16th Young Investigators' Meeting 2024

ABSTRACT BOOK

IndiaBioscience

IISER Bhopal

IndiaBioscience

IndiaBioscience fills a unique niche in the ecosystem of the life sciences in India by being a catalyst to promote the change that affects the culture and practice of the field, through engagement with academia, government, and industry at various levels.

www.indiabioscience.org

ACKNOWLEDGEMENTS

IndiaBioscience and the organisers of YIM 2024 are thankful for the support they received from:

L S Shashidhara, Director, NCBS; IndiaBioscience Board Member
Gobardhan Das, Director, IISER Bhopal
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Rashna Bhandari, IndiaBioscience Board Member
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The Young Investigators' Meeting Series

Building a community of young Indian biologists.

The YIM series aims to build a vibrant community of biologists by allowing young Indian scientists from different regions and institutions to establish friendships, initiate collaborations, and learn from peer-to-peer mentoring.

The annual Young Investigators' Meeting (YIM) brings together exceptional young investigators and senior scientists, heads of institutes, and representatives from funding agencies for **four and a half days** of discussions and interactions focusing on science and careers in a broad range of disciplines of biology, as well as mentorship and networking.

Since its inception in 2009, the YIM has established its brand in the life science fraternity in India. The meeting creates a vibrant atmosphere for exchanging ideas and catalysing collaborations between life scientists in India. The YIM series also pairs Postdoctoral Fellows (PDFs) from India and abroad with Young Investigators (YIs) and senior scientists to promote new connections and facilitate a first-hand exchange on building and establishing a research group in India.

YIM 2024 will provide an opportunity for the participants to get a flavour of all the different components of this flagship meeting.

The meeting is divided into two parts: The first part is the three-day Young Investigators' Meeting, which will be attended by Young Investigators from all over India and Postdoctoral Fellows from across India and the world. The second part is the one-and-a-half-day Postdoctoral Satellite Meeting for the Postdoctoral Fellows at YIM 2024.

YIM 2024 will feature mentor talks by renowned scientists, special talks on a range of science topics, poster sessions, interactive workshops, icebreaker sessions, round table discussions and networking events, that focus on a wide range of subjects and issues, including starting and building an independent research career in India, contemporary conversations on funding for science in India, international funding opportunities for scientists in India, science education, science communication and outreach, and workshops on science journalism and research ethics.

The **Postdoctoral Satellite Meeting** at YIM 2024 will enable invited Postdoctoral fellows to learn about jobs in India and meet Directors/Vice-Chancellors of institutes and universities from across India. Although YIM makes an effort to facilitate job searches for Postdoctoral fellows, it is not a job fair. The meeting revolves around doing science in India and mentoring Young Investigators and Postdoctoral Fellows.

Please write to us at ***yim2024[at]indiabioscience[dot]org*** for queries.

YIM 2024 Organisers

Karishma Kaushik

Karishma is a physician-scientist who has led and been involved in a range of initiatives across the scientific landscape in India. After her MBBS and MD in Clinical Microbiology from the Armed Forces Medical College, Pune, Karishma moved to the US to pursue a PhD. She completed her PhD at the University of Texas at Austin and returned to India as a Ramalingaswami Re-entry Fellow. She ran her independent research group at Savitribai Phule Pune University from 2018-2023. In this new avatar as Executive Director, IndiaBioscience, she looks forward to expanding the impact of IndiaBioscience, by facilitating the scientific ecosystem across India and fostering partnerships between communities in India and across the world.

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Lipi Thukral

Lipi Thukral did her PhD from the University of Heidelberg, Germany and Postdoctoral research at the University of Southampton, UK. In 2012, she obtained the prestigious DST- INSPIRE Faculty fellowship and started working as a computational biologist at the CSIR - Institute of Genomics and Integrative Biology. She is the recipient of the CSIR- Young Scientist Award in Biological Sciences and, recently, the India Alliance Intermediate Fellowship supported by DBT and Wellcome Trust. At present, she is a Principal Scientist at IGIB and an AcSIR Associate Professor. Her research involves understanding how biomolecular contacts at the structural level especially protein-membrane interactions within autophagy drive autophagosome formation.

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Ragothaman M. Yennamalli

Ragothaman M. Yennamalli is a computational biologist at SASTRA Deemed to be University at Thanjavur, Tamil Nadu. He has a vast experience in the areas of predictive modelling and biomolecular simulation. After the completion of his PhD degree from Jawaharlal Nehru University, he worked as a postdoc at Iowa State University, University of Wisconsin-Madison, and Rice University, USA. In 2018, he was featured in the Early-Career Researcher series of Communications Biology journal. He is currently the chair of the publication committee of the International Society for Computational Biology. He has been a member of the Early Career Committee of the Biophysical Society, USA since 2018.

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Varun Chaudhary

Varun Chaudhary is a developmental biologist working at the Indian Institute of Science Education and Research (IISER) Bhopal, Madhya Pradesh. He uses *Drosophila* (fruit flies) as a model system to study the mechanisms of cell-cell communication and tissue growth. He did his PhD at the University of Sheffield, England, followed by a postdoc at the German Cancer Research Centre (DKFZ), Heidelberg, Germany. He established his lab in 2015 and received the Ramalingaswami Re-entry Fellowship in 2017.

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IndiaBioscience Team

Ankita is a science and technology (S&T) researcher and science communication practitioner in India. Originally trained as a lab-bench researcher, with a Bachelor's in Biomedical Sciences and Master's in Toxicology, she did her PhD in S&T communication from the National Institute of Science Communication and Policy Research (CSIR-NIScPR), New Delhi. After her master's, she worked as a Research Officer at CIB-RC, Faridabad in Regulatory Toxicology and later moved to Mohali, Punjab to work as a Junior Research Fellow to investigate hyperthermia-based treatment for Glioblastoma Multiforme (GBM). At IndiaBioscience, she takes care of the science communication vertical, where she aims to actively engage—online and offline—with networks of writers, scientists, educators, researchers, students and experts.

Ankita Rathore

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Program Manager - Science Communication

Arushi is a passionate and accomplished genome informatician with a background in genomics. She is pursuing her PhD at CSIR-IGIB, New Delhi, where she focuses on understanding the genomics of intellectual disabilities and has developed a strong foundation in scientific expertise. However, her intrinsic motivation to bridge the gap between scientists and the broader community has led her to explore opportunities beyond the laboratory, delving into the realm of science communication. With her new role as a Program Manager (Digital Initiatives) at IBS, she is enthusiastic about driving the organisation's digital initiatives forward.

Arushi Batra

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Program Manager - Digital Initiatives

Manjula holds a Master's degree in Microbiology and an MBA in Human Resource Management. She has been an integral part of the IndiaBioscience team since 2016, working closely with the life science community, optimising processes, and contributing to numerous projects. Currently, she leads the 'Community Building' initiative striving to find innovative ways to engage and expand the community. She manages projects like IndiaBioscience Outreach Grants (IOG) and expanding the life scientist (LS) database. She is also actively involved in our outreach activities, workshops, conferences, building resource materials and organising our flagship event - the Young Investigators' Meeting (YIM).

Manjula Harikrishna

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Rohini completed her PhD from the Department of Biosciences and Bioengineering, IIT Bombay. During her doctoral work, she developed an interest in science teaching and writing. She then switched to science education, as a post-doctoral fellow at the Homi Bhabha Centre for Science Education (HBCSE, TIFR) in Mumbai. Later, she worked with three different organizations involved in science communication and education. Rohini is also experienced in communicating science in the Marathi language. In her new role as an associate director, Rohini is excited to take on the new challenges in bolstering IndiaBioscience's efforts in bringing science and society closer. She currently manages the skill-building vertical and assists in other projects at IndiaBioscience.

Rohini Karandikar

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Associate Director

Shwetha graduated with an M.Com and joined IndiaBioscience in 2018. She manages the finances of all the initiatives at IndiaBioscience. She plays a key role in raising indents, evaluating vendor proposals and coordinating with the accounts and purchase departments at NCBS. She manages logistics including transportation, reimbursements, bill-processing and settlements. She also shoulders office administrative responsibilities such as maintaining records of hardware and equipment, posting jobs, grants and events on the IndiaBioscience website, and maintaining social media memberships among many other miscellaneous duties as needed. More recently, she leads the IndiaBioscience Jobs and Internships monthly newsletter.

Shwetha C

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Vijeta did her PhD in biophysics at the Centre for Cellular and Molecular Biology (CCMB), Hyderabad and postdoctoral research in molecular neuroscience at the Vollum Institute, Portland, Oregon, USA. Her strong interest in science communication and education drew her to IndiaBioscience, where she aims to grow the nationwide network of biology educators at the undergraduate level and showcase their experiences and opinions, and the latest innovations in pedagogy. She is also an associate editor of a bi-annual science magazine for school teachers called "i wonder...", published by Azim Premji University. The magazine presents basic science concepts in a new light through storytelling, classroom activities, interviews, and more. Through her contributions to the magazine, Vijeta hopes to reinvigorate science education in schools.

Vijeta Raghuram

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About IndiaBioscience

IndiaBioscience

IndiaBioscience is an organisation that fills a unique niche in the ecosystem of the life sciences in India, by being a catalyst to promote changes that affect the culture and practice of the field, through engagement with academia, government and industry at various levels. IndiaBioscience aims to increase the visibility of science in society, by being a hub for policy discussions, science communication, and as an aggregator of information

IndiaBioscience plays an administrative and organisational role in each year's YIM, but its engagement with the participants extends beyond the meeting. IndiaBioscience sets out to forge a long-standing bond with the YIM alumni to promote the development of their careers and aid the flourishing of their research groups. Through this sustained ripple effect, it hopes to create a meaningful and lasting impact on the research ecosystem in the life sciences in India.

www.indiabioscience.org

Engage with us

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Write for us.
Advertise jobs, events, and grants on our website

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IndiaBioscience Educators' Newsletter

IndiaBioscience Monthly Newsletter

IndiaBioscience Jobs & Internships Newsletter

International Grants Awareness Programme (iGAP) Newsletter

YIM Advisors

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Programme Schedule

The Programme Schedule may change as we approach closer to the meeting. Please visit the website of YIM 2024 for the most updated schedule.

11 March 2024

DAY 1: Young Investigators' Meeting 2024 (Courtyard by Marriott, Bhopal)
Moderator: Karishma Kaushik, IndiaBioscience

12:00 - 14:00	**Lunch | Registration** Check in to Courtyard by Marriott, Bhopal
14:00 - 14:15	**Welcome Note** L S Shashidhara, Board Member, IndiaBioscience
14:15 - 14:45	**Keynote address** Rajesh Gokhale, Secretary, Department of Biotechnology, GoI, New Delhi
14:45 - 15:00	**Engaging communities, enabling change** Karishma Kaushik, Executive Director, IndiaBioscience
15:00 - 15:30	**Seeking form and patterns in cancer; trials, twirls, and thrills** Ramray Bhat, Indian Institute of Science, Bengaluru
15:30 - 16:00	Tea | Coffee | Light refreshments
16:00 - 16:30	**Life science funding in India** Sanjay Mishra, Senior Advisor, Department of Biotechnology, GoI
16:30 - 16:45	**Digital footprint at YIM 2024** Arushi Batra, IndiaBioscience
16:45 - 17:30	**The icebreaker at YIM 2024** Ankita Rathore, Arushi Batra, Karishma Kaushik and Rohini Karandikar, IndiaBioscience
17:30 - 18:00	**My dog diaries and silver linings** Anindita Bhadra, Indian Institute of Science Education and Research Kolkata
18:00 - 18:30	**From a non-model organism to models and back: How to ignore misleading top-down strategies from funding agencies (EMBO Global Lecture Series)** Frederic Berger, Gregor Mendel Institute of Molecular Plant Biology GmbH, Austria
18:30 - 19:30	Networking mixer | Light refreshments
19:30 onwards	Dinner

12 March 2024

DAY 2: Young Investigators' Meeting 2024
Indian Institute of Science Education and Research Bhopal (IISER Bhopal)
Moderator: Varun Chaudhary, IISER Bhopal

08:30 - 10:00	**Travel to IISER Bhopal**
10:00 - 10:30	**Bridging boundaries: Surprises and triumphs in navigating interdisciplinary terrain** Abhijit Majumder, Indian Institute of Technology Bombay
10:30 - 11:00	**Advancements in microscopy imaging** Rishi Kant, Zeiss Technologies
11:00 - 11:30	Tea | Coffee | Light refreshments
11:30 - 12:15	**International funding for scientists in India** Sayam Sen Gupta, Alexander von Humboldt-Stiftung — 15 mins **International funding for scientists in India** Leonor Teles-Grilo Ruivo, The European Molecular Biology Organization — 15 mins **iGAP: How can YIs and PDFs leverage this program?** Rohini Karandikar, IndiaBioscience — 15 mins
12:15 - 12:30	**Move from CS2 building to Visitor Hostel**
12:30 - 13:00	**Poster session for 40 YIs**
13:00 - 14:00	Group photo | Lunch at IISER Bhopal
14:00 - 15:30	**Workshops at YIM 2024** ***Workshop for YIs*** Mini-workshop: 'How can YIs engage with science journalism in India' Dinsa Sachan and Shakoor Rather, Science Journalism Association of India (SJAI) ***Workshop for PDFs*** Mini-workshop: 'Research ethics for PDFs' Madhurima Kahali, Taylor and Francis
15:30 - 15:45	**Move from Visitor Hostel to CS2 building**
15:45 - 16:00	**Rediscovering school science** Vijeta Raghuram, IndiaBioscience
16:00 - 16:30	**Novel pedagogical practices for science educators** Tamralipta Patra, Azim Premji University, Bengaluru
16:30 - 17:00	Tea | Coffee | Light refreshments
17:00 - 17:30	**Wandering the landscapes of research and academia starting from the end of the world** Cesar A. Ramirez-Sarmiento, Pontificia Universidad Catolica de Chile
17:30 - 18:00	**Ask Us Anything (interactive panel): 'Starting and building a research group in India'** Abhijit Majumder (Indian Institute of Technology Bombay), Andrew Lynn (Jawaharlal Nehru University, New Delhi), Anindita Bhadra (Indian Institute of Science Education and Research Kolkata), VijayRaghavan, (Former PSA to the Government of India), Ramray Bhat (Indian Institute of Science, Bengaluru), Ritu Trivedi (CSIR-Central Drug Research Institute, Lucknow), Roop Mallik (Indian Institute of Technology Bombay) and Sunando Datta (Indian Institute of Science Education and Research Bhopal) Moderator: Varun Chaudhary, Indian Institute of Science Education and Research Bhopal
18:00 - 18:45	**Walking tour of IISER Bhopal** Ram Kumar Mishra, IISER Bhopal
18:45 - 21:15	Cultural program | Banquet dinner | Return to Courtyard by Marriott, Bhopal

13 March 2024

DAY 3: Young Investigators' Meeting 2024 (Courtyard by Marriott, Bhopal)
Moderator: Ragothaman Yennamalli, SASTRA Deemed to be University, Thanjavur

09:00 - 09:30	**Membrane protein barrels: Biophysical and functional studies** Mahalakshmi Radhakrishnan, Indian Institute of Science Education and Research Bhopal
09:30 - 10:00	**Sequences, structures, systems and data science: My journey through the evolution of bioinformatics** Andrew Lynn, Jawaharlal Nehru University, New Delhi
10:00 - 10:15	**Science communication at IndiaBioscience** Ankita Rathore, IndiaBioscience
10:15 - 10:30	**IndiaBioscience Outreach Grants at 5 years** Manjula Harikrishna, IndiaBioscience
10:30 - 11:00	**CARBON Exhibition-in-a-Box** Shelwyn James and Ahalya Acharya, Science Gallery Bengaluru
11:00 - 11:30	Group photo | Tea | Coffee | Light refreshments
11.30 - 12:00	**Aspiring minds: Journey as an academic scientist pioneering meaningful innovations in bone health** Ritu Trivedi, CSIR-Central Drug Research Institute, Lucknow
12:00 - 12:30	**Bringing biotech and public health under one umbrella: Breaking barriers** Senjuti Saha, Child Health Research Foundation, Bangladesh
12:30 - 13:00	**The road towards making research human-relevant: Status quo and challenges in India** Surat Parvatam, Humane Society International
13:00 - 14:00	Lunch
14:00 - 14:30	**Design thinking for life science research environments** Vikash Kumar, Shiv Nadar University, Greater Noida
14:30 - 15:00	**American Chemical Society (India): Enabling science for everyone** Ajay Kumar Jha, American Chemical Society (India)
15:00 - 15:30	**Exploring perspectives: The influence of Large Language Models (LLMs) in research and publishing** Neelanjan Sinha, TNQ Technologies
15:30 - 16:00	**Power of translation in science: Inventions to profitable technologies** Ramjee Pallela, Atal Incubation Centre—Centre for Cellular and Molecular Biology, Hyderabad
16:00 - 16:30	Tea | Coffee | Light refreshments
16:30 - 17:00	**YIM: 15 years on** Ron Vale, Janelia Research Campus, HHMI, US
17:00 - 17:15	**Summary of YIM 2024 and the year ahead for IndiaBioscience** Karishma Kaushik and Shwetha C, IndiaBioscience
17:15 - 17:30	**Closing remarks** Roop Mallik, Board Member, IndiaBioscience
17:30 - 18:30	**Free time**
18:30 - 19:00	**YI-PDF mixer with institutional representatives** (light refreshments)
19:00 onwards	Dinner

14 March 2024

DAY 4: PDF Satellite Meeting (Courtyard by Marriott, Bhopal)
Moderator: Karishma Kaushik, IndiaBioscience

10:00 - 10:10	**Introduction to the PDF Satellite Meeting** L S Shashidhara, National Centre for Biological Sciences, Bengaluru
10:10 - 11:10	**Institutional talks session 1** L S Shashidhara (National Centre for Biological Sciences, Bengaluru), Aprotim Mazumder (Tata Institute of Fundamental Research Hyderabad), Mohan Wani (National Centre for Cell Science, Pune), Usha Vijayraghavan (Indian Institute of Science, Bengaluru) and Vinay K Nandicoori (CSIR-Centre for Cellular & Molecular Biology, Hyderabad)
11:10 - 11:40	Group photo | Tea | Coffee | Light refreshments
11:40 - 12:30	**PDF talks session 1** 10 PDF talks—5 mins each
12:30 - 13:30	**Institutional talks session 2** Anil Kumar Tripathi (Banaras Hindu University, Varanasi), Divya Uma (Azim Premji University, Bengaluru), Maneesha Inamdar (Institute for Stem Cell Science and Regenerative Medicine, Bengaluru), Rakesh Mishra (Tata Institute for Genetics and Society, Bengaluru) and Swaminathan S (SASTRA Deemed to be University, Thanjavur)
13:30 - 14:30	Lunch
14:30 - 15:20	**PDF talks session 2** 10 PDF talks—5 mins each
15:20 - 16:20	**Institutional talks session 3** Deepak Sharma, (CSIR- Institute of Microbial Technology, Chandigarh), Prasanna Venkatraman (ACTREC—Tata Memorial Centre, Navi Mumbai), Prashant K Dhakephalkar (Agharkar Research Institute, Pune), Murali Dharan Bashyam (Centre for DNA Fingerprinting and Diagnostics, Hyderabad) and Sanjeev Galande (Shiv Nadar University, Greater Noida)
16:20 - 17:10	**PDF talks session 3** 10 PDF talks—5 mins each
17:10 - 17:40	Tea | Coffee | Light refreshments
17:40 - 19:10	**Live interactions - PDFs and institutional heads on start up funding and faculty fellowships in life science in India**
19:30 onwards	Dinner and informal discussion

15 March 2024

DAY 5: PDF Satellite Meeting (Courtyard by Marriott, Bhopal)
Moderator: Rohini Karandikar, IndiaBioscience

10:00 - 11:00	**Institutional talks session 4** Anurag Agrawal (Ashoka University, Sonepat), Balaji P V (Indian Institute of Technology Bombay), Gobardhan Das (Indian Institute of Science Education and Research Bhopal), Prasanta K Panigrahi (Indian Institute of Science Education and Research Kolkata), Sagar Sengupta (National Institute of Biomedical Genomics, Kalyani)
11:00-11:30	**Tea | Coffee | Light refreshments**
11:30-12:20	**PDF talks session 4** 10 PDF talks—5 mins each
12:20 - 13:20	**Live interactions - PDFs and institutional heads on project administration and grant management in life science in India**
13:20 - 13:30	**Closing remarks to the PDF Satellite Meeting** Rashna Bhandari, Board Member, IndiaBioscience
13:30 onwards	**End of PDF Satellite Meeting followed by Lunch**

Supporters of YIM 2024

ACS INDIA, NEW DELHI

ACS is a non-profit scientific organisation with more than 140 years of experience; they are a champion for chemistry, its practitioners, and the global community of members.

ATAL INCUBATION CENTRE-CENTRE FOR CELLULAR & MOLECULAR BIOLOGY

Atal Incubation Centre – Centre for Cellular and Molecular Biology (AIC-CCMB) is a premier incubator focused on promoting entrepreneurship in life sciences, supporting startups in Health, Pharmaceuticals and Biotechnology. CSIR-CCMB is one of the first 10 institutes to establish the Atal Incubation Centre under the Atal Innovation Mission (AIM) of National Institution for Transforming India (NITI Aayog).

ALEXANDER VON HUMBOLDT FOUNDATION, GERMANY

The Alexander von Humboldt Foundation is a renowned institution fostering international academic cooperation, particularly in the sciences. Named after the eminent naturalist and explorer Alexander von Humboldt, the foundation provides fellowships and grants to outstanding researchers worldwide, facilitating collaborations, promoting academic exchange, and supporting cutting-edge research across disciplines. It catalyzes innovation and collaboration, nurturing a global network of scholars and contributing significantly to advancements in science and knowledge-sharing on a global scale.

ASHOKA UNIVERSITY, NEW DELHI

Ashoka University, a pioneering institution in India, offers a multidisciplinary education focusing on liberal arts and sciences. It is renowned for fostering critical thinking and leadership while emphasising holistic learning. By encouraging diverse perspectives and societal contributions, Ashoka cultivates innovative thinkers poised to tackle global challenges through academic excellence and a commitment to social impact, creating a new generation of thoughtful leaders adept at addressing complex issues.

AZIM PREMJI UNIVERSITY, BENGALURU

Azim Premji University in Bengaluru, India, stands as a distinguished institution dedicated to fostering social change through education and research. Renowned for its commitment to social development and inclusive education, the university offers programs in various disciplines, focusing on the intersection of social sciences, humanities, and development. With a strong emphasis on practical learning and community engagement, Azim Premji University equips students with the tools to critically analyse societal challenges and drive meaningful change, making it a hub for social impact and transformative education in India.

DEPARTMENT OF BIOTECHNOLOGY, GOVT. OF INDIA

This Department set up in 1986, gave a new impetus to the development of the field of modern biology and biotechnology in India. In more than a decade of its existence, the department has promoted and accelerated the pace of development of biotechnology in the country. DBT is the largest supporter of both YIM and IndiaBioscience.

Supporters of YIM 2024

DBT/ WELLCOME TRUST INDIA ALLIANCE, HYDERABAD

DBT/Wellcome Trust India Alliance (India Alliance) is an independent, dynamic a public charity that funds research in health and biomedical sciences in India. India Alliance invests in transformative ideas and supportive research ecosystems to advance discovery and innovation to improve health and well-being. India Alliance stands for diversity, inclusivity, and transparency in science and works to facilitate the engagement of science with society. India Alliance is funded by the Department of Biotechnology (DBT), the Government of India, and the Wellcome Trust, United Kingdom.

EUROPEAN MOLECULAR BIOLOGY ORGANIZATION (EMBO), GERMANY

EMBO is an organisation of more than 1,900 leading researchers that promotes excellence in the life sciences in Europe and beyond. The major goals of the organisation are to support talented researchers at all stages of their careers, stimulate the exchange of scientific information, and help build a research environment where scientists can achieve their best work. The EMBO communities are global networks of top-level scientists at various stages of their careers. They give privileged access, particularly to young researchers, to cutting-edge science and the opportunity to build international contacts.

HUMANE SOCIETY INTERNATIONAL (HSI), HYDERABAD

Humane Society International (HSI) and its affiliates together constitute the world's largest force for animal protection, working lawfully and professionally, building relationships with government authorities and elected officials, business leaders, and other decision-makers to identify and implement workable solutions to animal welfare concerns. HSI/India was formally incorporated in 2012, and today works toward eradicating rabies through humane street dog population management, capacity building for Indian animal welfare organizations, strengthening farm animal and wildlife protections, and minimising animal testing. In partnership with HSI's global team of scientists and policy experts, they advocate for an accelerated transition to a "21st-century" paradigm in toxicology and health research based on human biology, non-animal tools and technologies.

INDIAN INSTITUTE OF SCIENCE EDUCATION AND RESEARCH (IISER) BHOPAL

The Indian Institute of Science Education and Research (IISER) Bhopal, established by the Ministry of Education, Government of India in 2008, stands as a premier autonomous research institute in Bhauri, Bhopal district, Madhya Pradesh. It excels in fostering excellence in science education and research, emphasising both undergraduate and graduate-level fundamental science education. Renowned for its rigorous academic programs, state-of-the-art facilities, and commitment to innovation, IISER Bhopal provides a dynamic environment where students engage in cutting-edge research across various scientific disciplines.

PREMAS LIFE SCIENCES PVT. LTD., NEW DELHI

Premas Life Sciences (PLS) is a young, dynamic, and focused organization introducing game-changing niche technologies in Genomics, Cell Biology, and Biopharma to boost innovative research and diagnostics in India. They are also the knowledge partners to several reputed research institutes and hospitals, enabling them to set up core genomics facilities with complete support at all fronts.

Supporters of YIM 2024

SHIV NADAR UNIVERSITY, NEW DELHI

Shiv Nadar University, Delhi NCR is a multidisciplinary, research-focused, and student-centric University offering a full range of academic programs at the undergraduate, postgraduate, and doctoral levels. The University's goal is to become internationally recognised for the quality of its research and creative endeavours and their applicability to improving quality of life, generating new insights, and expanding the boundaries of human knowledge creativity. Committed to excellence in teaching, research and service, the University aims to serve the higher education needs of India and the world beyond.

TATA INSTITUTE FOR GENETICS AND SOCIETY (TIGS), BENGALURU

The UC San Diego campus has been fortunate to receive a path-breaking gift from the Tata Trust in India to create the Tata Institute for Genetics and Society (TIGS). TIGS will have operations on the UC San Diego (TIGS-UCSD) campus and at inStem, within the campus of the National Center for Biological Sciences, in Bangalore, India (TIGS-India).

TAYLOR & FRANCIS GROUP, UNITED KINGDOM

For more than two centuries Taylor & Francis has been committed to the highest quality scholarly publishing, and this remains their goal today. Their purpose is to foster human progress through knowledge – something they've been doing since the Enlightenment. They aim to promote a positive future for everyone through their work.

TNQ TECHNOLOGIES, CHENNAI

TNQ is a publishing technology and services company based in Chennai, India. Founded in 1998, TNQ serves some of the world leaders in STM publishing - like Elsevier, Wolters Kluwer, Royal Society of Chemistry - across time zones from Australia to North America, specialising in Roman script composition and XML-first production processes.

V.K. TRADERS

V.K. Traders, initially a distributor of chemicals and glassware, has evolved into a specialised provider of Life Sciences, Diagnostics, and Turn Key Services over 25 years. With headquarters in Bhopal and a branch in Indore, the team serves customers across Madhya Pradesh, partnering with industry leaders like Merck Life Sciences and Thermo Fisher to deliver top-notch solutions and swift after-sales support. Customer satisfaction is paramount, with a focus on providing choices, expertise, and innovation to build enduring relationships and empower customers.

ZEISS, BENGALURU

ZEISS is an internationally leading technology enterprise operating in the optics and optoelectronics industries. As a company wholly owned by a foundation, ZEISS is rooted in and committed to responsibility in all its activities. As the pioneers of scientific optics, they continue to challenge the limits of human imagination. ZEISS in India is headquartered in Bengaluru and is present in the fields of Industrial Quality Solutions, Research Microscopy Solutions, Medical Technology, Vision Care, and Sports and Cine Optics.

Keynote Talk

Rajesh Gokhale

Secretary,
Department of Biotechnology, GOI
Email: secy@dbt.nic.in

Special Talks

Rishi Kant

Advancements in microscopy imaging

National Manager Sales,
Zeiss Technologies

Sanjay Mishra

Life science funding in India

Senior Advisor,
Department of Biotechnology, GoI

Surat Parvatam

The road towards making research human-relevant: Status quo and challenges in India

Senior Strategist, Research and Regulatory Science,
Humane Society International

Tamralipta Patra

Novel pedagogical practices for science educators

Faculty (Science Education),
Azim Premji University, Bengaluru

Vikash Kumar

Design thinking for life science research environments

Assistant Professor, School of Humanities and Social Sciences,
Shiv Nadar University, Greater Noida

Mentor Talks

Abhijit Majumder
Bridging boundaries: Surprises and triumphs in navigating interdisciplinary terrain

Andrew Lynn
Sequences, structures, systems and data science: My journey through the evolution of bioinformatics

Anindita Bhadra
My dog diaries and silver linings

Cesar A. Ramirez-Sarmiento (EMBO Global Lecture Series)
Wandering the landscapes of research and academia starting from the end of the world

Frederic Berger (EMBO Global Lecture Series)
From a non-model organism to models and back: How to ignore misleading top-down strategies from funding agencies

Mahalakshmi Radhakrishnan
Membrane protein barrels: Biophysical and functional studies

Ramray Bhat
Seeking form and patterns in cancer; trials, twirls, and thrills

Ritu Trivedi
Aspiring minds: Journey as an academic scientist pioneering meaningful innovations in bone health

Senjuti Saha
Bringing biotech and public health under one umbrella: Breaking barriers

Abhijit Majumder

Indian Institute of Technology Bombay
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Bridging boundaries: Surprises and triumphs in navigating interdisciplinary terrain

Abstract

To me, research is akin to a treasure hunt where you don't know a priori if the treasure is even present. The challenges intensify when you decide to explore an unfamiliar terrain. In the past decade, while leading my independent lab, I have frequently encountered a common question from research scholars: "Should I transition to a more interdisciplinary research field?" Unfortunately, the answer isn't a simple yes or no. In this talk, my aim is to address this question by drawing from my personal journey, acknowledging mistakes, and distilling lessons learned from others.

The central focus of my research group revolves around mechanobiology and microfluidics, seamlessly integrating principles from chemical engineering, physics, material science, and biology. It's a journey that necessitates the adept wearing of different hats. Using the lens of successfully completed projects, I will delve into the inherent challenges of interdisciplinary research for both scholars and principal investigators. Additionally, I will discuss strategies to navigate these challenges and underscore the associated rewards.

Andrew Lynn

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Website: cdri.res.in/1603.aspx?id=1603

Sequences, structures, systems and data science: My journey through the evolution of bioinformatics

Abstract

India's Biotechnology program and Information Technology revolution entered their log growth phase at the time of economic liberalisation in the early 1990s. I was fortunate to start my research career at this time at Jawaharlal Nehru University in an area that was in the confluence of both. Computers in Life Science laboratories were first used to analyse the data required for determining protein structures, and to access digital records of DNA and protein sequences and perform rudimentary sequence analysis at specialised Bioinformatics Centers established at institutions in the pre-internet age. By the turn of the century, with the internet established, access to information stored locally was rapidly becoming redundant, and the need of these centres was to shift to educational and research objectives. Cyberinfrastructure for the life sciences, and the need to look at multivariate datasets through a systems approach - both with the data from "omics" experiments and analytical models now dominated the field. Opportunities that arose from distributed computing and networked teams borrowed from the Open Source software world was one major accomplishment through the Open Source Drug Discovery program of CSIR. Basic research problems that were earlier intractable due to the lack of sufficient computing power were also now reaching the desktop with the current flavour being driven by machine learning methods that power artificial intelligence applications in the biomedical field. This talk will cover my own contributions to this evolution through the development of computer infrastructure, methods and applications.

Anindita Bhadra

Indian Institute of Science, Bengaluru
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My dog diaries and silver linings

Abstract

I am a behavioural biologist, working on the behavioural ecology of free-ranging dogs in India. I obtained my PhD from the Centre for Ecological Sciences, IISc, working on wasp politics. My son was born during my PhD, and I made a conscious decision to not go abroad for the usual postdoctoral stint. I started my journey as an independent researcher in 2009, when I established The Dog Lab at IISER Kolkata. It has been an amazing journey of nearly 15 years since then, peeping into the private lives of dogs on streets, learning to manoeuvre through the winding roads of academia and realising my dream of teaching. When I began, nobody really took research on stray dogs seriously. Today, we are considered pioneers for laying down the path for researching free-ranging dogs, and multiple research groups across the world are following in our footsteps. There have been bottlenecks, barriers, and major setbacks in the journey, but on the whole, it has been a highly rewarding experience. I will speak about this journey, with some glimpses into our research and I hope this will inspire some young people, especially women, to pave their own paths.

Cesar A. Ramirez-Sarmiento

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Wandering the landscapes of research and academia starting from the end of the world (EMBO Global Lecture Series)

Abstract

It was during the last years of my undergraduate program that I found out I wanted to be a protein scientist. It happened after a random encounter at a conference with one of my best friends from the University, who was delivering a poster presentation about how substrate specificity was determined in a set of archaeal glucokinases using a combination of enzyme kinetics, molecular docking, and molecular dynamics.

Several years later, my research group and I have been focusing on understanding the folding-function-evolution relationships of proteins of biomedical and biotechnological interests. On the one hand, we study metamorphic proteins, which switch their structures to encode different functions and constitute prototypical models to understand the emergence of novel protein folds in nature. On the other hand, we work on the discovery, characterisation and engineering of enzymes that hydrolyse PET, a widely used plastic that accumulates as waste in landfills and natural environments at similar rates to its production.

But what happened in between? I will tell you about the decisions, risks, chances, and wholesome encounters – many of which happened during my PhD – that enabled me to delve in the realm of protein biophysics, biochemistry, and bioinformatics. I will also tell you why I decided to work on metamorphic proteins and plastic-degrading enzymes, how the research skills that my research group and I have acquired are allowing us to connect with peers and do research beyond protein science, and how we are propelling our careers as scientific researchers from the southernmost country in the world.

Frederic Berger

Gregor Mendel Institute of Molecular Plant Biology GmbH, Austria
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From a non-model organism to models and back: How to ignore misleading top-down strategies from funding agencies (EMBO Global Lecture Series)

Abstract

What are the favoured trajectories to become PI? This seminar will illustrate how one may choose non-model organisms and venture outside of Cambridge and Boston to train to become a curiosity-driven group leader.

Starting my PhD with a failed PhD project on cell polarity reoriented my scientific interest in cell fate. This theme was pursued during my post-doc this time using the well-established model organism Arabidopsis, which remained the main model in my lab for a decade.

My lab gradually moved its focus to chromatin and epigenetics and now explores this theme using a variety of organisms from yeast to plants. I do hope that this journey will expand to explore the origins of chromatin using archaea and synthetic approaches in bacteria and yeast.

Various topics regarding why certain decisions were made in terms of places, hiring and career moves will be discussed.

Mahalakshmi Radhakrishnan

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Website: bio.iiserb.ac.in/faculty_profile.php?id=NA==&lname=bWFoYQ==

Membrane protein barrels: Biophysical and functional studies

Abstract

Human mitochondria possess three unique β-barrel membrane protein channels that regulate protein assembly and transport of biomolecules (from proteins to ions) across the outer membrane (OMM). These are the core translocase protein Tom40 of the Translocase of the Outer Mitochondrial Membrane (TOM), the three metabolite flux voltage-dependent anion channels (VDACs 1–3), and Sam50 chaperone of the Sorting and Assembly Machinery (SAM). Of these three proteins, Sam50 shares evolutionary ancestry with BamA of the β-Barrel Assembly Machinery (BAM) found in the outer membrane of Gram-negative bacteria. Both Sam50 and BamA are 16–stranded β-barrels. Tom40 and VDACs have no bacterial ancestry, form structurally unique 19–stranded β-barrels with a regulator N-terminal helix. All three β- barrels (Tom40, VDAC, Sam50) are indispensable for mitostasis, and regulating mitoptosis. Under adverse cellular conditions, these proteins are specifically implicated in interaction with α- synuclein, Aβ42, tau, Parkin, and tubulin, affecting muscular and neuronal function and triggering the onset of neuropathies. Despite their physiological relevance, and involvement in human pathologies, we have limited knowledge of how these proteins are assembled in the mitochondrial membrane, and what molecular factors regulate their myriad of functions in the cell. Our studies, using biophysical, biochemical, and functional approaches, have bridged the knowledge gap surrounding these proteins, allowing us to develop targeted peptidomimetics for neurodegenerative diseases caused by mitochondrial disorders.

Ramray Bhat

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Seeking form and patterns in cancer; trials, twirls, and thrills

Abstract

Cancer at its simplest can be described as a disease in which cells acquire mutations that disrupt mechanisms regulating their proliferative and mobile capacities. This results in afflicted tissues and organs losing their characteristic pattern, which essentially is what is used by the pathologist for diagnosis of the disease. However, is the 'grammar' of morphology and organisation truly lost in cancer? is it possible to observe new multicellular organisation as the disease progresses? If so, can we use this knowledge to devise novel therapeutic strategies? Such questions have motivated me to develop a research program around them. Mostly aided, and sometimes impeded, by the vagaries of the research milieu in India, we have managed to make interesting discoveries on what may be called 'rogue morphogenesis': studying novel rules of interactions between cancer cells, non-cancerous cells and their microenvironment that helps the disease spread to different parts of the body. These observations were possible only through an intensely interdisciplinary approach that combined classical cell and molecular biology with multiscale computer modelling, physical conceptualisation and engineering techniques. In addition to discussing these observations and the future directions of my group's research, I will also share my experiences with research funding and attempts to juggle time between teaching, research and administrative obligations.

Ritu Trivedi

CSIR-Central Drug Research Institute, Lucknow
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Website: cdri.res.in/1603.aspx?id=1603

Aspiring minds: Journey as an academic scientist pioneering meaningful innovations in bone health

Abstract

Trivedi's impactful journey as an academic scientist in the realm of meaningful technologies for bone health (one for accelerating fracture healing by the name "REUNION" and the other dedicated to addressing osteoarthritis by the name "JOINT FRESH") offers a profound source of inspiration for young students venturing into the field of science. Her relentless pursuit of answers to pivotal questions and commitment to creating solutions that truly matter serve as a beacon of motivation.

The narrative emphasises that innovation isn't just about groundbreaking ideas but is, at its core, a collaborative effort involving people. This insight can encourage young minds to value teamwork, diverse perspectives, and the collective power of a dedicated community.

The acknowledgement of the challenges posed by the rapid pace of technological evolution instils a sense of urgency and excitement for innovation. Dr. Trivedi's story encourages students to view these challenges not as obstacles but as opportunities for growth and discovery.

Furthermore, the metaphor of the light bulb symbolises the transformative potential inherent in each individual's ideas. This metaphorical "light bulb moment" is something every student can aspire to and is a reminder that their unique contributions can illuminate new pathways in science.

In essence, Dr. Trivedi's narrative inspires young students to approach their scientific pursuits with purpose, collaboration, and an unwavering belief in the meaningful impact they can make on the world through their scientific endeavours.

Senjuti Saha

Child Health Research Foundation, Bangladesh
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Bringing biotech and public health under one umbrella: Breaking barriers

Abstract

My transition from Canada to Bangladesh marked the beginning of a scientific journey characterised by challenges, achievements, and continuous learning, demanding nonstop grit and resilience. The journey has led to the establishment of a productive genomics lab of the country, dedicated to bridging the gap between biotechnology and public health in tackling diseases endemic to South Asia. Among my team's notable scientific accomplishments is the development of Paratype, a tool for the precise genotyping of *Salmonella* Paratyphi A, significantly enhancing our understanding of bacterial pathogenesis on a global scale. Our team's extensive genomic sequencing efforts, particularly with *Salmonella* Typhi and *Klebsiella pneumoniae*, have been pivotal in better understanding the complex mechanisms of antimicrobial resistance. Sequencing of over 6000 diverse pathogens, including bacteria, viruses, and fungi, has led to the creation of an extensive pathogen atlas, focusing on pediatric diseases prevalent in the region. This comprehensive database not only propels scientific discovery but also serves as an invaluable resource for the international research community. As our team continues to grow and evolve, we face new challenges and opportunities for growth, reinforcing our commitment to science. The journey is not getting any easier. However, as I realise the crucial role of scientists from the global south in driving innovation and developing localised solutions to address global health challenges, it definitely gets more rewarding, and my determination gets stronger.

Spotlight Talks

American Chemical Society (India): Enabling science for everyone

Ajay Kumar Jha

American Chemical Society (India)
Email: ajha@acs-i.org

Exploring perspectives: The influence of Large Language Models (LLMs) in research and publishing

Neelanjan Sinha

TNQ Technologies
Email: neelanjan.sinha@tnqsoftware.co.in

Power of translation in science: Inventions to profitable technologies

Ramjee Pallela

Atal Incubation Centre—Centre for Cellular and Molecular Biology, Hyderabad
Email: ramjee@ccmb.res.in

International funding for scientists in India

Sayam Sen Gupta

Alexander von Humboldt-Stiftung (AvH)
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Leonor Teles-Grilo Ruivo

The European Molecular Biology Organization (EMBO)
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Science Exhibit

CARBON Exhibition-in-a-Box

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Science Gallery Bengaluru
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Shelwyn James
Science Gallery Bengaluru
Email: shelwyn.james@bengaluru.sciencegallery.com

Workshops

Mini-workshop 1: How can YIs engage with science journalism in India

Workshop for YIs

Dinsa Sachan
Science Journalism Association of India (SJAI)
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Shakoor Rather
Science Journalism Association of India (SJAI)
Email: amanshakoor@gmail.com

Mini-workshop 2: Research ethics for PDFs

Workshop for PDFs

Madhurima Kahali
Taylor and Francis
Email: madhurima.kahali@tandfindia.com

Panel Discussion

Ask Us Anything (interactive panel)

Starting and building a research group in India

Moderator: **Varun Chaudhary**

Indian Institute of Science Education and Research Bhopal

Abhijit Majumder
Indian Institute of Technology Bombay
Email: abhijitm@iitb.ac.in

Andrew Lynn
Jawaharlal Nehru University, New Delhi
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Anindita Bhadra
Indian Institute of Science Education and Research Kolkata
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K. Vijayraghavan
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Roop Mallik
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Sunando Datta
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Institutional Heads and Representatives

Each year, representatives from various institutions across India attend the YIM, particularly the Postdoctoral Fellows' Satellite Meeting and give talks about their institutes. Listed below are the institutions and representatives at YIM 2024.

