12th

Young Investigators' Meeting 2020

14-18
February 2020
Mahabalipuram

IndiaBioscience

INDIAN INSTITUTE OF TECHNOLOGY MADRAS · सिद्धिर्भवति कर्मजा ·

The Young Investigators' Meeting Series

Building a community of young Indian biologists

The YIM series aims to build a community of well-networked 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 an eclectic mix of India's best early-career life science researchers, postdoctoral fellows, reputed Indian and international scientists, administrators of institutions, funding agency representatives and science policymakers for 5 days of discussions and interactions focusing on science and careers in science.

The program features talks, posters and panel discussions, where participants examine a wide variety of topics ranging from picking research problems, publishing, personnel management and mentorship. Senior scientists describe their own scientific journeys, providing inspirational as well as amusing anecdotes about their experiences of starting their scientific careers. Interactions between young Indian investigators and post-docs aspiring for jobs in India ensures that the postdocs get a first-hand account of finding jobs and setting up labs in India. Experiences shared by senior scientists enable young Indian investigators and future recruits to imbibe the scientific ethos in India and further them towards making the Indian life sciences sector internationally competitive.

Perhaps the greatest accomplishment of the YIM series is building a future community of well-networked biologists, allowing young Indian scientists from different regions and institutions to establish friendships, initiate collaborations, and learn from peer-to- peer mentoring.

Every year the YIM is organised by a different committee, comprised of young faculty members from institutions across the country. IndiaBioscience plays an administrative and advisory role in each year's YIM. YIM 2020 is the twelfth in a series that began in 2009, and has grown in popularity, size and content since then.

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YIM 2020 Organizers

VAISHNAVI ANANTHANARAYANAN

Indian Institute of Science, Bangalore

http://www.be.iisc.ernet.in/~vaish/

Vaishnavi Ananthanarayanan is an Assistant Professor at the Centre for BioSystems Science and Engineering at the Indian Institute of Science, Bangalore. She obtained her Ph.D. from the Max Planck Institute of Molecular Cell Biology and Genetics, Dresden. Prior to her Ph.D., Vaishnavi pursued a dual degree in M.Sc. Biological Sciences and B.E. Computer Science at BITS, Pilani. She was awarded the INSPIRE Faculty Award in 2014, the Innovative Young Biotechnologist Award in 2015, SERB Early Career Research Award in 2016 and was elected Associate of the Indian Academy of Sciences in 2018. In 2019, she was granted the Wellcome Trust/DBT India Alliance Intermediate Fellowship, SERB Women Excellence Award, BITSAA 30u30 Award, and named RI Mazumdar Young Investigator and EMBO Young Investigator. Her lab focuses on developing and employing light microscopy and image processing techniques coupled with genetic manipulation in living cells to better understand processes mediated by the cytoskeleton and associated proteins.

SMITA JAIN

IndiaBioscience, Bangalore

https://indiabioscience.org/

Smita has a PhD from the Indian Institute of Science, Bangalore in the field of Cancer Biology. After exploring industry for couple of years, she moved into the field of scientific management. With her keen interest in management, ability to communicate, she played a key role in establishing the business and processes at C-CAMP, Bangalore. She also has experience of working as a research analyst with a digital content organization. She is deeply motivated to take the activities of IndiaBioscience to all possible corners of the country and make a strong knit network of Indian life science researchers and professionals.

YIM 2020 Organizers

ATHI N NAGANATHAN

Indian Institute of Technology Madras, Chennai

http://pbl.biotech.iitm.ac.in/athi-n.-naganathan.html

Athi N Naganathan is an Associate Professor and a Wellcome Trust-DBT India Alliance Intermediate Fellow at the Department of Biotechnology, Indian Institute of Technology Madras. His research group employs an interdisciplinary approach involving experimental spectroscopy, functional studies, simulations and theoretical modeling to understand and manipulate the basic energetic and entropic factors governing the folding of proteins, with implications in protein function, design and engineering.

V. ARAVINDHAN

University of Madras, Chennai

https://www.unom.ac.in/index.php?route=department/department/profile&deptid=33&facultyid=345

V. Aravindhan is currently an Assistant Professor at the Dept of Genetics, University of Madras. His current research focus is to look at chronic inflammation and impaired immunity in diabetes. His serendipitous discovery on inverse relationship between the prevalence of diabetes and lymphatic filariasis paved the way for using LF antigens as anti-diabetic vaccines, which is actively being perused at his lab. He was invited to deliver a keynote lecture at The 9th International Science and Maths Symposium at California State University Fullerton, USA on this topic. The second topic in which he is working on is Diabetes-Tuberculosis co-morbidity in India. He has won several international fellowships including AIDS International Training & Research Program, Global Infectious Diseases Fellowship Program and DST-DAAD scientist exchange program. Apart from research and teaching he enjoys scientific writing, scientific dissemination and is an activist against pseudoscience.

IndiaBioscience

IndiaBioscience
ENGAGING COMMUNITIES ENABLING CHANGE

IndiaBioscience is an organization 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.

Team Members from left to right: Manjula, Shantala, Smita, Shreya, Shwetha, Lakshmi and Vijeta

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Program Schedule

14 February

Day 1: Young Investigators' Meeting 2020

12.00 - 14.30	**Lunch**
14.30 - 14.45	**Welcome Note** by YIM Organisers
14.45 - 15.15	**Keynote address** by Renu Swarup, *Secretary, Department of Biotechnology, Govt of India, New Delhi* **Launch of** *Disha: A Career Resource Book for Life Science and Biotechnology Students*
15.15 ~ 15.45	**Mentor Talk-1/ EMBO Global Lecture** **Microtubule Organisation and Dynamics: From Cells to Single Molecules** by Anna Akhmanova, *Utrecht University, Netherlands*
15.45 - 16.15	**Mentor Talk-2/ EMBO Global Lecture** **A Little Fly and Big Questions Can Keep You Busy Throughout Your Career** by Elizabeth Knust, *Max Planck Institute of Molecular Cell Biology and Genetics, Germany*
16.15 - 16.40	**Tea/Coffee**
16.40 - 17.00	**Special Talk-1** **Engaging Communities, Enabling Change** by Smita Jain, *IndiaBioscience, Bangalore*
17.00 – 18.15	**Panel Discussion-1** Translational Research *Moderator:* Taslimarif Saiyed, *C-CAMP, Bangalore* *Panelists:* Navakanta Bhat, *IISc, Bangalore;* Jugnu Jain, *Sapien Bio, Hyderabad &* Guhan Jayaraman, *IIT Madras*
18:15 - 19.45	**YI Poster session** (YIs with even poster numbers present their posters)
19.45 onwards	**Dinner on the lawn**

Program Schedule

15 February

Day 2: Young Investigators' Meeting 2020

09.00 - 09.30 **Mentor Talk-3**

Codes for the making of a rice flowering stem

by Usha Vijayraghavan, *IISc, Bangalore*

09.30 - 10.00 **Mentor Talk-4**

What I talk about when I talk about biology

by Gautam Menon, *Ashoka University, Sonipat & IMSc, Chennai*

10.00 - 10.30 **Mentor Talk-5**

Adaptive Evolution of a Researcher in Indian Academia

by Guhan Jayaraman, *IIT Madras*

10.30 - 11.00 **Tea/Coffee**

11.00 - 11.30 **Mentor Talk-6**

The Chaos Between the Intention of Becoming a Scientist and Being One

by Maitrayee DasGupta, *University of Calcutta*

11.30 - 13.00 **Panel Discussion-2**

Funding for Science in India

Moderator: Aravindhan Vivekanandhan, *University of Madras*

Panelists: Meenakshi Munshi, *DBT;* Shahid Jameel, *Wellcome Trust/DBT India Alliance;* Balachandar Venkatesan, *SERB*; Maitrayee DasGupta, *University of Calcutta*

13.00 - 13.50 **Lunch**

13.50 - 15.20 **Breakout session-1**

Getting started - 1 (*Setting up labs and lab management, Picking up the right research question*

15.20 - 16.45 **YI Poster session** with Tea/Coffee (YIs with odd poster numbers present their poster)

16.45 - 17.15 **Mentor Talk-7/ EMBO Global Lecture**

Centrosomes in Development, Disease and Evolution

by Mónica Bettencourt-Dias, *Instituto Gulbenkian de Ciência, Portugal*

17.15 - 18.00 **Keynote Lecture**

Biology across Scale: Should we Reconfigure our Approach

by K VijayRaghavan, *Principal Scientific Adviser to the Government of India, New Delhi*

