *Akkermansia muciniphila*, were associated with responsiveness to immunotherapy. In contrast, *Escherichia coli*, *Bacteroides thetaiotaomicron*, and *Veillonella* genus causing gut dysbiosis have been linked with resistance spanning different cancer types. Additionally, at family level, *Lachnospiraceae, Ruminococcaceae*and *Akkermansiaceae* were more prevalent in effective group, whereas *Bacteriodiaceae, streptococcaceae,* and *Veillonellaceae* were abundant in non-effective group.

Conclusion: We present a consensus microbial dysbiosis signature predictive of worse immunotherapy outcomes. We also present an easy-to-use database of gut microbiomes, aiding further research to improve treatment strategies across cancers.

Keywords: Cancer, Gut microbiome, Immunotherapy, Metagenomic Sequencing, Database

Studying the binding multiplicity of steroid hormone receptors and ligands in triple negative breast cancer

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Background: Triple negative breast cancer (TNBC) lacks PR, ER and HER2. Thus, therapies targeting these receptors are ineffective, leading to poor prognosis and high recurrence rate. However, TNBCs express androgen (AR), glucocorticoid (GR) and mineralocorticoid (MR) receptors. Thus, we aimed to understand roles of these steroid hormone receptors in TNBC and identify drugs that bind them.

Materials and Methods: We performed *in silico* molecular docking experiments to identify natural/synthetic compounds (n=117) that can bind to nuclear and membrane AR/GR/MR. Further, we performed a cross-recognition experiment to identify multitarget potential of these drugs. We performed molecular docking using AutoDock Vina, followed by post-docking analyses (binding affinity and active site prediction criteria) to confirm receptor-ligand interactions.

Results: Analyses identified novel natural/synthetic ligands to bind nuclear and membrane AR/GR/MR with binding affinity similar or more than that of their cognate ligands. Further, we identified additional ligands that show multitarget potential in their interactions with AR/GR/MR (cross-docking). Post-docking analyses identified drugs that bind receptors with high affinity. Further, we will perform ADME, MD simulations, and functional cell-based validations in TNBC cells.

Conclusion: We identified several potential ligands that can interact with AR/GR/MR, and hence, may make TNBC amenable for endocrine therapy. Moreover, study results may serve as paradigm shift in cancer therapeutics by making available ligands that can function even in absence of their cognate receptors in TNBC—a potential drug-repurposing approach.

Keywords: Triple-negative breast cancer, steroid hormone receptors, cancer therapeutics, molecular docking, MD simulation.

Development of Saliva-based biosensor for non-invasive detection of oral cancer

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Background: Oral cancer has poor response rates and patients show poor survival outcomes. Therefore, early detection is necessitated to improve treatment outcomes. A majority of diagnostic techniques are either invasive or costly, limiting their utility. This study aims to develop an economical, non-invasive biosensor for quantifying levels of pathogenic bacteria as a means of detecting oral cancer.

Materials and Methods: We are developing an aptamer-based biosensor that would quantify levels of certain proteins secreted by *Fusobacterium*, *Porphyromonas* and others, which are associated with oral cancer. The biosensor is prepared using aptamers against these proteins, conjugated to gold nanoparticles and attached to screen-printed electrodes. We will use saliva sample for detecting the protein levels.

Results: We have synthesized gold nanoparticles and obtained preliminary spectrometric standardization results. We have isolated *Fusobacterium*-like bacteria as one of the isolates, and are currently confirming its identity. We are also standardizing the aptamer-gold nanoparticle-conjugated SPE for detection of bacterial proteins secreted in liquid growth medium. Once successful, we will test the applicability of the biosensor for detection of pathogen-secreted proteins in whole saliva of pathologically normal and patients with oral cancer, possibly of varying stages.

Conclusion: The development of a biosensor using pathogen as a biomarker may serve as a promising, cost-effective, non-invasive, rapid, and reliable approach for detection of oral cancer, potentially improving early detection and outcomes, especially in settings with limited resources.

Keywords: Biosensor, biomarker, early detection, oral cancer, oral health, pathogens

Investigating the binding potential of a novel peptide targeting platinum-resistant ovarian cancer

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Background: Peptides have emerged as potential therapeutic agents due to their ability to bind to specific receptors on tumour cells. Using phage display technology, a novel heptapeptide was identifiedtargeting platinum-resistant ovarian cancer. This study aims to identify the specific peptide receptors that are differentially expressed in resistant ovarian cancer populations and explore the functional effects of peptide-receptor interactions.