Ashoka University,
Sonipat

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Pune

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Azim Premji University,
Bengaluru

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Banaras Hindu University,
Varanasi

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Professor, School of Biotechnology
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CSIR-Centre for Cellular & Molecular Biology (CCMB), Hyderabad

VINAY K. NANDICOORI
Director
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Institutional Heads and Representatives

CSIR- Institute of Microbial Technology (IMTECH), Chandigarh

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Principal Scientist
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Indian Institute of Science (IISc), Bengaluru

USHA VIJAYRAGHAVAN

Dean, Biological Sciences Division
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Indian Institute of Science Education and Research Kolkata (IISERK)

PRASANTA K PANIGRAHI

Professor, Department of Biological Sciences
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Indian Institute of Science Education and Research Bhopal (IISERB)

GOBARDHAN DAS

Director
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Institute for Stem Cell Science and Regenerative Medicine (DBT-InStem), Bengaluru

MANEESHA INAMDAR

Director
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Indian Institute of Technology Bombay (IITB)

BALAJI P V

Professor, Department of Biosciences and Bioengineering
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Institutional Heads and Representatives

Each year, representatives from various institutions across India attend the YIM, particularly the Postdoctoral Fellows' Satellite Meeting and give talks about their institutes. Listed below are the institutions and representatives at YIM 2024.

National Centre for Biological Sciences (NCBS), Bengaluru

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Director
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National Centre for Cell Science (NCCS), Pune

MOHAN WANI
Director
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National Institute of Biomedical Genomics (NIBMG), Kalyani

SAGAR SENGUPTA
Director
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SASTRA Deemed to be University, Thanjavur

SWAMINATHAN S
Dean, Planning & Development
Director - CeNTAB
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Shiv Nadar University, Greater Noida

SANJEEV GALANDE
Dean, School of Natural Sciences
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Tata Institute of Fundamental Research (TIFR), Hyderabad

APROTIM MAZUMDER
Associate Professor
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Institutional Heads and Representatives

Tata Institute for Genetics and Society (TIGS), Bengaluru

RAKESH MISHRA

Director
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Tata Memorial Centre - Advanced Centre for Treatment, Research and Education in Cancer (ACTREC), TMC, Navi Mumbai

PRASANNA VENKATRAMAN

Principal Investigator
Email: vprasanna@actrec.gov.in

Young Investigators at YIM2024

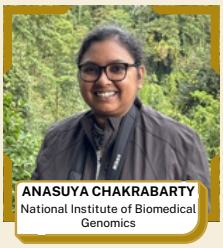
ABHISHEK DEY
National Institute of Pharmaceutical Education and Research (NIPER)- Raebareli

ABHISHEK SUBRAMANIAN
Indian Institute of Technology Hyderabad

AJAY TIJORE
Indian Institute of Science

AMIT RANJAN
TNJFU- Institute of Fisheries post graduate studies

ANANNYA BANDYOPADHYAY
University of Delhi



ANASUYA CHAKRABARTY
National Institute of Biomedical Genomics

ATANU BANERJEE
Amity University Haryana

CHARUKESI RAJULU
JSS Academy of Higher Education & Research

DEBANJAN MUKHOPADHYAY
Presidency University

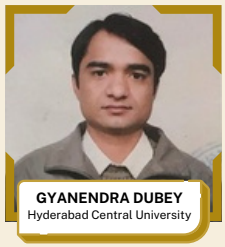
DEVESH BHIMSARIA
Indian Institute of Technology Roorkee

DHANJAI
University of Allahabad

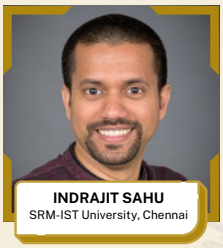
DHANAWANTARI L SINGHA
Rabindranath Tagore University

GAJANAN KENDRE
National Institute of Technology Rourkela (NITR)

GAURAV SHARMA
Indian Institute of Technology Hyderabad



GYANENDRA DUBEY
Hyderabad Central University



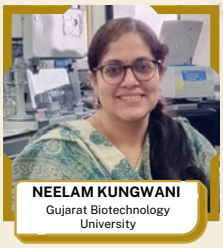
INDRAJIT SAHU
SRM-IST University, Chennai

INDUMATHI SATHISARAN
National Institute of Technology Calicut

JANVIE MANHAS
VMMC & Safdarjung Hospital

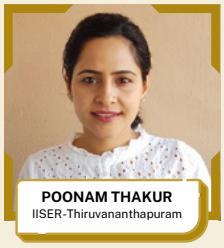
JAYAKUMAR SUNDARRAJ
Bhabha Atomic Research Centre

JUNAID JAWED
Presidency University



NEELAM KUNGWANI
Gujarat Biotechnology University

NITHYA N KUTTY
Dr. Vishwanath Karad MIT World Peace University



POONAM THAKUR
IISER-Thiruvananthapuram

PRIYADHARISHINI VEERARAGHAVAN
PSG Institute of Advanced Studies

RAJNISH KUMAR
Indian Institute of Technology (B.H.U.) Varanasi

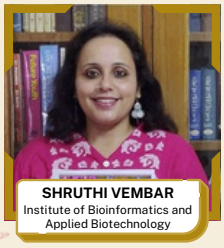
RAMA RAO DAMERLA
Kasturba Medical College Manipal, Manipal Academy of Higher Education

SADHAN DAS
Indian Institute of Science Education and Research (IISER) Mohali

SATYAJEET KHARE
Symbiosis International (Deemed University)

SESHADRI K S
Ashoka Trust for Research in Ecology and the Environment

SHASHI KIRAN
University of Hyderabad



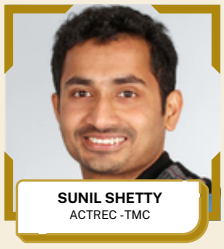
SHRUTHI VEMBAR
Institute of Bioinformatics and Applied Biotechnology

SHYAM KUMAR SUDHAKAR
Krea University

SIVARAJ SUNDARAM
Indian Institute of Technology Indore

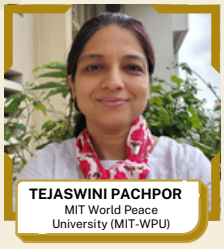
SOWMYASHREE MAYUR KAKU
St. John's Medical College Hospital and Research Institute

SRINIVASARAO REPUDI
DBT-inStem



SUNIL SHETTY
ACTREC -TMC

SUPHIYA PARVEEN
JAIN (Deemed-to-be University)



TEJASWINI PACHPOR
MIT World Peace University (MIT-WPU)

VIJAY SINGH
ICMR-National Institute of Research In Tribal Health

VINI GAUTAM
Indian Institute of Science (IISc)

Young Investigators' Abstracts

The abstracts have been printed exactly as submitted by the participants.
The organisers of YIM 2024 are not responsible for any errors in them.

YI 01 **Abhishek Dey**
Conformational ensembles of RNA Frameshift element are essential for Frameshifting in RNA Viruses

YI 02 **Abhishek Subramanian**
Computational systems biology approaches to study biological systems: Overview of past & current research interests

YI 03 **Ajay Tijore**
Confinement suppresses mechanical force-mediated cancer cell apoptosis

YI 04 **Amit Ranjan**
Approaches to enhance the effective utilisation of de-oiled rice bran in the diet of Labeo rohita using solid-state fermentation and exogenous enzymes

YI 05 **Anannya Bandyopadhyay**
Expanding the outer membrane protein repertoire of *Borrelia burgdorferi*

YI 06 **Anasuya Chakrabarty**
Widespread cross-sex negative genetic correlations between traits suggest extensive sexual antagonism in humans

YI 07 **Atanu Banerjee**
Investigating the "Ins and Outs" across fungal membranes: Paving the way towards mitigating antifungal resistance

YI 08 **Charukesi Rajulu**
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Young Investigators' Abstracts

The abstracts have been printed exactly as submitted by the participants.
The organisers of YIM 2024 are not responsible for any errors in them.

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Optoelectronic biointerfaces for stimulating neuronal cells

YI 01

Abhishek Dey

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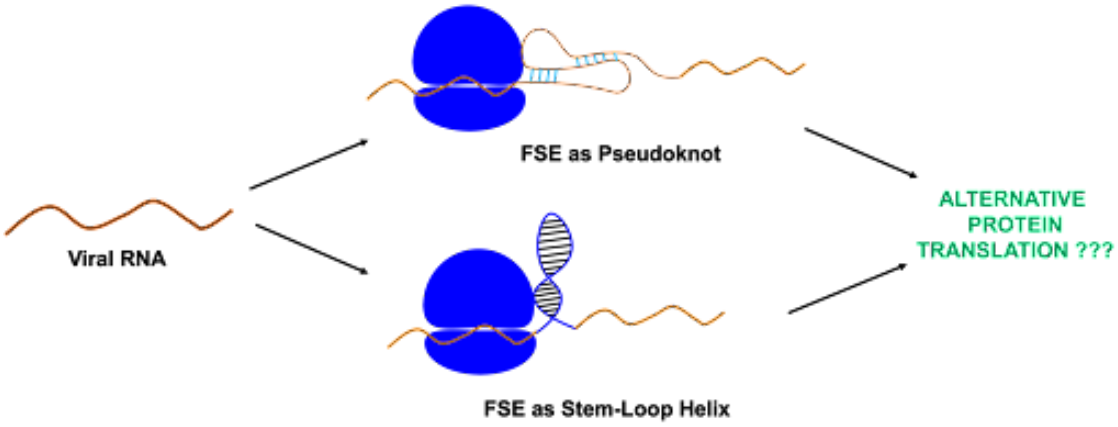
Conformational ensembles of RNA Frameshift element are essential for Frameshifting in RNA Viruses

Keywords: RNA biology, RNA modifications, RNA nanoparticles, structural biology, RNA-protein interactions

Abstract

Programmed ribosomal frameshifting (PRF) is the regulatory mechanism engaged by many RNA viruses to regulate the translation of multiple proteins from alternative, overlapping open reading frames (ORFs). This mechanism involves a controlled slippage (by slippery sequence) of translating ribosomes over the alternative ORF. To enhance its effectiveness, ribosomes also encounter a conserved RNA structural element when translating. These specific RNA structures can block the movement of the translating ribosomes on the slippery site thus receding them by 1 nucleotide which then translates proteins from -1 position. This mechanism is known as -1 PRF. Collectively, the slippery sequence and the RNA structures are called Frameshift element (FSE). Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), Hepatitis C virus (HCV) and many other RNA viruses employs -1 PRF to code viral polyproteins from two alternative ORFs. In SARS-CoV-2, ORF1a usually translates proteins during the early phase of viral infection while ORF1b encoded proteins that are generated during the late phase. Previous computational and secondary structural analyses from various laboratories have shown that the FSE adopts multiple secondary structure conformations. In the present study we identified multiple ensembles of RNA FSE from SARS-CoV-2, HCV, and West Nile Virus (WNV). Initial studies from HCV and WNV suggest the presence of pseudoknots stabilising their RNA FSE. We have also generated stabilising mutants that favours each alternative secondary structure of the SARS-CoV-2 FSE. Functional assays of these mutants reveal decline in frameshifting efficiency suggesting suppression of conformational transitions and that multiple conformations are required for function. Thus SARS-CoV-2 FSE is therefore an ideal system for evaluating how different computational analyses of structure probing data correlate with observed structure/function observations in RNA.



Conformational landscape of viral RNA FSE critical for alternative protein translation | Credits: Abhishek Dey

YI 02

Abhishek Subramanian

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Computational systems biology approaches to study biological systems: Overview of past & current research interests

Keywords: Computational systems & network biology, omics data analysis & bioinformatics, metabolism & gene regulation, mathematical, statistical modelling and machine learning, parasitology and immunology

Abstract

Biological function is an outcome of the integrated behaviour of simultaneously functioning components at heterogeneous biological time and length scales [1]. Although high-throughput experiments measure changes in specific biological quantities at different time-length scales, information regarding mechanisms underlying these changes is often overlooked/misinterpreted based on our limited, accumulated knowledge of biological mechanisms.

Systems biology approaches provide a birds-eye perspective into biological mechanisms. Using comparative genomics, influence of GC-rich codons in governing translational efficiency in Leishmania species was discovered [2]. Biological processes and cell subtypes emerging during angiogenesis in wet age-related macular degeneration (wet-AMD) could be captured using bulk & single-cell transcriptomics [3]. Kinetic models predicted an ultrasensitive switching of hedgehog signaling response in cancers [4]. Using genome-scale metabolic models, stage-specific adaptations in Leishmania and aspects of metabolic organisation were outlined [5]. Integration of tissue-specific single-cell transcriptomics data with genome-scale models of metabolism identified enzymes essential for pathological angiogenesis [3]. Modeling endemic spread of Leishmaniasis among multi-species host populations modeled using compartmental models prioritised optimal control strategies for controlling infectivity [6]. Machine learning classification, regression models enabled to identify minimally essential metabolic genes in Escherichia coli and evolutionary conserved metabolic genes in Leishmania infantum [7,8], both aspects linked to metabolic network organisation.

Currently, our research group @IITH is interested in understanding condition-specific adaptations of microeukaryotic parasites, interspecies interactions during infection and effects of gene regulation on host immunometabolism.

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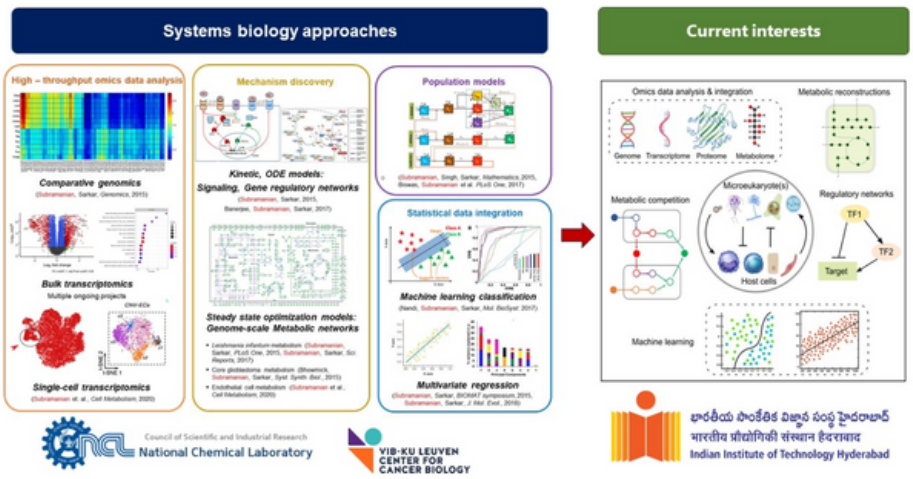

Overview of systems biology approaches & current research interests

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YI 03

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Confinement suppresses mechanical force-mediated cancer cell apoptosis

Keywords: Mechanobiology, cell biology, biomaterials, cancer, stem cells

Abstract

During cancer cell invasion, cancer cells migrate through '3D channel-like tracks' present in the tissues' interstitial extracellular matrix (ECM). Cancer cell migration through these 3D confined channels leads to confinement-induced cell deformation. Recent studies show that cancer cells are susceptible to mechanical stretch/ultrasound (US)-mediated mechanical forces and undergo calcium-dependent apoptosis under conditions that promote normal cell growth. Surprisingly, we find that the confinement-induced cell deformation suppresses US-mediated cancer cell apoptosis. A low level of apoptosis is observed upon US treatment in the confined breast cancer cells and primary oral squamous cancer cells. Also, apoptosis level was found to increase with a decrease in the degree of confinement. The absence of mature adhesions, low myosin IIA contractility and diffuse mechanosensitive Piezo1 channels are responsible for low apoptosis levels in confined cancer cells.

Thus, these findings suggest that confined cells, due to the absence of mature FAs, could not sense and transduce the mechanical forces and generate enough myosin IIA contractility required to trigger apoptosis.

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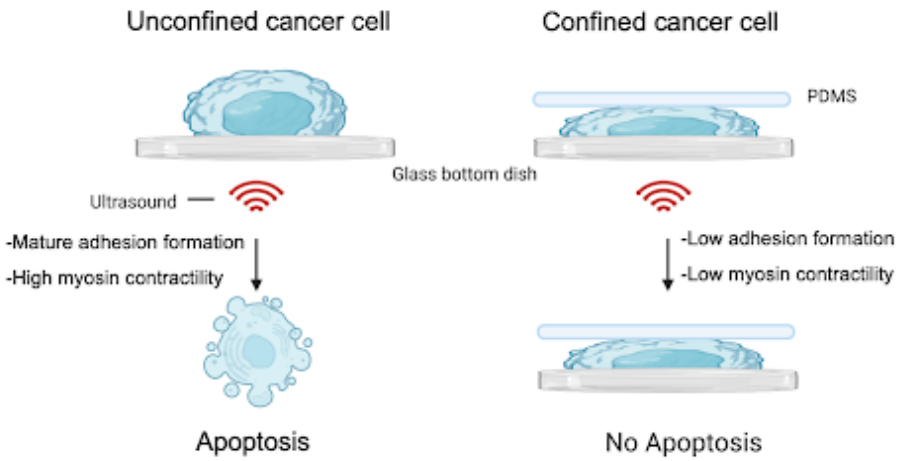

Confinement suppresses mechanical force-mediated apoptosis | Credits: Alka Kumari

Amit Ranjan

YI 04

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Approaches to enhance the effective utilisation of de-oiled rice bran in the diet of Labeo rohita using solid-state fermentation and exogenous enzymes

Keywords: Fish nutrition, aquaculture, sustainable aquaculture, solid state fermentation, exogenous enzyme supplementation

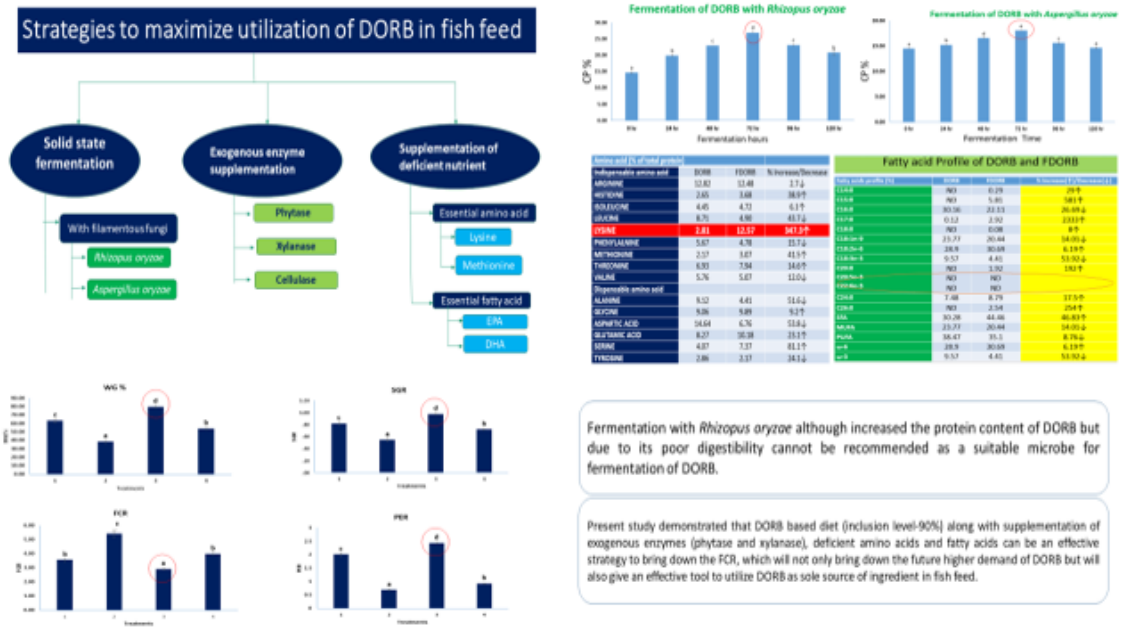
Abstract

De-oiled rice bran (DORB) is often used alone or in combination with other ingredients in fish feed. It is an agro-industrial byproduct following rice bran oil extraction. DORB presents challenges due to its high crude fiber, non-starch polysaccharides, and anti-nutritional factors that hinder digestibility in fish diets. To overcome these challenges, two experiments were conducted:

1. Solid-state fermentation (SSF) of DORB using *Rhizopus oryzae* and *Aspergillus oryzae*, resulting in improved nutrient profiles, and notably increased protein content of DORB.

2. Evaluation of the impact of exogenous enzymes (xylanase and phytase) supplementation in both non-fermented and fermented DORB diets for *Labeo rohita*, leading to significant improvements in the growth performance of *labeo rohita*.

The findings offer potential solutions to the challenges posed by DORB, making it a more effective and sustainable ingredient in aquaculture diets. By enhancing the nutritional content and digestibility of DORB through SSF and enzyme supplementation, these studies contribute to the development of cost-effective and efficient strategies for utilising this by-product in the aquaculture industry, benefiting both farmers and the environment.



Strategies for maximising utilisation of de-oiled rice bran in fish feed

YI 05

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Expanding the outer membrane protein repertoire of Borrelia burgdorferi

Keywords: Molecular bacteriology, antibacterial resistance, novel intervention strategies, protein structure-function, protein homeostasis

Abstract

In this study we have computationally identified and characterised novel outer membrane beta-barrel (OMBB) proteins in gram-negative spirochete *Borrelia burgdorferi*, the causative agent of Lyme disease. Lyme disease is an emerging vector-borne zoonotic disease affecting various regions worldwide [1]. OMBB proteins are crucial for specific and non-specific import, efflux, adhesion, proteolysis, membrane biogenesis, and protein assembly [2]. Understanding the structural and functional aspects of OMBBs is crucial for elucidating the pathogenesis and developing potential intervention strategies. Despite previous research, a comprehensive understanding of these proteins remains elusive in Borrelia. We have employed an integrated in silico approach, combining multiple outer membrane protein prediction tools and beta-barrel structure prediction methods. From these analyses, 17 putative OMBBs were manually selected. Homology-based models were constructed to determine their three-dimensional structures, revealing structural insights into these proteins.

Additionally, amino acid sequence variations in these OMBBs, obtained from clinical strains, were mapped onto the structural models, highlighting the significance of surface-exposed loops in these proteins' adaptation and evolution. The findings suggest that these surface-exposed regions are under constant selection pressure, which implies their importance in bacterial pathogenesis. Furthermore, we identified linear and conformational epitopes in these 17 putative OMBBs, offering potential targets for the development of peptide-based vaccines. Through this work we have identified 17 novel OMBBs in *B. burgdorferi*, highlighting their structural features and their potential role in bacterial pathogenesis.

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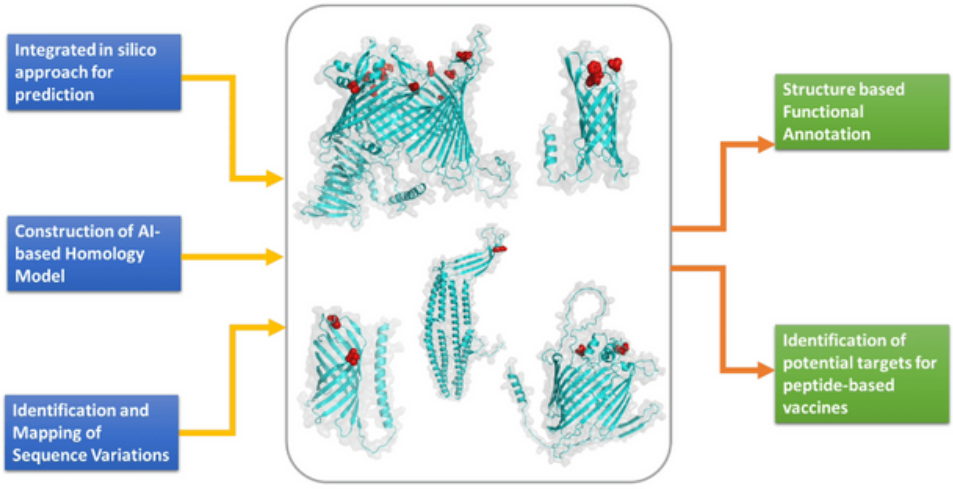

Unveiling Membrane Arsenals of Lyme Disease Pathogen
Credits: Amisha Panda, Sanjiv Kumar, Anannya Bandyopadhyay

YI 06

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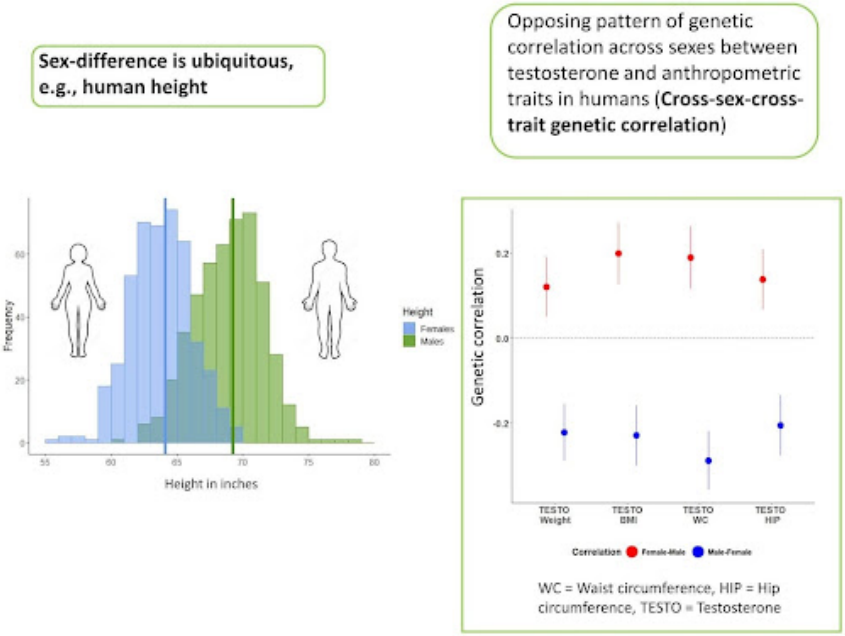
Widespread cross-sex negative genetic correlations between traits suggest extensive sexual antagonism in humans

Keywords: Quantitative genetics, sexual selection, sexual dimorphism, genetic correlation, human complex disorders

Abstract

Sex-difference is extremely prevalent in humans despite a shared genetic architecture between the sexes. Studying sex-difference in single traits does not provide a holistic biological overview, because traits are not independent and are genetically correlated. One way to overcome this issue is by estimating the genetic correlations between two traits in different sexes, i.e., cross-sex-cross-trait genetic correlation, e.g., between height in males and weight in females, instead of correlation between the same trait in the two sexes, e.g., between height in males and females. Using such a multivariate approach, we investigated sex-difference in the genetic architecture of 12 anthropometric, fat depositional, and sex-hormonal phenotypes. We found that besides the sexes having a different genetic architecture, intriguingly, the directions of most of the cross-sex-cross-trait genetic correlations were opposite, most prominently between testosterone and the anthropometric traits (weight, BMI, waist-to-hip ratio etc.). We also identified variants (SNPs) which were associated with testosterone only in males, but with BMI in females, although annotated genes revealed association with obesity in both the sexes. We estimated an overwhelming number of negative genetic correlations, 28 out of 66 pairs in cross-sex-cross-trait, which indicates sexual antagonism in humans. Such negative genetic correlations across sexes implies that variants which affect trait A positively in males, affect trait B negatively in females, and generally signifies trade-offs and genetic constraint to evolution. Most genetic correlations reported in non-human species are found to be positive, and this opposing direction of correlations in humans are probably the signatures of sex-specific selection which led to the sex-difference that we observe in contemporary humans.



Opposing patterns of genetic correlations between testosterone and anthropometric traits in human males and females
Credits: Anasuya Chakrabarty, Saikat Chakraborty, Diptarup Nandi, Analabha Basu

YI 07

Atanu Banerjee

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Investigating the "Ins and Outs" across fungal membranes: Paving the way towards mitigating antifungal resistance

Keywords: Membrane transporters, antifungal resistance mechanisms, multidrug efflux pumps, peptide permeases, peptide-based therapeutics

Abstract

The emergence of the new multidrug-resistant species *Candida auris* demands urgent intervention from the mycology community. In this direction, our research group at Amity University Haryana focuses on two major areas: understanding the contribution of efflux pumps in antifungal resistance of *C. auris* and identifying and characterising importer proteins that can facilitate in the uptake of peptidomimetic drugs. Towards our first goal, we have prepared an inventory of ATP-binding cassette (ABC) superfamily and Drug/H+ antiporter (DHA1) family proteins in *Candida auris* using our in-house bioinformatic pipeline. With the help of genetic manipulations and drug screens, we identified several azole drugs as substrates for a DHA1 pump, CauMdr1 [1]. On the other hand, our analyses with ABC transporter genes in *C. auris* unveiled novel roles of HST6 and MDL2 in cell wall and plasma membrane homeostasis, and biofilm development. For the second frontier, we have comprehensively analysed the peptide transport (PTR) family and identified a PTR transporter Ptr_C in *C. auris*, which is central for the import of chitin synthesis inhibitors [2]. Our ongoing studies are aimed at delving deeper into the functional relevance of these membrane transporters in antifungal resistance and finding ways to mitigate it.

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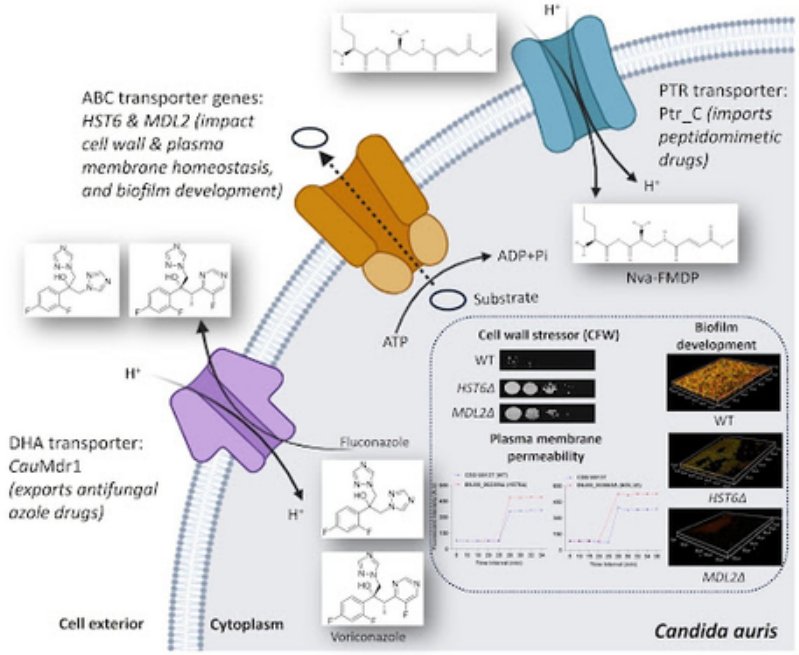

Candida auris membrane transporters involved in antifungal export/import and cellular physiology | Credit: Atanu Banerjee

YI 08

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Integrated omics approaches to elucidate the low phosphate stress tolerance mechanisms in climate resilient weed and crop species

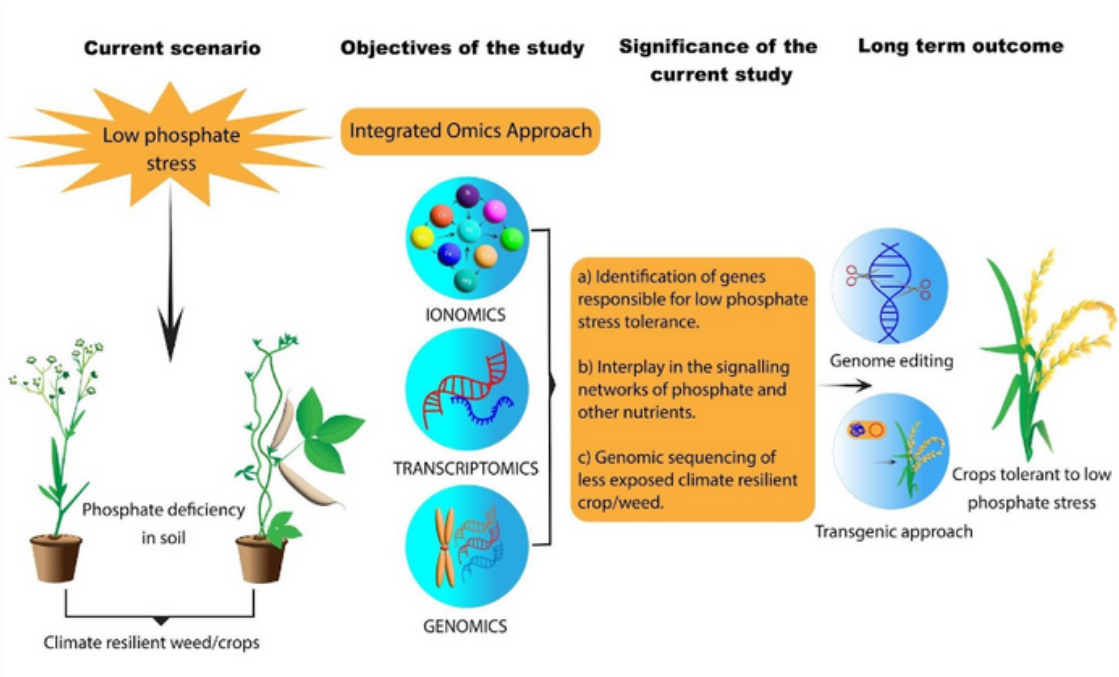
Keywords: Plant omics, low phosphate stress, horse gram, *Parthenium hysterophorus*, crop improvement

Abstract

Phosphorous nutrient deficiency in soil represents a significant challenge, leading to reduced crop yields. The production cost associated with chemical Phosphate (Pi) fertilizers places a heavy economic burden, while their use contributes to severe environmental pollution. One promising solution is the engineering of crops with improved Pi utilisation efficiency and greater tolerance to low Pi stress. This approach can help mitigate Pi pollution and reduce dependence on non-renewable Pi reserves.

To enhance Pi use efficiency in crops, it is crucial to identify novel molecular regulators governing a plant's response to low Pi stress. To tackle this, I am focusing on two less-explored yet robust plant models: Parthenium hysterophorus, a widely distributed weed, and horse gram (*Macrotyloma uniflorum*), an indigenous, climate-resilient crop. The mechanisms underlying their responses to low Pi stress remain unexplored. My current research involves employing integrated omics methods, including de novo transcriptomics and ionomics, to identify the novel genes responsible for Pi uptake under limiting conditions and to unravel the intricate signaling interactions between Pi and other nutrients.

In the case of Parthenium weed, our immediate goal is to identify the low Pi stress responsive regulators. In the long term, we aim to use genome editing techniques to engineer homologous genes in stress-susceptible crops, ultimately optimising Pi use efficiency. In our study with the horse gram model, we seek to identify horse gram varieties with superior Pi acquisition and utilisation capabilities and to unravel novel genes controlling low Pi stress tolerance by de novo transcriptomics. We would also decipher the interplay in the signaling of Phosphate with other nutrients by Ionomics.



Plant omics-based crop engineering: Enhancing resilience to low phosphate stress | Credits: Subramanya Hegde

Debanjan Mukhopadhyay

YI 09

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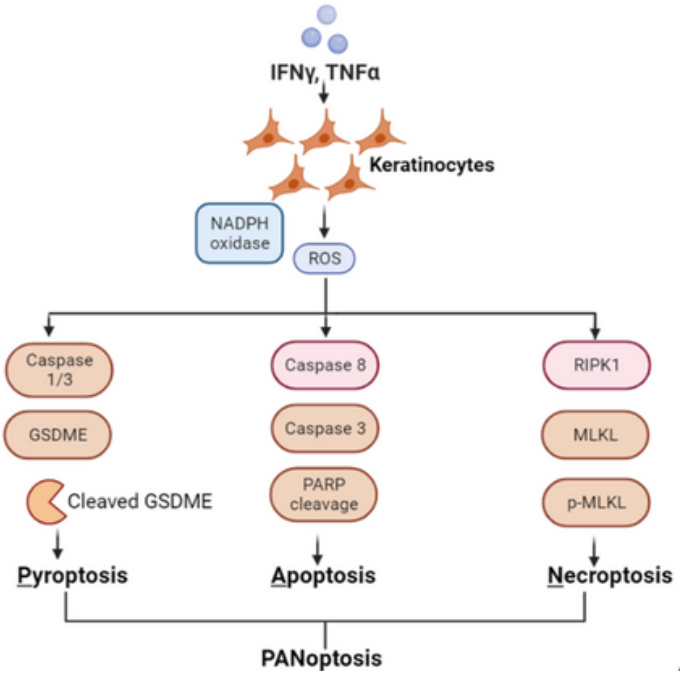
IFNγ and TNFα induced PANoptosis in keratinocytes: Implications in inflammatory skin disorders

Keywords: Interferon, host-pathogen interaction, virulence factors, immune signaling, cell death

Abstract

Introduction: Interferon gamma (IFNγ) and tumor necrosis factor alpha (TNFα) play a critical role in inflammatory skin disease pathologies. Keratinocytes are highly active and one of the most affected cells in inflammatory skin disorders. Although, IFNγ induced cell death in keratinocytes but the mechanism of this cell death is not known. Aim/Objectives: In this study, we investigated the mechanism of cell death induced by IFNγ and TNFα alone and in combination in human keratinocytes. Methods: HacaT cells (immortalised human keratinocyte line) were treated with the IFNγ and TNFα alone or in combination. Cell viability was measured by MTT assay. Cleavage of Caspase 1, 3 and 8, PARP, GSDME, and phosphorylated MLKL were measured using western blotting. Reactive oxygen species (ROS) and nitric oxide (NO) were measured using H2DCFDA and Griess assay respectively. Results: IFNγ alone and together with TNFα triggers cell death in keratinocytes which is associated with cleavage of Caspase 3, 8, PARP and GSDME along with phosphorylation of MLKL. IFNγ and TNFα triggered ROS within an hour of the co-treatment. The cell death is rescued with cell death inhibitors of apoptosis, pyroptosis and necroptosis. Discussion: Our result indicates that IFNγ and TNFα co-treatment induces both pyroptosis, apoptosis and necroptosis which is termed PANoptosis. Furthermore, we showed that unlike murine cells, in human keratinocytes, the trigger for PANoptosis is ROS. Conclusions: This is the first report of PANoptosis in human keratinocytes which can be used as a druggable target to reduce the disease pathology in inflammatory skin disorders.



IFNγ and TNFα induced PANoptosis in human keratinocytes
Credits: Debanjan Mukhopadhyay and Jyotirmoyee Roy

Devesh Bhimsaria

YI 10

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MinSeq Find algorithm: Unravelling multiple modes of DNA-protein interaction

Keywords: Protein-DNA binding, bioinformatics, computational modeling, machine learning, artificial transcription factors

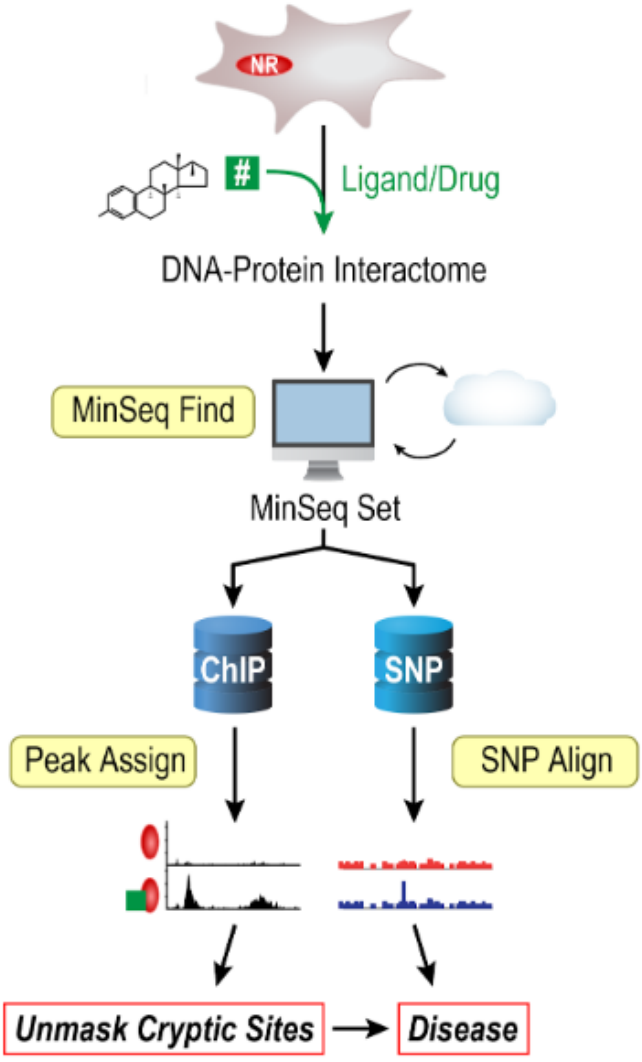
Abstract

Transcription factors (TFs) are pivotal proteins within cells, orchestrating gene regulation and influencing diverse cellular functions. Mutations in TFs or their DNA-binding partners can disrupt this vital interaction, contributing to diseases like cancer, diabetes, and various disorders. To investigate these intricate interactions, labs worldwide employ high-throughput (HT) techniques and computational methods for in vivo and in vitro DNA binding analysis.

Typically, computational methods focus on the most prominent binding patterns, overlooking medium-to-low affinity sequences and multiple binding modes critical for distinguishing related TFs. In response, we have pioneered a ground-breaking search algorithm called MinSeq Find, inspired by MinTerms in electrical engineering. MinSeq Find unveils concealed binding sites within the DNA-protein interactome data, enriching our understanding of TF binding diversity.

This innovative approach has revealed complex trimer and tetramer binding patterns of various TFs, shedding light on previously obscured binding modes. Moreover, when applied to public SNP databases, the MinSeq model identified both known and up to 14% of previously unassigned disease-linked SNPs as novel TF binding sites. This discovery has profound implications, enabling the repurposing of FDA-approved drugs for diseases previously not linked to these TFs.

In essence, MinSeqs offer a ground-breaking method to capture multiple TF binding profiles within a single model, unraveling the molecular underpinnings of poorly understood genetic diseases. This advancement is pivotal for advancing precision medicine, as it opens new avenues for targeted therapeutic interventions and enhances our comprehension of complex diseases at the molecular level.