Program Schedule

18.00 - 19.30 **EMBO Grant Awareness Workshop**

19.30 onwards **Banquet Dinner on the lawn**

16 February

Day 3: Young Investigators' Meeting 2020

09.00 - 09.30 **Special Talk-2**

Why and How to integrate Research and Education

by LS Shashidhara, *Ashoka University, Sonipat & IISER Pune*

09.30 - 10.00 **Mentor Talk-8**

Balancing Act of Modern Age Women

Shakila H, *Madurai Kamraj University, Madurai*

10.00 - 11.15 **Panel Discussion-3**

Science Outreach & Communication

Moderator: Gautam Menon, *Ashoka University, Sonipat & IMSc, Chennai*

Panelists: Shakila H, *MKU, Madurai;* Elizabeth Knust, *MPI-CBG, Germany;* Kollegala Sharma, *CFTRI, Mysuru;* Dinabandhu Sahoo, *University of Delhi;* Priyanka Pulla, *Freelance Journalist*

11.15 - 11.45 **Tea/Coffee**

11.45 - 12.15 **Mentor Talk-9**

Joys and Confusions of Being a Scientist at the 'Interface'

Sudipta Maiti, *TIFR, Mumbai*

12.15 - 12.45 **Mentor Talk-10**

Revisiting the journey towards an Independent Researcher

by AK Munirajan, *University of Madras*

12.45 - 13.45 **Lunch**

13.45 - 15.00 **Breakout session-2**

Getting started-2 (*Research ethics, Research output, Peer recognition)*

15.00 - 17.00 **PDF poster session** with Tea/Coffee

17.00 - 18.00 **Panel discussion-4**

Breaking Barriers in Science

Moderator: Rashna Bhandari, *CDFD, Hyderabad*

Program Schedule

Panelists: Sudipto Maiti, *TIFR, Mumbai;* AK Munirajan, *University of Madras;* Anna Akhmanova, *Utrecht University, Netherlands;* Mónica Bettencourt-Dias, *Instituto Gulbenkian de Ciência, Portugal;* Usha Vijayraghavan, *IISc, Bangalore*

18.00 - 18.30 **Special Talk 3**
A Decade of Recognizing the Best Contemporary Research and Science:
by Bhavna Mehra, *Infosys Science Foundation, Bangalore*

18.30 - 18.45 **Summary** by Aravindhan Vivekanandhan (YIM 2020 Organizer)

18.45 - 19.00 **Closing remarks**
by Satyajit Mayor, *NCBS, Bangalore, India*

19.30 onwards **Banquet Dinner on the lawn**

17 February
Day 4: PDF Satellite Meeting

09.00 - 09.10 **Introduction to The PDF Satellite Meeting**
by Rashna Bhandari, *CDFD, Hyderabad*

09.10 - 10.10 **Institutional Talks Session 1**
(LS Shashidhara, *Ashoka University, Sonipat*; Satyajit Mayor, *NCBS, Bangalore*; Subhash C Lakhotia, *BHU, Varanasi*; Saikrishnan Kayarat, *IISER Pune*; AK Munirajan, *University of Madras;* Manjula Reddy, *CSIR-CCMB Hyderabad*)

10.10 - 11.00 **PDF Talks Session 1** (10 PDFs talk for 5 mins each)

11.00 - 11.20 **Tea/Coffee**

11.20 - 12.10 **Institutional Talks Session 2**
Govindan Rangarajan, *IISc, Bangalore*; Ranjith Padinhateeri, *IIT Bombay*; Pragasam V, *VIT, Vellore*; R. Sankar, *IIT Kanpur*; BJ Rao, *IISER Tirupati*

12.10 - 13.00 **PDF Talks Session 2** (10 PDFs talk for 5 mins each)

13.10 - 14.00 **Lunch**

14.00 - 14.50 **PDF Talks Session 3** (10 PDFs talk for 5 mins each)

14.50 - 15.40 **Institutional Talks Session 3**
Apurva Sarin, *InStem, Bangalore*; Pushkar Sharma, *NII, New Delhi*; Pennathur Gautam, *Anna University, Chennai*; Guhan Jayaraman, *IIT Madras*; Himanshu Sinha, *IBSE, IIT Madras*

Program Schedule

15.40 - 16.20	**PDF Talks Session 4** (10 PDFs talk for 5 mins each)
16.20 - 18.20	**PDF Poster Session** with Tea/Coffee
19.30 onwards	**Dinner and Informal Discussion**

18 February

Day 5: PDF Satellite Meeting

09.00 - 10.00	**Institutional Talks Session 4** (Yogendra Sharma, *IISER, Berhampur*; Neeraj Jain, *NBRC, Manesar*; Chandan Goswami, *NISER, Bhubaneswar*; Vivek Tanavde, *Ahmedabad University*; Appa Rao Podile, *University of Hyderabad*; Roop Mallik, *TIFR, Mumbai*)
10.00 - 11.30	**PDF Poster Session** with Tea/Coffee
11.30 - 12.20	**PDF-Institutional Heads Open Session** Moderated by Roop Mallik, *TIFR, Mumbai* & Rashna Bhandari, *CDFD, Hyderabad*
12.20 - 12.45	**Closing remarks to the PDF Satellite Meeting** by Roop Mallik, *TIFR*, *Mumbai*
12.45 onwards	**Interaction with Institutional Heads,** lunch and departure

Keynote Speakers

K VIJAYRAGHAVAN

Principal Scientific Advisor to the Government of India, New Delhi

RENU SWARUP

Secretary, Department of Biotechnology, Government of India, New Delhi

Special Lecture

BHAVNA MEHRA

General Manager, Infosys Science Foundation

www.infosys-science-foundation.com

Infosys Prize: A decade of recognizing the best contemporary research and science

Governed by the Infosys Science Foundation, the Infosys Prize was established, keeping in mind that it is important to encourage both fundamental and applied research and science. Distinguished awards world over recognize a lifetime of achievement and some others reward only breakthroughs. The Infosys Prize is given to mid-career researchers with a focus on encouraging them and allowing them to continue comfortably in the field.

Translational Research

Panel Discussion-1

Moderator

Taslimarif Saiyed, Centre for Cellular And Molecular Platforms (C-CAMP), Bangalore

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Funding for Science in India

Panel Discussion-2

Moderator

Aravindhan Vivekanandhan, University of Madras, Chennai

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Science Outreach & Communication

Panel Discussion-3

Moderator

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Breaking Barriers in Science

Panel Discussion-4

Moderator

Rashna Bhandari, CDRI, Hyderabad

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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 2020.

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Supporting Organizations

DEPARTMENT OF BIOTECHNOLOGY, GOVT. OF INDIA, NEW DELHI

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.

WELLCOME TRUST/DBT INDIA ALLIANCE (INDIA ALLIANCE), NEW DELHI

India Alliance is an independent, dynamic 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. It is funded by Department of Biotechnology, Govt. of India and Wellcome Trust, UK

INDIAN INSTITUTE OF TECHNOLOGY MADRAS, CHENNAI

IIT Madras was established in 1959. It is one of the foremost institutes in the country to impart higher technological education, and conduct basic and applied research. The institute comprises academic departments and centers of advanced research in various disciplines of engineering and pure sciences.

UNIVERSITY OF MADRAS, CHENNAI

Established in 1857, the University of Madras is one of the oldest and prestigious universities in India. It imparts undergraduate and postgraduate education through its affiliated institutions and remotely through the Institution of Distance Education. It also conducts teaching and research programmes in its campuses and has been recognized by UGC as one of the centres for “potential for excellence” in the country.

INDIAN INSTITUTE OF SCIENCE, BANGALORE

IISc is India’s leading institution in advanced research and education in the areas of science and engineering. Since its establishment in 1909, the institution has vigourously pursued both fundamental and applied investigations in these areas.

Supporting Organizations

EUROPEAN MOLECULAR BIOLOGY ORGANIZATION (EMBO)

EMBO was established in 1964 and it is currently home to more than 1800 leading life science researchers across Europe and beyond. Its goals 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.

NATIONAL CENTRE FOR BIOLOGICAL SCIENCES (NCBS), BANGALORE

NCBS is a premier research institution under the aegis of the Tata Institute of Fundamental Research, Mumbai. The mandate of NCBS is fundamental research in the frontier areas of biology. Research interests range from the study of single molecules to ecology and evolution.

INSTITUTE FOR STEM CELL SCIENCE AND REGENERATIVE MEDICINE, BANGALORE

inStem is an autonomous research institute funded by the Dept of Biotechnology, Govt. of India. It emphasizes collaborative research efforts and the use multi-pronged approaches, with a goal to bridge clinical and fundamental research in stem cell and regenerative biology.

CENTRE FOR CELLULAR AND MOLECULAR PLATFORMS (C-CAMP), BANGALORE

C-CAMP occupies a unique niche that is at the interface of academia and industry. It stimulates entrepreneurship and innovation through its involvement in seed-funding schemes, entrepreneur mentorship programs and bio-incubation facility for start-ups, in and around an academic environment. It also provides training and services in state-of-the-art technology platforms.