Materials and Methods: FACS and confocal microscopy were performed to assess peptide-receptor interactions. The impact of peptide binding on cell viability, adhesion, and migration will be evaluated using MTT, PI staining, Matrigel, and wound healing assays. In silico-target prediction and molecular docking are being conducted to identify putative receptors.

Results: The peptide binding was higher in early platinum-resistant (ER) cells compared to late-resistant(LR) and sensitive ovarian cancer cells. The binding was also significantly higher in tumour cells obtained from malignant ascites of High-Grade Serous Ovarian Cancer patients and the Patient-Derived Xenograft model. In silico analysis using the *Swiss-target prediction* tool indicated a 66.7% probability of the peptides binding to members of the GPCR (G-Protein Coupled Receptor) family. Among several GPCRs associated with ovarian cancer, the Endothelin Type A receptor was identified as a likely target, showing strong polar interactionsat the ligand-binding site.

Conclusion: This preliminary study suggests that the peptide has the potential to specifically bind to a subset of ovarian cancer cells. The ongoing investigation aims to identify the peptide-targeted putativereceptor(s) and assess the functional consequences of peptide-receptor interaction.

Keywords: Peptides, Platinum-resistant ovarian cancer, Peptide-receptor interaction, GPCR

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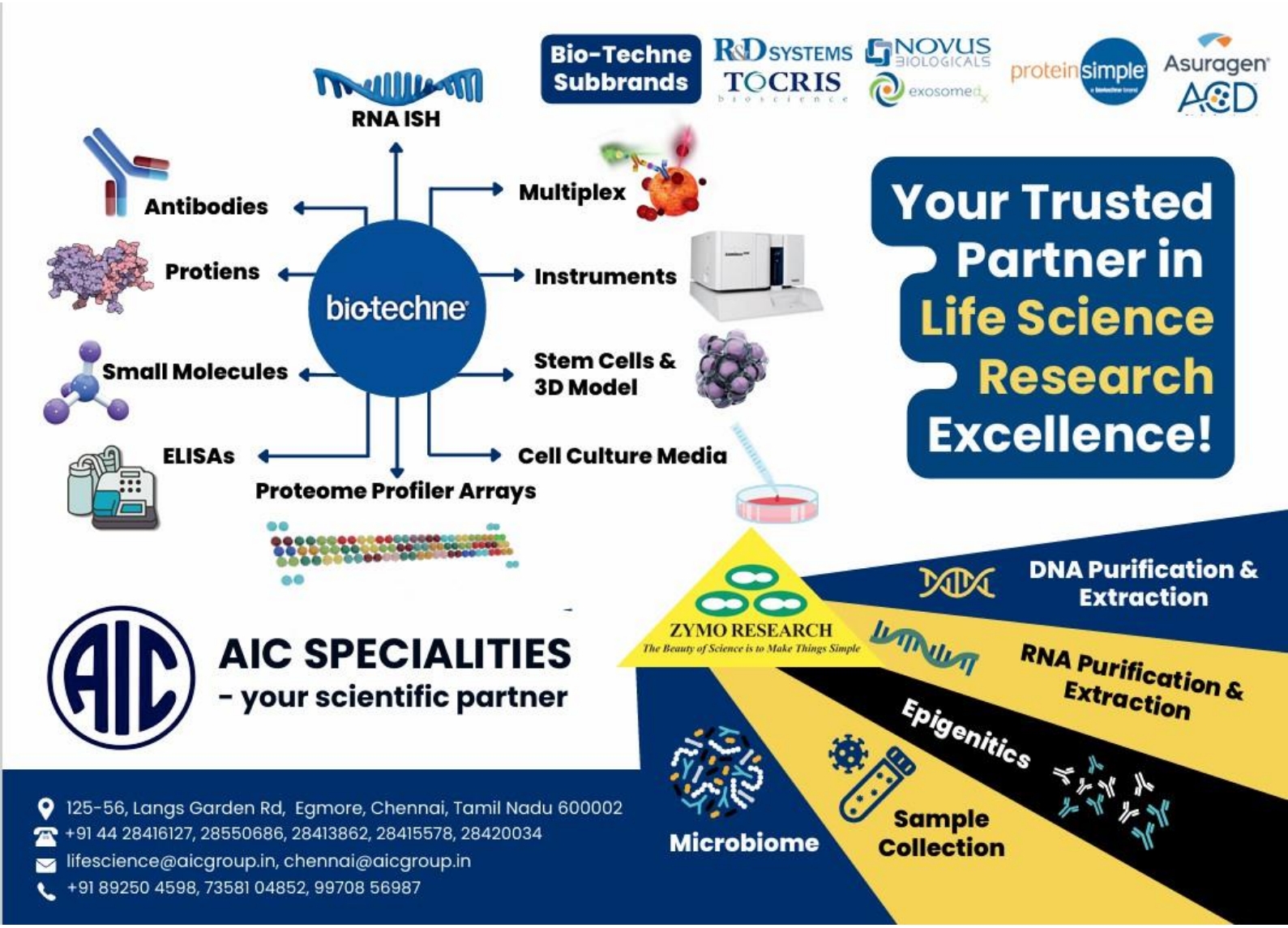