MinSeq set derived from the DNA–Protein Interactome (DPI) involving nuclear receptor (NR) proteins, employing the innovative MinSeq Find algorithm, which not only enhances the prediction of ChIP-seq binding but also concurrently assesses the influence of disease-associated SNPs on NR-binding sites.
Credits: Laura Vanderploeg for graphic design

YI 11

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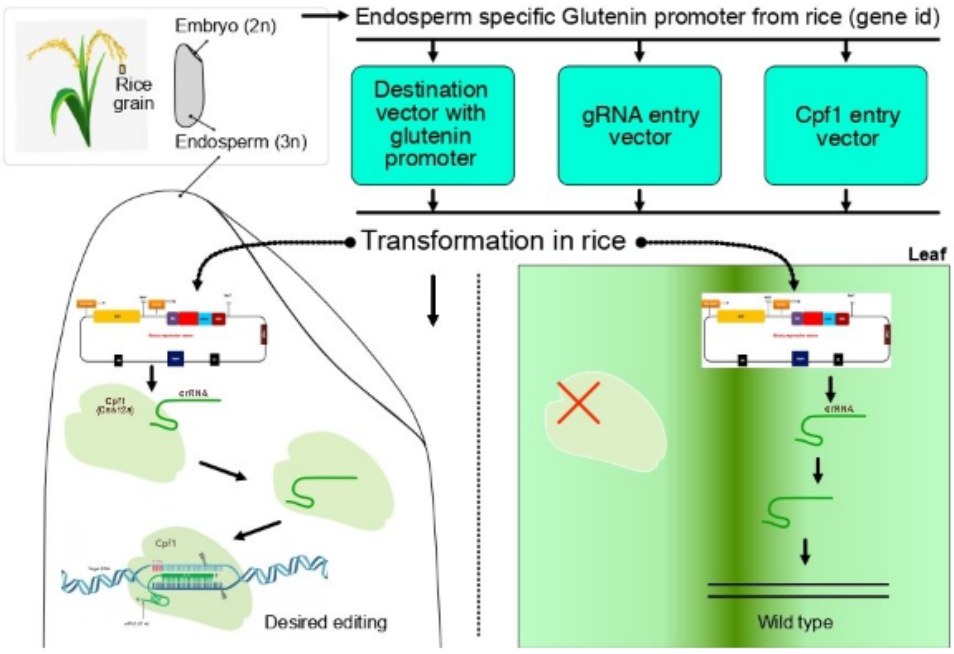
CRISPR/Cpf1-ESGE: Designing and development of endosperm specific genome editing in rice

Keywords: Molecular Biology, CRISPR/Cas technology, crop improvement, genome editing, plant tissue culture

Abstract

Editing of the targeted gene in localised tissue can minimise the pleiotropic effects of the gene in other non-targeted tissues and reduce the risk of unintended consequences. Further, tissue specific genome editing (TSGE) cut down the metabolic load to the plant through its limited editing in the conscious areas. Genome editing technologies, particularly the clustered regularly interspaced short palindromic repeats (CRISPR) system and CRISPR-associated protein (Cas) has emereged as a promising avenue within this realm. It allows for targeted genetic modifications in specific tissues or organs minimising off-target effects. Tissue-specific editing enables researchers to dissect the roles of specific genes in various tissues, contributing to the identification of important genes. Further, some genes are present in many isoforms in the genome. Selection of the precise isoform is crucial for successful editing. In this study, we have designed and developed an endosperm specific genome editing (ESGE) and a additional process for selecting suitable isoforms of target gene in rice. The Cas gene was exclusively expressed only in the endosperm.



Endosperm specific CRISPR/Cas12a targeting | Credits: Jeetendra Maharana

YI 12

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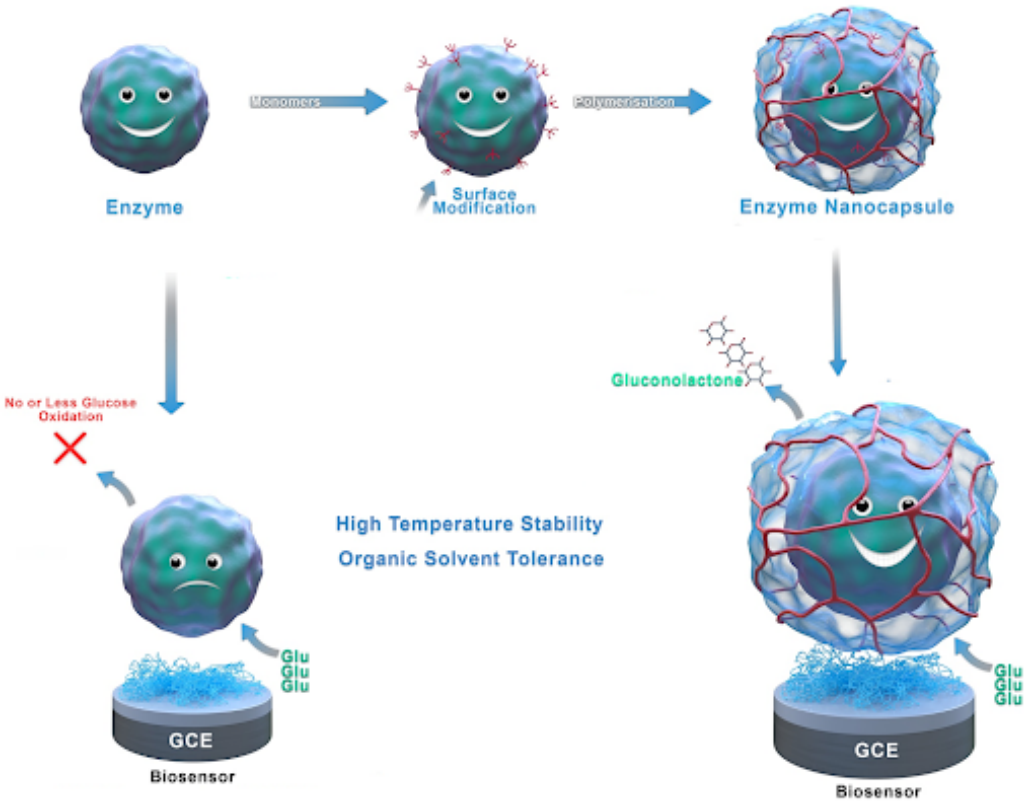
Biosensing strategies for screening of biomolecules: Their applications

Keywords: Biosensors, disease detection, biomolecules, food safety, analytical sensors

Abstract

Biomolecules such as glucose, adrenaline, dopamine are integral elements of living organisms and control many biochemical functions of the body. Such biomolecules are generally termed as biomarkers for body metabolite or disease detection. Increasing imbalance in the natural metabolism of human body results in irregular secretion/absorption and alteration in biomolecule concentration which may lead to various genetic, metabolic, and cancerous diseases. Therefore, there is a great need for highly sensitive, accurate and stable detection platforms for their fast and specific detection.

My research focusses on the development of advanced biosensing devices based on new generation nanostructures and biomaterial for fast screening of disease biomarkers and contaminants for point-of-care diagnostics, food safety and environmental protection. State of the art fabrication approaches such as screen/3D printing are being used and developed to fabricate the portable, integrated electrochemical devices which will help in solving the problems of society.



Stable enzyme nanocapsules for detection of glucose in different working environments
Credits: This figure was prepared by Ella Maru Studio, USA on the paid service using author's basic design

Gajanan Kendre

YI 13

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Co-mutational spectrum in intrahepatic cholangiocarcinoma: Evaluation of 6130 patients

Keywords: Cancer biology, precision medicine, cholangiocarcinoma, fusion genes, mouse model

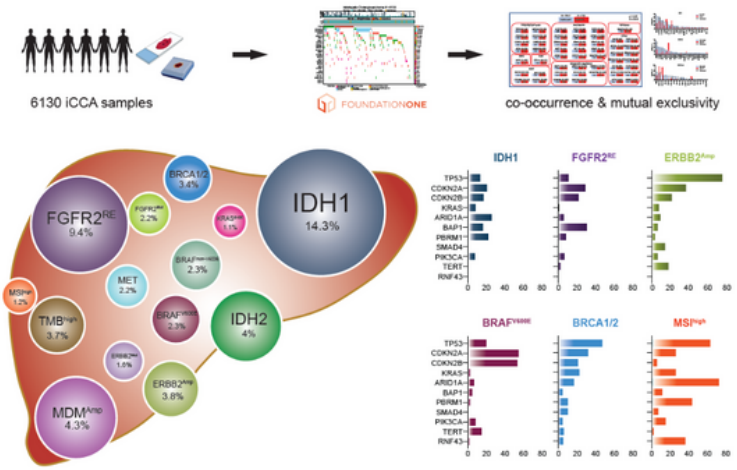
Abstract

Background and Aims:
Intrahepatic cholangiocarcinoma (iCCA) is a fatal disease with an overall 5-year survival below 10%. In recent years, iCCA has evolved as a "role model" for precision oncology in GI cancers. However, it is a rare and heterogeneous cancer that challenges the development of targeted therapies. Interrogating large, standardized datasets drive better understanding of the characteristics of molecular subgroups of iCCA and allows the identification of genomic patterns that remain unrecognized in smaller cohorts.

Methods:
We performed a retrospective analysis of 6130 iCCA patients from the FoundationCORE database who received diagnostic panel sequencing on the hybrid capture-based Foundation One platform. Short variants/fusion-rearrangements and copy number alterations in >300 tumor associated genes were evaluated, and the tumor mutational burden (TMB) as well as the microsatellite instability (MSI) status, was available for the majority of the cohort.

Results:
We provide the genomic landscape of iCCA and outline the co-mutational spectra of seven therapeutically important oncogenic driver genes: IDH1/2, FGFR2, BRAF, ERBB2, BRCA1/2, MDM2, MET and KRASG12C which alredy used in targated theripies in iCCA. We observed a negative selection of RTK/RAS/ERK pathway co-alterations, and an enrichment of epigenetic modifiers such as ARID1A and BAP1 in IDH1/2 and FGFR2 altered patients. RNF43 and KMT2D occurred with high frequency in MSIhigh and TMBhigh patients.

Conclusion:
A detailed knowledge of the most prevalent genomic constellations is fundamental to accelerate therapeutic developments in a rare cancer such as iCCA. Our study provides a valuable resource for feasibility assessment of clinical trials and subgroup analyses, helps the development of translationally relevant preclinical models, and generates a knowledge ground to anticipate potential resistance mechanisms to targeted therapies in genomically defined subgroups of iCCA patients.



Co-mutational Spectrum in Intrahepatic Cholangiocarcinoma | Credits: Kendre et.al. 2023; Journal of Hepatology

YI 14

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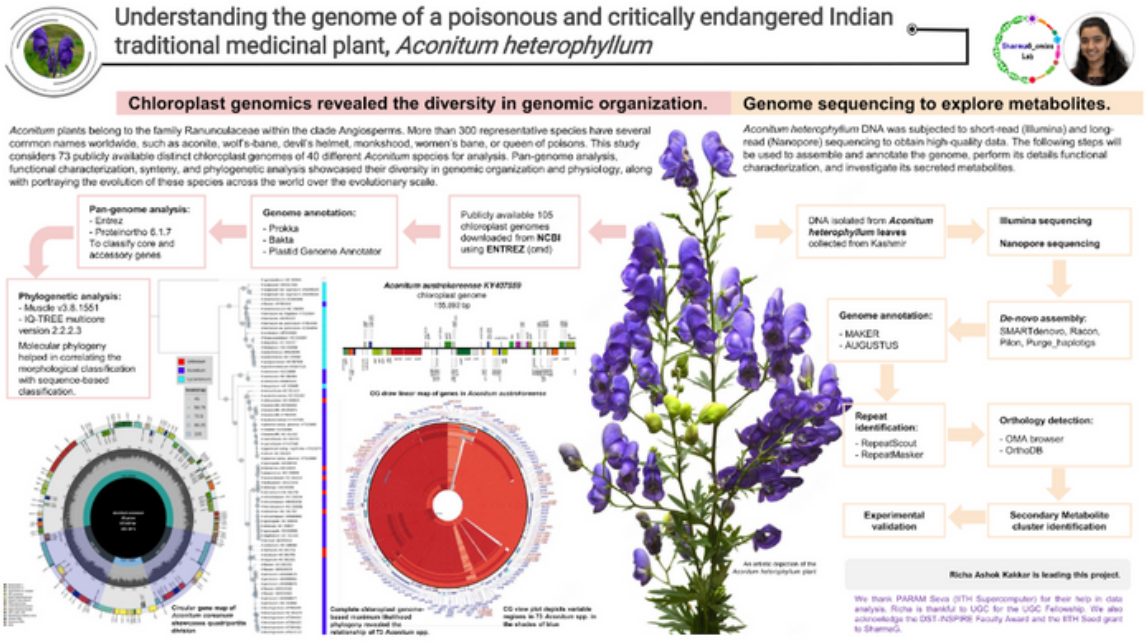
Plant health, growth, and productivity are intertwined with their associated microbiota

Keywords: Microbial Genomics, microbial evolution, metagenomics, computational biology, plant-microbe interactions

Abstract

The halobiome (genome of the plant and its microbiota cumulatively) keeps the holobiont (plant and its microbiota) fit amidst all biotic and abiotic (drought, temperature, marsh, snow, or salinity) factors. Traditional medicinal plants secrete a massive spectrum of natural metabolites. For centuries, they have assisted humankind in attaining accessible health care, and for many rural populations, they are still an indispensable part of survival. Phytotherapeutic properties of medicinal plants might be coupled with their plant-microbe interactions; however, this scientific knowledge is not benchmarked appropriately.

Aconitum heterophyllum (Ativisha) is a Critically Endangered Traditional Indian Medicinal plant, well known for its analgesic, anthelmintic, antipyretic, aphrodisiac, astringent, expectorant, diuretic, and poisonous properties attributed majorly via a diverse array of secreted alkaloids, i.e., aconitine, hypaconitine, heteratisine, benzoylmesaconine, atidine, isotisine, hetidine, etc. present in their rhizomes. High-throughput sequencing data procured via Nanopore and Illumina platforms will help us produce their good-quality nuclear genome assembly. Access to the genome will facilitate the discovery of alkaloid biosynthesis pathways via comparative genomics and in-depth data mining, further helping in benchmarking their medicinal properties. The chloroplast genome sequencing will expedite population, phylogenetic, and genetic engineering research. Metagenomic NGS data will help to profile the unique microbial diversity present in their poisonous rhizomes along with generating their draft/complete genome assemblies. Overall, this project will excavate plant-microbial interactions that might be defining the plant's medicinal properties, along with an exploration of multidrug resistance and next-generation antibiotics potential.



Benchmarking the Traditional Medicinal plant Properties using Genomics and Metagenomics
Credits: Richa Kakkar: leading the genomics aspect of this project and created this poster. Mariam Azeezuddin Haneen: leading the genomics aspect of this project. Gaurav Sharma: Designed this project

YI 15

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Decrypting the edge of bacterial cell-to-cell and gut symbiotic bacterial-intestinal host cell interaction

Keywords: Microbiology, microbiota, inter-bacterial cell-to-cell communication, bacterial cell biology, bacterial multicellurity (e.g. biofilms, swarming)

Abstract

It is evident that bacteria directly interact with their encounter parts in 'inter-and-intra species' manner, and also interact with their host/s 'in-and-on'. I will discuss that bacterial cells directly communicate via their membranous inter-connecting intercellular nanotubes. I will present that when bacteria reside 'close-by', they inter-connect with each other via these tubes and exchange their cytoplasmic molecules, importantly resistance to the antibiotics both in transient and hereditary manner. I will describe how bacteria start building these nano-tubular networks and their molecular architectures, independently from the classical conjugation. Notably, such bacterial attributes are highly dominant in the host microbiota, where bacteria not only communicate with each other but also interact with the host cells by sensing their environments. We recapitulated to grow the premier gut symbiotic bacteria, Segmented Filamentous Bacteria (SFB) in an in vitro with intestinal cells and in vivo conditions in germ free mice models. Utilising higher resolution cell biology tools, we found that only the single-celled intracellular offspring (IOs), and not filamented SFB, harbors flagella. IOs flagella is specific to their holdfast which attaches with host epithelium, thus regulating almost all the immune systems and host pathophysiology. I believe that such novel bacterial physiology is likely to change our view on how molecular cross-talk, the ongoing «war-and-peace» between bacteria and host cells, results in the emergence of symbiosis and/or pathogenesis.

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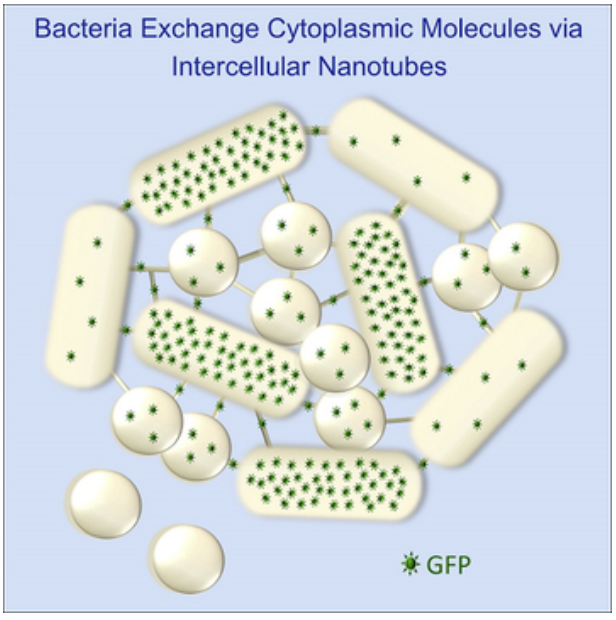
3. Nkamba I, Mulet C*, Dubey GP*, *et al.*, Sansonetti PJ and Schnupf P. Intracellular offspring released from SFB filaments are flagellated. Nature Microbiology, 2020, 1: 34-39. (*Second co-author).



Bacteria exchange cytoplasmic molecules via their intercellular nanotubes

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YI 16

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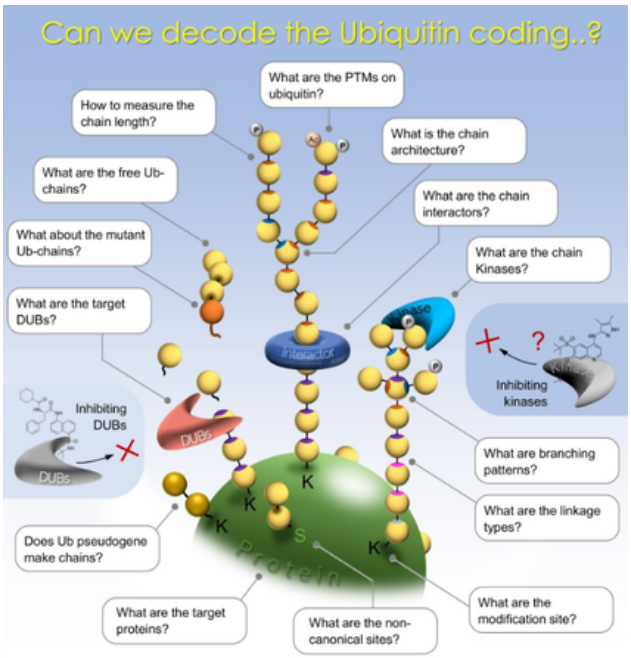
Can we decode the Ubiquitin coding...?

Keywords: Ubiquitin-Proteasome-System, targeted protein degradation, ubiquitinomics & degradomics, neurodegenerative diseases, molecular glues & PROTACs

Abstract

The expanded knowledge of ubiquitin landscape has already convinced us to consider ubiquitination as a major post-translational modification (PTM) that regulates almost all signaling pathways in the cells. Ubiquitin is a uniquely complex PTM that maintains normal cellular function and when dysregulated leads to diverse pathophysiology. A critical component toward achieving this potential is being able to investigate Ub PTMs, and how they change in a spatiotemporal fashion in a given disease state and/or in response to stimuli or pharmacological agents. This is no easy task given the complexity of the ubiquitin landscape. Nonetheless, the development of new reagents and methods provides a powerful toolbox to accelerate our understanding of ubiquitin as a complex regulatory signal. The recent technological advances enabled us to appreciate the explored ubiquitin codes as well as the existence of the unexplored ones. Despite these successes, there are many blind spots in our understanding of cellular ubiquitination diversity, polyubiquitin chain architecture, and ubiquitin interactome. Taking recent progress as our guide, we are trying to combine the existing knowledge with the appropriate understanding of the abilities and limitations of the current proteomic methods. We are confident that enabling improvements in the conventional techniques and developing new tools and approaches would fill these technological gaps and provide a full resolution of the ubiquitin landscape in human cells and tissues. A number of drugs and drug candidates that modulate ubiquitination through targeting proteins that add, remove, or read ubiquitination have now been developed, although these only scratch the surface of harnessing the ubiquitin system for therapeutic value. Decoding this major ubiquitination PTM and the biological importance of such an intricate landscape could help researchers exploit the ubiquitin code for tools and leverage the ubiquitin pathways for a plethora of therapeutic interventions.



Can we decode the Ubiquitin coding...? | Credits: Indrajit sahu

Indumathi Sathisaran

YI 17

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Crystal engineering of curcumin for enhanced bioavailability

Keywords: Crystal engineering, 3D cell culture, biomimetic materials, personalised drug formulations, 3D bioprinting

Abstract

Biopharmaceutics Classification System (BCS) of drugs had classified the poorly water-soluble drugs into BCS Class II and Class IV categories. Several Active Pharmaceutical Ingredient (API) molecules, in spite of possessing significant medicinal properties, have been restricted for therapeutic use because of their poor aqueous solubility, which limits its bioavailability. We report crystal engineering of CUR using different geometrically compatible coformers to enhance the dissolution and bioavailability of curcumin (CUR) (a BCS class IV polyphenolic compound). The so formed new cocrystal phases were found to exhibit enhanced dissolution. Such solid phases with improved dissolution profiles are of significant importance for pharmaceutical industries. Further, we have investigated the bioavailability of some of the CUR multicomponent solids in 2D monolayers and 3D tumor models of triple-negative breast cancer cells, MDA-MB-231 cells. The cytotoxicity and internalisation assays on 2D monolayers revealed that all CUR multicomponent solid forms except Curcumin-Folic Acid Dihydrate (CUR-FAD) (1:1) coamorphous solid exhibited enhanced bioavailability than raw CUR. Cell invasion assay conducted on 3D tumor spheroid models showed that Curcumin-Hydroxyquinol (CUR-HXQ) cocrystal inhibited cell invasion while CUR-FAD (1:1) coamorphous solid promoted enhanced invasion of cells from spheroids.

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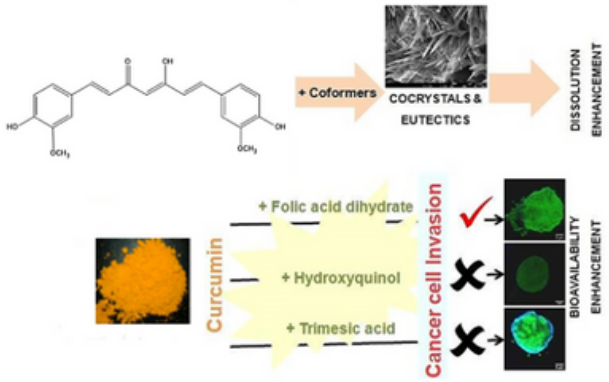

Anti-invasion activity of curcumin multicomponent solids against tumor spheroids
*Credits: Indumathi Sathisaran, Dhiraj Devidas Bhatia, Sameer Vishvanath Dalvi**

YI 18

Janvie Manhas

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TUSC1 drives oxidative phosphorylation and tumor cell death in colon cancer

Keywords: Cell therapy, gene therapy, synthetic biology, biochemistry and molecular biology, diagnostics

Abstract

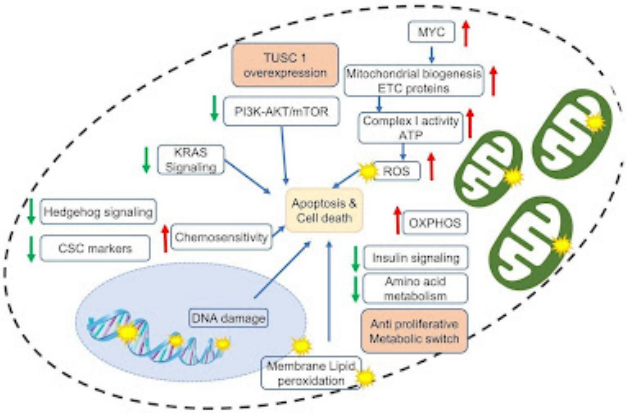
Tumor Suppressor Candidate 1 (TUSC1) is an intronless gene located in on the 9p21.2 genomic region. In our initial studies, we did a microarray of colon cancer cell lines (cancer stem cells vs. non-stem cells) and identified that TUSC1 expression was significantly downregulated in the cancer stem cell fraction. Its expression has previously been found to be repressed in numerous cancers. In this study we aimed to delineate the mechanistic role of TUSC1 in colon cancer.

TUSC1 expression was analysed in human colon cancer tissue and control colon tissues and found to be repressed in primary colon cancer. TUSC1 overexpression studies were performed using a pHAGE6 based lentiviral vector in human colon cancer cell lines HCT116 and SW480. Cell proliferation assay showed a significant decline in cell proliferation and subsequent cell death on TUSC1 over expression. TUSC1 overexpression was observed to decrease cell migration and reduced tumor development in xenograft model in NOD-SCID mice.

Whole transcriptome analysis was done using RNA sequencing in both cell lines after TUSC1 overexpression. Data was analysed using Galaxy Server and pathway analysis done by GSEA. Oxidative phosphorylation (OXPHOS) was one of the top pathways enriched which suggested a reversal of Warburg phenomenon.

A live cell metabolic flux analysis for mitochondrial respiration and glycolysis was performed using a Seahorse analyser. It was observed that TUSC1 expression significantly increased the spare respiratory capacity, ATP production and maximal respiration along with an increased glycolytic reserve. This was accompanied by an increase in reactive oxidation species (ROS) generation leading to subsequent apoptosis.

We have characterised a novel anti-proliferative role of TUSC1 in metabolic reprogramming of cancer cells where it appears to mediate a bioenergetic shift from aerobic glycolysis to oxidative phosphorylation which can be utilised therapeutically.



TUSC1 overexpression promotes ROS mediated cell death in cancer
Credits: Janvie Manhas

YI 19

Jayakumar Sundarraj

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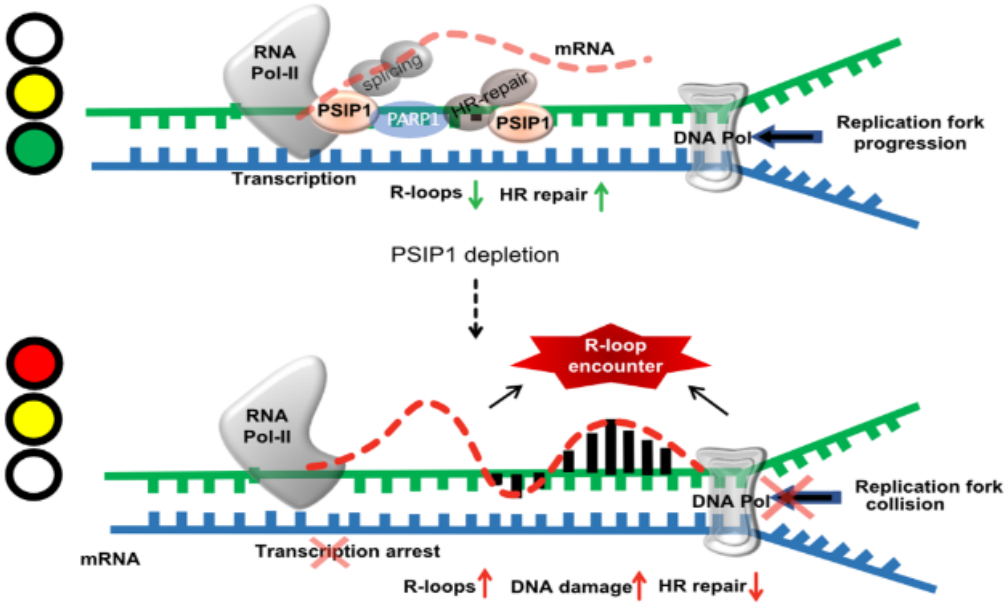
PSIP1 reduces R-loops at transcription sites to maintain genome integrity

Keywords: Cancer cell biology, epigenetics, molecular therapeutics, dna repair, genomic instability

Abstract

R-loops (DNA-RNA hybrids) are transcriptional by-products that cause a persistent threat to the genome and is linked with accelerated aging and cancer. Hence it is important to identify factors and mechanisms that underlie R-loops removal in the cells. PC4 SRSF interacting protein 1 (PSIP1) is a histone reader protein that reads H3K36me3 and known to associate with transcriptional elongation complex. In a proteomics study, we found that PSIP1 proteome is enriched with proteins involved in R-loop biology. Moreover, the recombinant PSIP1 protein showed the ability to bind to the RNA-DNA hybrids in cell free system, the immunoprecipitation of R-loops showed the heavy presence of PSIP1 and proximity ligation assay showed the close association of PSIP1 with R-loops. Hence we hypothesised that PSIP1 could be playing role in resolving un-scheduled R-loops in the cells during transcription. The depletion of PSIP1 led to the stark increase in R-loop levels in slot blot and mmunofluorescence studies. This R-loop accumulation could be reversed by RNaseH overexpression or rescued by PSIP1 re-expression indicated the role of PSIP1 in reducing R-loop burden in the cells. This R-loop accumulation further led to the accumulation of DNA damage. Genome-wide mapping of PSIP1, R-loops and γ-H2AX in PSIP1-depleted cells by CUT&Tag-seq revealed an accumulation of R-loops and DNA damage at gene bodies in the absence of PSIP1. This PSIP1 depletion mediated R-loop accumulation further caused reduction in transcriptional output, local transcriptional arrest and transcription-replication conflict, leading to DNA damage. We found that PSIP1 depletion increases 53BP1 foci and reduces RAD51 foci, suggesting altered DNA repair choice. Furthermore, PSIP1 depletion increased the sensitivity of cancer cells to PARP1 inhibitors and DNA-damaging agents that induce R-loop-induced DNA damage. These findings provide novel insights into the mechanism through which PSIP1 maintains genome integrity at the site of transcription.



Working model showing the role of PSIP1 in reducing R-loop level at transcription sites to minimise transcription-replication conflict leading to DNA damage | Credits: S. Jayakumar

Junaid Jawed

YI 20

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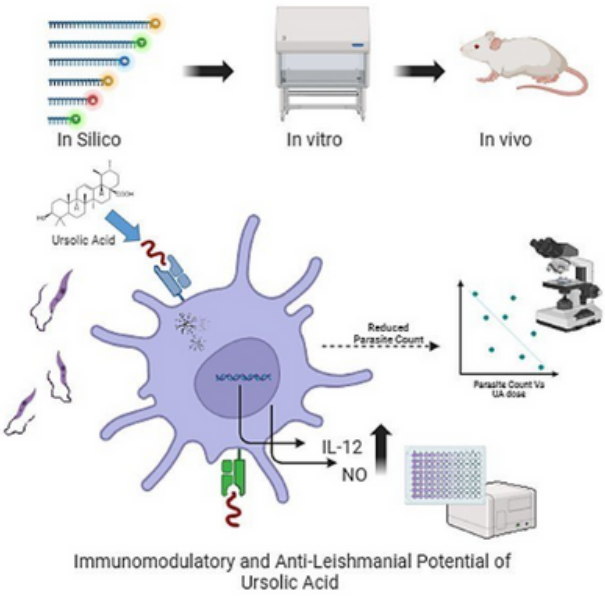
Immunomodulatory molecule Ursolic acid as a potential drug target for Leishmania specific Trypanothione Synthetase: In silico and In vitro approach

Keywords: Microbiology, immunology, parasitology, infectious disease, host-pathogen interaction

Abstract

Drug resistance and inefficiency is constantly emerging as a serious threat for human health. Multi drug resistance pathogens are extremely difficult to target with available spectrum of potential molecules. Investigation regarding search for novel molecules from scratch can incurred high cost also becoming cumbersome due to long time requirement. Application of bioinformatics tool made such investigation extremely easy. In this study we have investigated the difference in the sets of genes of Leishmania donovani parasite which have significant difference in sequence with human counterpart. 5876 out of 8014 genes have shown significant difference based on >40% pident value and >75% query coverage. 476 out of 5876 have their structure in PDB data base out of which 205 were found to be of known function. 42 genes out of 205 were conserved across all major leishmania species. Total 13 genes of leishmania specific origin were prioritised based on their virulency, stage specific expression and druggability. Docking study were performed for the 13 proteins with different molecules and it was found that Ursolic acid (UA) have significant good docking score against Trypanothione synthetase, a specific enzyme of Leishmania origin. We analysed the effect of UA in promastigotes which shows dose dependent increase in parasite death with increasing ROS generation. In vitro experiments revealed that UA can significantly reduce the parasite burden in RAW264.7 murine macrophage cells with EC50 value of 0.6 µg/ml.

Further experiment revealed that UA can modulate immune response by elevating the expression of IL-12 cytokines and subsequent increased in nitrite generation. Overall, the combination of in silico and in vitro approach shows a significant immunomodulatory and anti-leishmanial potential of ursolic acid.



Immunomodulatory and anti-leishmanial potential of Ursolic Acid
Credits: Created using Biorender

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YI 21

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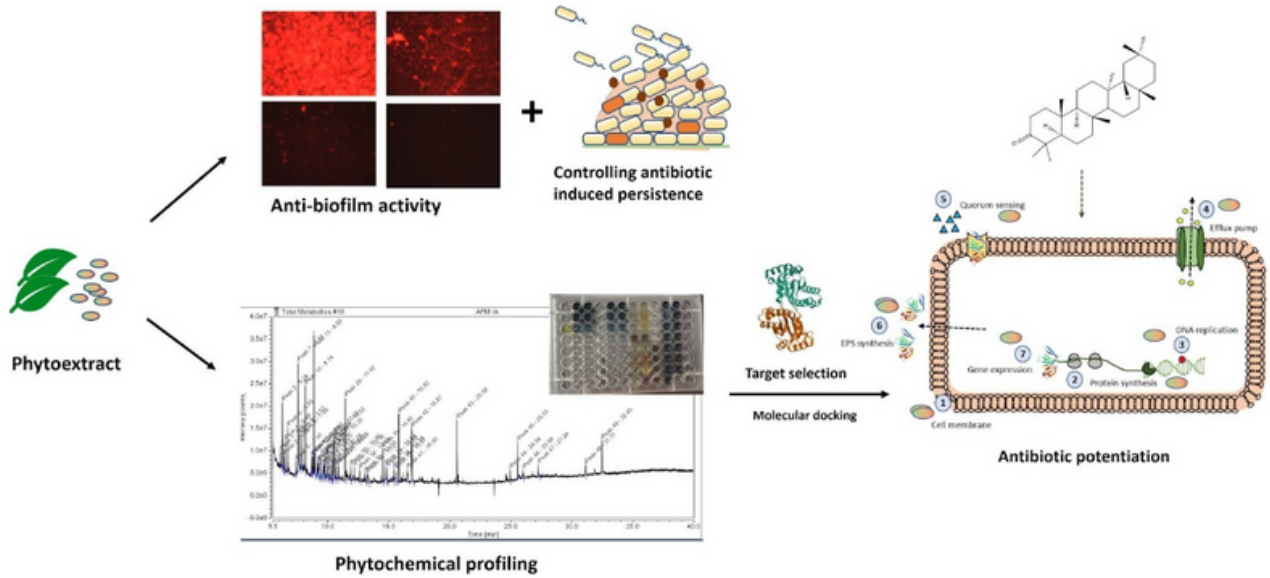
Synergism between phytochemicals and antibiotics to control Pseudomonas aeruginosa biofilm and antibiotic induced persistence

Keywords: Biofilms, quorum sensing, bioremediation, AMR, marine pollution

Abstract

There are numerous infections caused by bacteria and ocular infection is one of them. Bacterial keratitis (BK) is one such ocular ailment caused by the inflammation of clear tissue of cornea due to microbial infection. Contact lens (CL) users are more prone to BK as it provides ideal substratum for bacterial adherence and formation of biofilm. *P. aeruginosa* is key biofilm forming pathogen causing common ocular infections. With an aim to control antibiotic resistance in ocular pathogens we are looking for natural products derived from medicinal plants such as *Curcuma amada* (CA), *Andrographis paniculate* (AP), *Alpinia glanza* (AG), *Tribulus Terrestris*, *Bryonia laciniosa* (BL), *Avicennia marina* (AM), *Withania somnifera* (WS), *Glycyrrhiza glabra* (GG), *Psoralea corylifolia* (PC) etc. as antibiotic adjuvant to control biofilms and antibiotic induced persister cell formation by *P. aeruginosa*. Our finding shows that GG extract is effective in controlling biofilm formation on contact lens surface. GG, AP and Quercetin (Q) Gallic acid (G), Cinnamic acid (C) and Ascorbic acid (A) had shown antibiotic-potentiating effect. Combinational use of phytochemicals with antibiotic cause significant decline (> 30%) in the formation of persister cells. LC-MS and GC-MS profile of plant extract showed presence of numerous phytochemicals (morin, quercetin, cinnamic acid derivatives, β-amyrin etc.) which can as be used as antibiotic potentiators. Molecular docking studies of phytocompounds show multiple potential proteins in *P. aeruginosa* which can be targeted to potentiate antibiotic activity. We found that quercetin, which is a known antibiofilm phytocompound, can interfere quorum sensing (lasI, pqsR) biofilm associated EPS production (pelA, pelB) and gene associated with persistence (relA, spot). The approach can be useful in phytochemical repurposing and development of unconventional yet environmentally friendly antimicrobial drugs.



Synergism between phytochemicals and antibiotics | Credits: Dr. Neelam Amit Kungwani

Nithya N Kutty

YI 22

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Green extracts of waste marigold flowers as eco-friendly plant protective agents

Keywords: Metabolomics, floral volatiles, aromatic plants, green chemistry, plant-microbe interactions

Abstract

Green extracts of waste marigold flowers as eco-friendly plant protective agents Indian floriculture market is the second largest globally and amongst which marigold flowers accounts for nearly 75% of total production worldwide. However, mass production of marigolds generates large amounts of floral waste daily and without any sustainable method of disposal creates huge pollution in land and water bodies1. The present study involves the use of natural deep eutectic solvents (NADES) as a green method of pigment extraction from used marigold flowers2. In this study, different combinations (molar ratios) of glucose and citric acid, tartaric acid and choline chloride were used to prepare NADES systems. Ultrasound-assisted NADES based extraction of carotenoids using dried floral tissue was carried out. Further, total carotenoid content was estimated for NADES-based floral extracts. A combination of glucose: citric acid in optimised molar ratio showed higher extraction power with respect to other solvent systems. Further, thermal, photo and storage stability of these extracts in these solvent systems were assessed. Degradation rate analysis showed that the half-life of carotenoids was comparatively higher in NADES-based systems. Further we also assessed the antifungal activity of these extracts with plant pathogens viz. Sclerotia rolfsii and Botrytis cinerea. Interestingly, it was observed that eutectic solvents and marigold flower extracts showed antifungal activities. This preliminary study shows valorisation of waste marigold flowers and also potency of eutectic solvents as crop protective agents.

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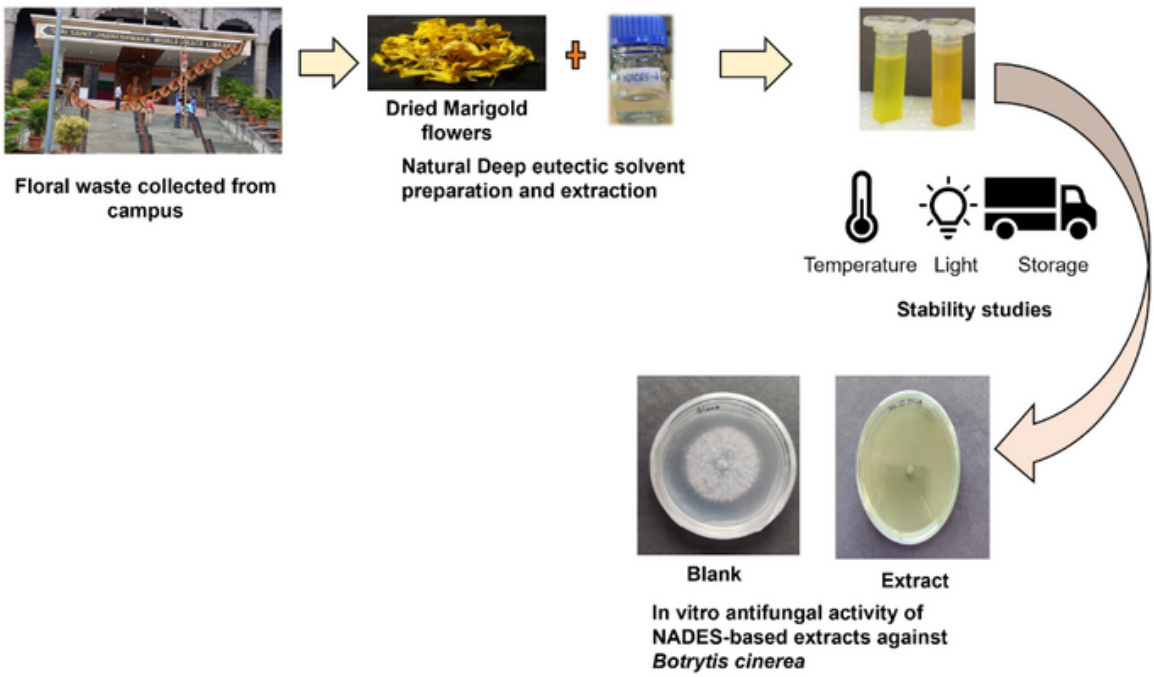

Natural deep eutectic solvent based extracts of used marigold flowers show higher stability and act as crop protective agents | Credits: Siddhi Hire, Prithviraj Gavai and Nithya N Kutty

Poonam Thakur

YI 23

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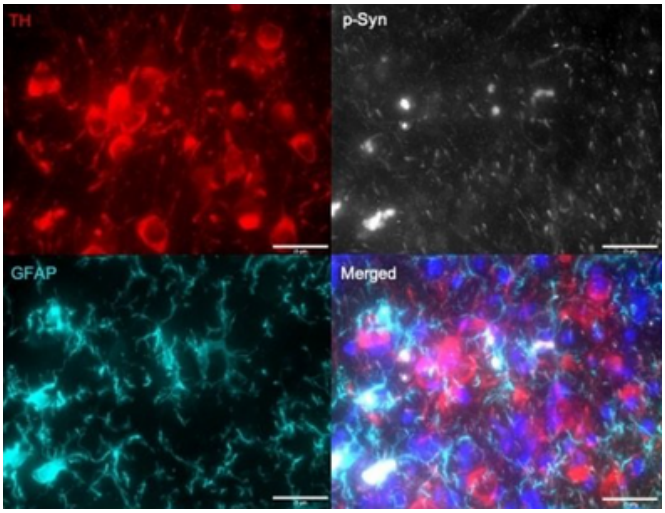
c-Abl inhibition as a therapeutic target for Parkinson's disease

Keywords: Parkinson's disease, neuroscience, dopamine, alpha-synuclein, autophagy

Abstract

Parkinson's disease (PD) is characterised by a progressive loss of substantia nigra dopaminergic neurons. This cell loss is believed to be driven by the accumulation of α-synuclein aggregates in the Lewy bodies in neurons. c-Abl, a non-receptor tyrosine kinase, has been implicated as an important player in PD pathogenesis. c-Abl affects several pathways involved in PD, such as α-syn aggregation, oxidative stress, synaptic dysfunction, and autophagy. Thus c-Abl inhibition presents a potential therapeutic target. The present study was designed to evaluate the therapeutic potential of a potent c-abl inhibitor drug PD180970.