Supporting Organizations

AHMEDABAD UNIVERSITY, AHMEDABAD

Ahmedabad University is a private, non-profit institution established in 2009 by the Ahmedabad Education Society. The university offers a range of academic programmes to enable students to grow into well-rounded leaders. These programmes include undergraduate, graduate and doctoral studies in the areas of engineering, life sciences, management, arts, and computer science.

INDIAN INSTITUTE OF SCIENCE EDUCATION AND RESEARCH (IISER), TIRUPATI

IISER Tirupati is the sixth Institute in the chain of IISERs established by the Govt. of India under the Ministry of HRD. Its goal is to impart quality education in basic sciences and to set up state-of-the-art research facilities for cutting-edge research in science.

TOSHNIWAL BROTHERS (SR) PRIVATE LIMITED, BANGALORE

Toshniwal Brothers (SR) Private Limited, are a technical sales & service group, with the aim of bringing high technology instrumentation to the Indian scientific community both in industry and academia, backed by committed services. They have a strong presence in the fields of material sciences, life sciences, bio-pharma & nanosciences.

ADDGENE, USA

Addgene is a global, nonprofit repository created to help scientists share high-quality plasmids. Addgene also provides a variety of educational resources, including protocols, blog posts, and eBooks. Its mission is to accelerate research and discovery by improving access to useful research materials and information.

CACTUS COMMUNICATIONS, MUMBAI

Editage, the flagship brand of Cactus Communications, was established in April 2002. It is one of the largest scientific communication companies in the world. Editage supports researchers, especially from non-English-speaking countries, with an array of publication support services, including language editing, translation, technical review, journal selection, and artwork preparation. It also provides services to boost the reach and impact of scientific research via videos, infographics, and news stories.

Advancing Discovery and Innovation to Improve Health

The Wellcome Trust/DBT India Alliance (India Alliance) is an independent, dynamic 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 is funded by the Department of Biotechnology (DBT), Government of India and the Wellcome Trust, UK.

BUILDING CAPACITY IN BIOMEDICAL AND HEALTH RESEARCH

Fellowships and Grants

With a commitment to build research capacity in India and catalyse internationally competitive research, India Alliance has successfully steered three types of fellowship programmes to support researchers at different stages of their career—**Early Career, Intermediate**, and **Senior**—under the tracks of **Basic Biomedical Research and Clinical and Public Health Research**. The focus of our Fellowship programme is to set the funded researchers on a leadership track through a continuous system of engagement and mentoring.

To enhance India's health research ecosystem and address major health challenges for India and the world, India Alliance also offers funding for collaborative research projects and clinical research training through its **Team Science Grants** and **Clinical/Public Health Research Centres**, respectively.

Team Science Grants fund interdisciplinary teams that bring together high-quality scientists from multiple institutions with complementary skills, knowledge, and resources to address an important health challenge for India. Clinical/Public Health Research Centres (CRC) are envisioned as virtual, research-oriented centres focused either on crosscutting or vertical research themes. To build clinical research capacity, integrate basic with clinical/public health research, and develop physician scientists, **CRCs** can have an embedded **Clinical Research Training Programme (CRTP)**—funding 3 to 4-year mentored research training fellowships for medical graduates (MBBS) and post-graduates (MD/MS).

India Alliance is also the implementation partner of the joint research initiative of Cancer Research UK and DBT called **Affordable Approaches to Cancer.**

Research Capacity Workshops

In addition to the funding programmes, India Alliance runs workshops aimed at building capacity in biomedical and health research. **Developing Indian Physician Scientists (DIPS)** workshops, launched in 2017, are designed to encourage young physicians to participate in research by facilitating exposure to the scientific methodology and inspirational role models. **Research Methodology workshops** are an attempt to enhance technical skills of researchers by providing training in epidemiology, study design, data collection, and analysis.

FOSTERING INTERDISCIPLINARY AND INTERNATIONAL COLLABORATIONS

Finding innovative and sustainable solutions to modern problems requires interdisciplinary and collaborative science, which extends beyond borders. Besides its Fellowship programmes, India Alliance funds major scientific meetings and provides travel grants aimed at resource-sharing and forging national and international research collaborations.

IndiaAlliance
DBT wellcome

India | EMBO Symposia

India Alliance and EMBO co-fund up to three scientific meetings per year in India. The meetings facilitate discussions on important global challenges in the context of the life sciences and aim to promote discovery and innovation through an interdisciplinary approach. This programme has now been discontinued.

Africa-India Mobility Fund

India Alliance, in partnership with the African Academy of Sciences, steers the Africa-India Mobility Fund (AIMF), which is designed to provide researchers from Africa and India a travel grant for short visits in either direction. Since Africa and India face similar health challenges, the AIMF initiative intends to encourage South-South collaborations, improve research capacity, and build leadership in biomedical and health research in Africa and India.

STRENGTHENING RESEARCH ECOSYSTEMS IN INDIA

In addition to identifying and supporting the best scientific talent in India, India Alliance supports and implements enabling policies and interventions to create a robust research ecosystem in the country.

Research Leadership Workshops

Scientists have to manage people and projects, and this makes leadership skills critical to a successful career. India Alliance, in partnership with EMBO, organises Research Leadership workshops for early- and mid-career Indian researchers to help them recognise and cultivate their leadership style and develop management skills.

India Research Management Initiative

Institutions in India currently lack a well-developed research management system, which is important for them to navigate the high demands for funding, outreach, and governance of research. To address this lacuna, India Alliance launched the India Research Management Initiative (IRMI), a Research Management programme for India, which aims to strengthen institutional ecosystems. IRMI will also provide opportunities to Indian research managers to receive training and create a network of practitioners for serving broader career development needs.

ENABLING ENGAGEMENT WITH SCIENCE

At India Alliance, we empower researchers to make their science accessible and engaging through open access publication, science communication, and public engagement.

Open Research

Open research ensures an unbiased, instantaneous, and unhindered flow of knowledge produced by researchers, thereby promoting innovation, communication and collaborations. To keep all of India Alliance-funded research openly accessible, India Alliance joined Wellcome Open Research and Europe PMC in 2017-2018. Adoption of the open research policy is bound to improve the relationships between researchers, policymakers, educators and the society at large.

Science Communication Workshops

Effective communication of scientific facts and findings helps science to thrive and people to better appreciate its value for the society. In addition to organising various unique science communication events, the India Alliance regularly conducts Science Communication Workshops in three different formats: Pan-India SciComm (a two-day workshop in which participation is based on a pan-India competition), SciComm 101 (a one-day workshop held at institutions on request), and Science Communication and Career workshop (a one-day workshop conducted in partnership with Nature India and Nature Careers at major scientific meetings).

Public Engagement

India Alliance aims to bridge the gap between science and society through public engagement programmes that bring the scientific community and the public together to share, debate, and deliberate on important matters of science, especially those relevant to human health, which have implications for the society.

India Science Media Fellowships

India Alliance in collaboration with Nature India launched the India Science Media Fellowship in 2019 to strengthen science journalism in the country and help establish science as a distinct genre of journalism. This fellowship will enable journalists to apply the craft of journalism to science and write nuanced science stories.

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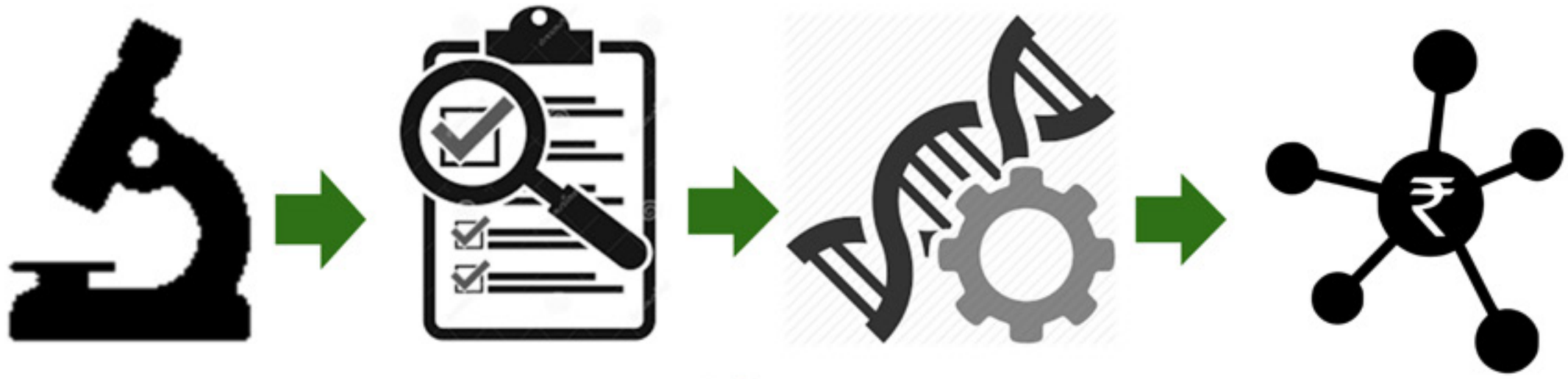