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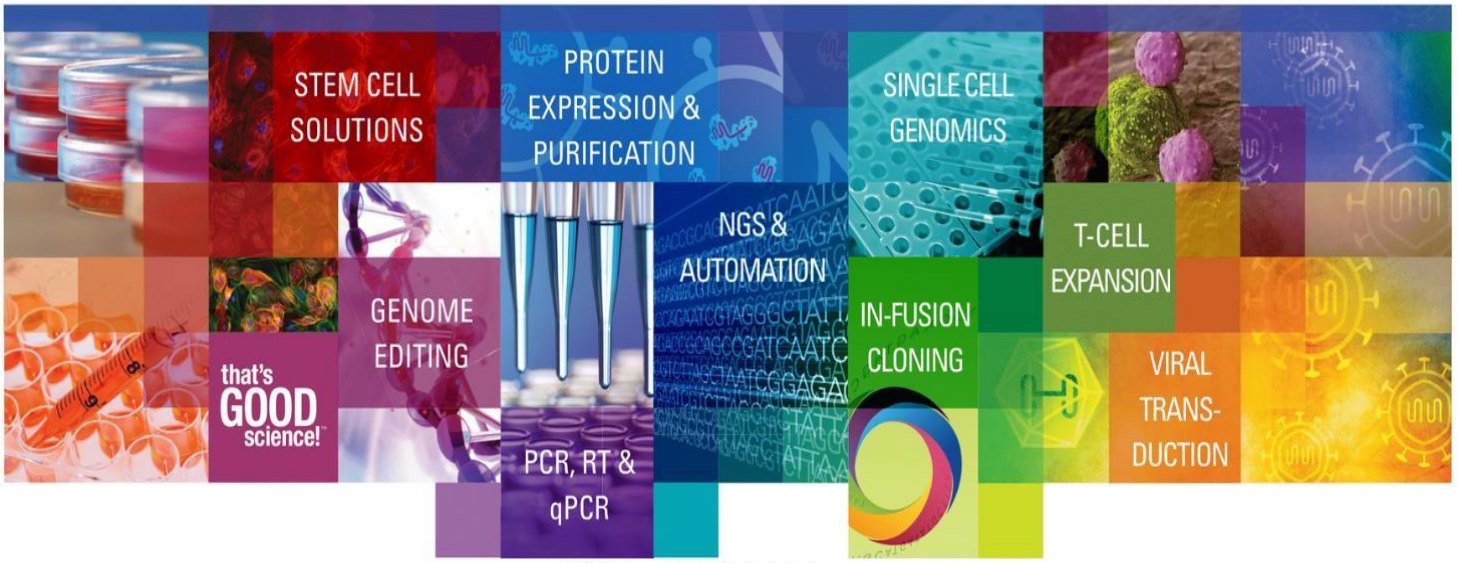

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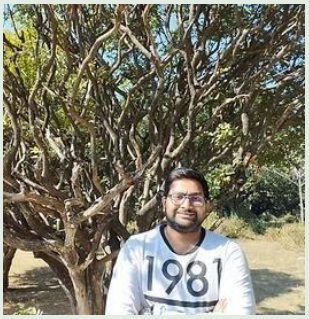

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