Our results suggest that PD180970 can effectively cross the blood-brain barrier upon systemic injection and is detectable in the brain for up to 24 hours. Long-term dosing with the compound in an alpha-synuclein injection-based chronic mouse model of PD showed significant rescue from neurodegeneration at 16-week time points. Our results show that the drug was able to inhibit c-abl and cause a reduction in alpha-synuclein aggregation and neuroinflammation. Further mechanistic studies are currently underway. Thus, our studies support PD180970 as a potential drug candidate for treating PD pathology.



An image showing the appearance of aggregated alpha-synuclein (white) in the dopaminergic neurons (TH, red). IBA-1-positive microglia (cyan) can be observed engulfing these aggregates.
Credits: Jyotirmay Srivastava

YI 24

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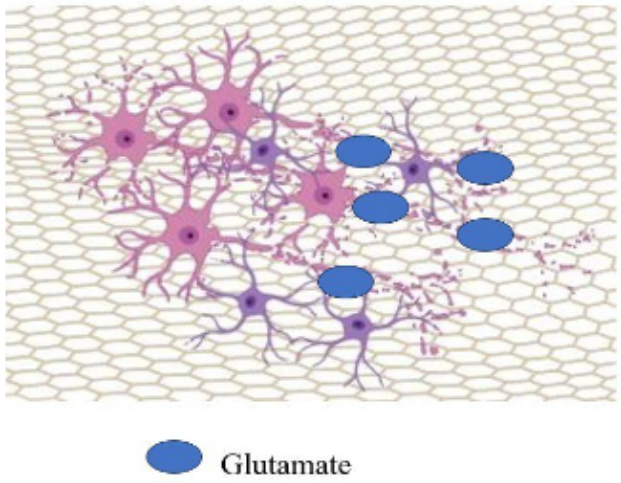
Graphene based nanomaterial: A tool for simultaneous sensing and support after neuronal injury

Keywords: Neurophysiology, spinal cord injury, synaptic physiology, voltage gated calcium channels, glutamate sensing

Abstract

Glutamate is a neurotransmitter released at synapses during any physiological activity involving excitatory neurons. After signaling or communication, glutamate is rapidly cleared from the synapses to prevent prolonged excitatory stress on neurons. However, in cases of neuronal injury, there is uncontrolled glutamate release, and the uptake mechanisms may also be compromised, leading to excitotoxicity and neuronal loss. Therefore, it is important to understand the dynamics of glutamate levels at various time points following injury to assess the extent of damage and develop a treatment plan for recovery. To achieve this goal, we use a non-enzymatic graphene-based biosensor for the detection of glutamate from bio fluid samples and to directly grow neurons for live sensing. Graphene, due to its large surface area-to-volume ratio and high conductivity, is an excellent material for precise, fast, and reliable biosensing. It could be utilised as a cost-effective point-of-use device. In this study, we propose the use of reduced graphene oxide decorated with metal oxide nanoparticles as a detection tool for both glutamate in fluid and live neurons. The metal oxide nanostructure on the reduced graphene oxide will enhance the conductivity and sensitivity of glutamate oxidation detection. Consequently, the outcome of this study promises to deliver an ultrafast glutamate sensing product suitable for both research and clinical applications following neuronal injury.



Real Time Glutamate Sensing | Credits: image edit from Biorender

Rajnish Kumar

YI 25

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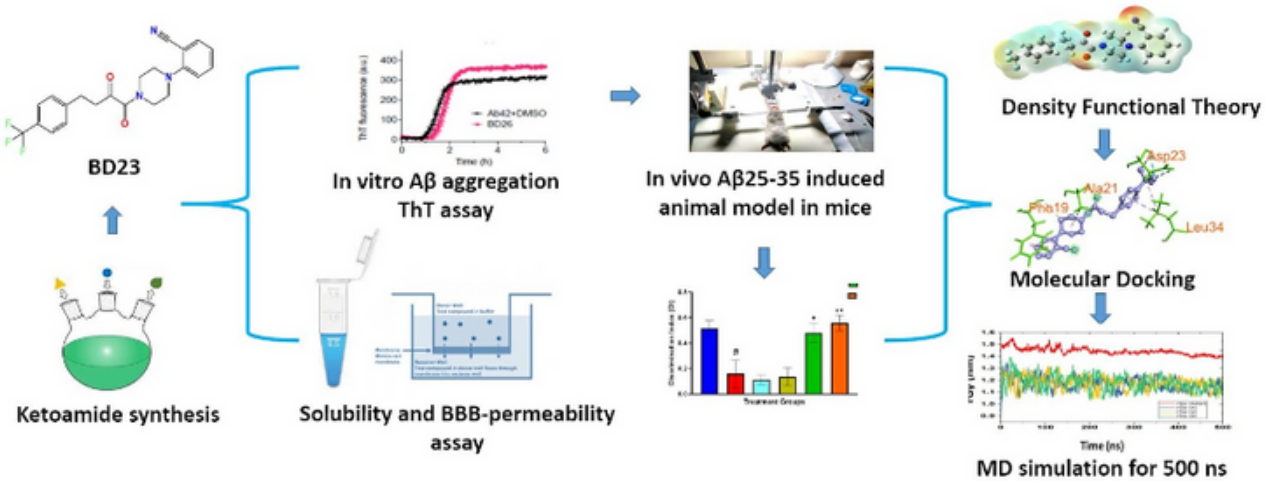
Discovery of novel α-ketoamide derivatives as protein aggregation modulators as potential therapeutics for Alzheimer's disease

Keywords: Drug discovery, alzheimer's disease, protein aggregation, amyloid beta, AI-based drug design

Abstract

The prevalence of Alzheimer's Disease, a multifactorial disorder, is steadily increasing. Given that there is no current effective therapy available, there is an urgent need for the discovery of novel therapeutic agents. Ketoamides have been found tremendous biological significance in several neurological disorders like AD and Parkinsons' disease by inhibiting calpain, caspase, and other proteases. The failure of a multitude of target-based therapeutics against AD motivated researchers to explore novel ways to treat the disease. However, the recent success of the amyloid beta targeted immunotherapies has motivated us to design and develop some amyloid beta aggregation inhibitors having α-ketoamide scaffold. In this study, we have synthesised several piperazine as well as piperidine-substituted ketoamide derivatives and evaluated them for their potential to modulate amyloid beta aggregation. In vitro, ThT-based aggregation kinetic assay revealed that several compounds

Further, solubility and blood-brain-barrier permeability studies established compound BD23 as a potent lead compound having optimal physicochemical properties. Moreover, in vivo study in an amyloid beta induced cognitive deficit mice model showed that compound BD23 improved learning and memory in a battery of behavioural tests and didn't show any motor toxicity evaluated through rotarod test at a dose of 5 mg/kg. Additionally, the compound BD23 was able to inhibit the tau aggregation in an in vitro assay at a concentration of 100 µM. Overall, the study reports the potential of α-ketoamide based compound BD23 as a potential lead that can be developed into a drug candidate for the treatment of AD.



Discovery of BD23 as a potential protein aggregation modulator | Credits: Bhanurajan Das

YI 26

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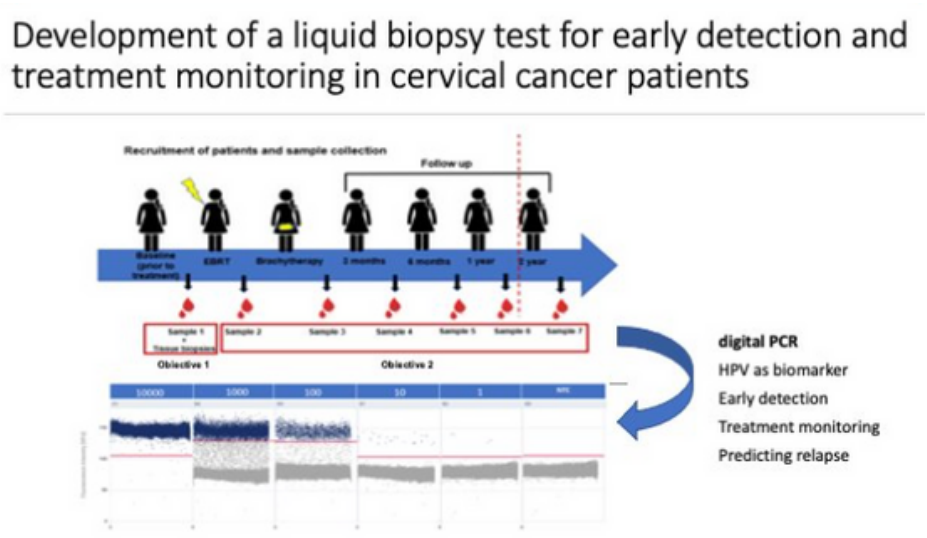
Liquid biopsy strategies for early detection and treatment monitoring of human papilloma virus associated cancers in india

Keywords: Liquid biopsy, cancer genetics, genomics, human papillomavirus, nanopore sequencing

Abstract

Detecting circulating tumor DNA (ctDNA) in the blood using minimally invasive techniques known as a "liquid biopsy", is gaining tremendous popularity in oncology research. Integration of human papillomavirus (HPV) DNA and the overexpression of the E6 and E7 oncogenes from high risk strains of HPV are crucial steps in the development of cervical cancer. We investigated the potential utility of HPV ctDNA as a biomarker for monitoring treatment outcomes in patients with cervical cancer. We use droplet digital PCR (ddPCR) to measure the amount of HPV16/18 ctDNA in plasma of cervical cancer patients. HPV standards GP5+/6+ primers were used to determine HPV positivity in our patients followed by HPV typing specifically the E6 oncogene of HPV16 and HPV18. Plasmids containing would act as a positive control for the assay. HPV16 and 18 plasmids were serially diluted and tested in qPCR as a template using different primer sets. Standard curves were made from the recombinant plasmids. This will serve as a positive control and will also provide a correlation between the sensitivity and specificity of qPCR vs ddPCR. We hypothesize that our dPCR test will be able to detect minute quantities of HPV ctDNA in plasma of cervical cancer patients as ctDNA levels are expected to be decrease as treatment progresses. We will now use the digital PCR system to understand HPV ctDNA levels in our patient cohort. We believe that our comprehensive sample collection after every treatment milestone and thorough follow-up for upto 2 years after diagnosis will allow us to study the utility of this sensitive test in monitoring disease and relapse.



Development of a liquid biopsy test for early detection and treatment monitoring in cervical cancer patients | Credits: Preetiparna Parida

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YI 27

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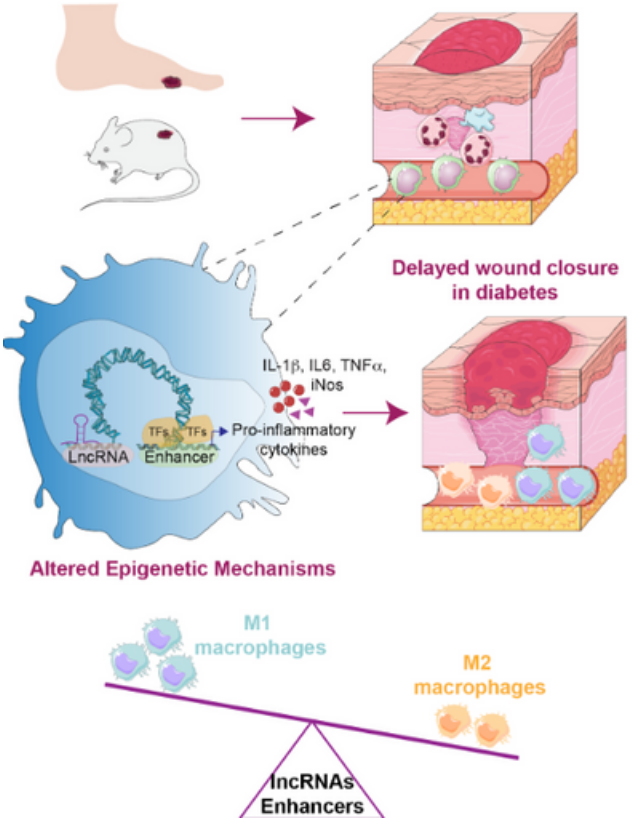
Understanding the role of the non-coding portion of the genome in diabetic wound-healing

Keywords: Diabetes complications, long noncoding RNAs, enhancers, epigenetics, wound-healing

Abstract

Accelerated diabetes can lead to chronic wounds due to impaired wound-healing, which causes severe morbidity and mortality in diabetic patients. Macrophage dysfunction is an important feature of impaired wound-healing characterised by altered macrophage polarisation. Although biochemical mechanisms involved in wound-healing have been studied, contributing epigenetic mechanisms are poorly understood. Transcriptional regulatory elements; enhancers, and long noncoding RNAs (lncRNAs) are implicated in several diseases, but their role in diabetic wound-healing are unclear. We hypothesise that transcriptional control by enhancers and lncRNAs might contribute to macrophage dysfunction in diabetic wound-healing. To address this, we differentiated splenic monocytes from diabetic (db/db) and non-diabetic (db/+) mice into uncommitted (M0), pro-inflammatory (M1), and anti-inflammatory (M2) macrophages. We observed increased M1 and decreased M2 signatures in macrophages from diabetic mice. RNA-sequencing analysis identified differentially expressed coding and non-coding genes among these macrophage populations in db/db compared to db/+. Several novel lncRNAs were dysregulated, amongst which we focused on two M2-specific lncRNAs. These lncRNAs MSTRG.21350 and MSTRG.708 were present near coding genes Ccr5 and Cxcr4, respectively, which were also dysregulated, indicating possible cis-regulation by these lncRNAs. Moreover, these lncRNAs and associated genes showed similar dysregulation in expression in the skin wound-tissues of normal mice, suggesting they play essential roles in wound-healing. To identify the transcriptional regulatory mechanisms underlying increased M1 signatures, we integrated our RNA-seq dataset with publicly available H3K27ac ChIP-seq/ATAC-seq datasets from bone marrow-derived M0 and M1 macrophages of control and diabetic mice. We identified 349 M1-specific enhancers, which were mapped to M1-specific genes. ATAC-seq integration confirmed the presence of open chromatin sites on these enhancers. Current experiments are focusing on elucidating the functional and mechanistic role of these lncRNAs and enhancers in impaired macrophage polarisation associated with delayed wound-healing in diabetes.



Role of transcriptional regulatory element in diabetes wound-healing
Credits: Ankita Priyadarshini

Satyajeet Khare

YI 28

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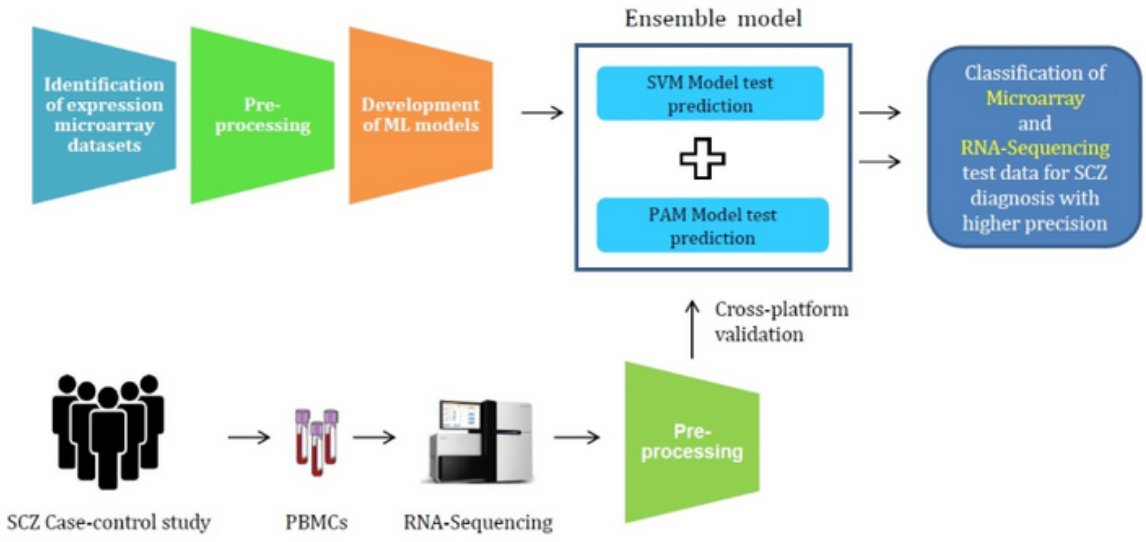
Ensemble learning for higher diagnostic precision in schizophrenia using peripheral blood gene expression profile

Keywords: Genomics, proteomics, machine learning, schizophrenia, diabetes

Abstract

Stigma contributes to a significant part of the burden of schizophrenia (SCZ) (Fox et al. 2018). The stigmatization associated with schizophrenia advocates the need for high-precision diagnosis. In this study, we present an ensemble learning-based approach for high-precision diagnosis of SCZ using peripheral blood gene expression profiles (Wagh *et al.* 2021). The ML models, support vector machines (SVM), and prediction analysis for microarrays (PAM) (Spang & Markowetz 2002) were ensembled using expression-array datasets with differentially expressed genes (DEGs) as features. The microarray-based learning was used to classify the RNA sequencing samples from our case-control study (Pune-SCZ). The ensemble learning predicted independent dataset samples with a precision of 78.97 % (SD: 0.06). The microarray-based learning classified the RNA sequencing samples from our case-control study (Pune-SCZ) with moderately high precision (66.00%, SD: 0.07). The feature genes were enriched in biological processes such as response to stress, regulation of the immune system, and metabolism of organic nitrogen compounds. RBX1, CUL4B, DDB1, PRPF19, and COPS4 were identified as hub genes. To the best of our knowledge, this is the first report on the use of ensemble learning for higher diagnostic precision in psychiatric disorders. Future efforts will be directed towards multi-omic integration and developing 'explainable' diagnosis methods.

1. Fox AB, Earnshaw VA, Taverna EC, & Vogt D. 2018. Conceptualizing and measuring mental illness stigma: The mental illness stigma framework and critical review of measures. Stigma and health 3(4): 348.
2. Spang R & Markowetz F. 2002. Microarray Analysis Classification by SVM and PAM. Molecular Biology: 1-9.
3. Wagh VV, Vyas P, Agrawal S, Pachpor TA, Paralikar V & Khare SP. 2021. Peripheral blood-based gene expression studies in schizophrenia: A systematic review. Frontiers in genetics 12: 736483.



Blood based SCZ diagnosis using ensemble learning for higher precision | Credit: Vipul Wagh

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YI 29

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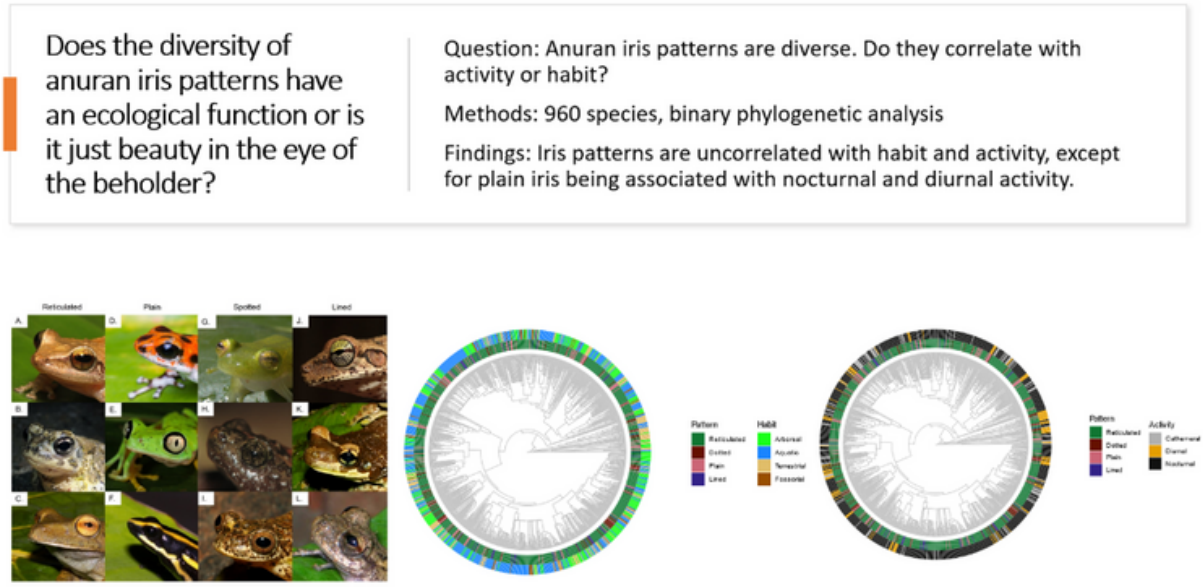
Does the diversity of anuran iris patterns have an ecological function or is it just beauty in the eye of the beholder?

Keywords: Animal behaviour, evolutionary ecology, terrestrial ecology, ecological restoration, forest canopies

Abstract

Iris patterns in the animal kingdom are incredibly variable, with anurans having some of the most diverse and intricate patterns. Although the shape and colouration of anuran eyes seem to be correlated with ecological factors, the evolution of iris patterns remains unexplored. We used a large-scale phylogenetic comparison, with 960 anuran species to examine the evolutionary and ecological correlates of iris patterns. We classified iris patterns into four categories: Reticulated, Plain, Dotted, and Lined, and examined whether iris pattern was correlated with diel activity (diurnal, nocturnal, and cathemeral activity) and habit (aquatic, arboreal, terrestrial, and fossorial) or both. Our analysis suggests that reticulated irises are the most common pattern in anurans and are the most likely ancestral character. The evolution of iris patterns across the anuran phylogeny best matched Brownian expectations, with many transitions between the four pattern types. Iris patterns, however, were mostly uncorrelated with diel activity or habit. The only exception was an association between plain irises and diel activity. Specifically, anurans with plain irises were more likely to be diurnal and less likely to be nocturnal; and the evolution of plain irises seemed to have preceded the evolution of diel activity. Overall, iris patterns across anurans are mostly unrelated to ecological factors, suggesting that this trait may be important for other functions, such as inter- or intra-specific interactions, or that the incredible diversity has evolved through neutral processes. Our findings open avenues for further research, especially to understand the potential adaptive value of the striking ornamentation in iris patterns across taxonomic groups.



Graphical abstract for the YIM 2024 application. Seshadri K S. Co-authors: Gangothri S and Maria Thaker

Image explains the research question, methods and key findings with graphs

Shashi Kiran

YI 30

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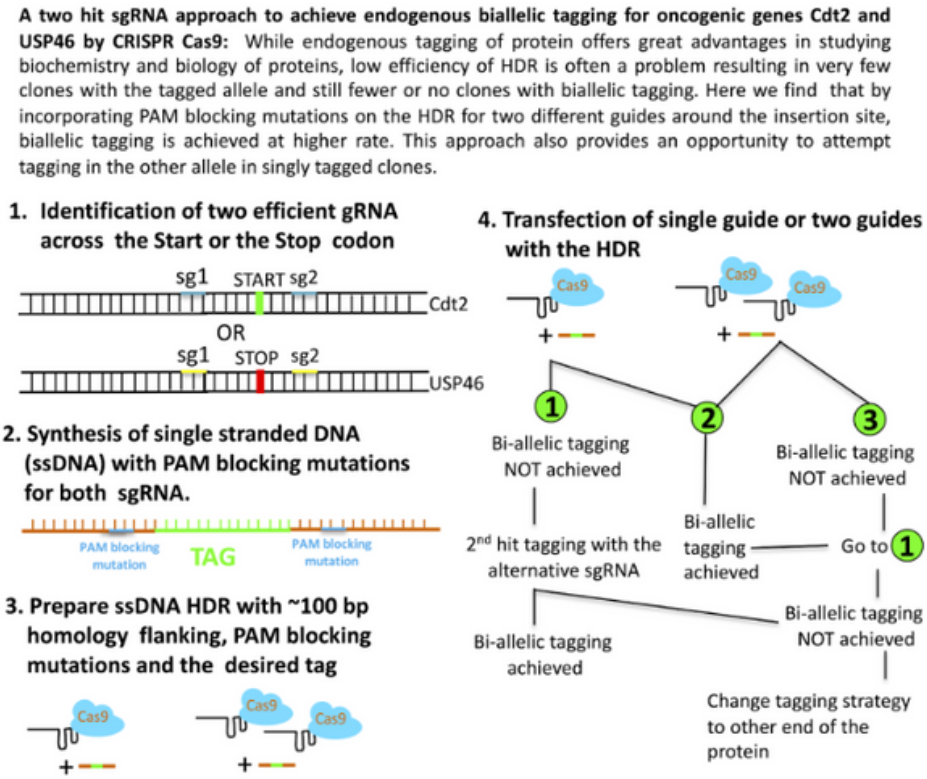
Identifying substrate repertoire of the oncogenic ubiquitinase CRL4Cdt2 and the USP46 deubiquitinase complexes through endogenous gene tagging

Keywords: Ubiquitination signaling, genome editing, oncology, DNA repair

Abstract

The CRL4Cdt2 ubiquitination complex and USP46 are crucial to the proliferation of cervical cancers and are present in a protein complex mediated by the HPV-E6 protein. While the CRL4-Cdt2 complex itself is critically essential to the proliferation of most cancers, USP46 is critical to the stabilisation of Cdt2 protein in HPV-induced cancers. We aim to characterise the Cdt2 and USP46 complexes by identifying substrate repertoire in primary and transformed cells. For this, we tagged endogenous genetic loci of USP46 with Strep-tag-II at the C-terminus and Cdt2 with the Flag-tag at the N-terminus using CRISPR-based genome editing. Here we present the strategy of generating such clones by genome editing and their usefulness. We first generated single-stranded DNA (ssDNA) with desired tags flanked by homology arms and PAM blocking mutations to be used as homology repair template. We tested different lengths of homology arms sufficient for gene integration. The ssDNA that has a homology of about 100 bp on either end was most efficient for site-specific integration of the tags. Longer lengths than 100bp did not improve the efficacy of edits. We found that the Cdt2 and USP46 gene locus yielded clones tagged at only one allele. The tagging of 2nd allele required a two-hit strategy by CRISPR Cas9. For this, two sgRNA were identified near the edit site. This strategy required prior mutation of the 2nd sgRNA on the ssDNA so that upon the 2nd hit, only the tagged allele is targeted, not one that was tagged earlier. These clones maintain the endogenous levels and stoichiometry of the endogenous Cdt2 and USP46 complexes and will be used to identify genuine interactors by tag pull-down and mass spectrometry.



A two hit sgRNA approach to achieve endogenous biallelic tagging for oncogenic genes Cdt2 and USP46 by CRISPR Cas9
Credits: Harsitha G.V.; Shashi Kiran

Shruthi Vembar

YI 31

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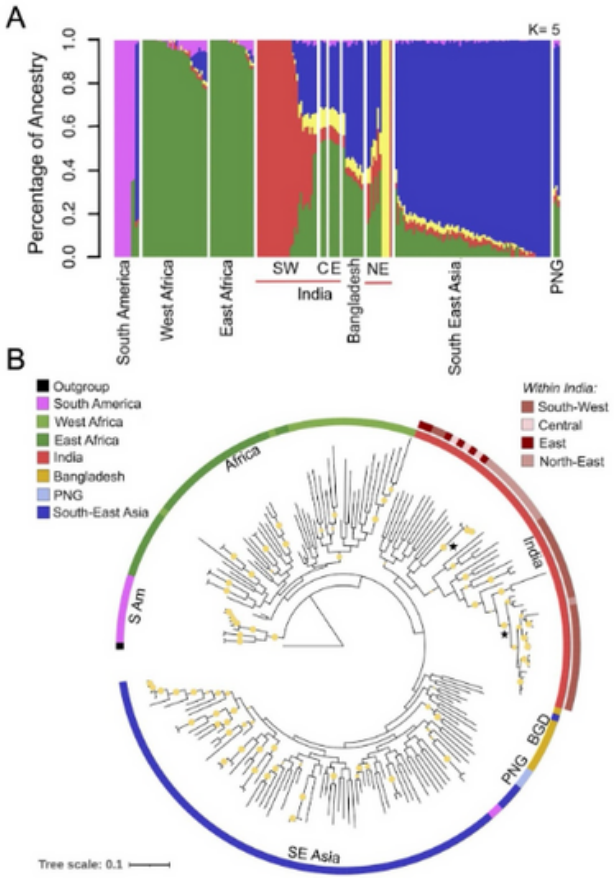
Genetic diversification of gene regulatory mechanisms in malaria parasites

Keywords: Molecular biology, genome editing, omics, gene regulation, parasitology

Abstract

In the past decade, the advent of faster and cheaper sequencing technologies has led to a rapid increase in the volume of genomic data available for pathogenic organisms such as the malaria parasite Plasmodium falciparum. This has in turn improved our understanding of parasite population structure and transmission patterns at the local and global scales, their adaptation to drug and vaccine administration, and genetic determinants of host-parasite interactions. However, a country that has been poorly represented in these studies is India, despite bearing the highest burden of disease in the South-East Asia Region. To fill this knowledge gap, we evaluated the genomic diversity of P. falciparum within India by sampling clinical isolates from four geographically distinct regions: South-West, Central, East and North-East India, and show for the first time the high genomic divergence of P. falciparum within the Indian sub-continent. Moreover, by comparing whole genome sequences of Indian P. falciparum isolates to those from across the globe, including other regions in India, we conclude that P. falciparum from the Indian sub-continent forms a genetic bridge between Africa and Asia. Yet, we find evidence of bottleneck events in the genomes of select isolates from South-West and North-East India which have led to the fixation of divergent ancestries in these regions. We are currently exploring the major genes/gene families that contribute to this divergence by estimating FST, IBD, Tajima's D and nucleotide diversity values. Overall, the exploration of Indian P. falciparum genomes significantly advances our understanding of malaria population structure and opens doors to investigate region-specific selection pressures that drive parasite evolution.



Population structure of malaria parasites inferred through genomics
Credits: Anitha Bavikatte

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YI 32

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Discovering disease comorbidities in mild traumatic brain injury patients using graph network approach: A traumatic brain injury model systems study

Keywords: Traumatic brain injury, neurodegeneration, bio-simulation, comorbidities, computational modeling

Abstract

Disease comorbidity is the occurrence of two or more diseases in the same individual, simultaneously or sequentially. The study of disease comorbidity has become increasingly valuable due to the growing burden of chronic diseases, aging populations, and the need for more integrated and personalised healthcare. One approach to studying disease comorbidities uses graph networks and mathematical representations of entity relationships. This network is a graphical representation of the relationships between diseases based on their co-occurrence patterns within a given population. The motivation for using disease comorbidity networks is threefold. First, a disease comorbidity network lends itself to analysis through well-established graph-theoretic algorithms that have been widely successful in numerous domains in biology and medicine. Second, the study of co-occurrence patterns between diseases enables the identification of common risk factors and shared pathophysiological pathways between diseases. Third, disease comorbidity networks can facilitate recognising high-risk groups within a patient population and developing targeted and preventative healthcare interventions. Recently, disease comorbidity networks have emerged as a powerful tool for understanding the complex relationships between medical conditions. However, one area that has been largely overlooked in this field is the application of these networks to populations with Traumatic Brain Injury (TBI). This study aims to investigate diseases comorbid in patients with mild TBI using a disease comorbidity network. We chose Traumatic Brain Injury Model Systems Database (TBIMS) as our data source, the largest longitudinal TBI dataset.

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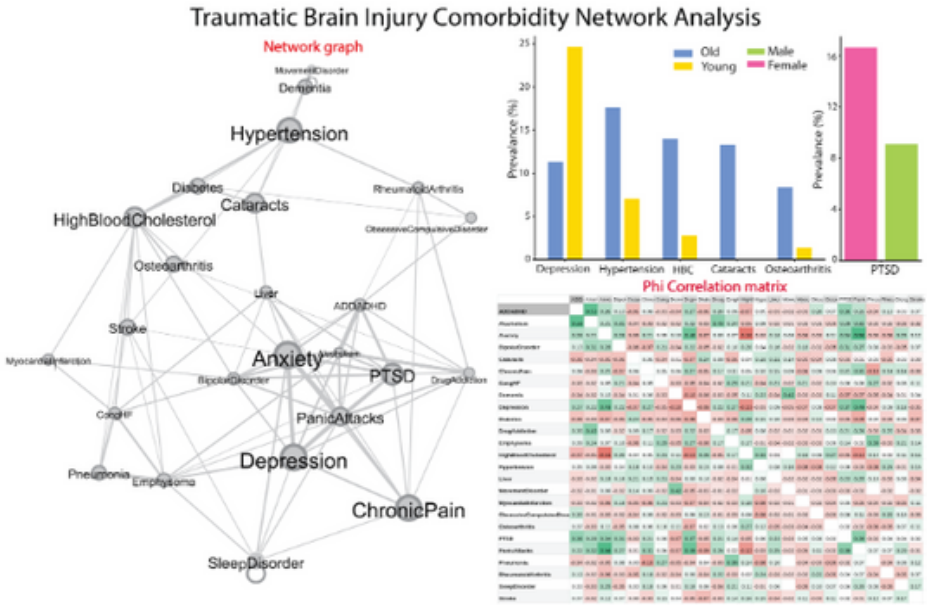
2. Traumatic Brain Injury Model Systems Program (2021). Traumatic brain injury model systems national database. Traumatic Brain Injury Model Systems National Data and Statistical Center, doi: 10.17605/OSF.IO/A4XZB



Traumatic Brain Injury Comorbidity Network Analysis | Credits: Shyam and Kaustav

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YI 33

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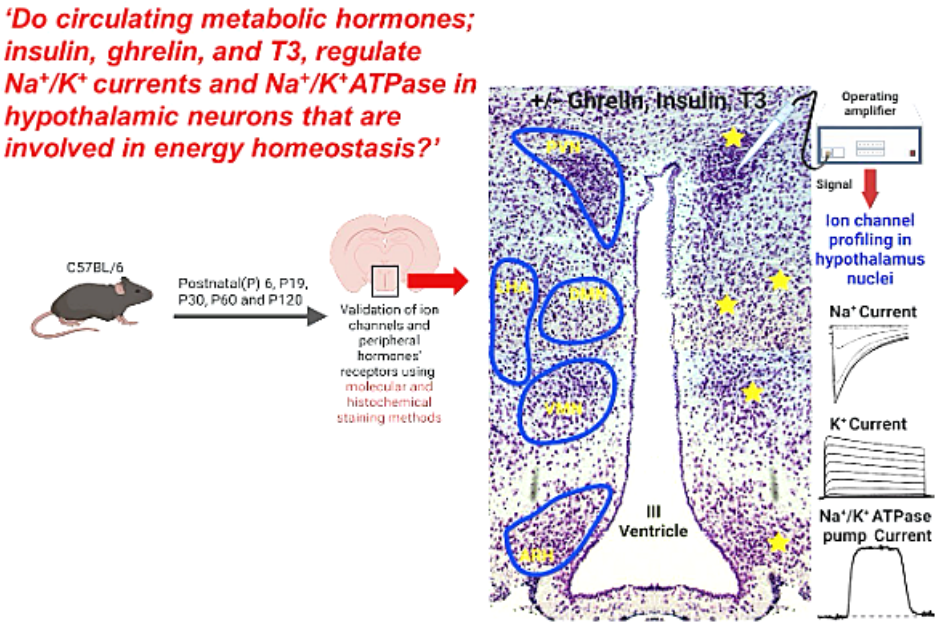
Regulation of ion channels in hypothalamic neurons governing energy homeostasis

Keywords: Neuroendocrinology, cell-energy metabolism, hypothalamic- pituitary communication , neuroanatomy, neural network and eating behaviour

Abstract

Obesity is one of the major global public health problems. Currently, India is facing the double burden of undernutrition as well as too much food intake. There are >135 million obese people in India. Therefore, any practical solution in combating this dreadful health condition will be of paramount importance. Primarily, food intake is controlled by brain hypothalamic nuclei in the central nervous system (CNS); such as paraventricular nucleus (PVN), ventromedial nucleus (VMN), dorsomedial nucleus (DMN), Arcuate nuclei (ARH) and lateral hypothalamus area (LHA). By integrating peripheral metabolic hormones (e.g. ghrelin, insulin, and thyroid hormone), specialised hypothalamic neurons maintain a homeostatic balance between food intake and energy expenditure. This process may become dysregulated in obesity and other metabolic disorders. About 40% of total testing energy is consumed by the Na+/K+ATPase, an integral membrane protein, which transports 3Na+ out and 2K+ into the cells by spending one ATP per cycle. Na+/K+ATPase acts as a regulator of neuronal activity. After periods of enhanced neuronal activity, the Na+ load increases, and Na+/K+ATPase (α-1,2,3 and β1,2 isoforms) cycle until the Na+ binding sites in the pump are no longer occupied. Therefore, any alterations that might happen in this ion exchange cycle would deteriorate the neuronal membrane potential and energy status and, consequently neuronal functions. Considering the interconnection between neuronal activity and cellular energy status, I have designed my research goal to address the effect of circulating metabolic hormones in ion channel modulation in hypothalamic nuclei which is involved in hunger and satiety. Further development of effective drugs targeting important ion channels may be promising for the treatment of metabolic diseases including obesity.



'Do circulating metabolic hormones; insulin, ghrelin, and T3, regulate Na+/K+ currents and Na+/K+ATPase in hypothalamic neurons that are involved in energy homeostasis?'
Credits: Biorender and powerpoint

YI 34

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A survey of epileptiform discharges in children with autism spectrum disorders and a pilot study of outcomes with exposure to anti-epileptic medication

Keywords: Autism, epilepsy, EEG

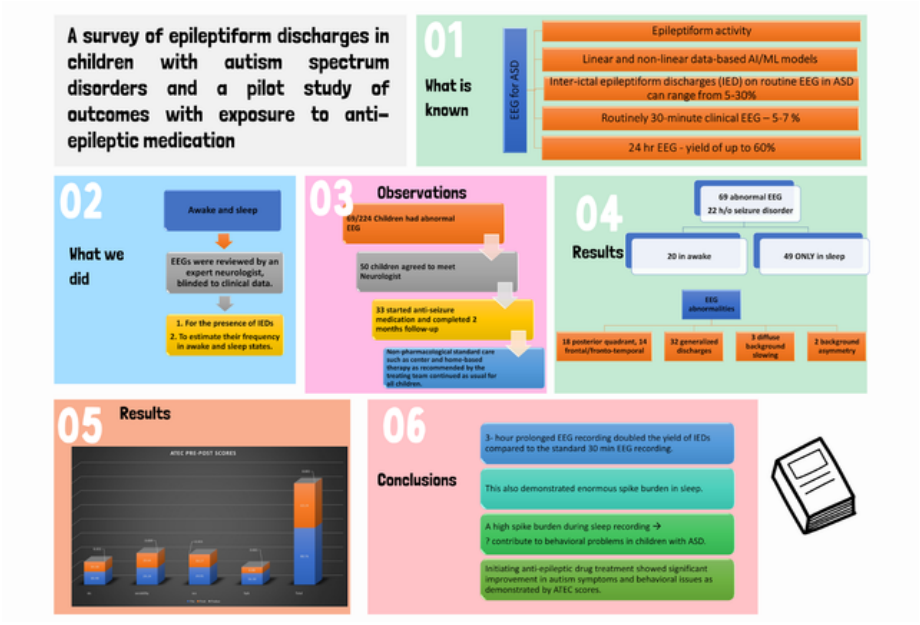
Abstract

Introduction: Children with Autism Spectrum Disorder (ASD) have increased prevalence of epilepsy and/or abnormalities in EEG associated with behavioural issues. The role of anti-epileptic drugs (AEDs) in such cases remains uncertain. Preliminary studies using EEG have suggested that prolonged EEG (up to 3 hours) recordings, including awake and sleep states, increase identification of significant epileptiform abnormalities in ASD. We conducted this study to measure the prevalence and frequency of interictal epileptiform discharges in children with ASD in both awake and sleep states and explore short term clinical response to AEDs in those with IEDs.

Method: 133 children with ASD aged 2-17 years underwent EEG recording using a 64-channel Philips Geodesic EGI 400. Children predominantly had moderate to severe ASD. EEGs were reviewed by the neurologist to assess for IEDs and estimate their frequency in awake and sleep states. For 12 children with abnormal EEG, AEDs were started. A pre and post treatment (2 months) assessment was done using Autism Treatment Evaluation Checklist (ATEC).

Results: Of the 133 children, 20 (15%) had IEDs in their awake-records. This yield increased to 47 children (35.3%) with extended-records. Frequency of IEDs increased from 'rare' to 'very frequent'/'continuous spikes' in sleep. 12 children who were exposed to AEDs were followed up after 2 months. There was significant improvement on the Autism Treatment Evaluation Checklist Scores. None of these children had additional interventions compared to baseline.

Conclusion: Prolonged EEG recording increases the yield of IEDs in children with ASD. High spike burden in sleep could arguably contribute to the behavioural problems in children with ASD. This reasoning led to use of AEDs with observed behavioural improvement. We provide pilot evidence to show that AEDs may be beneficial in severe forms of ASD. Well-controlled interventional studies with larger samples, to explore cognitive and behavioural outcomes are necessary.



This is the summary of my abstract

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YI 35

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Modeling and characterising developmental epileptic encephalopathy – 28: From basic science to translational medicine

Keywords: Neurodevelopmental, neurological disease, induced pluripotent stem cells, human brain organoids, regenerative medicine

Abstract

Rationale: Developmental epileptic encephalopathy-28 (DEE28, OMIM 616211), also known as WWOX-related epileptic encephalopathy (WOREE) syndrome is caused by human germline biallelic mutations in WW domain-containing oxidoreductase (WWOX). DEE28 is a neurodevelopmental disorder characterised by intractable epilepsy, severe developmental delay, ataxia and premature death at the age of 2-4 years. The underlying mechanisms of WWOX actions in DEE-28 development are poorly understood. Methods: Using genetic mouse modeling and patient-derived induced-pluripotent stem cells (iPSCs) and brain organoids, we studied WWOX in brain homeostasis and in its loss of function in DEE-28/WOREE syndrome. WWOX restoration was achieved using an adeno-associated viral vector (AAV9) harboring human WWOX cDNA and driven by the human neuronal Synapsin I promoter (AAV9-SynI-WWOX). Results: We demonstrated that specific neuronal deletion of murine Wwox produces phenotypes typical of the Wwox-null .In-depth characterisation of these mice revealed a major myelination defect that results in reduced maturation of oligodendrocytes, reduced myelinated axons and impaired axonal conductivity. Brain hyperexcitability as well as dramatic cellular and molecular CNS abnormalities, were also revealed in human unpatterned brain organoids derived from CRISPR-engineered human ES cells and from patient-derived iPSCs. Furthermore, we provide a proof-of-concept that ectopic WWOX expression, using AAV9-SynI-WWOX, could rescue these phenotypes.