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Codes for the making of a rice flowering stem

M 01

Microtubule Organisation and Dynamics: from Cells to Single Molecules

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Since my student days at Moscow State University in Russia, I have always been fascinated by how biomolecules self-organize to form cellular structures and whole cells. Throughout my research career, I have tried to address this question in a broad variety of systems, ranging from halophilic archaebacteria to ciliates dwelling in a cockroach gut and human cells. Currently, my lab focuses on studying microtubules - dynamic cytoskeletal filaments that control different aspects of cell architecture. Microtubules are intrinsically asymmetric polymers, with fast-growing plus ends, which in cells serve as major sites of microtubule assembly and disassembly, and slow-growing minus ends, which are often stabilized and attached to different cellular structures. Our initial work has been focused on cell biological aspects of microtubule organization and function, and we still actively employ live cell imaging to study how microtubules contribute to cell polarity, migration, division and differentiation. However, over the years, we became increasingly interested in biophysical approaches, such as in vitro reconstitution and single molecule assays to dissect how the proteins that bind to microtubules control their nucleation and dynamics. The combination of experiments in cells and assays with purified components allows us to decipher how the specific molecular properties of microtubule regulators contribute to cellular function.

M 02

A Little Fly and Big Questions Can Keep You Busy Throughout Your Career

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Children are extremely curious, and can give us a hard time with their never-ending questions. However, most of them stop asking when they are grown up, except a few, who are likely to become scientists.
I was privileged to work as a scientist throughout my career, performing curiosity-driven research, focusing on problems that I found exciting and worth to explore. And I was very lucky to find young people – PhD students and postdocs, who shared my interest in fundamental questions in developmental and cell biology, using Drosophila as the model system most of the time. The major topics - from cell polarity to retinal degeneration – were not predetermined, nor actively chosen, but rather naturally emerged from the previous work. Overall, the scientific journey, which included both research and teaching, was a wonderful journey, not always straight-forward and sometimes bumpy. And on top of it, allowed to get to know different cultures and to meet wonderful colleagues, many of whom became friends later on.

M 03

What I talk about when I talk about biology

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What we think of as the biological sciences today uses tools and methods from physics, applied mathematics, chemistry, engineering and computer science. (Think of the latest breakthroughs in microscopy, in statistical image analysis or in mechanobiology.) Yet, we don't naturally train either students or practicing biologists and physicists to reach across disciplinary boundaries. I'll describe some examples of how methods from physical and mathematical modelling can be used to address some interesting open questions in biology, with examples from my own work on large-scale nuclear architecture. This will illustrate my own journey from theoretical physics to biophysics and physical biology.

M 04

Adaptive Evolution of a Researcher in Indian Academia

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An academic career gives us a degree of freedom and flexibility, which is unimaginable in most careers. With many open roads at the beginning of a journey, what path do we follow? Whom do we follow as a role model? What do we value as an academic and how do we measure what we value? What will give us most happiness and fulfillment? These are not easy questions to answer and often not even questions researchers think about when they begin their careers. Most faculty and researchers in India start their careers based on their doctoral and post-doctoral experiences and their respective advisors as role-models. However, when they begin their independent journey, many constraining factors force them to adapt, change (mutate!) and evolve their careers in ways they would have not imagined when they started. Some evolve and grow successfully and some struggle.
In this talk I will explore, from my own personal experiences, the personal attributes and factors in different academic environments that can shape the trajectory of a scientific career. While scientific talent of a researcher is undoubtedly very important, it is not the main determinant of success. The success achieved during doctoral and post-doctoral studies, especially in a foreign environment, is also not a useful guideline for predicting success under Indian conditions. I will explore how the mindset and attitude of researchers (being open to changes, prepared to get out of one's comfort zone, ability to collaborate, ability to persevere in difficult times etc.) as well as their inter-personal skills are perhaps the most important attributes to success. I will also explore some of the more obvious pitfalls and misconceptions which could be avoided early in a career. Finally, I will address what ultimately contributes to happiness and fulfilment in an academic career.

M 05

The Chaos Between the Intention of Becoming a Scientist and Being One

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https://www.caluniv.ac.in/academic/department/Biochemistry/Maitrayee-DasGupta.pdf

Becoming a 'scientist' was never an option for me until I attended the mesmerising lectures on history of scientific experiments by Prof JJ Ghosh in Calcutta University. The intention was born. Contrasting experiences while practicing science shaped me up; first, a turbulent ride that almost knocked me off, and second, an antithesis to the first, took me to the heights of joy of learning about protein kinases as dynamic molecular switches. Both experiences left me with pearls of wisdom. That couldn't save me from another roller coaster ride through my own confusions and failures as I strived to evolve as a scientist. But they did save me from succumbing to the system.

My idea was to decipher the molecular codes that predisposed a selected group of plants to intracellular symbiosis with nitrogen-fixing bacteria. Two major approaches were undertaken (i) investigating symbiosis in plants that were near the point of predisposition with the hope of encountering a simpler process and (ii) investigating the significance of distinctive signs of adaptation in the ectodomain of Symbiosis Receptor Kinase in symbiosis competent plants. In the first approach, several genes that are essential for bacterial invasion through intracellular tunnels were found to be inessential in plants where bacteria invade through epidermal cracks. In the second approach, we elucidated signature phosphorylations coupled with ectodomain shedding of SYMRK that guide through the progress of symbiosis. Almost everything I understood, I understood through exciting discussions with excellent scholars that I am blessed with. It doubled the satisfaction of the endeavour.

M 06

Centrosomes in Development, Disease and Evolution

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In this mentoring/biographic talk I will discuss how I started to work on centrosomes during my postdoc and how that led me into different topics in my own lab. I will also discuss how I decided to run my own lab, and how more recently, to run a research institute. Along the way, how to choose research questions and how to choose, supervise and mentor people, as well as how to contribute to the broader science endeavour and its relation with society.

M 07

Revisiting the Journey Towards an Independent Researcher

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Oral cancer remains as a serious health threat and ranks number one among all cancers in India with approximate rate 32-40% of total malignancies and its incidence is directly linked with chronic exposure to diverse form of tobacco usage, where chewing tobacco stands a unique risk factor for Indian oral cancers. My lab has a long-standing interest in understanding the role of non-coding RNA in the aetiology of cancer with the hope of translating such knowledge to treat human diseases, particularly squamous carcinoma of oral cavity and cervix. To comprehensively understand the unique property of these non-coding RNAs, we are working on whole transcriptome analysis to identify the novel transcripts that play a major role especially in tobacco-induced oral squamous cell carcinoma and to validate them using qPCR. Our lab has shown that several microRNAs and lncRNAs dysregulated with reference to different clinical conditions which will be useful for early diagnosis and better therapeutic management of the oral cancer. My passion towards teaching and research is the driving force that keeps me motivated till date.

I will be sharing the experiences I had during my journey as a PhD student, postdoctoral fellow and as an independent researcher. Further, the decisions I made throughout the period of research that influenced my career and the ups and downs of establishing an independent research lab at the state university setting.

M 08

Balancing Act of Modern Age Women

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After I completed my PhD in the year 1998, at Chennai, I did my postdoctoral fellowship in Chennai itself since I had a family by then and was working in Chennai from 1998 to 2005. Then, during 2006, I had to leave my family and move alone to Madurai since I was recruited as a Reader at Madurai Kamaraj University, Madurai. From 2006 till now, I have been shuffling between Madurai and Chennai to look after both my profession and personal life. At MKU, our research lab is exclusively working towards the development of DNA Vaccines and Adjuvants for infectious diseases like TB and HIV and disorders like cancer, which is the area that I have more than two decades of experience in. My research area was related to focusing on small questions that needs to be answered in a particular topic. My mentor Dr. V.D. Ramanathan, who was the Deputy Director of NIRT, Chennai helped me a lot in showing my path clearly and he was the one who taught me even to balance the professional and personal life. Currently, as a Professor I have been guiding four full time and two part time PhD students at Madurai Kamaraj University, Madurai. I have completed four PhD students and they all are well placed in reputed national and international Institutes. The positive approach of doing things that I can do helps me a lot in achieving whatever I want to. There was no set career path, but I just took the opportunities that came my way. Women need to patiently balance their act both in the profession as well as at home which will one day take them to greater heights.

M 09

Joys and Confusions of Being a Scientist at the ‘Interface’

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Today’s buzzword is “Interdisciplinary science”, but make no mistake, once you are standing at the intersection of Biology, Chemistry and Physics, you are at the risk of not “belonging” to any one of them! I was trained as a physicist, learnt some biology while doing a Ph.D. in biophysics, and found a faculty position in a chemistry department. While it was easy to dazzle my colleagues from any one area with interesting factoids from another, trying to get published in a high profile traditional journal was quite a different experience. However, inter-disciplinarity has ultimately proved to be rather rewarding. We have pursued problems in the areas of neurotransmitter dynamics and neurodegenerative diseases, where our ability to develop appropriate tools has been quite effective. Recently, delving into the structure and dynamics of amyloids, we have found fresh new answers to the question: “How can a protein aggregate be toxic?”

M 10

Codes for the Making of a Rice Flowering Stem

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‘O Tiger-lily, I wish you could talk!' 'We can talk,' said the Tiger-lily: 'when there's anybody worth talking to”. Through the Looking Glass, Lewis Carroll

Unravelling the logic behind the development of multicellular organisms from a fertilized single cell has fascinated philosophers for millenia. In more recent times biologists use the tools of genetics and developmental biology to decipher the complex interactions between genes and environment in the making of the striking structure and patterns we see in the mature organism. Studies in convenient laboratory organisms, illustrate how a few key ‘master’ regulators can have large- cascading- and cumulative- effects on how growth and the emergence of form takes place.

In higher plants, flowering comes about by a remarkable transformation from a basal state where cells destined to be leaves or branches are transformed to a floral fate. Our knowledge on how this transfomation is controlled comes largely from experimental studies with Arabidopsis thaliana, a model laboratory plant. These studies have given a remarkable insight on key regulators of flower development. Yet, given the diversity in flowering time and floral architectures that occur in nature, an outstanding question is about how these evolutionarily conserved regulators relate to the emergence of new patterns and variations in flowering stems and flowers.

We study development of the rice flowering stem (inflorescence) and rice flowers with the overall goal to understand the relationship between factors and signals that control fate of plant stem cells (meristems) and those that determine the identity of organs formed from meristems. I will summarize our studies that identified novel functions in rice flowering, stem-branching and meristem development for a gene call RICE FLORICULA LEAFY (RFL), an evolutionarily conserved transcription factor whose functions in Arabidopsis thaliana are largely confined to floral meristems. We have also investigated, using functional genomic tools, the roles for other genes called MADS domain transcription factors, in floret meristem formation, organ development and meristem termination. Studies such as ours and those in leading laboratories worldwide on the genome-wide effects of rice transcription regulators would in the future allow one to build dynamic gene-regulatory networks. Comparisons with data emerging from other plant models including Arabidopsis will be insightful to understand how function in a specific species shapes the network properties.

Post Doctoral Fellows

PDF 01 **AARTHY M**

Genetically Encoding Metal Chelating Amino Acid Containing Congener Protein for Waste Water Treatment

PDF 02 **ABISHEK IYER**

Targeting Immunometabolism in Health and Disease

PDF 03 **ACHIRA ROY**

Regulated Phosphoinositide-3-Kinase Signaling is Essential for Normal Cortical Development and Function in Mice

PDF 04 **ADITYA SANKAR**

Kdm4a Mediates Maternal-Zygotic Transition in Mammals

PDF 05 **AMEY REDKAR**

Understanding the Biotrophic 'Black Box' of the Vascular Wilt Pathogen Fusarium Oxysporum During Multiple Host Interaction

PDF 06 **ASHUTOSH SRIVASTAVA**

Structural and Dynamical Insights into Functional Divergence in Mammalian Cryptochromes

PDF 07 **BHARTI BISHT**

ancreatic Progenitor Cells Plasticity is Restricted by DNA Methylation

PDF 08 **DIVYA VENKATESH**

Genetic and Antigenic Evolution of Swine Influenza A Viruses and Pandemic Risk

PDF 09 **ELAYANAMBI SUNDARAMOORTHY**

nderstanding the Stressed Proteome: A Ribosomal Perspective

PDF 10 **GAURAV GOYAL**

Sphingolipid Dependent Protein Sorting in Developing Neurons: Insights into Human Genetic Disorder Hereditary Sensory and Autonomic Neuropathy Type-1 (HSAN-1)

PDF 11 **HARSHINI CHAKRAVARTHY**

Establishment of Adult CNS Neurons: Applications in Modeling Hyperglycemia

PDF 12 **INDRAJIT SAHU**

How Ubiquitination Affects Substrate Processing by Different Proteasomes?

PDF 13 **KAPIL GUPTA**

Architecture of Human TAF11/TAF13/TBP Complex Suggests Novel Mode of TATA-box Binding

PDF 14 **KOUSIK KUNDU**

Genetic Associations at Multi-Level Regulatory Data Improve Fine-Mapping of Causal Variants for Twelve Autoimmune Immune-Mediated Diseases

PDF 15 **KSHIPRA NAIK**

Fabrication of Piezoelectric Contact Lens Based Pressure Sensor for Early Detection and Management of Glaucoma

PDF 16 **MADHUJA SAMADDAR**

Protein Quality Control in the Immortal Germ Lineage: Identifying Changes in Oocyte Cell Biology Triggered by Signals from Sperm

Post Doctoral Fellows

PDF 17 **MAHIPAL GANJI**

Unraveling the Spatial Organization of Chromosomes by Single-Molecule Imaging

PDF 18 **MAMATHA M PILLAI**

Development of Polymer Based Antimicrobial Wound Healing Dermal Patches for Chronic and Acute Wounds

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Generation and Maintenance of Smooth Endoplasmic Reticulum

PDF 20 **NIKITA ABRAHAM**

Structural Mechanisms of Atypical Conotoxin Modulators of the Nicotinic Acetylcholine Receptors

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Hippocampal-Thalamo-Cortical Network for Episodic Memory

PDF 22 **PAULOMI SANGHAVI**

Dynactin Function in Dynein Driven Motion of Phagosomes

PDF 23 **PRAKASH DEVARAJU**

Mitochondria and Neural Circuit Dysfunctions

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A Systems Biology Approach Identifies FUT8 as a Driver Of Melanoma Metastasis

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Actomyosin Contractility is Essential for the Structural Integrity of the Syncytial Germline in C. elegans

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GCN4 Directly Controls a Methionine Mediated Anabolic Program

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Nanoscale Architecture of Cellular Cytoskeleton Impacts its Mechanics as Revealed by In Situ Cryo-Electron Tomography

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Ifnγ-Induced Mechanisms Restrict Intracellular Replication of the Lysosome-Adapted Bacterial Pathogen, Coxiella Burnetii

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Exploring the Sequence of PIWI-interacting RNAs

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Novel Signaling Pathway Links EBNA1 mRNA Translation Stress With Cell Proliferation

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Environmental Factor Effects on Tree Seedling Recruitment in a South African Humid Savanna

PDF 34 **SREEJITH NAIR**

Physicochemical Properties of Ligand-Activated Enhancer Complex Determine Transcriptional Response to Signaling Programs

PDF 35 **SRIRAM VARAHAN**

Metabolic Constraints Drive Self-Organization Of Specialized Cell Groups

Post Doctoral Fellows

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SUNIL MUNDRA

Forest Tree Species Shift: Conseqeunces on Belowground Microbial Communities and Carbon Stock

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SUVRAJIT SAHA

Integrating Neutrophil Fronts and Backs with the mTORC2 Mechanotransduction Pathway

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VANIKA GUPTA

Cellular Heterogeneity Underlying Poly-Functional Drosophila Fat Body Tissue

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VARUN SREENIVASAN

Long-Range Control Of Striatal Interneuron Network Development

PDF 40

VIJI VIJAYAN

Osteocalcin Dependent Uptake of Abeta42 by Astrocytes and Subsequent Degradation: a Means to Manage Alzheimer's Disease

PDF 01

Genetically Encoding Metal Chelating Amino Acid Containing Congener Protein for Waste Water Treatment