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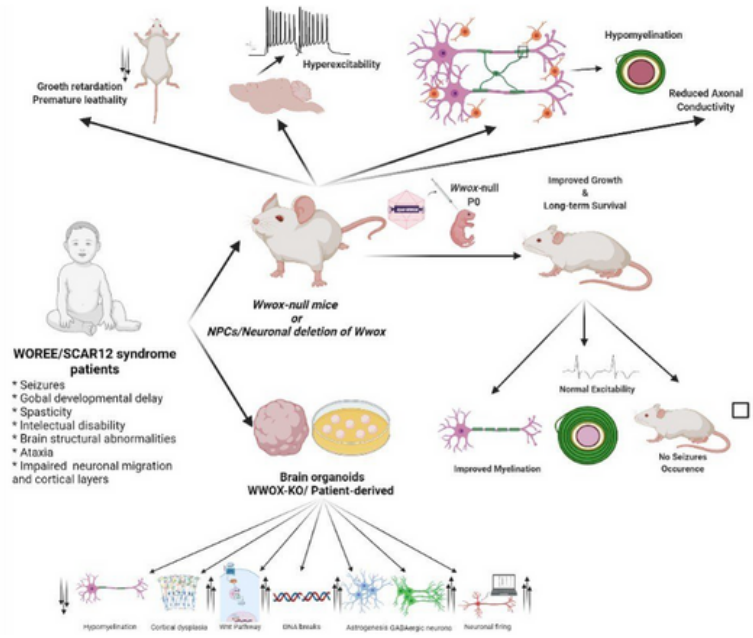
2. Steinberg DJ, Repudi S, Saleem A, Kustanovich I, Viukov S, Abudiab B Aqeilan RI. 2021. Modeling genetic epileptic encephalopathies using brain organoids. EMBO Molecular Medicine 13: e13610



Modelling neurodevelopmental disease: from Basic to Translational Medicine | Credits: from bench to bedside

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YI 36

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Uncovering novel mechanisms regulating protein synthesis under stress

Keywords: Protein synthesis, RNA biology, mTOR signaling, long noncoding RNAs, proteomics

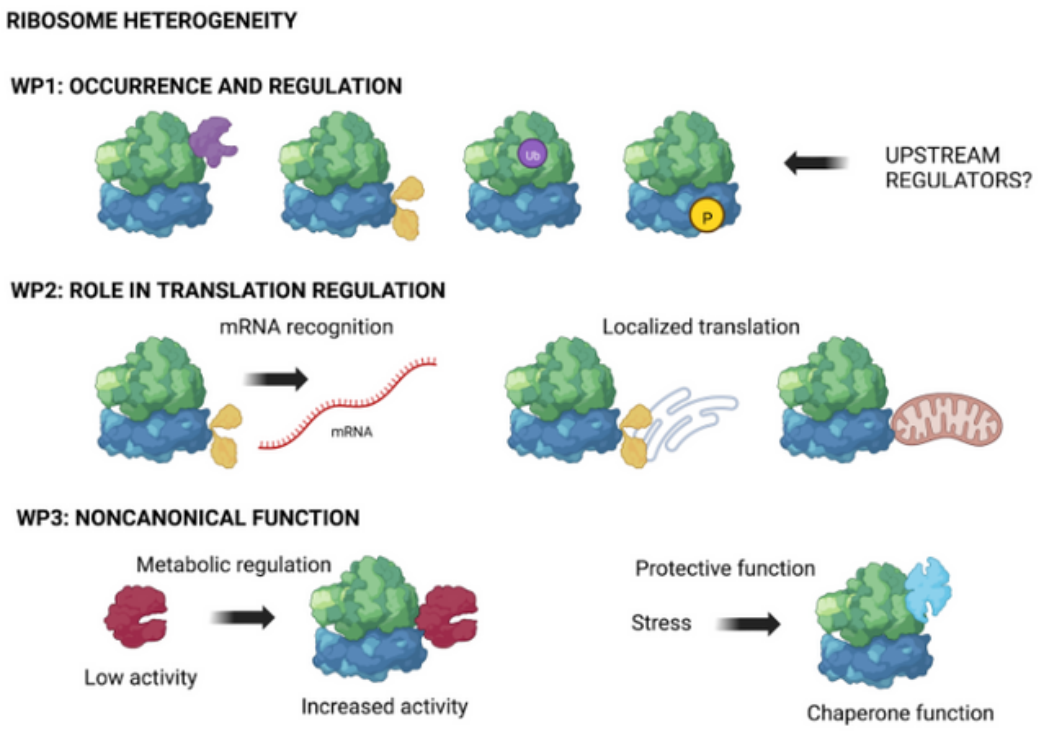
Abstract

Differential regulation of protein synthesis in response to changes in environmental and cellular conditions is an area of research that has implications in various diseases and developmental conditions. It is known that upon some stresses, which can range from nutrient deprivation to oncogenic insult, cells normally shut down global protein synthesis but allow translation of a subset of mRNAs which in turn help to cope with the stress. The signaling molecules or the cues that facilitate such selective translation in cells is of great significance to understand the biology of stress-responsive mechanisms and develop novel anti-cancer therapeutics.

Ribosomes are the ancient ribozymes which catalyse the reaction of peptide bond formation. Although core catalytic units of the ribosomes are highly conserved, there is a drastic increase in the complexity of ribosomes from bacteria to humans. Recent studies attribute the complex heterogeneity in the ribosome composition with respect to its associated factors, modifications, and rRNA sequence. However, regulation of protein synthesis, or translation of specific mRNAs by these ribosomal variants is still not widely explored. Furthermore, upstream regulators of ribosome compositions are not yet characterised. Hence, as a principal investigator, my group in ACTREC is interested in the following questions:

(1) How is protein synthesis regulated by nutrient sensing pathways?

(2) How is protein synthesis reprogrammed in cancer cells?



Ribosomal heterogeneity in gene regulation | Credits: Sunil Shetty

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YI 37

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Targeted phyto nanomedicine based delivery system for cancer therapy

Keywords: Nanotechnology, nanoparticles, drug delivery, cancer therapy and theranostics, phytomedicines

Abstract

Cancer is one of the most debilitating diseases in the world and in spite of a myriad of therapeutics; there is still need for safe, effective and targeted delivery system. Nanotechnology-based drug delivery can enhance therapeutic efficacy by reducing occurrence of adverse drug effects and allowing for less frequent administration, which can lead to greater patient compliance and higher adherence rates, ultimately resulting in improved treatment outcomes. On other hand, phytomedicines or herbal medicines in addition to their anticancer properties also provide other therapeutic benefits in terms of antimicrobial effects, antioxidant boosters, reducing inflammation, etc. The present investigation is aimed to synthesise various phytomedicine (Citrus, curcumin, gooseberry, aloe vera, etc.) blended multifunctional chitosan nanoparticles (PCNPs). The efficiency of the nanoparticles would be further enhanced by effectively targeting folate receptors (over-expressed in cancer cells), thus increasing therapeutic index of drugs. These would then be characterised by various analytical techniques. Toxicity testing of these novel formulations would be done on *drosophila melanogaster* to rule out the toxicity of blended-nanoparticulate carrier system. Additionally, the antimicrobial effectiveness of the nanoparticles (NPs) will be assessed by determining the minimum inhibitory concentration and minimum bactericidal concentration. The anticancer and targeting efficacy of these functionalised nanoparticles would also be tested on various cancer cell lines. The project is aimed at formulating a proof-of-concept non-toxic and targeted drug delivery vehicle aimed at minimising need for currently used chemotherapeutic drugs.

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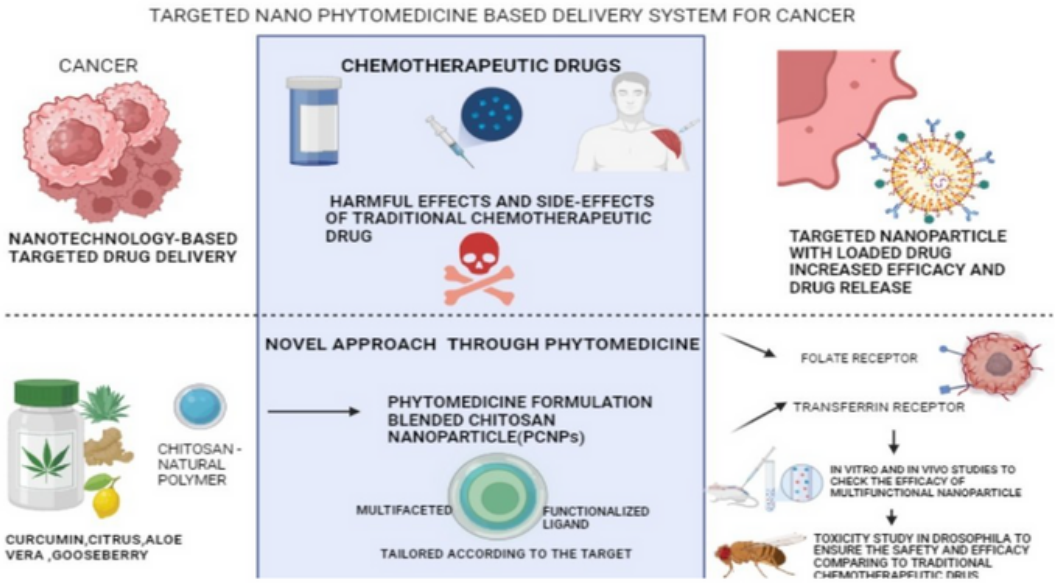

Targeted Phyto Nanomedicine Based Delivery System for Cancer Therapy | Credits: Suphiya Parveen, Abira R

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Synthesis of Butterfly Attractant for Pollination and Ecosystem Health

Keywords: Plant metabolites, nectar, network analysis, plant biomass, bioethanol

Abstract

Plant-pollinator interactions play a vital role in maintaining the health and stability of the ecosystem (Ollerton 2017). The decline in the number of insects due to climate change, excessive pesticide use etc., is affecting the plant-pollinator network (Sanchez Bayo and Wyckhuys,2019). Enhancement of floral visits by pollinators by developing natural attractants is one of the strategies to tackle this challenge. In this work, we have identified plants that are frequently visited by butterflies in the western ghats, one of the biodiversity hotspots. We performed extraction and isolation of essential oils and nectar from the flowers using standard methods. Characterization of essential oils and nectar was performed using GC-MS and LC respectively. The role of nectar and essential oils in attracting the pollinator was tested by devising a bioassay. We studied 62 endemic plant species which were visited by 105 butterfly species. A pollination network was created for the butterfly and plant species. The nectar was collected from 52 plant species and their standing nectar crop was estimated. We have characterised nectar composition for 23 plant species and essential oil from 3 plant species. We have performed a bioassay using formulation based on the nectar composition of the Ligustrum plant as it is the plant visited by most butterfly species. In conclusion, we found that the nectar volume, nectar composition, and plant pollination syndromes collectively contribute in attracting the pollinators.

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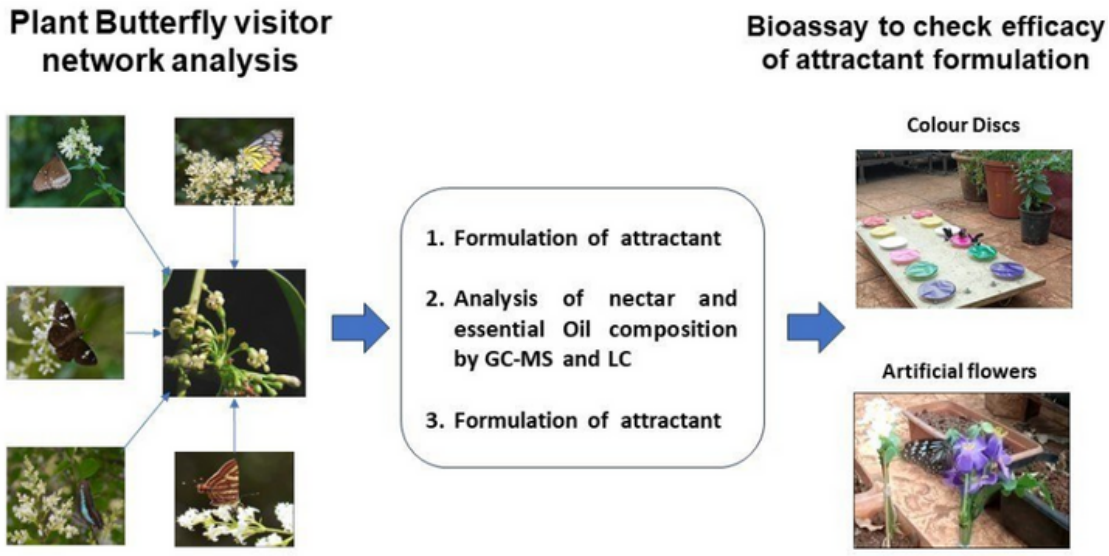

Synthesis of Butterfly Attractant for Pollination and Ecosystem Health | Credits: Mark Miller

YI 39

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Polyploidy and senescence in the placenta: Myc is having a (tropho) blast

Keywords: Placenta, development, DNA damage, polyploidy, senesence

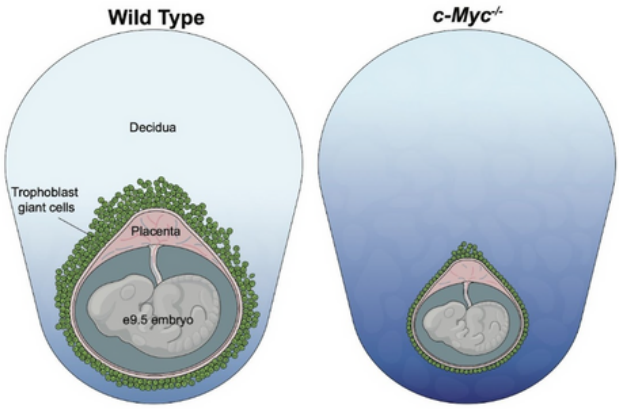
Abstract

Objectives:
The placenta is essential for reproductive success. The murine placenta includes polyploid giant cells that are crucial for its function. Polyploidy occurs broadly in nature but the regulators and significance in the placenta are not well characterised.

Methods:
We used fully developed mouse placenta to identify ploidy levels in several cell types and its molecular regulators using DNA-FISH and scRNA-seq. Further, using RNA-FISH, RNA-seq, histology and immunostaining techniques we characterised role of one of the molecular regulator Myc, in ploidy regulation and senescence in mouse placenta.

Results:
We discovered that many murine placental cell types are polyploid and identified several factors that license polyploidy using single-cell RNA seq. We characterised one of the molecular regulator Myc using a mouse model. Our result suggests that MYC is required for multiple rounds of DNA replication via endocycles in trophoblast giant cells. Furthermore, MYC supports the expression of DNA replication and nucleotide biosynthesis genes along with ribosomal RNA. Increased DNA damage and senescence occur in polyploid trophoblast giant cells without Myc, accompanied by senescence in the neighboring maternal decidua.

Conclusions:
These data reveal that Myc is essential for endocycling and polyploidy to support normalplacental development, thereby preventing premature senescence. Our study combined with the literature suggests Myc is an evolutionarily conserved regulator of polyploidy. Currently we are using a trophoblast stem cell model to screen for other molecular regulators of polyploidy and senescence using genome-wide approaches.



Role of Myc in the placental development | Credits: Mark Miller

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Optoelectronic biointerfaces for stimulating neuronal cells

Keywords: Bioelectronics, neuroscience, nanotechnology, tissue engineering, scaffolds

Abstract

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 regenerate neural circuits upon brain damage and injury.

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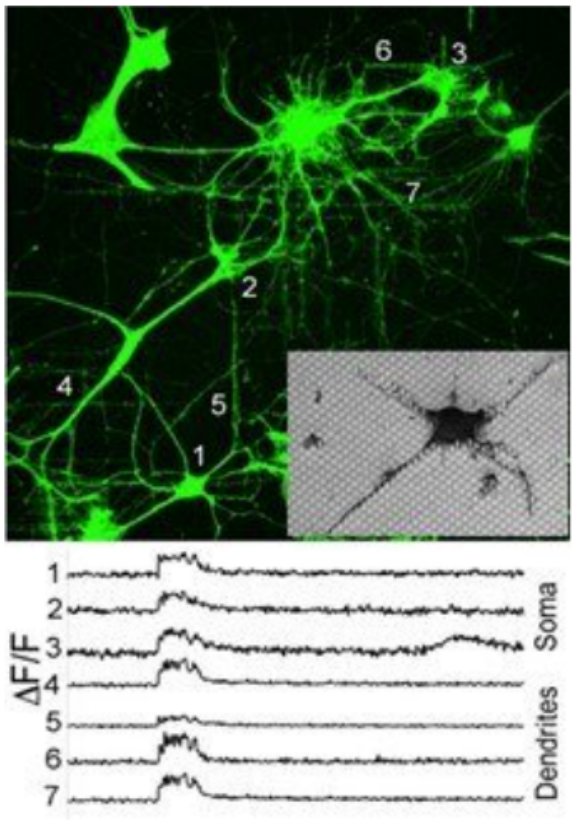

(Top) Functional Ca2+ imaging of neuronal cells and circuits on a semiconductor nanowire scaffold. (bottom) Ca2+ activity (F/F) as a function of time at the marked dendrites and soma. (inset) SEM image of a neuron on a nanowire scaffold.
Credits: Vini Gautam

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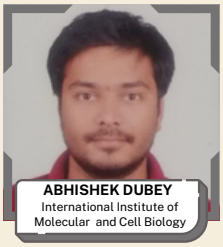

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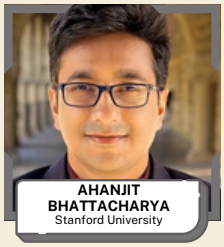

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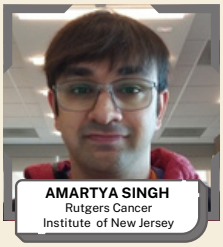

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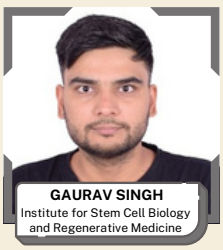

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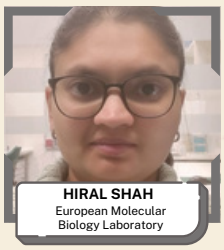

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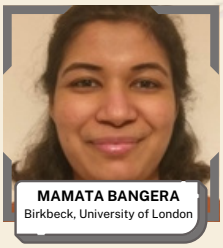

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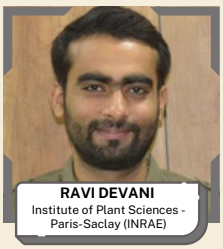

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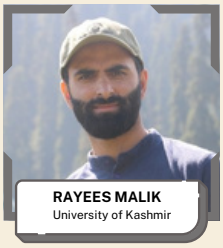

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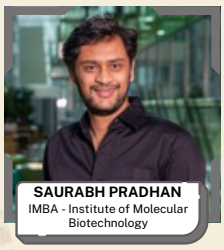

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Postdoctoral Fellow Abstracts

The abstracts have been printed exactly as submitted by the participants.
The organisers of YIM 2024 are not responsible for any errors in them.

PDF 01 Aara Patel
Developing targeted therapies for Norrie disease

PDF 02 Abhishek Dubey
Sterility-independent enhancement of proteasome function via floxuridine-triggered detoxification in *C. elegans*

PDF 03 Ahanjit Bhattacharya
A chemical synthetic biology approach to origin, structure, and dynamics of cellular membranes

PDF 04 Amartya Singh
Piccolo: A novel workflow for performing single-cell gene expression analysis

PDF 05 Amitabha Mukhopadhyay
Mechano-sensing enhances neutrophil defense and mitigates pulmonary infection

PDF 06 Angelina Thomas Villikudathil
An experimental machine learning study investigating the decision-making process of students and qualified radiographers when interpreting radiographic images

PDF 07 Aniruddha Panda
Direct determination of membrane protein complexes from lipid bilayer and its application in neuronal exocytosis

PDF 08 Ankit Tiwari
RAL-B dependent sensory neuron to cancer cell mitochondria exchange

PDF 09 Arpita Ghosh
Decoding the mechano-sensitive nature of NEAT1 lncRNA in glioblastoma: Implications for cancer progression and therapeutic strategies

PDF 10 Ashwini V Mohan
Comparative genomic architecture of chromosomal fissions and fusions in holocentric sedges

PDF 11 Debanjan Mukherjee
Does environmental heterogeneity impact Plasmodium parasites and severe malaria?

PDF 12 Dhananjay Huilgol
Generating excitatory neuronal diversity in the cerebral cortex

PDF 13 Fanindra Kumar Deshmukh
Structural elucidation of FAN1 protein complexes involved in Huntington's Disease and DNA Repair

PDF 14 Gaurav Singh
How dynamic modulation of mitochondrial inner membrane fluidity might regulate respiration

PDF 15 Gayatree Mohapatra
Understanding the lifeguard at the immunological barrier: The mechanism of patrolling by inflammasome at the gastrointestinal firewall

PDF 16 Gopal Chovatiya
Lineage-specific nascent transcription maps reveal molecular principles of tissue dynamics

PDF 17 Gyanendra Singh Sengar
Development of green nanoparticle-based bivalent paper-strip immune assay for simultaneous early detection of African swine fever and Classical swine fever viral antigens in pig

PDF 18 Hiral Shah
Lifecycle-coupled evolution of microtubule organising centres and mitosis in close relatives of animals

PDF 19 Kailash Chandra Mangalhara
Manipulating mitochondrial electron flow enhances tumor immunogenicity

PDF 20 Kartik Totlani
Unravelling bacterial transcription regulation in droplet-based microfluidics

Postdoctoral Fellow Abstracts

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PDF 21 **Mamata Bangera**
Tracing the cytoskeletal blueprint in vitro

PDF 22 **Manoj Kuamwat**
Emerging organic pollutants (EOPs) induce antimicrobial resistance in Salmonella: An experimental study

PDF 23 **Maya Raghunandan**
Translating genomic knowledge from bench to bedside advancements in cancer therapy

PDF 24 **Neetika Ahlawat**
Nutrient packaging alters adaptation and genetic divergence in *E. coli*

PDF 25 **Neha Dubey**
Autophagy pathway proteins plays distinct roles in regulating lung inflammation during tuberculosis infection and asthma

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PDF 27 **Prachi Nawkarkar**
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Early life adversity in rodents perturbs hippocampal mitostasis and drives inflammaging in age-dependent manner

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Precipitation reconstruction of Srinagar, Jammu and Kashmir, India from tree-rings

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Association of adiposity and its changes over time with COVID-19 risk in older adults with overweight/obesity and metabolic syndrome: A longitudinal evaluation in the PREDIMED-Plus cohort

PDF 32 **Sarita Sarita**
Molecular features of native and fibril form of AL55 light chain associated with AL amyloidosis

PDF 33 **Saurabh Pradhan**
Decoding species specific regulatory codes of trophectoderm specification and implantation

PDF 34 **Sayantan Panda**
A pair of microRNAs controls the unique pigmentation shift in developing eggplant fruit skin

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Neuron-specific CRISPR genetics to study the role of mitochondrial dynamics in aging Drosophila neurons

PDF 36 **Siddharth Jayakumar**
Neural and algorithmic bases of odor guided trail following in mice

PDF 37 **Sravanthi Nadiminti**
Mechanisms for synaptic vesicle biogenesis

PDF 38 **Sreeja J S**
Transporting Gli transcription factors to the cilium tip for Hedgehog signaling: A tale of two motor systems

PDF 39 **Tukki Sarkar**
Red and near-infrared light-triggered dual cancer phototherapy by using a dipyridophenazine Ni(II) dithiolene complex

PDF 40 **Vishnu Muraleedharan Saraswathy**
Regulation of adult neurogenesis and axon regrowth during spinal cord regeneration

PDF 01

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Developing targeted therapies for Norrie disease

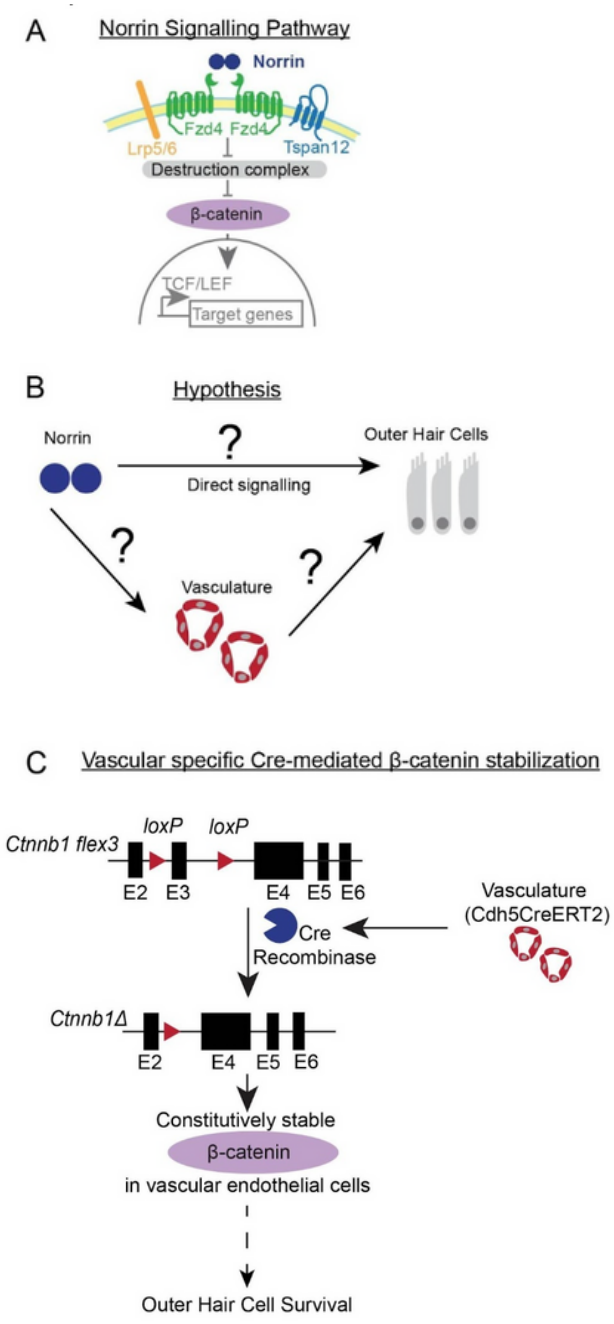
Keywords: Genetics, genomics, blindness, deafness, gene therapy

Abstract

Norrie disease is an X-linked recessive deaf-blindness condition. Congenital blindness and progressive hearing loss severely affect quality of life. It is caused by mutations in NDP. NDP encodes a secreted signaling molecule norrin, which binds to a receptor complex on target cells, activating canonical WNT signaling and stabilising β-catenin, which modulates downstream gene expression. Mice lacking a functional Ndp gene (Ndp-KO) show early abnormalities in the cochlear microvasculature, followed by sensory hair cell death and hearing loss. We recently showed that this phenotype can respond to AAV-mediated NDP gene replacement (1). To better target NDP gene therapy in patients we aimed to improve understanding of the requirement for norrin signaling in cochlea cells.

We hypothesised that vascular endothelial cells are the primary target of norrin signaling in the cochlea. We simulated the effect of norrin signaling to vascular endothelial cells only, using a tamoxifen-inducible Cdh5CreERT2 driver transgene and the Ctnnb1 flex3 allele to activate β-catenin constitutively in Ndp-KO mice. This intervention rescued cochlear microvascular abnormalities and gene expression. Importantly, it prevented the sensory hair cell death and hearing loss. Single-cell transcriptomic analysis of cochlea cells showed that norrin co-receptor expression coincides in vascular endothelial cells, supporting the importance of norrin signaling in maintaining vasculature integrity and a suitable cochlear micro-environment. These results are being used to inform the development, targeting and timing of NDP gene therapy for clinical translation and may have wider implications for more commonly occurring age-related hearing loss which may have a vascular origin.

1. Pauzuolyte V, Patel A, Wawrzynski JR, Ingham NJ, Leong YC, Karda R, Bitner-Glindzicz M, Berger W, Waddington SN, Steel KP & Sowden JC. 2023. Systemic gene therapy rescues retinal dysfunction and hearing loss in a model of Norrie disease. EMBO Mol Med: e17393.



Identifying cochlear vascular endothelial cells as the primary target of norrin signalling in the cochlea. Credits: Aara Patel

Abhishek Dubey

PDF 02

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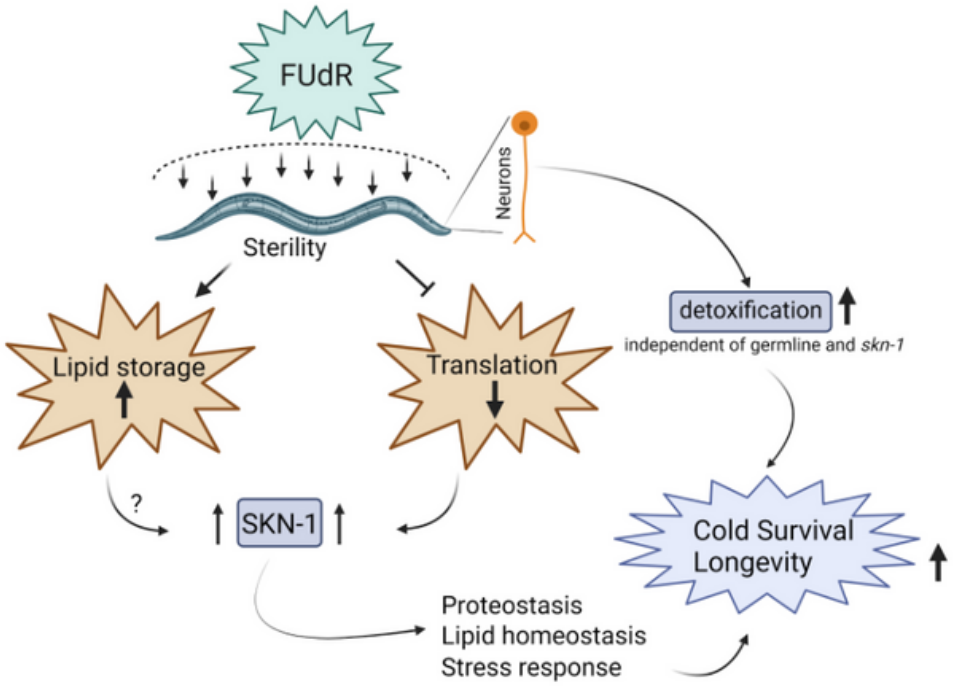
Sterility-independent enhancement of proteasome function via floxuridine-triggered detoxification in C. elegans

Keywords: Microbial physiology, synthetic microbiology, host-microbe interaction, aging and proteostasis

Abstract

Maintaining proteostasis is integral to cellular health and linked to stress resistance, longevity, and various metabolic processes. While most studies have centered on heat stress, recent findings suggest that low temperatures can promote proteostasis in Caenorhabditis elegans, specifically via PA28γ-activated proteasomes. In the absence of a germline, proteostasis is further modulated by specific proteasome subunits such as RPN-6.1. Our study investigates the role of 5-fluoro-2'-deoxyuridine (FUdR), a compound known for its sterility-inducing effects, in enhancing proteasome function and cold adaptation. Our results indicate that FUdR significantly bolsters cold tolerance in *C. elegans*, even without key proteasome subunits. This effect is partially mediated by SKN-1-regulated transcription but operates independently of other known proteostasis enhancers. Furthermore, FUdR activates a unique detoxification pathway, separate from SKN-1 and the germline, with GST-24 acting as a central player. Our findings provide previously uncharted aspects of cellular responses to hypothermia and proteostasis, establishing a foundation for prospective biomedical developments and enriched insights into protein turnover procedures.



FUdR's role in increasing lifespan and cold tolerance in C. elegans | Credits: Abhishek Anil Dubey

Ahanjit Bhattacharya

PDF 03

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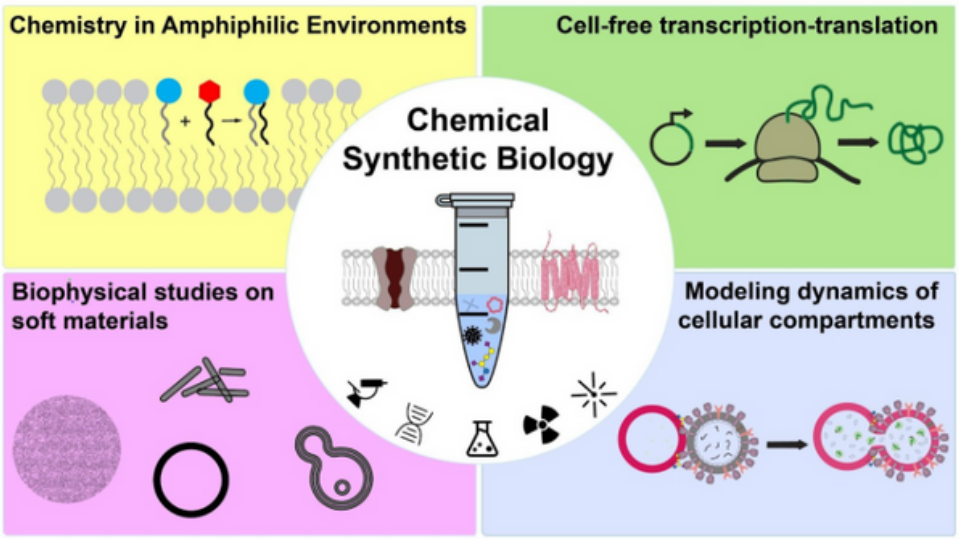
A chemical synthetic biology approach to origin, structure, and dynamics of cellular membranes

Keywords: Synthetic biology, chemical biology, soft materials, physical chemistry of viruses, origin of life

Abstract

Compartmentalisation is a defining feature of all forms of life. Amphiphilic lipid molecules are the primary building blocks of cellular membrane compartments. Numerous processes like signaling, transport, and biosynthesis take place in cells through the interplay between structure and dynamics of membranes. Here we take a bottom-up synthetic biology approach to develop a fundamental understanding of cellular processes involving lipid membranes. Various lipid architectures can be used to build functional models of the membranous structures found in cells. We utilized giant vesicles to recapitulate the basic membrane-bound structure of cells. To model membrane-rich organelles such as the endoplasmic reticulum, we utilized bicontinuous sponge phase lipid droplets. To understand the origins and evolution of cellular life, we developed various minimal chemoenzymatic pathways for de novo generation of lipid compartments. We further demonstrated a few primitive modes of growth and division of such compartments to provide a hint at how earliest cells may have proliferated. Given their central role in cellular physiology, lipid membranes are also key to understanding the fundamentals of many infectious diseases. For example, pathogens like viruses hijack the dynamics of the cellular membrane systems to gain entry. We describe the application of surface-immobilized lipid vesicles to model the events concerning cellular attachment, endosomal escape, and genome transfer of enveloped viruses such as influenza.



Chemical Synthetic Biology | Credits: Ahanjit Bhattacharya

PDF 04

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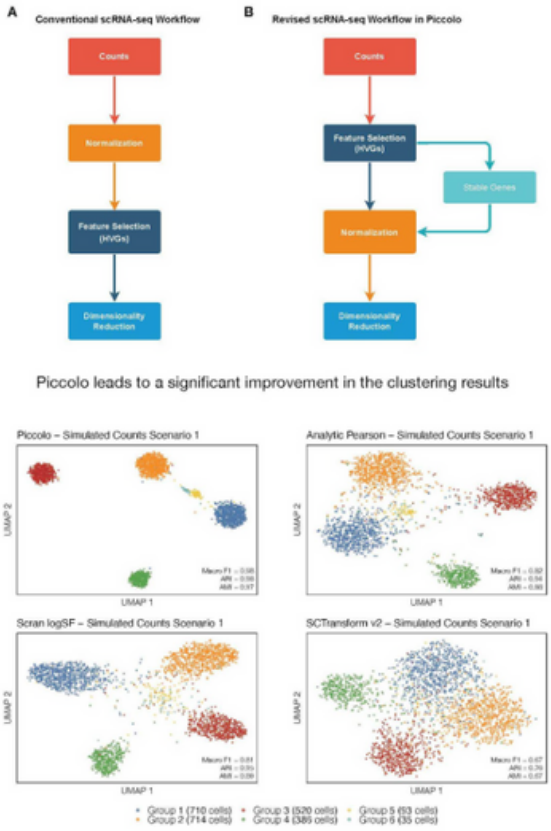
Piccolo: A novel workflow for performing single-cell gene expression analysis

Keywords: Bioinformatics, computational biology, single-cell transcriptomics, spatial transcriptomics, epigenomics

Abstract

Single cell gene expression studies are rapidly transforming our understanding of cellular processes at the level of single cells, especially in the case of complex diseases such as cancer. Despite rapid improvements in single-cell RNA sequencing (scRNA-seq) technologies over the past decade, significant challenges remain for computational analysis of the counts data. In particular, biases introduced through technical sources can obscure actual biological variation. These biases are typically addressed through a normalisation step. However, the conventional normalisation approaches show limited efficacy in reducing the impact of these biases. Recently, I proposed a revised workflow for analysing scRNA-seq data sets in which we first perform feature selection and then use a novel residuals-based normalisation to reduce the impact of the unwanted biases. This revised scRNA-seq workflow has been implemented in a tool called Piccolo. We showed by application to biological and simulated truth-known data sets that Piccolo outperforms popular single-cell workflows such as Seurat and Scanpy.



Piccolo: A novel workflow for performing single-cell gene expression analysis
Credits: Amartya Singh, Hossein Khiabanian

PDF 05

Amitabha Mukhopadhyay

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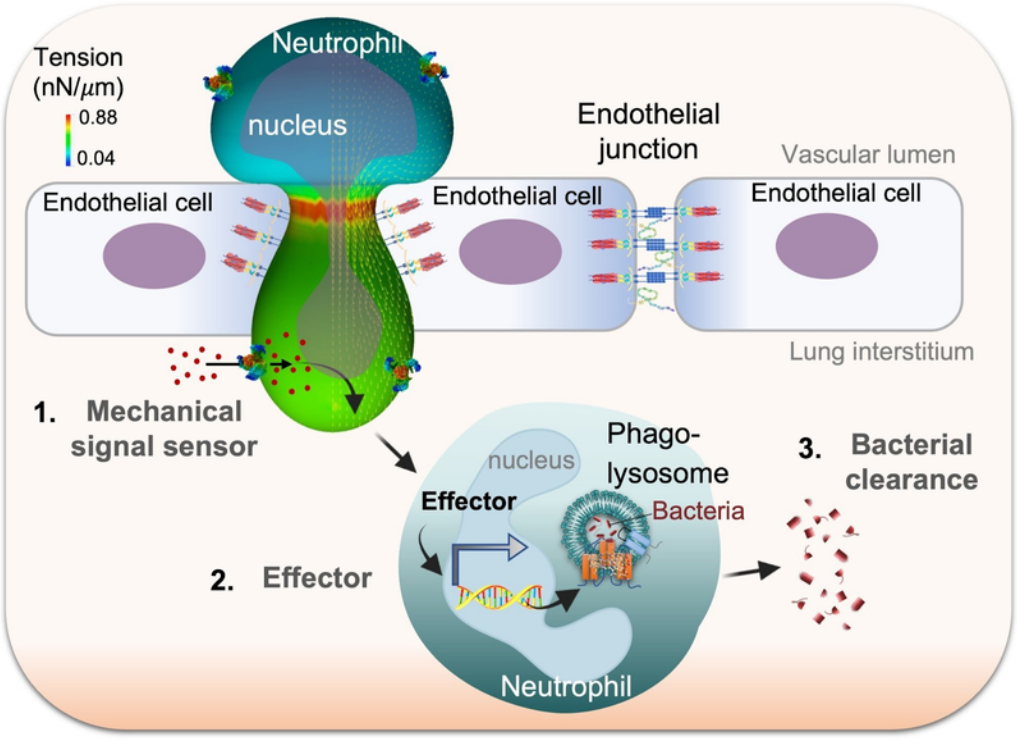
Email: amitabha@uic.edu

Mechano-sensing enhances neutrophil defense and mitigates pulmonary infection

Keywords: Mechanical signaling, neutrophil and innate immune response, endothelial barrier protection, respiratory inflammatory disease, mechano immuno-modulatory therapeutics

Abstract

The regulation of polymorphonuclear leukocyte (PMN) function by mechanical forces encountered during their migration across lung tissue is not well understood. We demonstrated that the mechano-sensors in PMN plasmalemma induced spike like Ca2+ signals. Adoptive transfer of mechanically activated PMN into lungs of *Pseudomonas aeruginosa* infected mice, or exposing PMN to defined mechanical forces in microfluidic systems, improved bacterial clearance phenotype of PMN. Mechanical signals activated phago-lysosomal machinery, crucial for the increased PMN bactericidal activity. Thus, mechanosensing of increased PMN tension while traversing lung tissue is a central mechanism activating the host-defense function.



Mechanical signaling influences neutrophil defense
Credits: Amitabha Mukhopadhyay

Angelina Thomas Villikudathil

Mahatma Gandhi University, India
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Website: https://www.mgu.ac.in

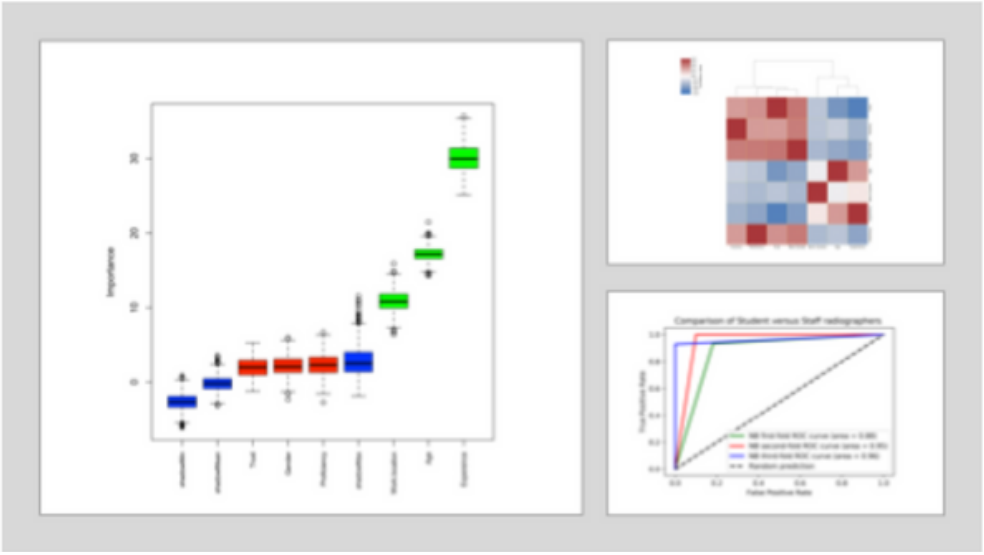
PDF 06

An experimental machine learning study investigating the decision-making process of students and qualified radiographers when interpreting radiographic images

Keywords: Bioinformatics, machine learning, multi-omics data analysis, computational biology, precision medicine

Abstract

Artificial intelligence (AI) is increasingly integrated into healthcare to alleviate the strain on the UK's National Health Service. Despite the NHS prioritising AI and digital health in its Long-Term Plan, limited research examines how healthcare professionals, especially radiographers, interact with AI systems. Understanding is needed of how certain user characteristics may impact how radiographers engage with AI systems in use in the clinical setting to mitigate against problems before they arise. This study investigates the impact of user characteristics on radiographers' engagement with AI. It focuses on the correlations between skills, confidence in AI, and perceived knowledge among student and qualified radiographers in the UK. A machine learning AI model was developed to predict whether an interpreter is a student (n = 67) or a qualified radiographer (n = 39) in advance, using key variables selected through the Boruta technique. A survey was conducted on the Qualtrics platform, shared through social media, inviting participation from all UK radiographers, including students and retired professionals. Participants were asked to interpret plain radiographic examinations with and without AI assistance. The analysis uncovered interesting patterns. Males with a high level of professional proficiency exhibited greater trust in AI compared to females. Trust in AI showed negative correlations with age and experience levels. The machine learning model achieved a 93% prediction accuracy with 0.93 area under curve, effectively distinguishing qualified radiographers. To assess the clinical applicability of this model, further testing with larger sample sizes in prospective validation cohorts is necessary.