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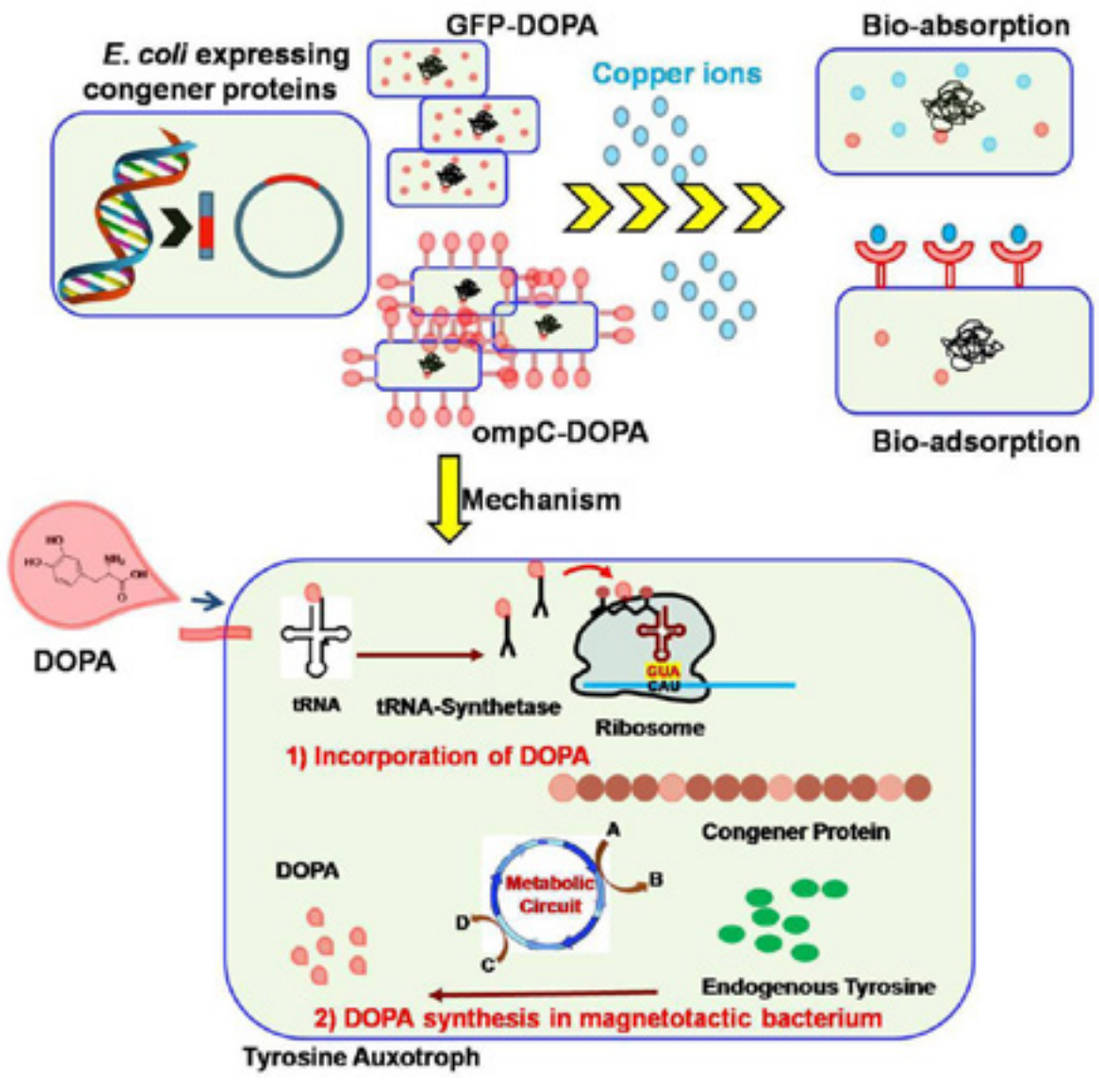
Genetic Code, Recombinant DNA, Congener Proteins, Collagen, Green Technology

Rapid industrialization has led to the indiscriminate discharge of heavy metals into the environment. In particular, the heavy metal copper is usually found at high concentrations in wastewater, because it is used in many industrial applications. Copper pollution poses serious threats to human health and various strategies have been adopted to tackle it. Physical and chemical treatment processes for copper removal are expensive and also result in secondary pollution. On the other hand, biological removal using native microbes suffer from poor efficiency due to metal toxicity at higher copper concentrations. In order to circumvent these drawbacks, we adopted a next generation strategy to adsorb copper ions present in wastewater by genetically encoding metal chelating amino acids for synthesis of congener proteins. Incorporation of metal chelating amino acids (MCAA) was used as a toolkit to construct proteins with increased affinity towards copper. Copper ions preferentially coordinate with the side chains found in the MCAA, 3,4-dihydroxy-L-phenylalanine (DOPA), making it a suitable candidate for incorporation. Congener variants of green fluorescent protein (GFP) and outer membrane protein C (ompC) containing DOPA were developed for intracellular absorption and surface mediated adsorption of copper ions, respectively. The success of these model proteins enabled us to design a magnetotactic bacterium by introducing a genetic circuit, which could biosynthesize DOPA. This proved to be a cost effective alternative to the costly incorporation process and facilitated scale-up. Effect of physio-chemical factors, cell permeabilization and immobilization on the metal binding efficiency was evaluated. Bioreactor studies revealed that 97% of copper was adsorbed from industrial effluent using consortia of congener protein expressing cells immobilized on functionalized granular activated carbon. This study will serve as a baseline for exploiting the potential of congener proteins in environmental research.



PDF 02

Targeting Immunometabolism in Health and Disease

Inflammation, Metabolism, Drug Discovery, Pharmacology, Cell Signalling

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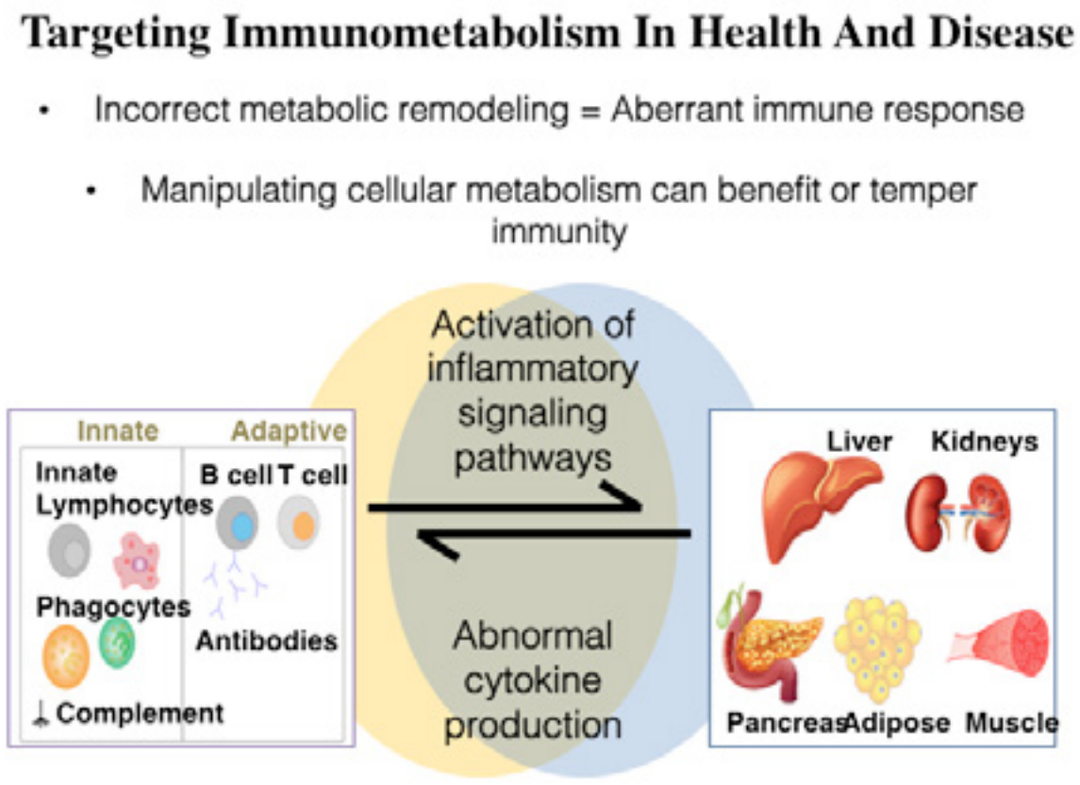
Diseases driven by chronic inflammation and metabolic dysfunction are major burdens on society. There are few effective treatments for these conditions, which are rapidly increasing as the population ages. There is an urgent need to better understand the mechanisms underlying these conditions, in order to identify new therapeutic targets and advance new drugs into the clinic. It is now evident that an integral component of immune regulation is through the metabolic pathways necessary to support energetically demanding protective or pathogenic responses. New discoveries from my research reveal important new links between basic biochemistry, cell activation, metabolism and immunity that suggest exciting new ways to target immunometabolism and develop new therapeutic agents. The overall goal of my research is to dissect newly identified roles of key cell surface receptor proteins such as G-Protein Coupled Receptor (GPCRs) and ion-channels in immunometabolic pathways in health and disease, using new ligands for these receptors in cellular and animal models, and monitoring the expression of these proteins in clinical samples from human patients. I study mechanisms of protein and cell activation, signalling pathways, biological processes, disease development and drug action. My central hypothesis is that an inability to maintain metabolic and immune homeostasis is a key contributor to the underlying pathology of many chronic inflammation- driven diseases, and that therapeutic targeting of key cell-surface proteins implicated in immunometabolism can reduce disease progression and restore tissue homeostasis. My research aims to: (1) Use new knowledge that my team has generated on cell-surface receptor mediated signaling pathways in adipose, epithelial and immune cells to now rationally modulate immunometabolism in vivo. (2) Use new pharmacological and genetic tools that I have developed to validate key cell-surface proteins as novel therapeutic targets for many immunometabolism-driven human diseases.