Feature selection using Boruta, the analysis of correlations, and the creation of machine learning models.
Credits: Angelina Thomas Villikudathil

Aniruddha Panda

PDF 07

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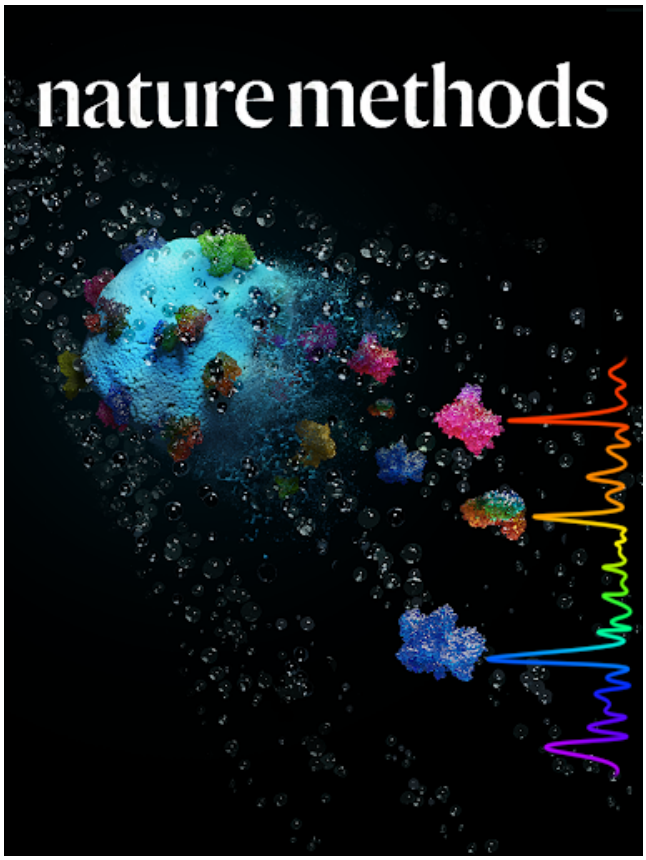
Direct determination of membrane protein complexes from lipid bilayer and its application in neuronal exocytosis

Keywords: Neurobiology, biochemistry, biophysics, lipidomics & proteomics, native mass spectrometry

Abstract

The molecular rationale behind the ultra-fast fusion of synaptic vesicles (SV) remains enigmatic due to limited understanding of the supra-molecular functional organisation of the involved proteins and lipids. To address this, we have developed a novel tunable lipid-vesicle native-mass spectrometry (nativeMS) platform that can determine membrane proteins-lipid complexes directly from membranes. The method enables us to introduce intact lipid membranes, embedded with target membrane proteins, directly into the MS. Subsequent gentle ablation of the protein-lipid complexes from the membrane inside MS enables determination of molecular organisation states, bound lipid, and the binding stoichiometry of the embedded target membrane proteins at precise molecular resolution. Utilising this platform, we discovered that VAMP2 exclusively exists as a monomer within the SV-bilayer. Through high-resolution nativeMS and top-down MS/MS analysis, we identified VAMP2's specific binding to phosphatidylcholine (PC) and cholesterol in the SV-membrane. Further investigations employing fusion assays show that specific interaction between VAMP2 and PC regulates the timing of vesicle fusion. We next turn our focus on understanding the role of Synaptophysin (Syp) in templating VAMP2 in SVs. By directly studying VAMP2-Syp from the lipid membrane, we show that Syp organises VAMP2 into higher-order complexes in an SV. To gain deeper insights into VAMP2's dimeric nature in the presence of synaptophysin, specific mutations were introduced to determine both the VAMP-VAMP and VAMP-Syp interfaces. Simultaneous vesicle fusion assays on these wt/mutant complexes reveal the functional role of these assemblies in regulating SV-fusion. Further expanding our platform, we screen specific VAMP2 mutations with pathophysiological effects. Together, our work presents a novel experimental platform to determine the oligomeric organisation of membrane proteins and lipids directly from lipid membranes. The application of this shows how VAMP2 is organised in the membrane by synaptophysin.



The lipid vesicle native mass spectrometry platform directly captures the organisation of membrane protein-lipid interactions from customisable lipid membranes, providing insights into how specific membrane lipids and biophysical properties influence these assemblies. An application of this shows the role of Synaptophysin (Syp) in guiding VAMP2 organisation within synaptic vesicles.
Credits: Hanna Wang, Yale University.

Ankit Tiwari

PDF 08

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RAL-B dependent sensory neuron to cancer cell mitochondria exchange

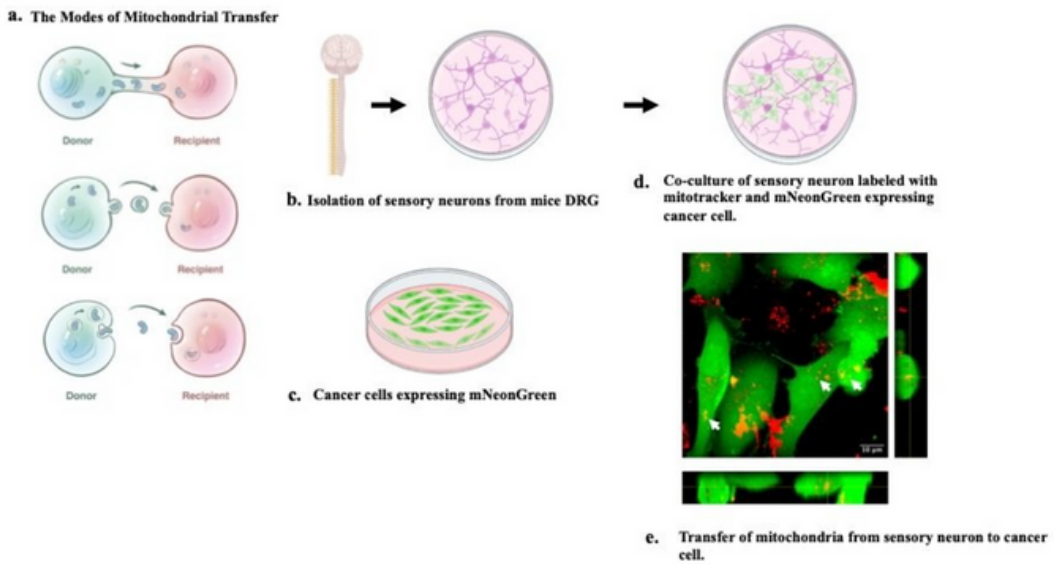
Keywords: Cancer neuroscience, intercellular communication, neuro-epithelial crosstalk, mitochondria exchange, tumor microtube formation

Abstract

Mitochondria are powerhouses of the cell, but the understanding of mitochondria has expanded beyond its role in ATP generation. Mitochondria play a significant role in biosynthetic reactions, stress responses, cell death, and cell differentiation. Recent studies have provided insights that mitochondria are significant for intercellular communication by lateral mitochondria transfer. The nervous system regulates organogenesis and oncogenesis. Recent discoveries have elucidated crosstalk between the nervous system and tumors, at both systemic and direct (paracrine or electrochemical) levels, with subsequent effects on tumor growth. Our laboratory recently discovered that sensory neurons are a reservoir of mitochondria that transfer to breast cancer cells. To our knowledge, this is the first evidence of neuron-to-cancer cell mitochondrial transfer. The density of transferred mitochondria from sensory neurons to the cancer cells was higher compared to normal epithelial cells indicating specific function of neuronal mitochondria. We have further observed that invasiveness of the cell type drives the acquisition of mitochondria from neurons.

The transfer of mitochondria between the cancer cells and neurons was a contact dependent mechanism suggesting involvement of open-ended tubular connections. To better understand the machinery involved for the mitochondria transfer we performed in silico proteomic network analysis for the proteins known for formation of open-ended tubular connections and identified RAL-B as being involved in mitochondria exchange. In conclusion this study makes the first observation of mitochondria transfer from neurons to cancer cells which is driven by invasiveness of the cancer cells and by formation of RAL-B dependent open-ended tubular connections leading to intercellular mitochondria exchange.

1. Saha T, Dash C,Jayabalanm R, Khiste S, Kulkarni A, Kurmi K,Mondal J, Majumder PK, Bardia A,HL, Sengupta S. 2021. Intercellular nanotubes mediate mitochondrial trafficking between cancer and immune cells. Nature Nanotechnology 17(1) :98-106



Lateral mitochondria transfer between sensory neuron and cancer cell and possible mechanism of lateral mitochondria transfer
Credits: Ankit Tiwari

PDF 09

Arpita Ghosh

Indian Institute of Technology Bombay
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Decoding the mechano-sensitive nature of NEAT1 lncRNA in glioblastoma: Implications for cancer progression and therapeutic strategies

Keywords: Long non-coding RNAs, cancer biology, cancer stem cells, tumor micro-environment, mechano-sensing

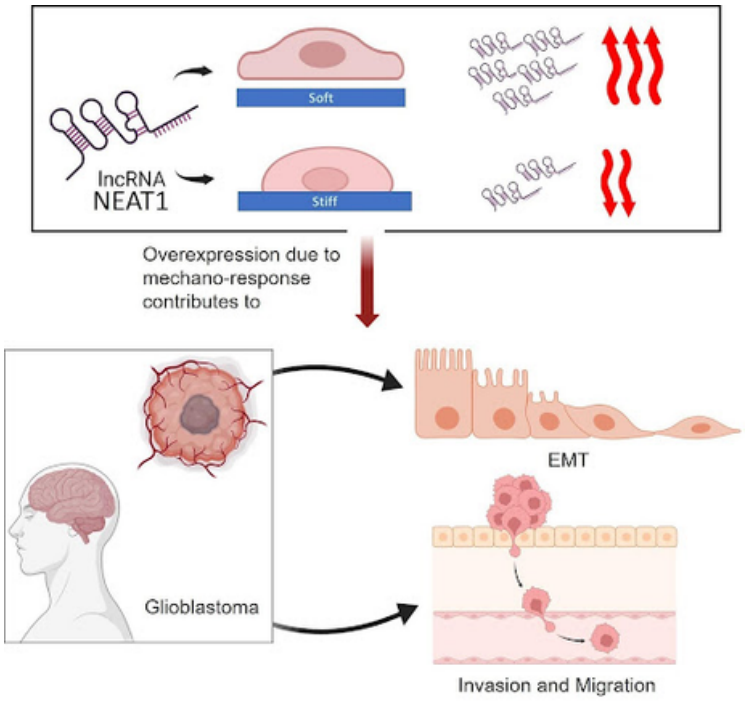
Abstract

Mechano-sensitivity, inherent to cells, profoundly influences physiological and pathological processes, particularly in cancer. The long non-coding RNA (lncRNA) NEAT1 significantly contributes to cancer, notably glioblastoma (GBM). Our study investigates NEAT1's relationship with substrate stiffness in GBM. Remarkably, GBM cells on a 0.5 kPa gel exhibit upregulated NEAT1 compared to those on stiffer substrates (40 kPa gel or 10 GPa tissue-culture plastic). This variance in NEAT1 expression correlates with increased cancer progression. Cells with higher NEAT1 on softer substrates show enhanced stemness, EMT, invasion, and migration capabilities. To reveal NEAT1's mechano-sensitivity, we downregulated NEAT1 in GBM cells on soft gels using siRNA. The results are striking: NEAT1's mechano-sensitive effect is reverted, reversing observed cancer progression properties. These findings highlight NEAT1's dynamic expression, intricately linked with the mechanical microenvironment.

Additionally, our comprehensive bioinformatics analysis of existing transcriptomic data from various cancer cells cultured on substrates of varying stiffness unveils a broader landscape of potential mechano-responsive lncRNAs. Pathway analyses shed light on their roles in distinct cancer types. Our goal is to target these mechano-responsive pathways associated with NEAT1 and other identified lncRNAs, opening innovative avenues for interventions not only in glioblastoma but also in other mechano-responsive cancers.

1.Liu, C., Gao, X., Li, Y. et al., 2022, The mechanosensitive lncRNA Neat1 promotes osteoblast function through paraspeckle-dependent Smurf1 mRNA retention. Bone Res, 10, 18.

2.Vanja Todorovski, Archa H. Fox, and Yu Suk Choi, 2020, Matrix stiffness-sensitive long noncoding RNA NEAT1 seeded paraspeckles in cancer cells. MBoC, 31, 16.



Mechano-sensing lncRNA NEAT1 contributes to GBM cancer progression | Credits: Arpita Ghosh

Ashwini V Mohan

PDF10

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Comparative genomic architecture of chromosomal fissions and fusions in holocentric sedges

Keywords: Speciation genomics, evolutionary ecology, molecular genetics, biogeography, population genetics, biodiversity crisis

Abstract

Speciation is the fundamental evolutionary process that generates and maintains biodiversity. The evolution of reproductive barriers between incipient species is a key component of speciation. In monocentric species where chromosomes contain a single centromere region, changes in karyotypes often promote reproductive isolation by causing constraints during cell division but such chromosomal rearrangements are less likely to establish in the first place. Holocentric species that lack a single centromere but have centromere-like structures across their chromosomes have repeatedly evolved. Chromosomal rearrangements through chromosomal fusion and fission may not result in a loss of genetic material for holocentric species and thus promote changes in karyotypes and rates of speciation. Sedges of the genus Carex are one such holocentric group with a high diversity of karyotypes between and within species. Chromosomal fusions and fissions are associated with changes in transposable elements (TEs)but the specific underlying genomic architecture is not fully understood. In this study, we utilise pairs of sibling species with different karyotypes and a case of karyotypic diversity to unravel the genomic architecture of chromosomal fission and fusion in holocentric species. For this, we (i) characterise the TEs across rearranged and non-rearranged chromosomes, (ii) measure synteny across species with different karyotypes, (iii) annotate genomes, and (iv) test whether non-conserved genomic areas have a lower gene density than conserved regions. We are assembling 10 reference-quality genomes from 8 species of Carex using the PacBio Revio and 3D genome-wide chromatin interactions using Hi-C sequencing. Through this rare comparative study, we will trace the evolution of changes in genomic architecture and regions associated with speciation in holocentric species providing unique insights into genome evolution.

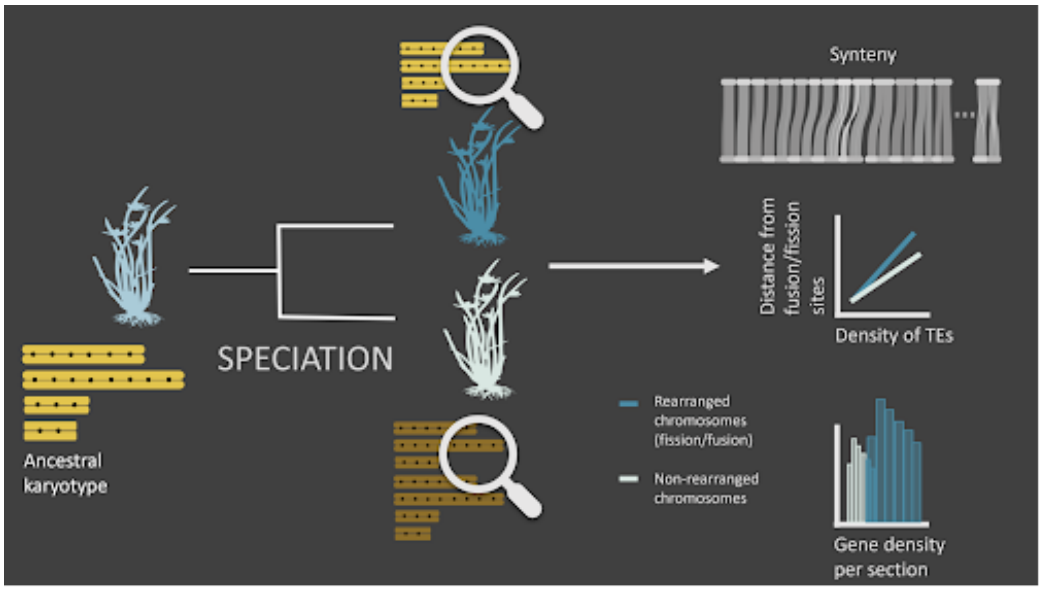

Illustration of speciation and differences in karyotypes and ongoing work | Credits: Ashwini V. Mohan

Debanjan Mukherjee

PDF 11

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Does environmental heterogeneity impact Plasmodium parasites and severe malaria?

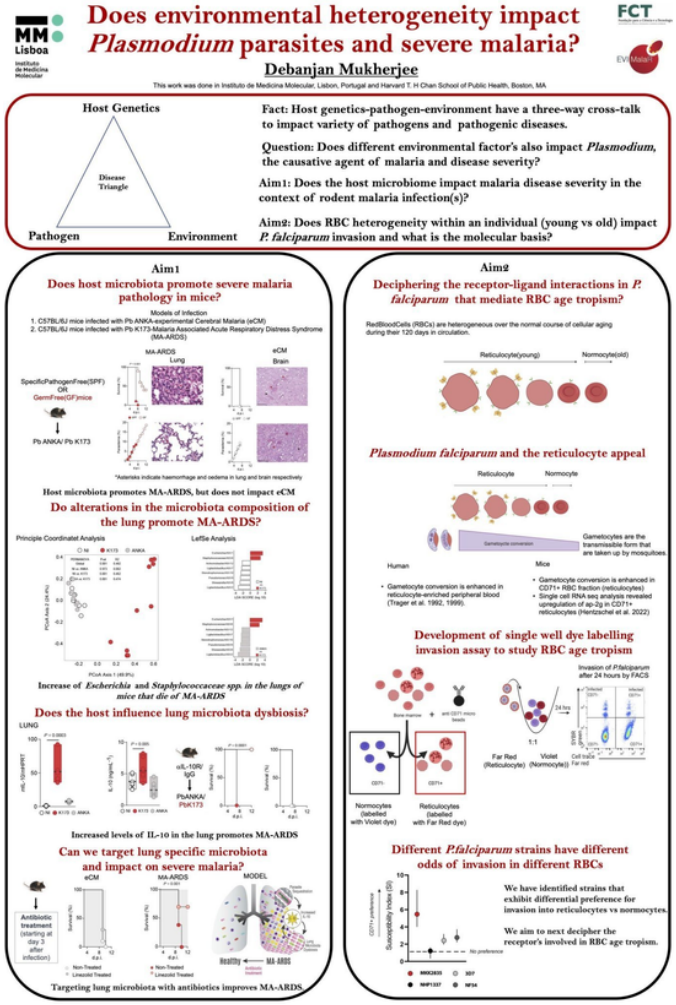
Keywords: Malaria, diet, microbiota, immune system, bacterio-therapies

Abstract

Acute respiratory distress syndrome (ARDS) is a life-threatening lung injury condition for which many possible causes have been identified, including local or systemic infections by a wide variety of pathogens, ranging from viruses to unicellular parasites, such as Plasmodium, the causative agent of malaria. ARDS is the most severe form of respiratory complications associated with malaria (malaria-associated ARDS; MA-ARDS) and has high mortality rates. Until now, the mechanisms leading to MA-ARDS remain utterly unexplored.

In my research we demonstrate a new discovery that alterations of the host microbiota colonising the lung are a critical determinant of host mortality in the context of ARDS during malaria infections. Sequestration of Plasmodium parasites in the lung causes persistent immune activation, ultimately resulting in the production of the anti-inflammatory cytokine IL-10 to curtail immunopathology. However, T cell production of IL-10 facilitates the outgrowth of the local microbiota, contributing to dysbiosis and resulting in MA-ARDS. Our data unequivocally shows that either depletion of microbiota by antibiotic treatment or blockade of the cellular or molecular immune mediators of microbiota alterations significantly suppress lung microbiota dysbiosis and is sufficient to prevent ARDS.

Red Blood Cell (RBC) heterogeneity: RBCs are heterogeneous over the normal course of cellular aging during their 120 days in circulation. We show that P. falciparum strains vary in the efficiency by which they invade normocytes (old RBCs) versus reticulocytes(young RBCs), suggesting that different parasites possess molecular determinants that vary for the propagation of parasites through RBCs of different age. Identifying the parasite molecules that mediate these differences in invasion would facilitate interventions for the radical cure of *P. falciparum*, eliminating parasites from these reservoirs and blocking transmission.



Host-pathogen-environment: A 3 way axis dictating disease severity
Credits: Biorender, Adobe Illustrator, Microsoft Powerpoint

Dhananjay Huilgol

Duke University, USA
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PDF12

Generating excitatory neuronal diversity in the cerebral cortex

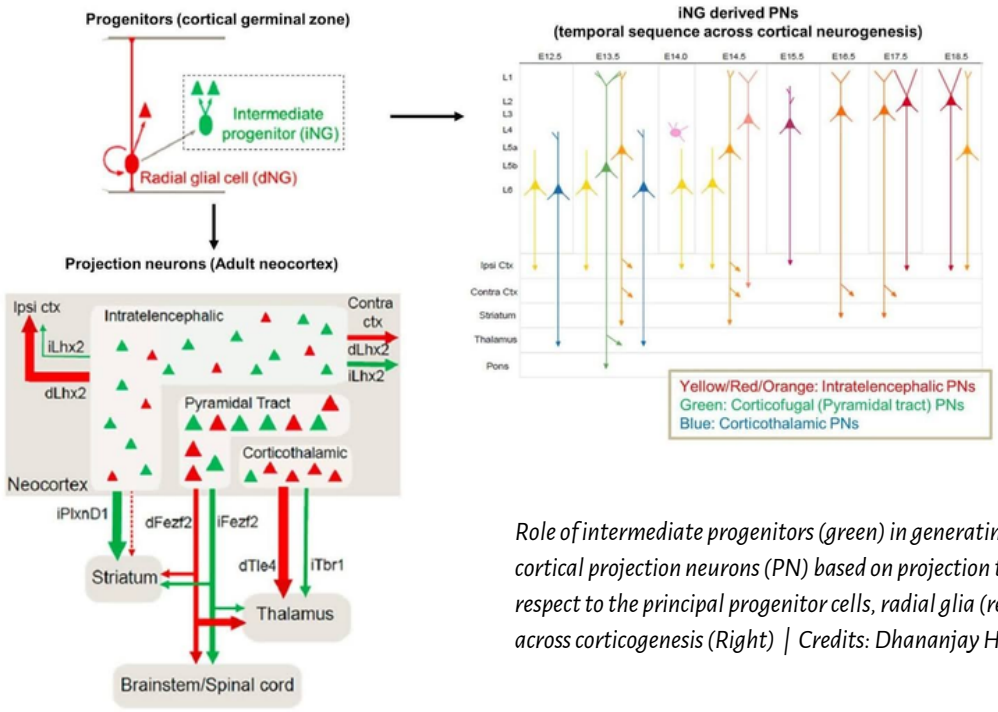
Keywords: Neurodevelopment, mouse genetics, progenitor diversity, projection neurons, forebrain evolution

Abstract

The neocortex is a recently evolved complex brain structure that performs multifarious higher-order brain functions. It comprises a vast number and diverse types of excitatory projection neurons (PNs) arranged in multiple layers that form information processing channels. These diverse PNs influence cortical size and complexity, rooted in cortical progenitors. However, mechanisms generating this PN diversity are poorly understood. Radial glia (RG) or intermediate-progenitors (IPs) produce PNs by direct (dNG) and indirect neurogenesis (iNG), respectively. While iNG increased with mammalian evolution, its contribution to PN diversification remains elusive. We established a novel fate-mapping method to differentially visualize and provide a quantitative assessment of dNG and iNG in mice. While dNG generates all major PN projection classes, iNG differentially amplifies and diversifies PNs within each class. Therefore, the two neurogenic pathways generate distinct PN types and assemble lineage-based cortical projections. Our results provide a fundamental framework of cortical development and evolution by linking neurogenic pathways to mature PN types.

A foundational concept in cortical neurogenesis is that PNs generated at different times are deployed in an "inside-out" order to establish cortical layers. To investigate the contribution of iNG to this lamination, we used novel genetic fate-mapping and viral tracing to link PN birthdate to projection patterns. We found that the generation of iNG-derived PNs substantially deviated from the "inside-out" rule. PNs destined to non-consecutive layers are generated simultaneously; PNs of the same layer are generated at non-consecutive times; and subsets of upper and deep layer PNs are generated early and late embryonically, respectively. Therefore, an overarching logic of iNG is the sequential specification and deployment of projection-defined PN types beyond their laminar position.

Overall, this unique developmental-genetic approach at a cell-type resolution reveals new insights in cortical circuit assembly and development.



Role of intermediate progenitors (green) in generating the diversity of cortical projection neurons (PN) based on projection targets, with respect to the principal progenitor cells, radial glia (red) (Left), and across corticogenesis (Right) | Credits: Dhananjay Huilgol

PDF13

Fanindra Kumar Deshmukh

University College London, UK
Email: fanidesh@gmail.com

Structural elucidation of FAN1 protein complexes involved in Huntington's Disease and DNA Repair

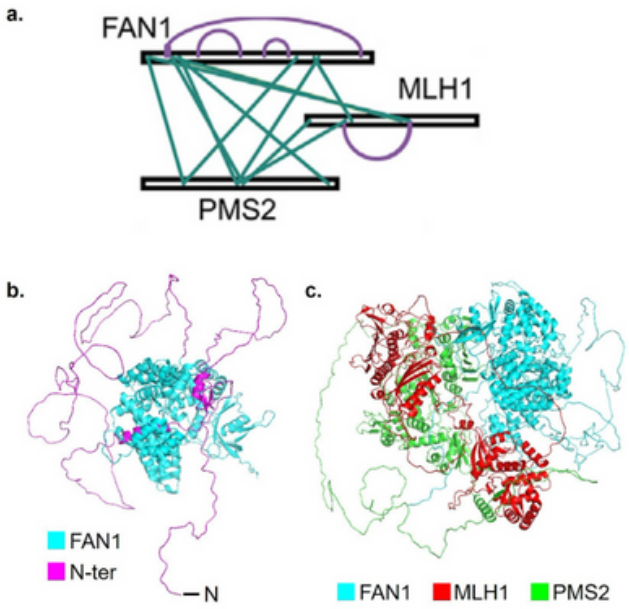
Keywords: Metabolic disorders, protein structure-function relation, protein dynamics in health and disease

Abstract

Huntington's disease (HD) is a dominantly inherited neurodegenerative disorder caused by expanded CAG repeats in the huntingtin gene HTT. Recent genome-wide association studies (GWAS) have uncovered the significant influence of DNA mismatch repair (MMR) and FAN1 (Fanconi-associated nuclease 1) on disease onset and severity (Genetic Modifiers of Huntington's Disease (GeM-HD) Consortium, 2015). FAN1, a non-MMR protein, interacts with MMR proteins MutLα (MLH1, PMS2) and plays a role in DNA mismatch repair and CAG repeat expansion regulation (Goold et al., 2021). This underscores the importance of the FAN1-MutLα complex in safeguarding against CAG repeat expansion.

Our study aims to elucidate high resolution structure of FAN1 in complex with MutLa complex, as a full length structure of these proteins is unavailable. Interestingly, N-terminus of FAN1 is predicted to be flexible, implying its role in complex formation and FAN1's function. Our preliminary cryo-EM data show structural variability within FAN1, potentially due to the flexible N-terminus complementing the prediction. Our future work aims to co-express FAN1 complexes under a single promoter, enabling co-purification and comprehensive structural analysis. This research enhances our understanding of the mechanisms behind CAG repeat expansion in HD, offering potential insights into disease pathology and novel therapeutic targets.

1. Genetic Modifiers of Huntington's Disease (GeM-HD) Consortium. (2015). Identification of Genetic Factors that Modify Clinical Onset of Huntington's Disease. Cell, 162(3), 516–526.
2. Goold, R., Hamilton, J., Menneteau, T., Flower, M., Bunting, E. L., Aldous, S. G., Porro, A., Vicente, J. R., Allen, N. D., Wilkinson, H., Bates, G. P., Sartori, A. A., Thalassinos, K., Balmus, G., & Tabrizi, S. J. (2021). FAN1 controls mismatch repair complex assembly via MLH1 retention to stabilize CAG repeat expansion in Huntington's disease. Cell Reports, 36(9).



Elucidating the structure of FAN1, MLH1, and PMS2 complex: (a) Interaction between FAN1 and MutLa complex (MLH1 & PMS2) revealed by the cross-linking mass spectrometry (b) AlphaFold predicted structure of FAN1 alone and (c) in complex with MLH1 and PMS2 (MutLa complex).

Credits: Goold, R., Hamilton, J., Menneteau, T., Flower, M., Bunting, E. L., Aldous, S. G., Porro, A., Vicente, J. R., Allen, N. D., Wilkinson, H., Bates, G. P., Sartori, A. A., Thalassinos, K., Balmus, G., & Tabrizi, S. J. (2021). FAN1 controls mismatch repair complex assembly via MLH1 retention to stabilize CAG repeat expansion in Huntington's disease. Cell Reports, 36(9).

Gaurav Singh

PDF14

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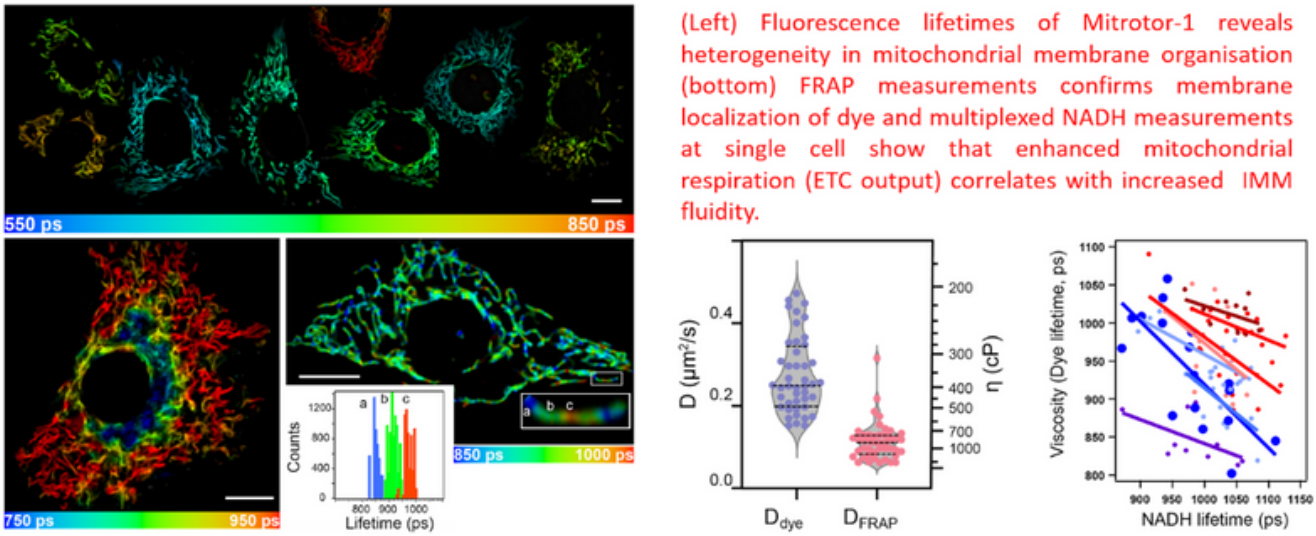
How dynamic modulation of mitochondrial inner membrane fluidity might regulate respiration

Keywords: Fluorescence lifetime imaging, mitochondrial membrane organisation and function, disease and diagnostics, high-resolution microscopy, biosensors

Abstract

Cellular respiration, a process fundamental to all life, involves the intricately complex electron transport chain (ETC) located in the inner mitochondrial membrane (IMM). Functioning in a densely packed mitochondrial membrane, electron transport chain requires the lateral movement of mobile charge (electron) carriers. Therefore, there has been a long standing (and often debated) view whether the lateral mobility of molecules and hence the 'fluidity' of IMM (particularly the charge carriers) should influence respiration rates and cellular energetics. An important question that has remained largely unanswered is: do cells modulate the fluidity of respiring membranes as energetic/respiratory demand changes? Specifically, do cells change the fluidity of the densely-packed IMM in response to metabolic stimuli? Answering these questions with any kind of spatial and temporal precision would require appropriate tools and methods for measuring and visualising inner mitochondrial membrane fluidity (in eukaryotes), especially for intact, living cells and tissues. We have developed a robust method to visualise IMM-fluidity in live-cells using a cell-permeable, fluorescent-molecular-rotor. Utilising fluorescence-lifetime readouts, this method eliminates probe concentration and intensity-fluctuations artefacts. FLIM-imaging reveals exquisite heterogeneity in IMM-fluidity, even across individual mitochondria. Multiplexing with single-cell NADH imaging reveals cells with higher mitochondrial respiration have increased IMM fluidity. Strikingly, cells rapidly modulate IMM fluidity upon stimulation. Thus, rapid modulation of IMM fluidity is a mechanism of adaptation to increased respiratory demand. Our findings open new lines of inquiry into how and when inner membrane fluidity may be tuned in cells – a new regulatory paradigm.

1. Singh, G., George, G., Raja, S., Kandaswamy, P., Kumar, M., Thutupalli, S., Laxman, S., Gulyani, A., A molecular rotor FLIM probe reveals dynamic coupling between mitochondrial inner membrane fluidity and cellular respiration. Proc. Natl. Acad. Sci. 120, e2213241120 (2023).



Visualising mitochondrial respiratory membrane fluidity in live cells | Credits: Gaurav Singh

PDF15

Gayatree Mohapatra

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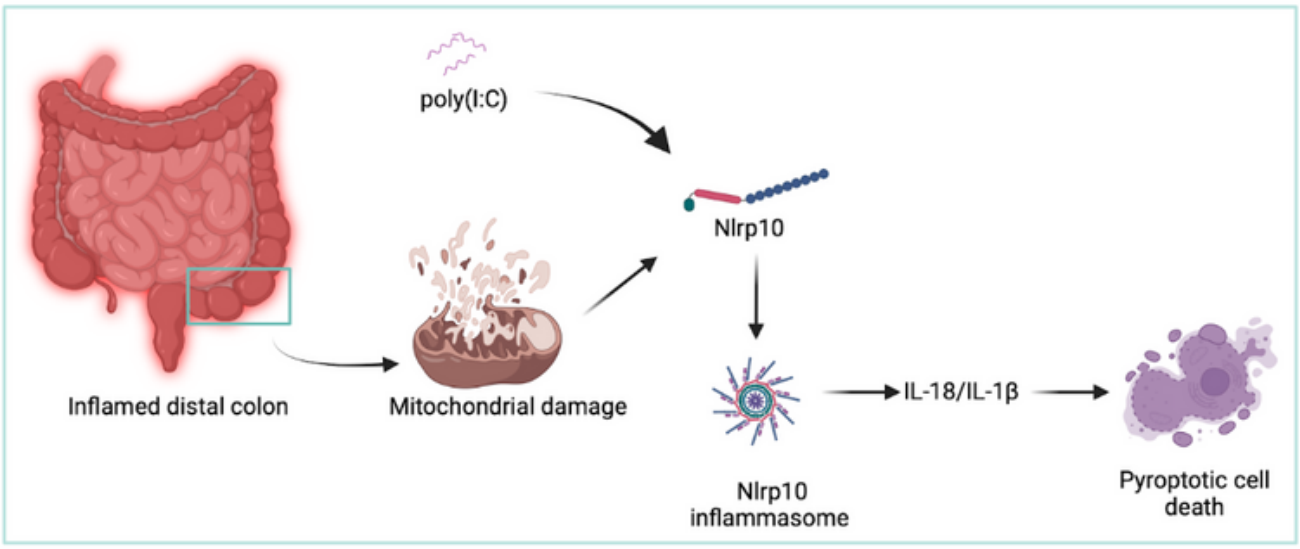
Understanding the lifeguard at the immunological barrier: The mechanism of patrolling by inflammasome at the gastrointestinal firewall

Keywords: Inflammasome, innate immunity, intestinal inflammation, intestinal epithelial cells, Nlrp10

Abstract

NOD-like receptors (NLRs) are cytosolic innate immune receptors that can recognise specific microbial- or damage-associated molecular patterns (MAMP or DAMP respectively). NLRs form an inflammasome complex in an apoptosis-associated speck-like protein containing a caspase-recruitment domain (ASC)-dependent or -independent manner. Inflammasome formation, in turn, initiates the enzymatic activation of canonical caspase-1, thereby leading to the maturation and secretion of the inflammatory cytokines interleukin-1β (IL-1β) and interleukin-18 (IL-18), as well as induction of pyroptotic cell death. The clinical significance of inflammasome has been studied beyond infectious disease, as a dysregulated activation can have a consequence to numerous autoimmune diseases or cancer.

Unlike other nucleotide oligomerisation domain-like receptors, Nlrp10 lacks a canonical leucine-rich repeat domain suggesting its incapability in signal sensing and activation. In our work, we show that Nlrp10 is expressed at the distal colonic epithelial cells (IECs) and expression is modulated by microbiota. In vitro, Nlrp10 forms an apoptosis-associated speck-like protein containing caspase recruitment domain (ASC), mitochondrial stress activated and polyI:C modulated inflammasome driving the secretion of IL-1 and IL-18. In vivo, Nlrp10 signaling is dispensable during steady state but becomes functional during autoinflammation in antagonising mucosal damage. Importantly, whole-body or conditional IEC Nlrp10 depletion leads to reduced IEC caspase-1 activation, coupled with enhanced susceptibility to dextran sodium sulfate-induced colitis, mediated by altered inflammatory and healing programs. Collectively, understanding Nlrp10 inflammasome-dependent and independent activity, regulation and possible human relevance might facilitate the development of new innate immune anti-inflammatory interventions.



Activation mechanism of Nlrp10 inflammasome at the gastrointestinal epithelial cells during inflammation
Credits: Created with BioRender.com

PDF16

Gopal Chovatiya

Cornell University, USA
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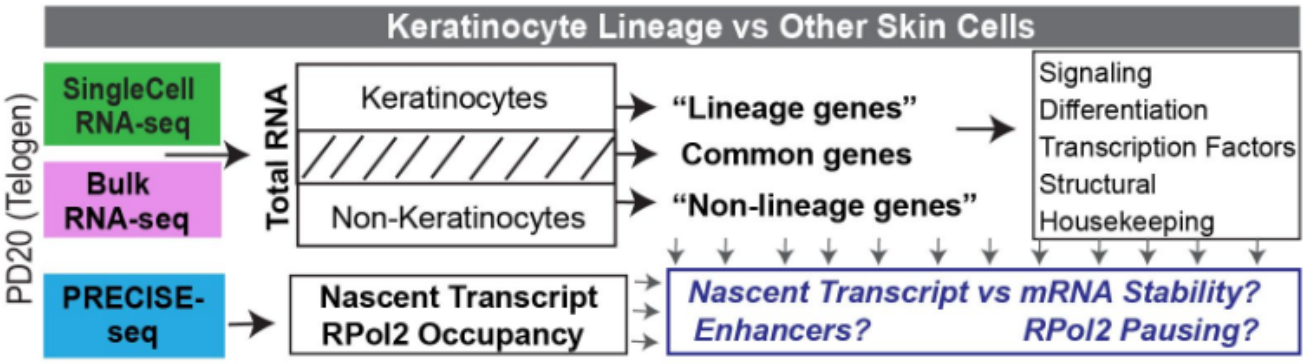
Lineage-specific nascent transcription maps reveal molecular principles of tissue dynamics

Keywords: Tissue stem cells, skin epithelium, transcriptional regulation, precise-seq, single cell transcriptomics

Abstract

Transcription precisely controls tissue regeneration by directing cell fate transitions and ensuring timely differentiation. These spatial and temporal shifts in cell fate are orchestrated by dynamic transcriptional changes, guided by niche factors. However, our understanding of the molecular intricacies underpinning these regulatory steps is hindered by heterogeneous tissue architecture and a lack of tools to study active transcription in unperturbed in vivo tissue. Here, we developed PRECISE-seq (Precision Run-on in Cell-type-specific In vivo System followed by sequencing) to directly analyse the cell-type-specific nascent transcriptome within its native in vivo microenvironment, circumventing cell isolation. Our approach utilises cell-type-specific inducible tagging of RNA Polymerase II with GFP, facilitating selective purification of transcriptionally engaged RNA Pol II and associated nascent RNAs. Using the K14Cre driver, PRECISE-seq profiling of keratinocytes revealed a robust enrichment of keratinocyte-specific target genes. Comparing nascent and bulk transcriptomes, we identified distinct gene classes, including actively transcribing yet unstable regulatory genes, consistently transcribing stable housekeeping genes, and genes exhibiting differential stability irrespective of their transcription rate. Furthermore, we detected differential RNA Pol II pausing patterns between lineage-specific and multilineage genes. Multilineage genes displayed elevated Pol II pausing, while lineage-specific genes lacked elevated Pol II density at the promoter-proximal region, hinting at regulation via promoter recruitment. These findings highlight the intricate molecular regulation of gene expression tailored to lineage maintenance and functional demands. Overall, PRECISE-seq provides a pivotal avenue for the scientific community to delve deeper into transcriptional dynamics, particularly RNA Pol II's role in promoter-proximal pausing and enhancer transcription, across varied in vivo tissue contexts throughout development and homeostasis.