PDF 03

Regulated Phosphoinositide-3-Kinase Signaling is Essential for Normal Cortical Development and Function in Mice

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Developmental Neurobiology, Translational Biomedical Research, Neurology, Neuro-Developmental Disorders, Animal Models

The phosphoinositide-3 kinase (PI3K) intracellular signaling pathway is conserved from yeast to mammals. Activating mutations of this pathway, especially PIK3CA, encoding the catalytic subunit of the PI3K enzyme, have long been linked to cancer. Strongly activating PIK3CA mutations, found commonly in cancer, also result in severe brain overgrowth and cortical malformations when acquired during embryogenesis. These often cause intractable epilepsy, hydrocephalus and intellectual disability.

I recapitulated the key human pathological features including brain enlargement, neocortical malformations and epilepsy in mouse models of human-related Pik3ca mutations1. Underlying mechanisms included increased proliferation, enlarged cell-size and altered cell migration. Phenotypic severity was dependent on the mutant allele and its time of activation. We also demonstrated acute treatment of epileptic seizures in these models with a Pik3ca inhibitor, promising new effective anti-epileptic therapy for intractable epilepsy patients.

We further demonstrated that PI3K and Hippo-Yap pathways interact to maintain the smooth nature of normal mouse brain2. Dysregulation in these interactions led to stereotypic cortical gyrification and ventriculomegaly in the mutants. Intriguingly, administration of Yap inhibitor attenuated these phenotypes by rescuing cell-cell adhesion deficits. This provides a potential new small-molecule therapy for developmental hydrocephalus, which currently lacks non-invasive treatments.

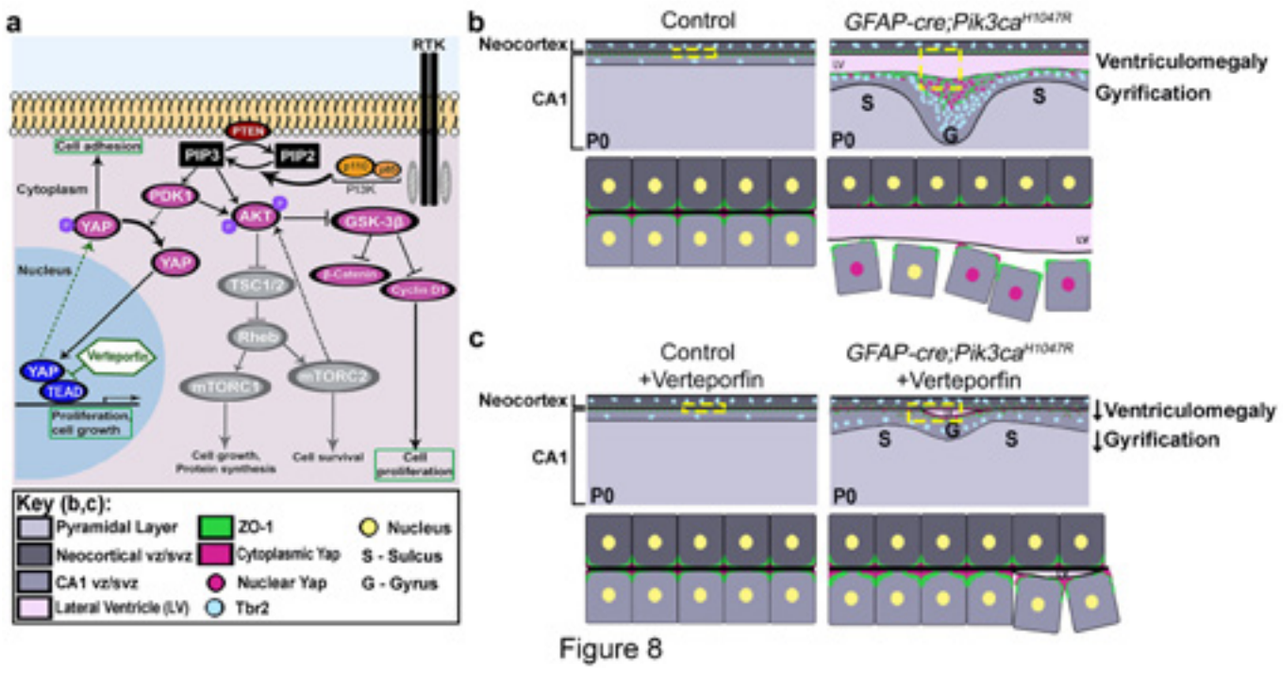

Figure 8

Future of these works would be to understand: a) how disease-causing gene function relates to cortical folding, b) whether any common druggable pathway exists to treat all kinds of hydrocephalus and epilepsy.

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PDF 04

Kdm4a Mediates Maternal-Zygotic Transition in Mammals

Epigenetics, Stem Cell Biology, Developmental Biology, Genetics, Chromatin

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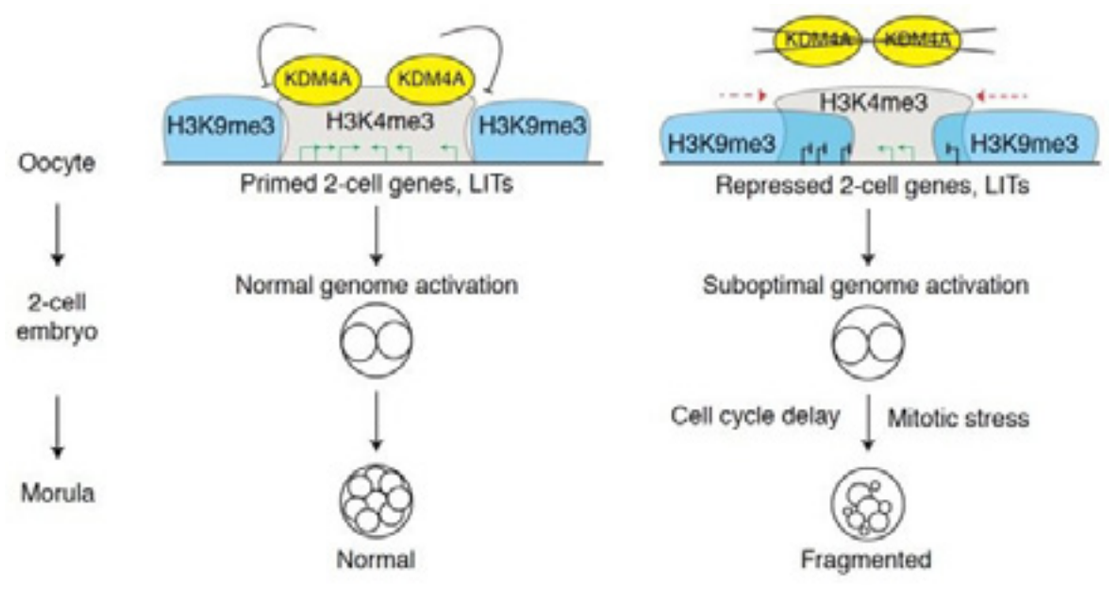
The importance of germline-inherited histone landscapes in priming early mammalian development is just emerging1-4. Post translationally modified histone H3 lysine 4 (H3K4me3) trimethylation and lysine 9 (H3K9me3) trimethylation are associated with active promotors and heterochromatic gene repression, respectively. Mature oocytes are transcriptionally quiescent and possess a unique epigenome exemplified by unusually broad H3K4me3 (bdH3K4me3) deposition1. It remains unknown as to which factors contribute to maintaining the bdH3K4me3 landscape. In the soma, lysine specific demethylase 4A and 4C (KDM4A, KDM4C) redundantly demethylate H3K9me3 at H3K4me3 positive promotors, thereby preserving an open chromatin state on transcriptionally active genes5. We report here that maternal KDM4A-mediated H3K9me3 demethylation in the oocyte is crucial for normal embryonic mitosis, establishing that H3K9me3 regulation in the oocyte is a necessary mechanism to ensure cell-fate change in preimplantation embryos. Oocytes lacking KDM4A display H3K4me3-H3K9me3 bivalency, causing impaired transcription activation of genes and transposons in 2-cell embryos. Ectopic expression of catalytically active KDM4A in the oocyte alone rescues developmental failure in embryos by reseting germline inherited H3K9me3. Hence, KDM4A confers oocyte competence by preserving maternal epigenome integrity and is necessary for epigenetic reprogramming in the embryo to ensure proper maternal-to-zygotic transition.