Interrogating cell-type-specific nascent transcription in vivo | Credits: Tudorita Tumbar, Gopal Chovatiya

Gyanendra Singh Sengar

PDF17

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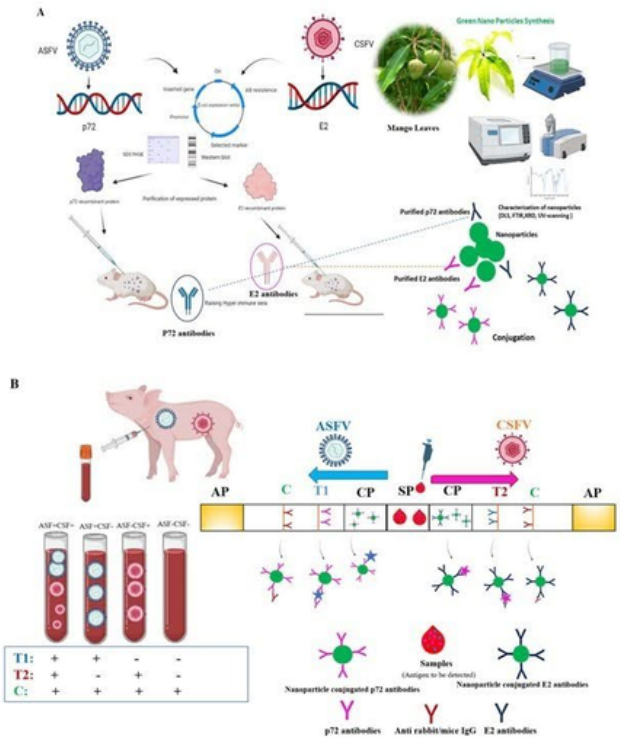
Website: https://nrcp.icar.gov.in/

Development of green nanoparticle-based bivalent paper-strip immune assay for simultaneous early detection of African swine fever and Classical swine fever viral antigens in pig

Keywords: Animal Biotechnology, molecular immunology, molecular diagnostics, vaccine development, therapeutics development

Abstract

India has 9.06 million pigs, with 0.88 million raised in urban settings and 8.17 million raised in biosecurity-challenged rural areas. Regardless, the pig population has fallen by 12.03 % since the last census. Various infectious diseases with high mortality rates compared to other livestock species, as well as ignorance and a lack of a suitable national program for controlling pig diseases in India, are among the key factors for the pig population's fall. The two most economically important infectious diseases of pigs in India are African swine fever (ASF) and Classical swine fever (CSF). ASF is currently diagnosed by polymerase chain reaction (PCR), Real-Time PCR, and detection of antibodies via enzyme-linked immunosorbent assay (ELISA), immunoblotting, or fluorescence antibody testing. However, these procedures are still time-consuming and need well-equipped laboratories and well-trained workers. According to recent reports, the cost of ASF detection tests ranges from roughly INR206 (US$ 2.78) to INR700 (US$ 9.46) per sample for antigen and real-time PCR-based testing, respectively. A wide range of nanoparticles are being utilized to construct rapid diagnostics for various infections of clinical importance. The lateral flow immune assay (LFIA) is one of them, and it has been shown to be an efficient analytical approach for detecting livestock viral infections such as ASF and CSF infection in pigs. However, in both diseases, antibodies emerged in the first or second week of infection, and thus early identification of infection can only be accomplished by identifying viral-specific antigens in biological fluids rather than antibodies. Here, we developed a smart and cost-effective green synthesis nano-sensor-based diagnostic for on-field simultaneous detection of ASF and CSF antigens as early indicators of both infections.



Development of green synthesised nanoparticle based lateral flo assay for simultaneous detection of African Swine Fever and Classical Swine Fever Virus | Credits: Gyanendra Singh Sengar

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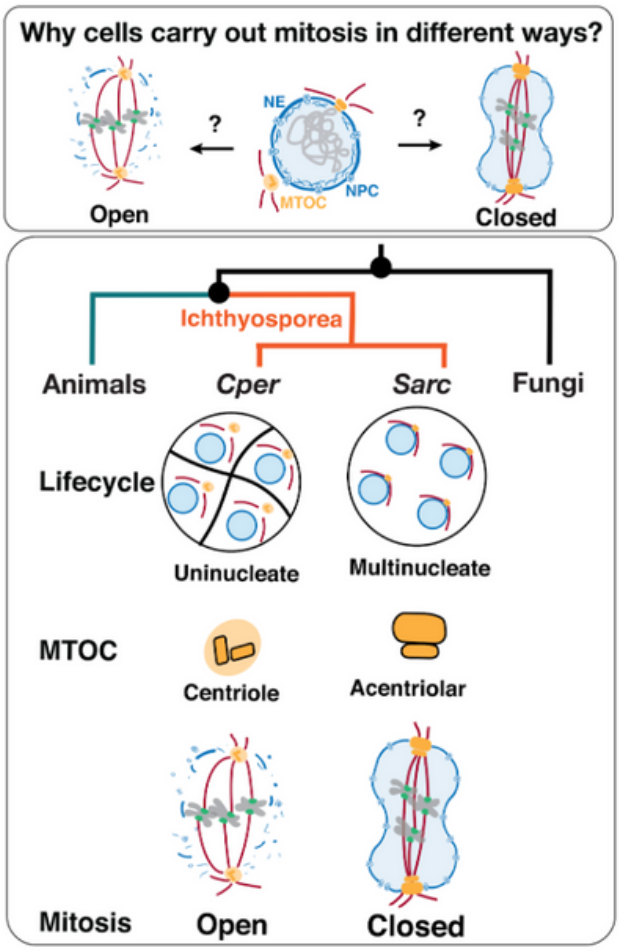
PDF18

Lifecycle-coupled evolution of microtubule organising centres and mitosis in close relatives of animals

Keywords: Mitosis, microtubule organising centre, evolution, microscopy, phylogeny

Abstract

Across eukaryotes, microtubule (MT) networks provide a framework for organelle positioning and global cellular organisation. MT networks are constantly remodelled to produce distinct cell stages, particularly as cells divide and nuclei are partitioned between daughter cells by a mitotic spindle. At the core of the MT networks are microtubule organising centres (MTOCs), that nucleate, organise and remodel MTs and are broadly categorised as centriolar or acentriolar based on their components and structure. Both types of MTOCs are widely distributed across many groups of the eukaryotic tree. While studies on animal centrosomes have shown some clear structural similarities among centriolar MTOCs, the acentriolar MTOCs are extremely diverse in structure, composition and sites, with fungal spindle pole bodies (SPBs) and amoebozoans providing the best studied examples. Here, we investigated mitotic machinery, including MTOCs, spindle and nuclear envelope (NE) components, in Ichthyosporea, which are early branching relatives of animals. Using comparative genomics, ultrastructural expansion microscopy and volume electron microscopy we find that there is a diversity in MTOC architectures within the Ichthyosporea. While the uninucleate Ichthyosporean Chromosphaera perkinsii has animal-like centrosomes, the multinucleate Sphaeroforma arctica has an acentriolar MTOC that shares features of close nuclear association and mitotic NE embedding with fungal SPBs. We show that these distinct MTOC architectures are also accompanied by different mitotic events with C. perkinsii undergoing open mitosis and assembling an animal-like spindle, while S. arctica forms an intranuclear spindle from NE embedded MTOCs to carry out a closed mitosis, a feature we believe is coupled to its multinucleate lifecycle. The presence of acentriolar MTOCs with SPB-like features within holozoans opens up the possibility to develop a broader understanding of the emergence and diversity of acentriolar MTOCs within the Opisthokonts and more broadly in eukaryotes.



Lifecycle-coupled evolution of mitosis | Credits: Hiral Shah

Kailash Chandra Mangalhara

PDF19

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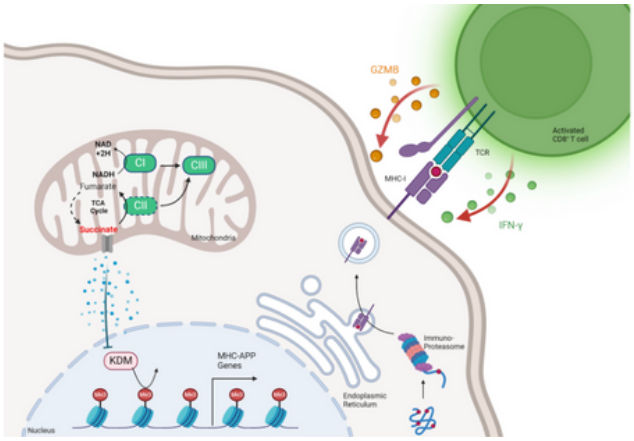
Manipulating mitochondrial electron flow enhances tumor immunogenicity

Keywords: Cancer metabolism, oncoimmunology, mitochondria, innate inflammation, antigen presentation

Abstract

Cancer cells rely on metabolic adaptations to survive in tumors. The mitochondrial electron transport chain (ETC) and tricarboxylic acid (TCA) cycle play crucial roles in these adaptations. The ETC comprises four multi-subunit complexes, with complex I (CI, NADH dehydrogenase) and complex II (CII, succinate dehydrogenase) acting as the gatekeepers of electron flow. CI and CII pass electrons from the TCA cycle generated NADH and FADH2, respectively, to ubiquinone, which are then delivered to complex III and finally to oxygen via complex IV. Recycling ubiquinone by complex III and IV is necessary for tumor growth. Loss of function mutations in genes encoding CI and CII subunits are better tolerated, as cancer cells can compensate for their loss through metabolic reprogramming. However, the individual contributions of CI and CII in tumor growth and immunogenicity were previously unclear. Our research shows that losing complex II, but not complex I, reduces melanoma tumor growth by increasing antigen presentation and T cell-mediated killing. This is due to succinate-mediated activation of major histocompatibility complex I-antigen processing and presentation (MHC-APP) genes, independent of interferon signaling. Our results indicate that rewiring the ETC, by knockout of MCJ, to enter electrons via CI preferentially can have anti-tumor effects without reducing mitochondrial respiration in non-cancer cells. This could be a potential therapy for tumors with reduced MHC-APP expression, a common mechanism of cancer immunoevasion.



Succinate accumulation by remodeling of mitochondrial ETC enhances tumor immunogenecity
Credits: Created using Biorender

PDF 20

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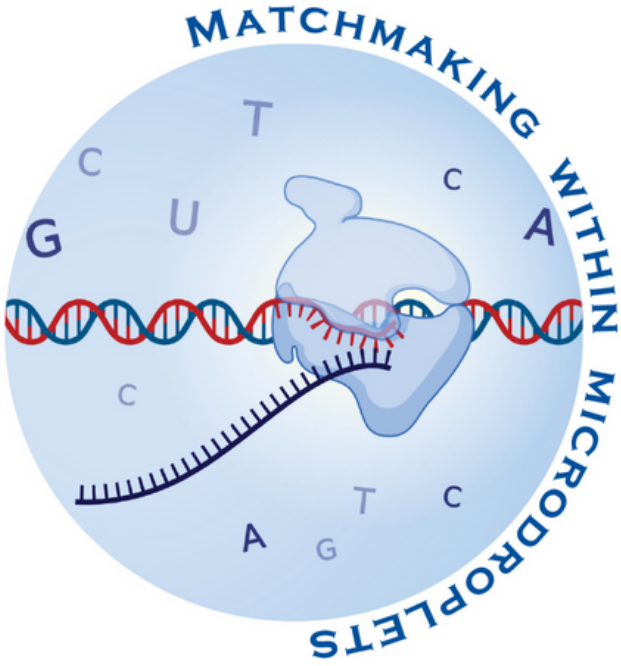
Unravelling bacterial transcription regulation in droplet-based microfluidics

Keywords: Droplet-based microfluidics, high throughput screening, bionanotechnology, micro & nano-fabrication, cells, organoids, and organs on-a-chip

Abstract

Bacterial transcriptional regulation plays an important role in adaptation to the changing environment and response to stimuli. Sigma (σ)-factors are subunits of bacterial transcriptional machinery that primarily determine the specificity of core RNA polymerase on the promoter region of the genes to initiate transcription. Bacteria has many σ-factors, but the knowledge of their specific binding sequences still remain limited. A long-term objective of our current research is to explore and map different sigma factor binding sequences in bacterial genome. In this work, we take a synthetic biological approach to understand the working of this transcriptional machinery using a droplet based microfluidic toolbox. Firstly, single DNA fragments are compartmentalised inside individual picolitre droplets along with PCR reagents and incubated for amplification. Thereafter, every droplet is coalesced with drops containing IVT reagents, specific sigma factor and a reporter dye. Finally, the droplets are sorted by di-electrophoresis based on the fluorescence intensity of the drops, where the dye specifically fluoresces after binding to the RNA aptamer in case of positive transcription reactions. Both, the original DNA fragments, and the generated mRNA transcripts would be sequenced, and the eventual goal would be mapping and pairing of sigma factors with promoter sequences from the original DNA. The database generated from such an approach would form a solid foundation towards enhanced understanding of transcriptional regulation in bacteria.



Synthesis of mRNA via in-vitro transcription inside a microfluidic droplet
Credits: Created using Biorender

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PDF 21

Tracing the cytoskeletal blueprint in vitro

Keywords: Cytoskeletal arrays, cryo-electron microscopy and tomography, neurodegeneration, cancer, plant stress response

Abstract

The cellular cytoskeleton is made up of actin, microtubule, and intermediate filaments that are dynamic polymers stabilised by associated proteins. During my post-doctoral research, I identified unique characteristics of microtubules and associated proteins in cilia, neuronal cells and parasitic systems. I purified a recombinant version of a ciliary junction protein called Flagellar associated protein 20 (FAP20) and identified its role in stabilising the microtubule lattice as well as in mediating lateral interactions with the building blocks called tubulin, critical in the assembly of doublet microtubules that make up the core of cilia (1). Further, I uncovered specialised microtubule architectures assembled with tubulin isolated from the malarial parasite, Plasmodium falciparum that are dependent on the conditions of polymerisation used (2). Comparison of Plasmodium microtubules with their mammalian counterparts is ongoing, which is particularly intriguing because of the differences observed in their polymerisation properties in the presence of plant tubulin targeting drugs such as oryzalin and amiprofos-methyl (APM).

Using my knowledge and expertise in the field, my future goal is to understand the coordinated working of cytoskeletal networks in diverse families of eukaryotes, including parasites, plants, animals and investigate the influence of environmental and disease-causing factors on filament systems. Through a combination of in vitro and cell-based studies brought about by collaborations, I envision obtaining critical insights into the framework of a cell that can be harnessed for practical solutions of disease control and sustainable farming.

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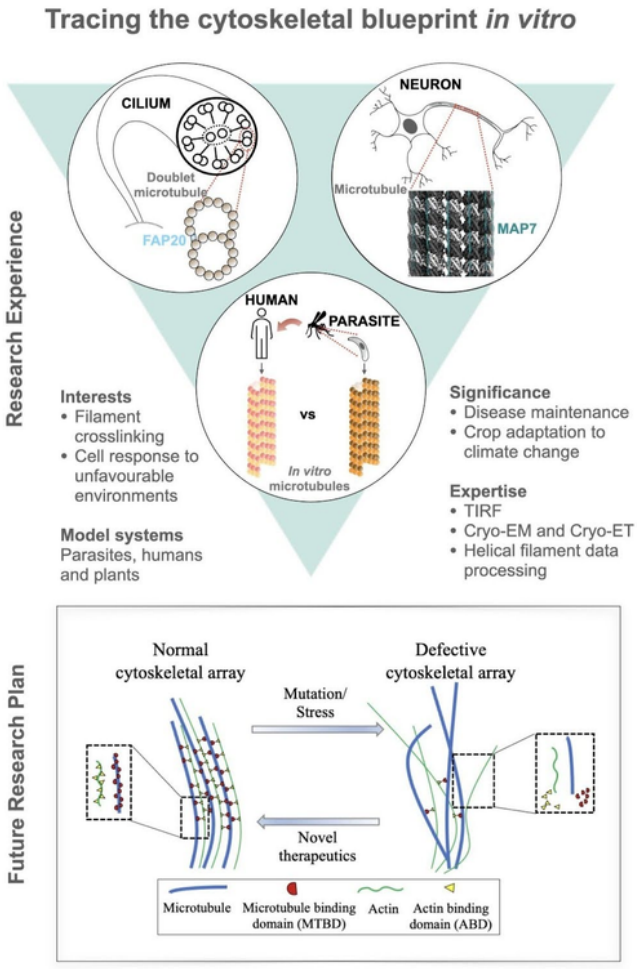
2. Hirst WG, Fachet D, Kuropka B, Weise C, Saliba KJ, Reber S. 2022. Purification of functional Plasmodium falciparum tubulin allows for the identification of parasite-specific microtubule inhibitors. Curr Biol. 32(4):919-926



The image provides a summary of the areas I worked in during my postdoctoral research and the knowledge distilled from my experiences that will assist me in achieving my long-term research goals.
Credits: Mamata Bangera

PDF 22

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Emerging organic pollutants (EOPs) induce antimicrobial resistance in Salmonella: An experimental study

Keywords: Biochemistry of endocrine disrupting chemicals, non-antibiotic antimicrobial resistance, proteomic, analytical biochemistry, one health

Abstract

Antimicrobial resistance (AMR) could render many of the current mainstay and last-resort antibiotics ineffective, leading to a significant increase in deaths from previously treatable infections (Kumar *et al.*, 2021). Microbes and pollutants coexisting can impact AMR evolution. Chemical stressors in water can induce mutations and select for resistant bacteria (Alderton et al., 2021). To understand the impact of the major emergence of bacterial antimicrobial resistance resulting from the presence of emerging organic pollutants (EOPs) on bacteria, we subjected the antibiotic-susceptible strain of Salmonella to different concentrations of Bis(2-ethylhexyl) phthalate (DEHP) and Bisphenol-A (BPA), along with a control. Antimicrobial susceptibility tests, bacterial survival, and whole-cell protein profiling were performed after 12, 24, and 36 hours of incubation. The results indicate that exposure to EOPs at concentrations of 4 µg/ml and 8 µg/ml significantly increases resistance in the bacterial strain after 36 hours of incubation. In contrast, some increase in antibiotic resistance was also observed for gatifloxacin, ofloxacin, cefpodoxime, ciprofloxacin, moxifloxacin, gentamicin, tobramycin, amikacin, kanamycin, streptomycin, nalidixic acid, and colistin. Moreover, whole-cell protein profiles revealed distinct variations in protein banding patterns even after 24 and 36 hours of incubation. The purpose of this research is to identify the role and possible mechanism of persistent organic pollutants in making bacteria antimicrobial-resistant.

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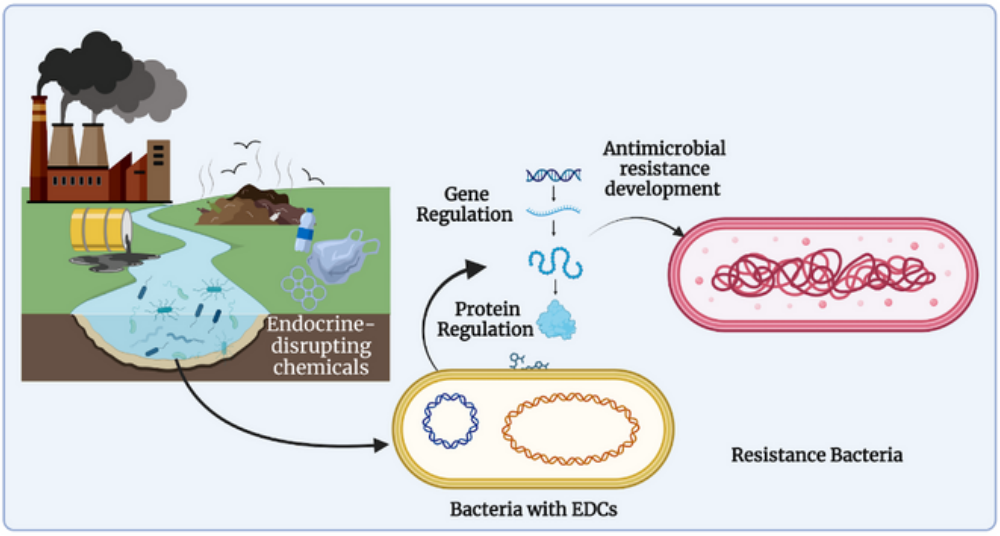
2. Kumar, M., Sarma, D.K., Shubham, S., Kumawat, M., Verma, V., Nina, P.B., Jp, D., Kumar, S., Singh, B. and Tiwari, R.R., 2021. Futuristic non-antibiotic therapies to combat antibiotic resistance: A review. Frontiers in microbiology, 12, p.609459.



Emergence of bacterial antimicrobial resistance due to emerging organic pollutants (EOPs)

PDF 23

Maya Raghunandan

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Translating genomic knowledge from bench to bedside advancements in cancer therapy

Keywords: DNA replication and repair, telomere biology, translational research, paediatric cancers, cancer genomics

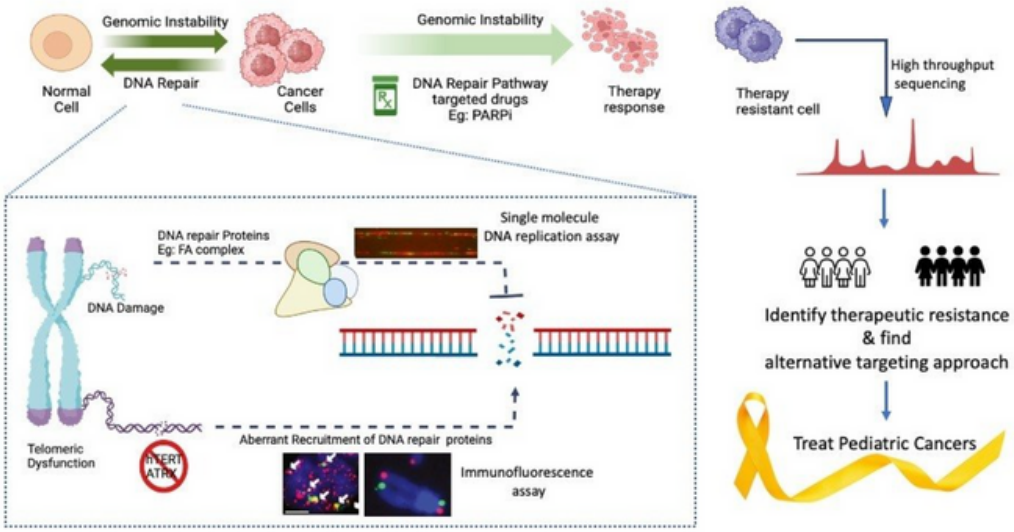
Abstract

Background: Genomic instability (GI) and replicative immortality (RI) are cancer cell hallmarks that confer targetable vulnerability. Mutations in DNA Damage Response (DDR) pathway proteins or dysfunction at chromosome ends – telomeres, cause GI. Telomere length maintenance in turn, enables RI in cancer cells: often by telomerase re-expression (TEL+) or occasionally by hijacking DDR proteins to dysfunctional telomeres (ALT+). Despite successfully targeting GI for therapeutic intervention, resistance emergence remains challenging.

Approach: Roles of DDR pathway proteins in overcoming DNA replication stress were investigated through single molecule DNA fibre assays. Impact of telomeric DDR-defects on genomic stability in ALT+ cancer cells was determined using biochemical/immunofluorescence assays. Blood biopsy-derived circulating-tumour DNA (ctDNA) sequencing was employed to investigate evolution of targeted therapy resistance.

Results: DDR proteins of 'Fanconi Anemia' pathway physically and functionally interact with a histone chaperone, ATRX, to restart stalled replication forks (Raghunandan *et al*. 2015, 2019). An interplay between ATRX-deficient telomeres and telomerase RNA subunit leads to inactivation of a DDR protein kinase – ATR, potentially causing cellular resistance to targeted ATR-inhibitor therapy in ALT+ cells (Raghunandan et al. 2021). ctDNA sequencing reveals parallel evolution of multiple mechanisms of resistance co-evolve in individuals in response to targeted therapy (PARPi) (Harvey-Jones et al. 2023).

Perspective: I'll combine my expertise in DDR, telomeres, and clinical research, to mechanistically understand ALT-pathway and identify novel therapeutic targets for ALT+ paediatric cancers. My genome stability focused research group will study DDR in ALT, with an overarching translational aim to improve clinical disease management via 3 avenues: 1) molecular pathways underlying cancer predisposition GI syndromes, 2) unravel fundamental ALT-specific molecular biology, and 3) establish clinical collaborations to access clinical material to perform DNA/RNA/methylome sequencing and develop experimental models to identify novel biomarkers and therapy avenues.



Genomic Instability & Replicative Immortality: Translating Genomic Knowledge from Bench to Bedside Advancements | Credits: Created using Biorender

PDF 24

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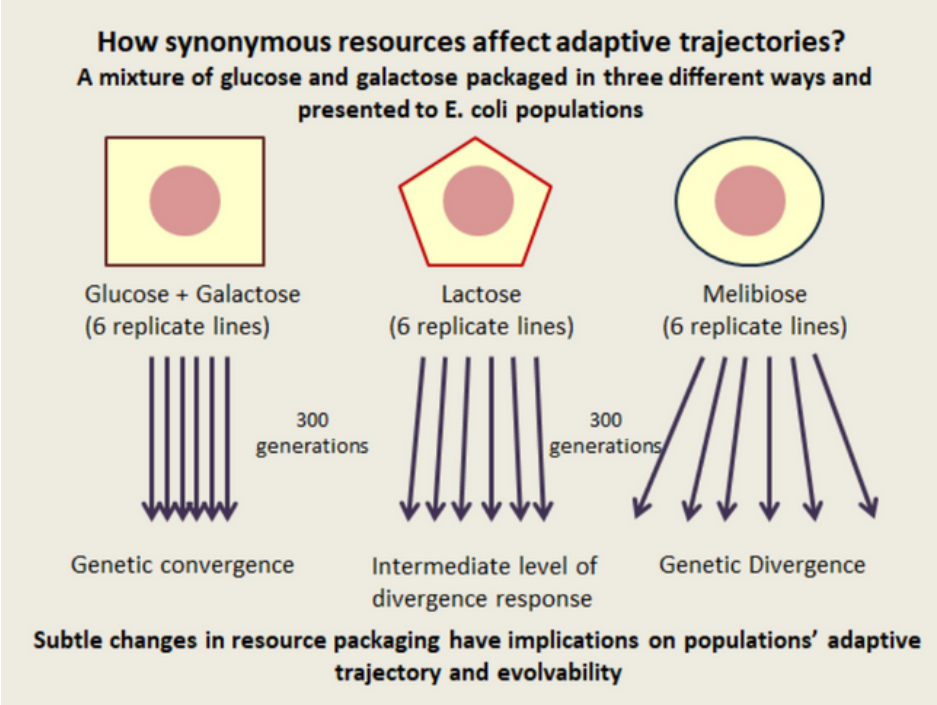
Nutrient packaging alters adaptation and genetic divergence in E. coli

Keywords: Evolutionary genetics, host-pathogen interactions, inter-microbial interactions, evolution of dominance and evolution of multicellularity

Abstract

How subtle changes in environment change adaptive trajectories? In this work, we investigate how an identical resource packaged differently influences genetic and phenotypic adaptation. In particular, we evolved *E. coli* populations in a mixture of glucose-galactose, lactose, and melibiose. The three environments contain an equal amount of glucose and galactose; albeit with different packaging in each environment. We call these three "synonymous" environments. Six independent lines were evolved in each of the three environments. After evolution for 300 generations, the melibiose-evolved lines exhibit maximum variability in their phenotypic response. Genome sequence revealed that the melibiose-evolved lines had the most diverse genetic targets of mutations; while targets of mutations were highly conserved in glucose-galactose evolved lines. Moreover, despite adaptation in melibiose, the melibiose-evolved lines were the most fit in lactose as well as in a glucose-galactose mixture. The genetic diversity in melibiose also likely has implications in future evolvability of these populations. Overall, our results show that subtle changes in resource presentation/packaging can have strong implications for a population's adaptive trajectory and evolvability.



Nutrient packaging alters adaptation and genetic divergence in E. coli | Credits: Neetika Ahlawat

Neha Dubey

PDF 25

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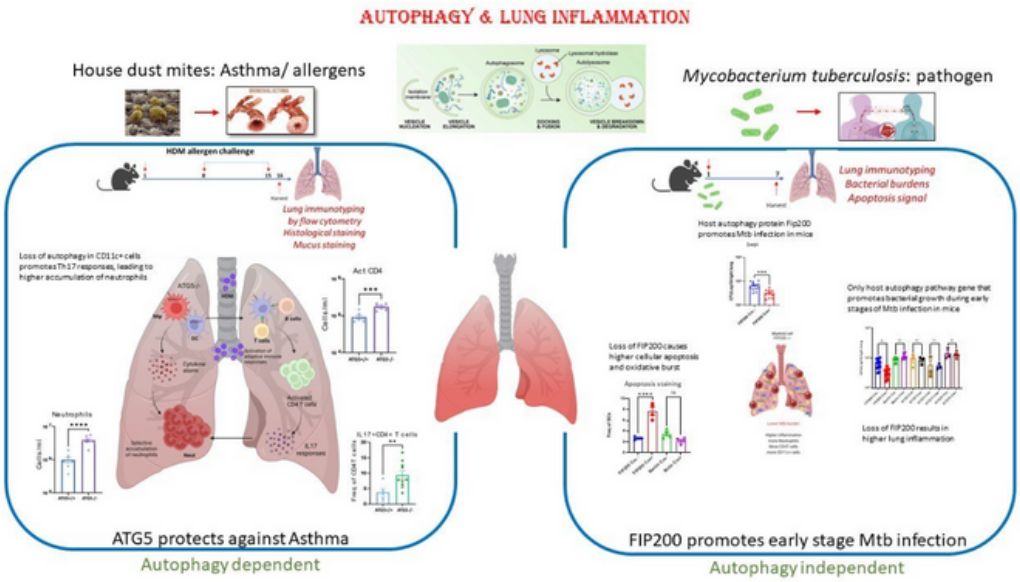
Autophagy pathway proteins plays distinct roles in regulating lung inflammation during tuberculosis infection and asthma

Keywords: *Mycobacterium tuberculosis* infection biology, lung pathologies including asthma, host-pathogen interface biology, host immunity, translational research and vaccine developments

Abstract

Dysregulation of innate cell mediated immune responses leads to inappropriate activation of adaptive immunity, hyperinflammation, & tissue damage. Autophagy, a fundamental cellular recycling process, have important contributions during several inflammatory disease conditions. Interestingly, proteins involved in the autophagy pathway could regulate inflammation in both an autophagy-dependent and independent manner. ATG5, an important autophagy protein was shown to play an autophagy-independent role in controlling neutrophilic inflammation and tuberculosis (TB) disease progression in mice lungs. Therefore, it is necessary to understand the functional relevance of these proteins with more precision. Towards this, my work explores the function of two autophagy proteins ATG5 and FIP200, in context of asthma and TB respectively. Asthma is a chronic lung condition arising from the lack of control of inflammatory responses. We identified that unlike TB, ATG5 protein plays an autophagy-dependent function in myeloid cells for protection against asthma. Loss of ATG5 and other autophagy proteins in macrophages and DCs results in higher neutrophil accumulation in mice lungs, leading to severe asthma phenotypes; indicating a protective function of autophagy during asthma. On the contrary, FIP200, another autophagy protein, was found to promote bacterial replication during *Mycobacterium tuberculosis* (Mtb) infection in mice. FIP200 plays a unique role in promoting cell survival, outside of its role in autophagy pathway, which consequently suppresses antimicrobial defense pathways and benefits Mtb replication in mice lungs during early stages of disease establishment. Loss of FIP200 specifically in alveolar macrophages results in higher cellular apoptosis and ROS, that leads to better pathogen clearance from mice lungs. Collectively, this work emphasizes the importance of both conventional and non-conventional functions of autophagy associated proteins to regulate pulmonary inflammation and, broadly affecting the outcomes of disease severities Tb infection and lung allergies.



Distinct functions of host autophagy proteins during lung inflammatory diseases | Credits: Created using Biorender

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PDF 26

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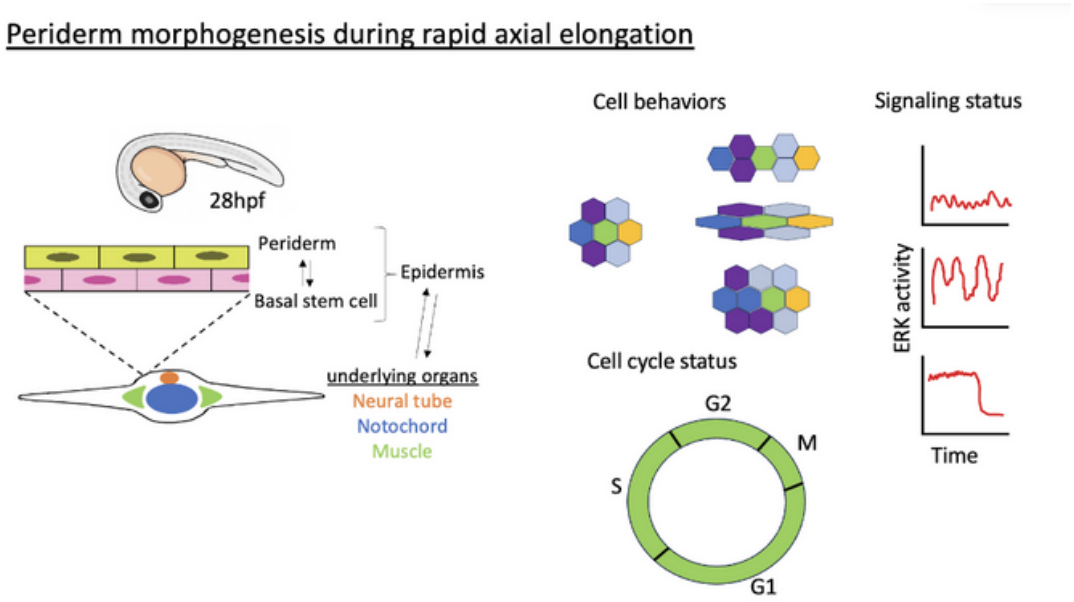
ERK mediated periderm growth during rapid axial elongation

Keywords: Cell and developmental biology, zebrafish transgenesis, in toto live imaging, quantitative biology, skin and corneal regeneration

Abstract

Morphogenesis of epidermis is particularly challenging during rapid phases of growth such as embryonic development and during regeneration of tissue lost by damage or disease. In addition to regulating its growth, epidermis would have to coordinate with underlying organs and grow together to ensure normal development and regeneration. Using zebrafish periderm, the outermost layer of the bilayer epidermis, we aim to understand how epidermis behaves and coordinates its growth when challenged with rapid embryonic axial expansion from 1–2 day post fertilisation. Using novel tools to visualise cell behaviors and signaling in the periderm and a platform to perform quantitative live imaging of the elongating embryonic epidermis, we find that the periderm experiences increased tension along the anterior-posterior axis, leading to oriented cell divisions, which facilitate directed growth of the tissue. Using the ERK-KTR sensor as a readout for the MAPK signaling activity, we find that increased MAPK signaling is associated with the ability of cells to undergo cell division. Further, inhibition of MAPK signaling leads to reduced proliferation, suggesting that MAPK signaling is instructive for cells to proliferate. To dissect this further, we developed a transgenic fish to define cell-cycle status specifically in the periderm. Co-imaging of ERK and Cdk2 activity, revealed that at 1dpf, cells are predominantly responsive to ERK for cell division. Post mitosis cells enter G1 indicated by the low Cdk2 activity. Interestingly, a fraction of cells switch-off ERK signaling and erase their ERK signaling history, while others maintain their ERK signaling status and respond by increasing cell size. With optogenetic approaches to spatially and temporally control MAPK signaling and mutants affecting embryonic axial expansion we aim to decipher the ability of MAPK signaling to translate mechanical stress and facilitate cells to undergo proliferation in the rapidly growing epidermis.



Periderm morphogenesis during rapid axial elongation in zebrafish | Credits: Nitya Ramkumar

PDF 27

Prachi Nawkarkar

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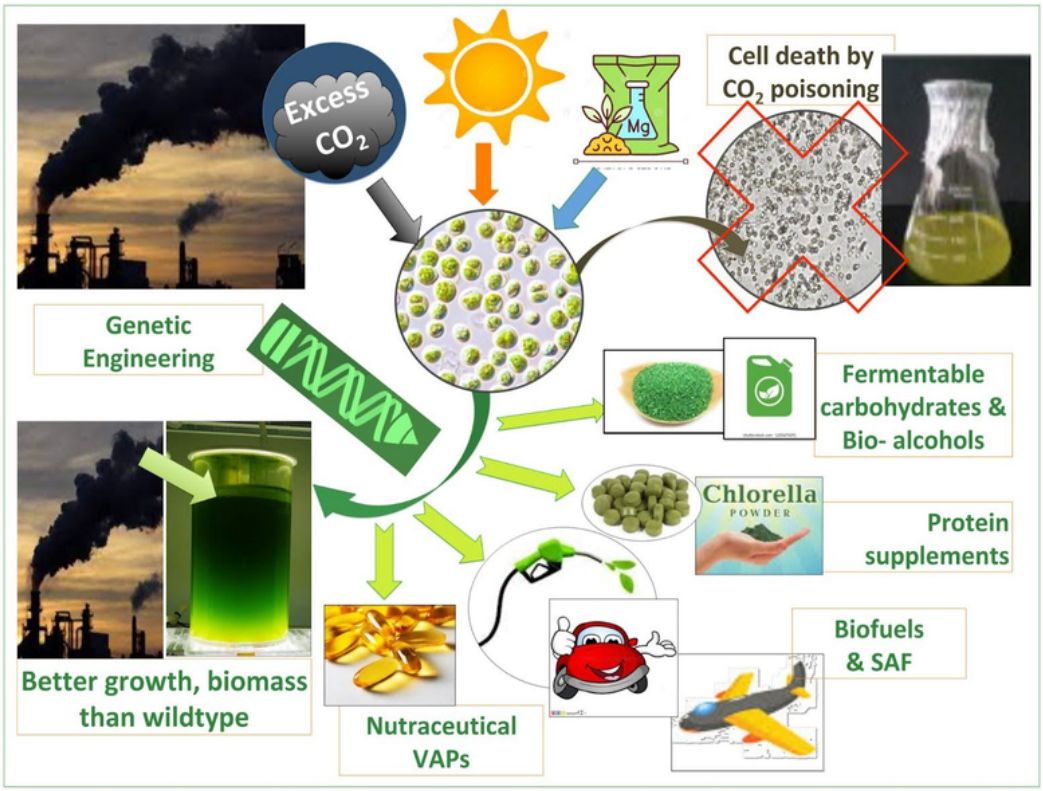
Enhancing Biological Carbon sequestration by GM Microalgae

Keywords: Biological carbon capture and utilisation, microalgal biotechnology, genetic engineering, biofuels, phyco-remediation

Abstract

The battle against climate change is getting hotter day by day. Of prime importance is CO2 which contributes to 76% of total global warming along with other NOx and SOx elements. Biological carbon capture & sequestration (Bio-CCS) using microalgae is a promising and safer means to reduce CO2 levels in the atmosphere. In algae, the Carbon Concentration Mechanism (CCM) facilitates CO2 assimilation via Carbonic Anhydrase (CA) enzymes and inorganic carbon transporters. The bicarbonate transporters are responsible for inorganic carbon uptake from the aqueous surroundings and channeling C towards RuBisCo for fixation. The transporters are required because of the very low availability of dissolved CO2 in aqueous environments. We have observed a significant increase in the bicarbonate uptake and algae biomass on overexpression of these transporters in microalgae. These modifications have led to enhanced biomass and lipid productivities of the strains than the wild type along with elevated carbon sequestration abilities. High CO2 causes acidification of media and lowers intracellular pH; which in turn compromises C assimilation. We have found that transcriptional silencing of CA via RNAi technology improved the ability of CO2 capture and sequestration in algae. This has also led to improved tolerance of the knockdown lines to high concentrations of CO2 in their environment.



Summary of Biological carbon capture technology using microalgae and its applications
Credits: Nawkarkar, P., Ganesan, A., & Kumar, S. (2022). Carbon dioxide capture for biofuel production. In Handbook of Biofuels (pp. 605–619). Elsevier. https://doi.org/10.1016/B978-0-12-822810-4.00032-4.

Pratik Chaudhari

PDF 28

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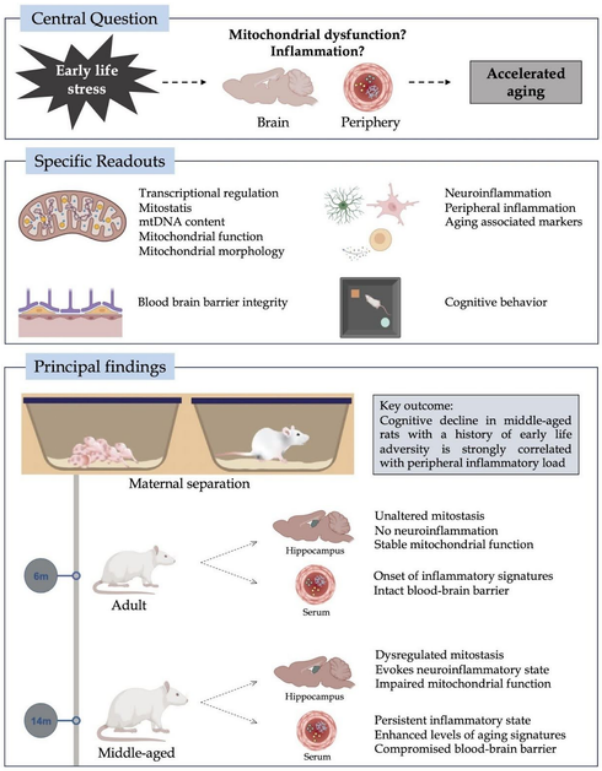
Early life adversity in rodents perturbs hippocampal mitostasis and drives inflammaging in age-dependent manner

Keywords: Neurobiology of stress, aging, neuro- and peripheral inflammation, neuropsychopharmacology, mental health

Abstract

Early life environment is a crucial in the development of neurocircuits involved in emotional behavior1. Adverse experiences during early life are known to program enhanced anxiety and depressive-like behaviors in adulthood, and to evoke perturbed neuroendocrine and behavioural responses to stress2. Early life adversity is also linked to accelerated aging-related changes including enhanced cognitive decline2. However, the molecular and cellular changes evoked by early adversity that contribute to these phenotype is not delineated. Aging is linked to mitochondrial dysfunction and inflammation2, and we hypothesized that early adversity may disrupt these processes thus impact the nature of aging. Using a rodent model of early adversity, maternal separation (MS), we addressed whether this was accompanied by perturbed mitostasis and peripheral-central inflammatory changes. We provide novel information that a history of MS is associated with a robust dysregulation in mitostasis accompanied by an inflammatory state evoked in the hippocampus, which emerges in an age-dependent manner. This is accompanied by impaired mitochondrial function, morphology and cognitive decline in middle-aged rats with a history of MS. The changes in the brain are also associated with robust peripheral inflammatory changes. Concomitantly, we note changes in permeability of blood brain barrier in the hippocampus of MS rats as compared to age-matched control rats later in life. Studies are under way to assess the influence of nutritional, metabolic and environmental interventional strategies that may serve to reverse the mitochondrial and inflammatory changes that we observe following early life adversity.



Early life adversity in rodents perturbs hippocampal mitostasis and drives inflammaging in age-dependent manner
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2. Chaudhari PR, Singla A, Vaidya VA. 2022. Early Adversity and Accelerated Brain Aging: A Mini-Review. Front Mol Neurosci. 15:822917.

Ravi Devani

PDF 29

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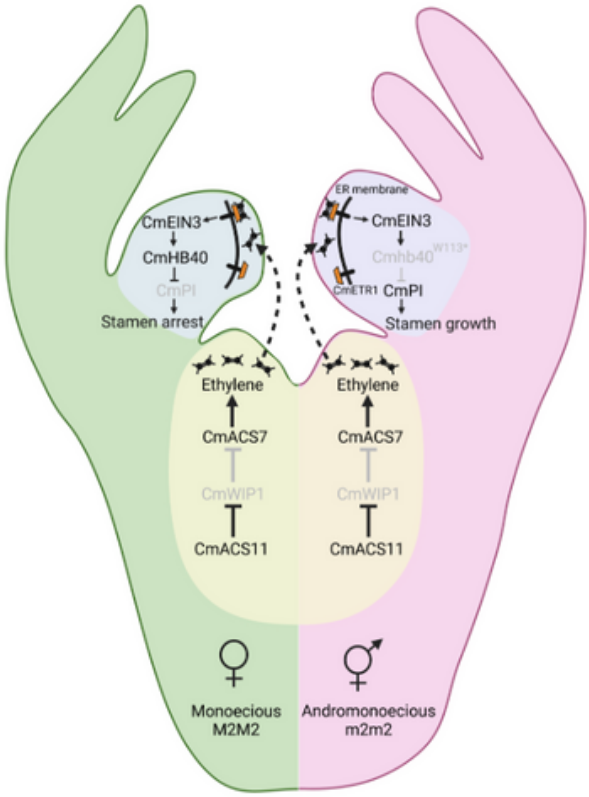
Compartmentalised ethylene signaling drives sex determination in cucurbits

Keywords: Plant Genetics, sex determination, crop improvement, cucurbitaceae, plant molecular biology

Abstract

Flowering plants have evolved intricate yet adaptable sex determination systems to increase genetic diversity and fitness of the offspring. Sex determination is also central in agriculture, as it determines how crops are cultivated and bred. We investigated how female flowers evolved from ancestral hermaphroditism in cucurbits. We characterised sex transition mutants and discovered a mechanism in which a versatile phytohormone, ethylene, produced in the carpel primordia is perceived in the stamen primordia through a spatially differentially expressed ethylene receptor, CmETR1. Subsequently, the tuning of the ethylene-insensitive 3 (CmEIN3) and EIN3-Like 1 (CmEIL1) signaling module, in stamen primordia, activates in a dose-dependent additive manner the expression of CmHB40, a homeodomain transcription factor. The expression of CmHB40 in stamen primordia of female flowers leads to the downregulation of key genes required for stamen development and upregulates genes associated with plant organ senescence. Investigation of melon genetic biodiversity revealed a haplotype, originating in Africa, altered in EIN3/EIL1 binding to CmHB40 promoter and associated with bisexual flower development. In contrast to other bisexual mutants available in cucurbits, CmHB40 mutations do not alter fruit shape. By disentangling the role of ethylene in fruit shape and sex determination pathways, our work opens up new avenues in plant breeding.



Ethylene produced in carpel primordia controls CmHB40 expression to inhibit stamen development

1. Rashid D*, Devani RS* (Co-first author), Rodriguez GN*, Choucha F*, Troadec C, Morin H, Tan F, Marcel F, Huang H, Hanique M, Zhang S, Verdenaud M, Pichot C, Rittener V, Huang Y, Benhamed M, Dogimont C, Boualem A, Bendahmane A. 2023. Ethylene produced in carpel primordia controls CmHB40 expression to inhibit stamen development. Nature Plants. 9: 1675–1687.

PDF 30

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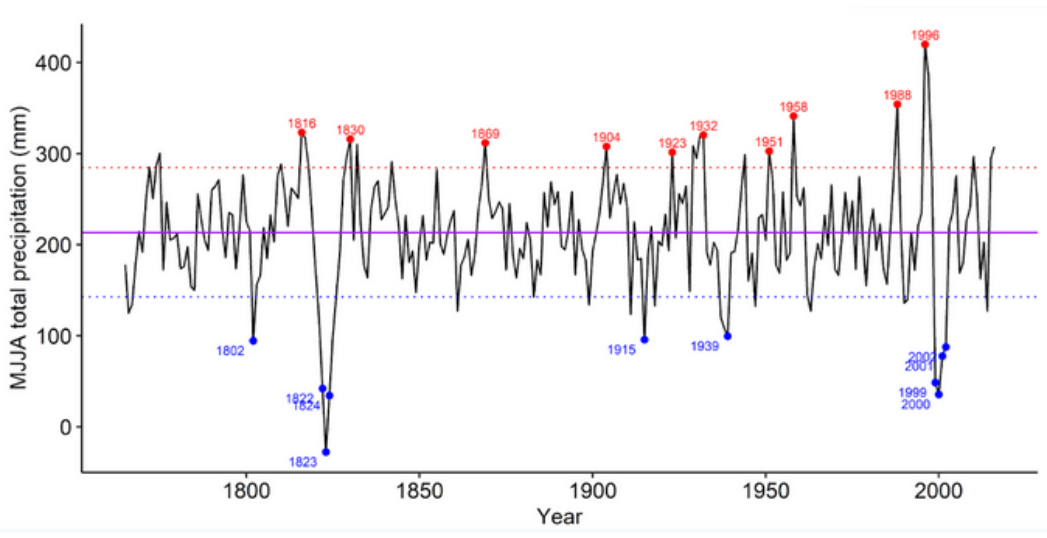
Precipitation reconstruction of Srinagar, Jammu and Kashmir, India from tree-rings

Keywords: Climate change, forest dynamics, tree ring research, R programming, species distribution modelling

Abstract

The ongoing climate change is affecting the plant growth and distribution pattern worldwide, with the impacts relatively more discernible at the higher latitudes, especially in the Himalayan ecosystems. Himalaya is among the most climatically important and sensitive regions, yet instrumental climate records are very patchy. The tree ring characteristics like ring-width, wood-density have long been used as tools to reconstruct past climate. The main advantage with the climatic data reconstructed from tree rings is that it is annually resolved and well calibrated and verified. We present a 226-year long reconstruction of growing season (May-August) precipitation for Srinagar, Jammu and Kashmir, India. A well replicated chronology of pindrow fir (Abies pindrow) tree ring-width measurements from 1791-2016 period was used as a hydroclimatic proxy. Residual tree-ring width indices were calibrated to monthly precipitation data from Srinagar meteorological station. The reconstruction explained 65% of total MJJA precipitation variability during the calibration period. Overall, there is no major trend in long-term precipitation. On the centennial scale, the 20th century is the wettest period. Identification of extreme dry and wet years based on 5th and 95th percentile distribution, respectively revealed twelve dry and wet years each. Twenty dry and twelve wet events of three or more years duration are present in the reconstruction with the longest dry period of ten years from 1933-1942 and longest wet period of nine years from 1902-1910. The driest event in the reconstruction was a five-year period from 1999 to 2003 while the wettest event was a four-year period between 1995 and 1998. On a decadal scale, 1911-1920 and 1811-1820 were the driest and the wettest decades, respectively. Further, there is some intermittent multi-year cyclicity present in the reconstruction. This reconstruction will help in better understanding of regional precipitation regime.



Reconstructed precipitation of Srinagar from tree ring-width chronology | Credits: Rayees Malik

Sangeetha Shyam

PDF 31

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Association of adiposity and its changes over time with COVID-19 risk in older adults with overweight/obesity and metabolic syndrome: A longitudinal evaluation in the PREDIMED-Plus cohort

Keywords: Nutrition, diabetes, dietary patterns, postprandial glycaemia, nutritional epidemiology

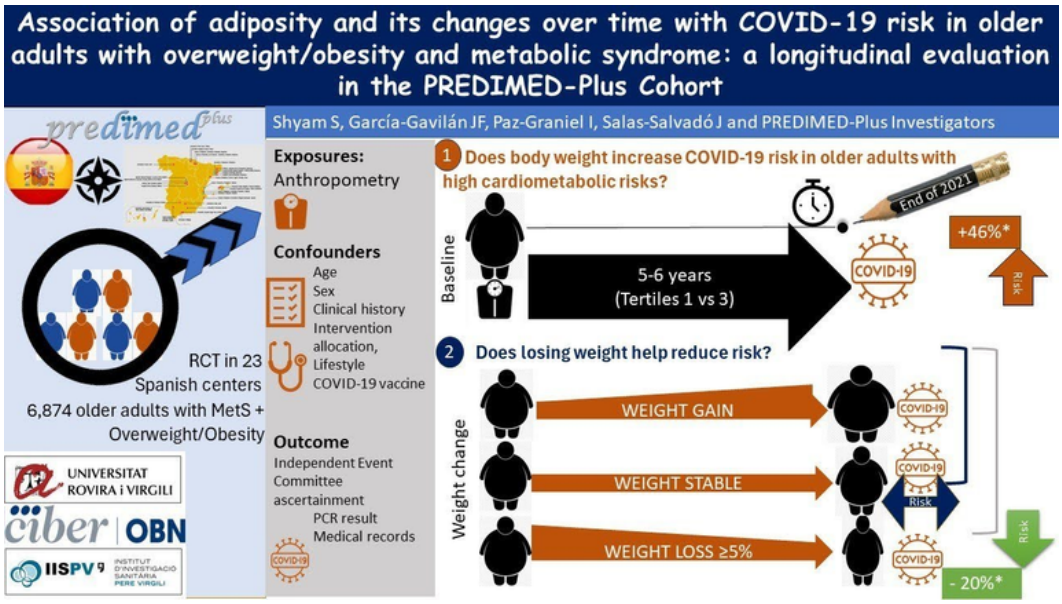
Abstract

Background: Cross-sectionally, older age and obesity are associated with increased coronavirus disease-2019 (COVID-19) risk. We assessed the longitudinal associations of baseline and changes in adiposity parameters with COVID-19 incidence in older adults at high cardiovascular risk.

Methods: This analysis included 6874 men and women (aged 55–75 years) with overweight/obesity and metabolic syndrome in the PREDIMED-Plus lifestyle intervention trial for cardiovascular risk reduction. Body weight, body-mass-index (BMI), waist circumference, waist-to-height ratio (WHtR), and a body shape index (ABSI) were measured at baseline and annual follow-up visits. COVID-19 was ascertained by an independent Event Committee until 31 December 2021. Cox regression models were fitted to evaluate the risk of COVID-19 incidence based on baseline adiposity parameters measured 5–6 years before the pandemic and their changes at the visit prior to censoring.

Results: At the time of censoring, 653 incident COVID-19 cases occurred. Higher baseline body weight, BMI, waist circumference, and WHtR were associated with increased COVID-19 risk. During the follow-up, every unit increase in BMI (HRadj: 1.04 (1.003, 1.08)) was associated with increased COVID-19 risk. Achieving≥5% reductions in body weight loss compared to having gains in these measures was associated with lower COVID-19 incidence even when adjusted for baseline adiposity.

Conclusions: In older adults with prior overweight/obesity, achieving clinically significant weight loss may be important to optimise immunity against COVID-19 and potentially other similar infections.



In older adults with prior overweight/obesity, achieving clinically significant weight loss may be important to optimize immunity against COVID-19 and potentially other similar infections | Credits: URV, IISPV, CIBEROBN and PREDIMED-Plus

Sarita Sarita

PDF 32

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Molecular features of native and fibril form of AL55 light chain associated with AL amyloidosis

Keywords: Protein aggregation, amyloid fibril structure, al amyloidosis, protein folding, cryo-electron microscopy

Abstract

AL amyloidosis is caused by the aberrant production of amyloidogenic light chains (LC) that accumulate as amyloid deposits in vital organs. Distinct LC sequences in each patient yield distinct amyloid structures. However, different tissue microenvironments may also cause identical protein precursors to adopt distinct amyloid structures. To address the impact of the tissue environment on the structural polymorphism of amyloids, we extracted fibrils from the kidney of an AL patient (AL55) whose cardiac amyloid structure was previously determined by our group. Here we show that the 4.0 Å resolution cryo-EM structure of the renal fibril, formed mainly by the variable domain of LC, is virtually identical to the cardiac fibril structure. These results provide the first structural evidence that LC amyloids independently deposited in different organs of the same AL patient share a common fold. Due to the variable domain's contribution to the amyloid fibril core, we recombinantly purified AL55 and its two domains (variable and constant) to compare the molecular properties of the native proteins with their aggregation properties. AL55 X-ray crystallographic structure reveals an open conformation with two variable domains far away from each other in native dimer over the closed conformations found in other known LCs, which may lead to greater accessibility of variable domains to proteolytic digestion and ultimately, to amyloid formation. We also found that the isolated variable domain is less structured, unstable, and flexible, which correlates with its increased aggregation propensity.

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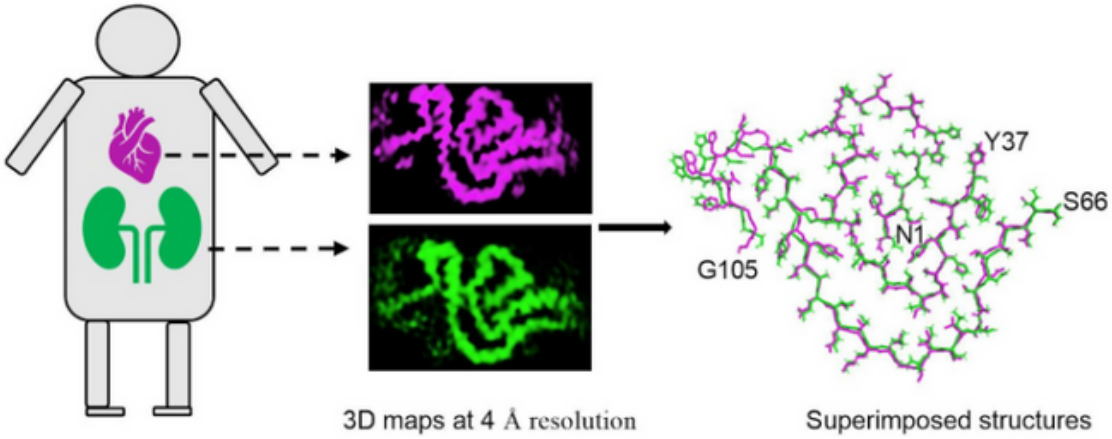

CryoEM-based structure maps and models of light chain fibrils extracted from the heart and kidneys of an AL amyloidosis patient. Credits: Sarita Puri, Stefano Ricagno

Saurabh Pradhan

PDF 33

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Decoding species specific regulatory codes of trophectoderm specification and implantation

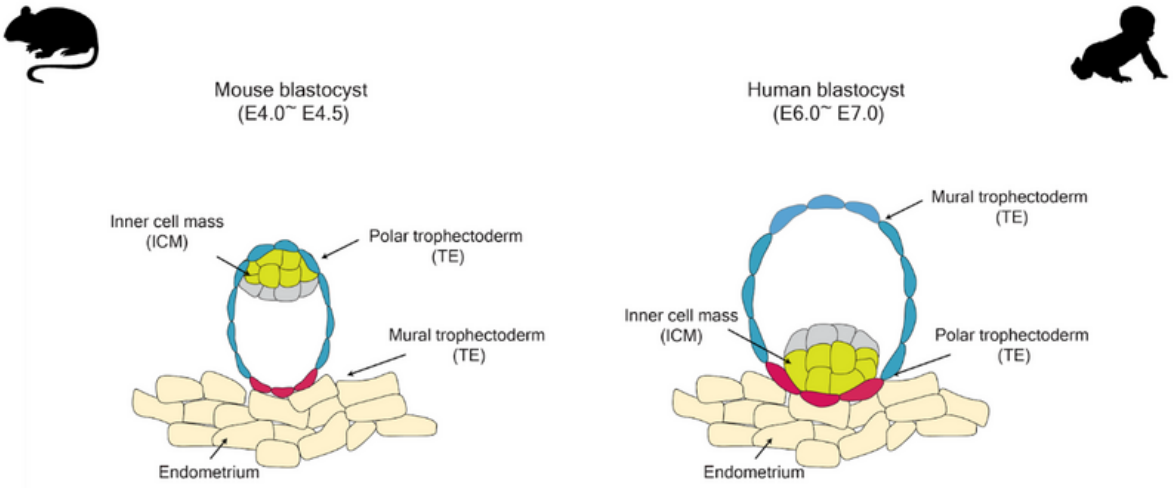
Keywords: Single cell multiomics- constructing gene regulatory networks, organoid research and phenotype screening, embryonic development and cell fate specification, chromatin biology and gene expression, cancer metastasis

Abstract

The intricacies of implantation, a pivotal event in establishing the connection between the developing embryo and the maternal environment, are essential for successful gestation. Across mammalian species, this process shares a common foundation but exhibits remarkable variations in attachment and invasion strategies. Notably, mouse embryos attach using mural trophectoderm cells, whereas human embryos employ polar trophectoderm. Furthermore, some species, like humans and cynomolgus monkeys, display a high potential for invasive implantation, while others, like marmosets, opt for a more superficial approach. The molecular mechanisms governing these differences have long eluded us.

In pursuit of these answers, our study harnessed cutting-edge techniques, including single-cell multiome (chromatin accessibility and transcriptome) analysis, to construct species-specific gene regulatory networks in humans and mice. We then compared these networks with data from cynomolgus monkeys and marmosets. Our findings shed light on a cadre of transcription factors acting in concert to regulate critical functions such as cell proliferation, translation of proteins, cell adhesion and invasion during the peri-implantation stage. To validate our discoveries, we combined in-silico perturbation with functional assays. We measured hCG secretion and in-vitro attachment potential to endometrial cells of knockout human blastoids. These experiments allowed us to delineate the roles of our candidate transcription factors which are at the core of our regulatory networks.

In summary, our study allows us to hypothesise that evolution of genomic traits is central to controlling these key functions and cell specification in a spatiotemporal manner. Moreover, these differences in cell fate and implantation strategies underscore the importance of evolutionary adaptations, empowering diverse mammalian species to thrive in their unique environments. This research not only expands our understanding of implantation but also holds potential implications for fertility and reproductive medicine.



Species specific differential mode of implantation | Credits: Saurabh J Pradhan

Sayantan Panda

PDF 34

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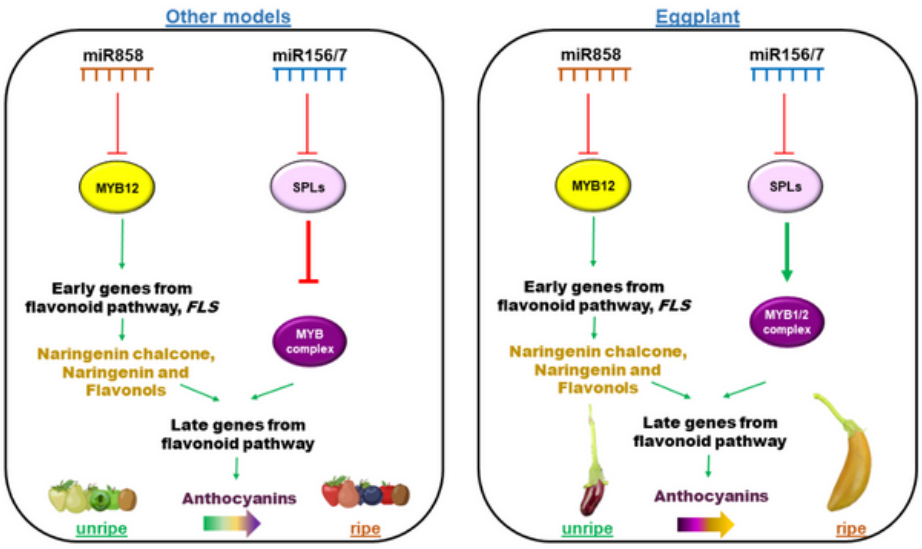
A pair of microRNAs controls the unique pigmentation shift in developing eggplant fruit skin

Keywords: Plant specialised metabolism, phytohormone metabolism, growth and defense tradeoff, host-microbiome interaction, fruit development and ripening

Abstract

Pigments are secondary metabolites present in fruit to attract animals for seed dispersal. In most fleshy fruit, green chlorophyll accumulates early in development and is replaced by a range of pigments during fruit ripening. In blueberries, grapes, and strawberries, chlorophyll is replaced by red anthocyanins generated downstream of the flavonoid biosynthetic pathway. Eggplant (*Solanum melongena*) fruit is unique in terms of pigmentation, as, according to our knowledge, is among very few fruits where anthocyanin is present from fruit set and is exchanged through maturation by a yellow pigment. We found that this colour results from naringenin chalcone, a flavonoid pathway intermediate that accumulates in tomatoes starting from the breaker stage of fruit development. To understand the genetic regulation of such an unusual shift, we integrated temporal transcriptomic data [microRNA (miRNA) and mRNA] obtained from developing eggplant fruit skin. We discovered that while Squamosa Promoter Binding-Like (SPL6a, SPL10, and SPL15), MYB1 and MYB2 transcription factors (TFs) regulate anthocyanin, the MYB12 TF controls naringenin chalcone. We prove that miRNA156/7 and miRNA858 negatively regulate SPLs and MYB12, respectively. Interestingly, in contrast to other plants, in eggplant SPLs positively regulate anthocyanin biosynthesis by transcriptional regulation of MYB1 and MYB2 TFs. Taken together, our model suggests that the opposing and complementary expression of miRNA157 and miRNA858 control various parts of the flavonoid pathway in developing eggplant fruit skin. This results in an unusual shift in eggplant fruit pigmentation in which anthocyanins are replaced through ripening by yellow intermediates of the flavonoid pathway. In summary, this work exemplifies how the different plant system vary in terms of their molecular regulation and why any single model should not consider as a proxy for every plant system.



A cross-species comparative model illustrating the transcriptional and post-transcriptional regulatory network governing flavonoid metabolism (other anthocyanin-rich fruits vs. eggplant; sharp arrow indicates activation, whereas blunt arrow represents repression)
Credits: Sayantan Panda (fruit images were created with BioRender.com)

Shlesha Richhariya

PDF 35

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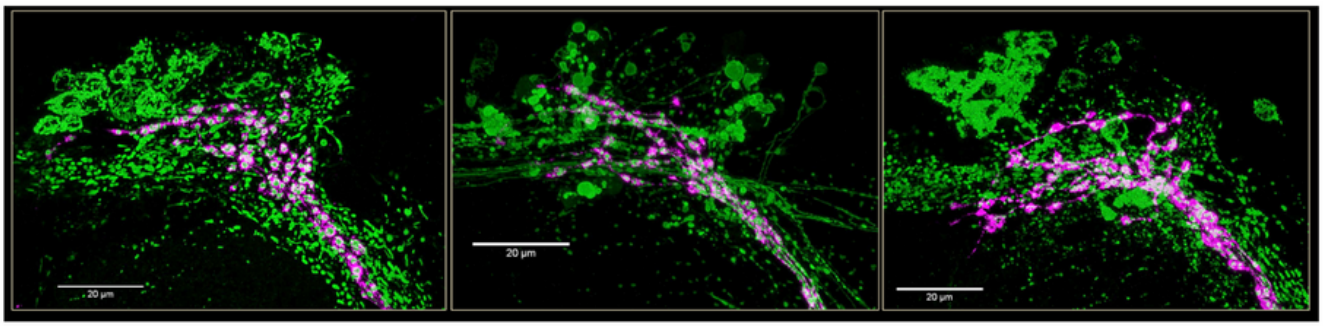
Neuron-specific CRISPR genetics to study the role of mitochondrial dynamics in aging Drosophila neurons

Keywords: Mitochondrial dynamics, neurodegeneration, CRISPR-based screening in Drosophila, circadian behavior, ageing

Abstract

Mitochondria are dynamic organelles that undergo fission and fusion for many reasons, including energy demands and stress. Altered mitochondrial dynamics are associated with several neurodegenerative diseases, yet the relationship of mitochondrial dynamics to neurodegeneration and aging is poorly understood. This is in part because the current understanding primarily relies on observations made in advanced stages of the disease or in cultured cells, which limits our understanding of disease etiology.

Since perturbing mitochondrial dynamics in broad sets of neurons causes lethality, we explored the consequences of altered mitochondrial dynamics in the clock neurons of Drosophila, which are largely inessential for viability. CRISPR-Cas9 based methods efficiently disrupt mitochondrial dynamics by targeting genes for mitochondrial fission and fusion in specific sets of neurons. Circadian behavioral assays indicate that blocking mitochondrial fusion in clock neurons leads to progressive age-dependent impairment of neuronal function, whereas blocking fission has much milder effects. To further understand the cellular effects of disrupted mitochondrial dynamics, we then performed transcriptomic analysis of clock neurons deficient in mitochondrial fusion and fission, in young and old clock neurons. Consistent with the behavioral effects, loss of fission had only a minor influence on the transcriptome, whereas loss of mitochondrial fusion led to differential expression of several genes, with bigger changes observed in older neurons. These transcriptional changes suggest reduced mitochondrial function and elevated translation upon loss of fusion, hinting at gene expression compensation mechanisms. Indeed, a CRISPR-Cas9 double gene knockout strategy identified Ldh as a key up-regulated gene that compensates for the loss of fusion associated decrease in mitochondrial function and prevents neurodegeneration. We are using this system to further explore the interactors of the mitochondrial fission-fusion pathway in "young-healthy" as well as in diseased and aging neurons.



Tissue specific CRISPR effectively alters mitochondrial morphology. Mitochondria labelled with mitoGFP (green) in the DN1p circadian neurons of Drosophila. Mitochondrial morphology in control neurons and their processes (left), hyperfused mitochondrial morphology seen in neurons with fission blocked (Drp1-mut, centre) and highly fragmented mitochondria in neurons with fusion blocked (Opa1-mut, right). In magenta is axonal projection of PDF neurons (neurons not in picture) stained with a PDF antibody.
Credits: unpublished image (Shlesha Richhariya)

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PDF 36

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Neural and algorithmic bases of odor guided trail following in mice

Keywords: Olfaction, closed-loop behavior, evolution of neural circuits, high speed videography, sensorimotor integration

Abstract

Animals actively sense the environment to acquire features of interest. An everyday example of active sensing behavior is our use of repeated visual saccades for scene recognition. Many behaviors in rodents are guided by odor cues, and active modulation of sniffing is likely to play important roles. Navigating odor trails involves bilateral comparison from both nostrils across multiple sniffs, followed by subsequent motor actions. Sensory neurons convey olfactory information from the nose to the olfactory bulb, where projection neurons relay it to higher brain regions that include olfactory cortical areas. However, the neural basis for such flexible yet precise odor-guided behavior remains poorly understood.

Here, we use an "infinite" paper treadmill with dynamic odor trails that continuously challenge mice to navigate with high precision. By combining high-speed videography with DeepLabCut, we estimate trail following with high accuracy.

We corroborated previous findings that occluding a nostril biases, but does not abolish, trail following. Although mice predominantly cast while trail-following, there exist other strategies for following a trail such as biased searches based on previous encounters with the trail. To address the neural basis of trail following, we chose to study the anterior olfactory nucleus (AON), an early olfactory cortical area that has privileged access to information coming from both nostrils and sends feedback projections to the bulb and the piriform cortex. Targeted unilateral chemogenetic perturbation in AON activity leads to lateralised trail following deficits, which we are characterising in greater detail. Using wireless methods to measure respiration we observe that mice use strategies beyond simple comparisons between two nostrils. We hope to understand the role of history dependent odor processing that might be especially relevant for accurately navigating odor trails.

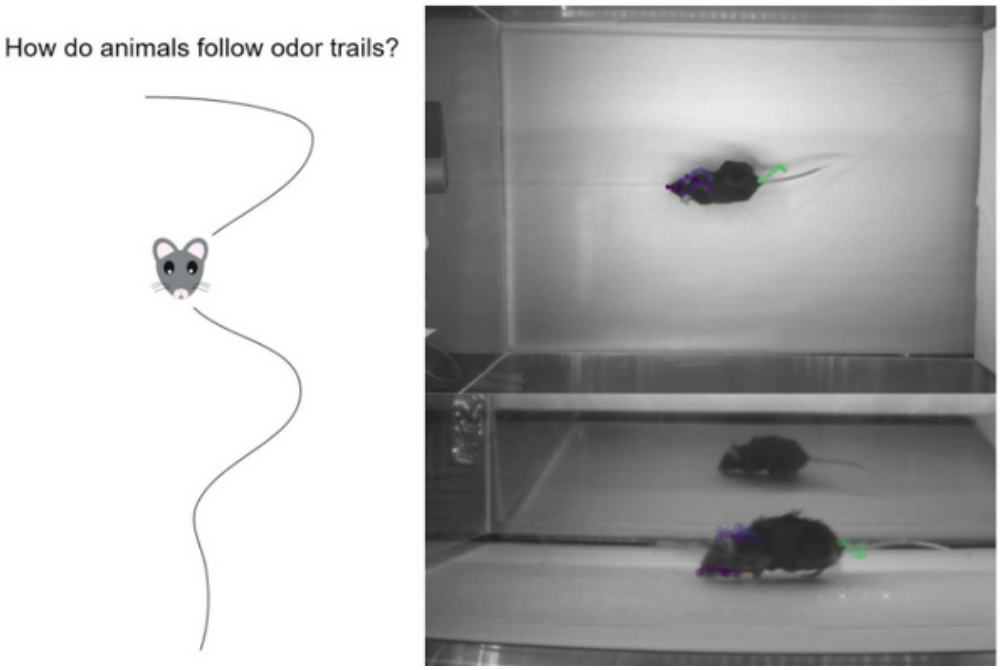

Image of a mouse following an odor trail with specific body parts identified through markerless methods in two synchronised views. Credits: Unpublished image (Siddharth Jayakumar)

Sravanthi Nadiminti

PDF 37

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Mechanisms for synaptic vesicle biogenesis

Keywords: Cell biology, protein trafficking, neurons, neurodegeneration, synaptic vesicle biogenesis

Abstract

Neurons are polarised cells that function to relay information via release of neurotransmitters from organelles known as synaptic vesicles (SVs). Several studies suggest that SVs are transported out of the neuronal soma as precursor vesicles, which through poorly known mechanisms, are converted into mature functional SVs [1-6]. The little information on SV biogenesis and maturation that we have currently comes largely from invertebrate models. My project therefore aims at uncovering the various molecular pathways regulating the formation and maturation of SVs in neurons in human neurons. In the long run my work may contribute to the development of novel treatment options for neurological diseases related to axonal and synaptic dysfunction.

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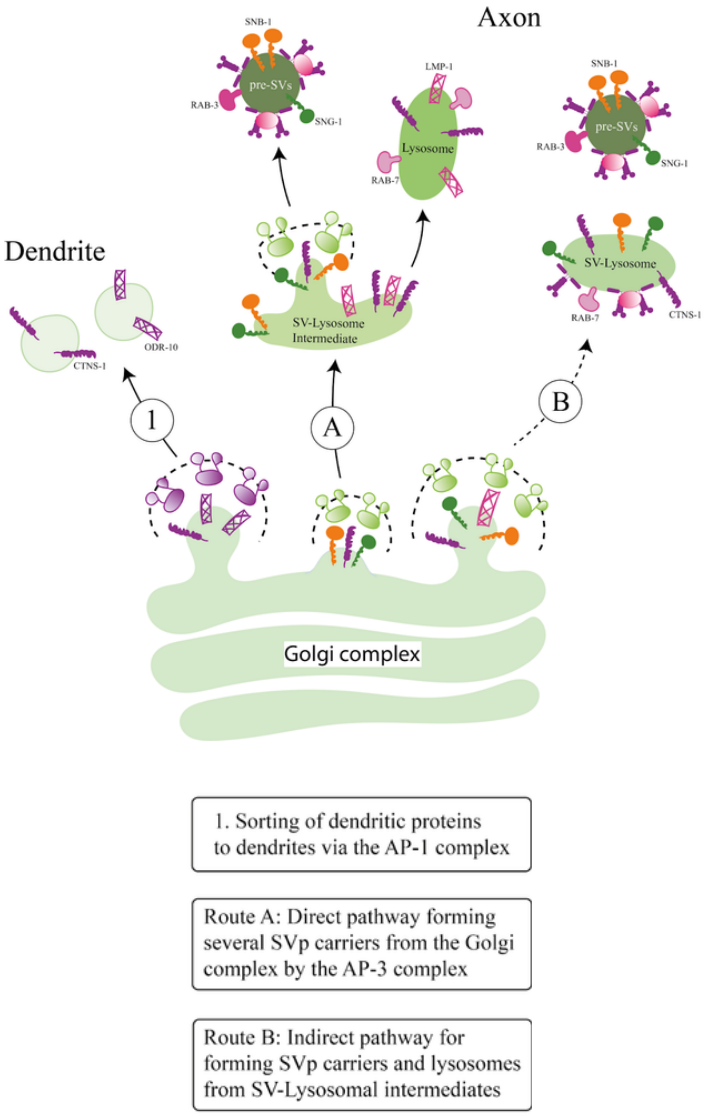

Genetic pathways for assembling synaptic vesicles
Credits: Sravanthi Nadiminti

PDF 38

Sreeja J S

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Transporting Gli transcription factors to the cilium tip for Hedgehog signaling: A tale of two motor systems

Keywords: Cilia, microtubules, neurodegeneration, transport, axoneme

Abstract

Primary cilium is a hub for cellular signaling pathways. A prime example is the Hedgehog (Hh) pathway important in embryonic development. A key step in Hh pathway activation is the accumulation of major pathway effectors, Gli transcription factors, at the distal cilium tip (1). The movement of Gli within the cilium has not been directly observed, hence the underlying trafficking mechanisms remain poorly understood. We developed a TIRF-microscopy-based live imaging assay to visualize Gli2 molecules in the cilium. Multi-hour imaging revealed that Gli2 tip accumulation occurs early, with maximum levels of Gli2 achieved within ~90 minutes of pathway activation. Imaging at higher temporal resolution, we observed directional movement of Gli2 molecules toward the distal cilium tip specifically during this initial time window. Through co-imaging Gli2 and the IFT88 subunit of Intra Flagellar Transport (IFT) machinery, we conclusively showed that Gli2 is a bonafide IFT cargo. Next, we examined the contribution of Kif7, a non-motile ciliary kinesin that is proposed to organise a ciliary tip compartment for Hh signaling. We found that in absence of Kif7, Gli2 is not efficiently loaded on IFT and is not exclusively concentrated at the cilium tip. This finding underscores the synergy between two cilium-specific cytoskeleton systems in enabling Hh-responsive trafficking of Gli2 to the cilium tip. Significantly, our findings address a long-standing conundrum and suggest that the function of IFT in vertebrate Hh signaling extends beyond maintaining cilium architecture. Instead, IFT is an integral component of the Hh pathway, with a direct role in Gli transport.

Reference:
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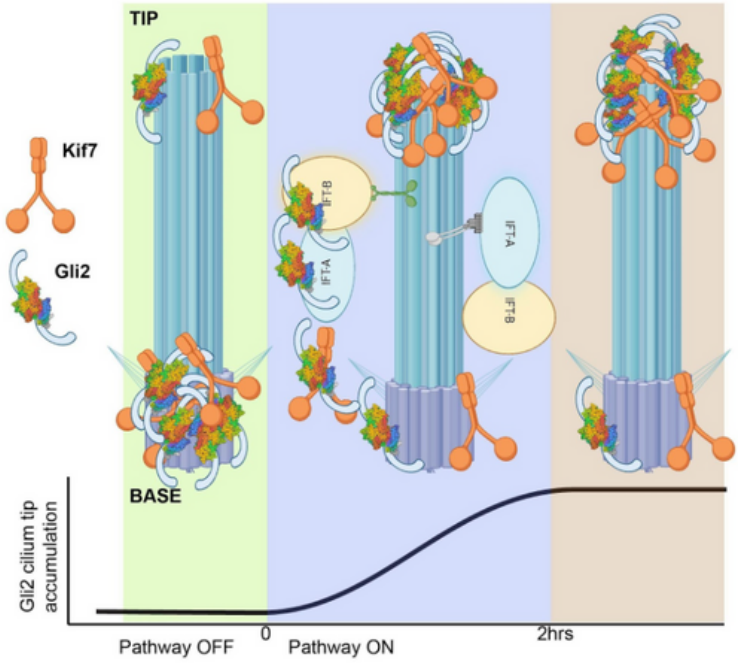

Gli2's ciliary journey: Dynamic interplay of IFT and Kif7 | Credits: Created using Biorender

PDF 39

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Red and near-infrared light-triggered dual cancer phototherapy by using a dipyridophenazine Ni(II) dithiolene complex

Keywords: Metal complex, cancer phototherapy, antimicrobial phototherapy, medicinal chemistry, inorganic chemical biology

Abstract

Combining photodynamic therapy (PDT) and photothermal therapy (PTT) within the phototherapeutic window (600–900 nm) holds immense potential for advancing cancer phototherapy, exceeding the efficacy observed with PDT or PTT alone. This study introduces a novel small-molecule mixed-ligand Ni(II)-dithiolene complex (Ni-TDD) featuring a dipyridophenazine ligand, showcasing potent red-light PDT and significant near-infrared (NIR) light mild-temperature PTT efficacy against cancer cells and 3D multicellular tumor spheroids (MCTSs). The four-coordinate square planar complex exhibited excellent dark and photostability in an aqueous phase. Ni-TDD induced a potent red-light (600–720 nm) PDT effect on HeLa cancer cells (IC50 = 1.8 μM, phototherapeutic index = 44), prompting apoptotic cell death through singlet oxygen generation. The complex induced mild hyperthermia and exerted a significant mild-temperature PTT effect on MDA-MB-231 cancer cells upon irradiation with 808 nm NIR light. Simultaneous irradiation of Ni-TDD-treated HeLa MCTSs with red and NIR light led to a remarkable synergistic inhibition of growth, surpassing the effects of individual irradiation, by generating singlet oxygen and inducing mild hyperthermia. Importantly, Ni-TDD demonstrated minimal toxicity towards noncancerous HPL1D and L929 cells, even at high micromolar concentrations. This research marks the first report of a Ni(II) complex displaying red-light PDT activity and represents the first instance of a first-row transition metal complex showcasing combined PDT and PTT effects within the clinically relevant phototherapeutic window. These findings open new avenues for developing metal-dithiolene complexes as dual-acting cancer phototherapy agents, utilising long wavelength lights for treating solid tumors.

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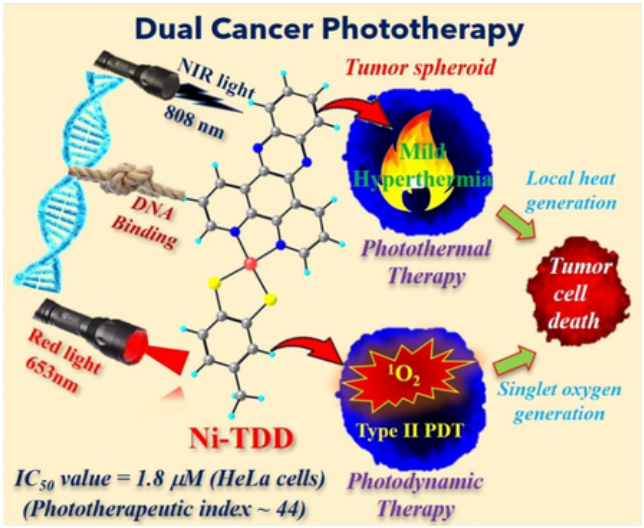

The Ni(II) dithiolene complex, Ni-TDD, displays potent red-light photodynamic therapy (PDT) activity via singlet oxygen and significant near-infrared light-induced mild-temperature photothermal therapy (PTT) effects through mild hyperthermia against HeLa cancer cells and multicellular tumor spheroids (MCTSs), with minimal toxicity towards normal cells in the absence of light.

Credits: Sarkar T, Sahoo, S, Neekhra S, Paul M, Biswas S, Babu B N, Srivastava R, Hussain A. 2023. A dipyridophenazine Ni(II) dithiolene complex as a dual-acting cancer phototherapy agent activatable within the phototherapeutic window. European Journal of Medicinal Chemistry 261: 115816.

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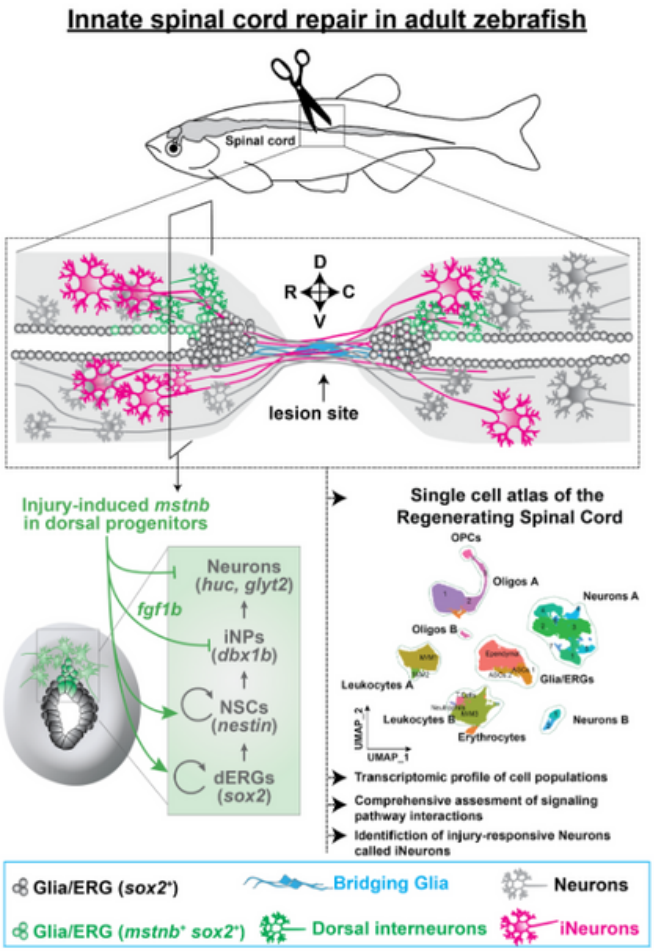
PDF 40

Regulation of adult neurogenesis and axon regrowth during spinal cord regeneration

Keywords: Neurogenesis, regeneration, single cell transcriptomics, plasticity, zebrafish spinal cord

Abstract

Recovery after spinal cord injury (SCI) in mammals is hindered by both neuron intrinsic and extrinsic factors. However, zebrafish have the innate ability to regenerate their spinal cord (SC) within 6-8 weeks post-injury. Progenitor cells in the zebrafish SC are shown to proliferate and produce different cell types after injury. Nonetheless, the mechanisms that lead to complete recovery after SCI are poorly studied. Using single-cell and genetic tools, we found that neurons are one of the most dynamic signaling populations during SC regeneration and uncovered local and global neuron intrinsic mechanisms that support innate SC regeneration. First, we found the TGF-β ligand myostatin b (mstnb) is expressed in a niche of dorsal progenitor cells post injury and regulates the profile of newborn neurons via Fgf1 signaling. This unanticipated neurogenic function for mstnb established the importance of local adult neurogenesis for innate SC repair 1. Next, we performed transcriptomic profiling of the regenerating SC through single nuclear RNA sequencing to understand global injury response and intercellular communications. We identified an injury-induced neuron subpopulation called iNeurons and hypothesized that genes expressed in iNeurons have pro-regenerative functions. HCR in situ hybridization confirmed the expression of iNeurons genes in vivo and high-efficiency CRISPR/Cas9 elucidated their importance during SC repair 2. Our studies provide mechanisms that direct successful SC regeneration and novel therapeutic targets for neural repair.



Mechanism regulating innate spinal cord regeneration
Credits: Vishnu Muraleedharan Saraswathy

1. Saraswathy VM, Zhou L and Mokalled MH. 2023. Single-cell analysis of innate spinal cord regeneration identifies intersecting modes of neuronal repair. bioRxiv, https://doi.org/10.1101/2023.05.19.541505

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*First authors

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