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PDF 05

Understanding the Biotrophic 'Black Box' of the Vascular Wilt Pathogen Fusarium Oxysporum During Multiple Host Interaction

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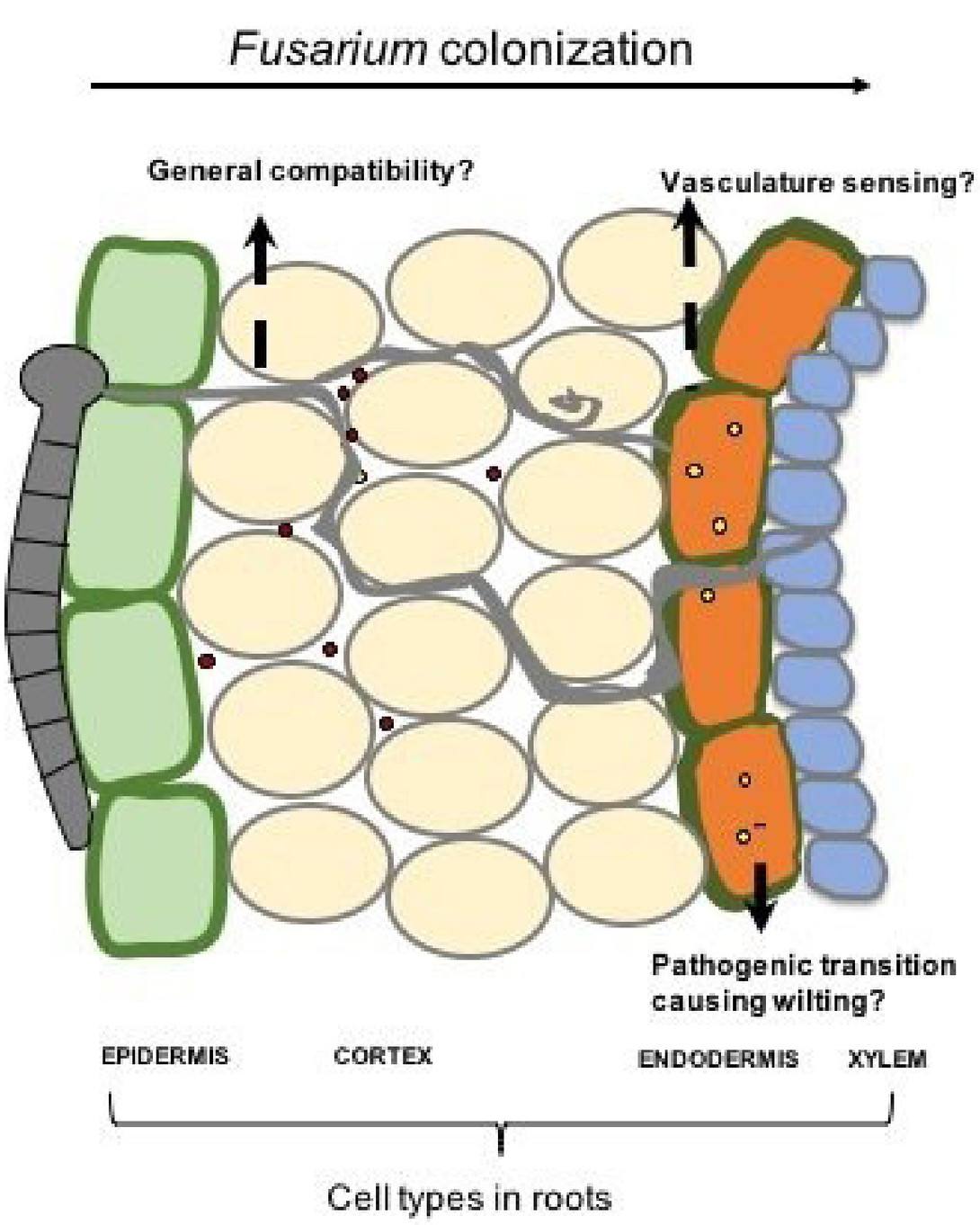
Plant Immunity, Fungal Pathogens, Effectors, Disease Resistance, Food Security

Fusarium oxysporum is a soil-borne pathogen that causes vascular-wilt disease with devastating agricultural losses. During early stages after penetration of roots, the pathogen grows asymptomatically and subsequently colonizes the vascular tissue, causing chlorosis and wilting.



Fusarium has evolved diverse infection strategies, but its biotrophic infection stage still remains puzzling. There is little information known on root cortex colonization to entering the vasculature. The fungus grows mostly intercellularly, but where it obtains nutrients and how it evades host recognition is unknown. Moreover, despite substantial research on Fusarium strains infecting dicots, how the fungus deals with stem/pseudostem in monocots is still elusive. Our work aims to understand cell-specific sensing by F. oxysporum during apoplastic intercellular growth and identify crucial pathogen-host components during infection of dicot and monocot. We use a proteomic and transcriptomic approach, where we analyze apoplastic fluid from infected tomato roots by Mass Spectrometry to identify secreted fungal and plant proteins. The results are compared with transcriptomic RNASeq during early colonization. Current experiments aim to compare the host processes that are modulated by Fusarium during infection of a tomato and banana. We will present the recent progress of our work on the biotrophic compatibility dialogue in life cycle of Fusarium that is crucial for establishing fusariosis in diverse hosts.

PDF 06

Structural and Dynamical Insights into Functional Divergence in Mammalian Cryptochromes

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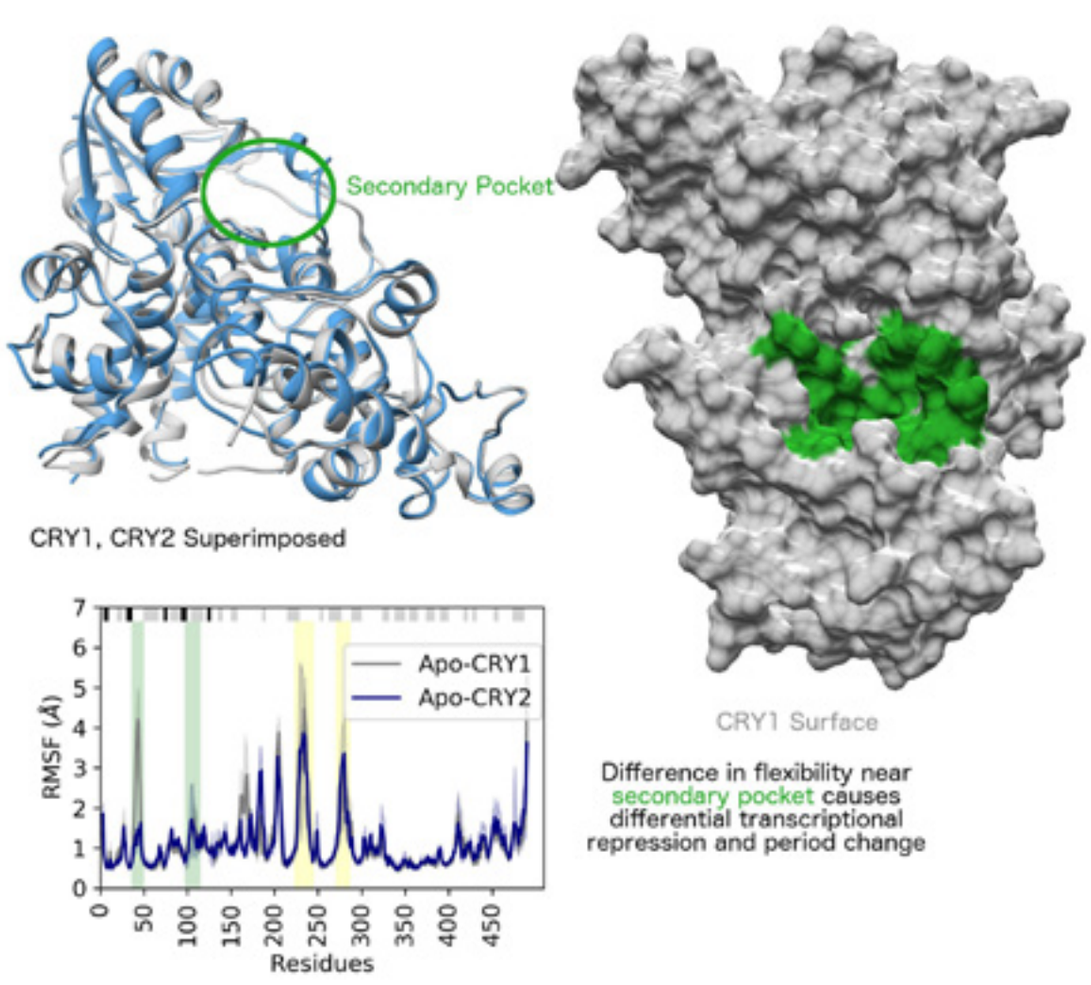
Integrative Modeling , Circadian Clock, Molecular Dynamics Simulations
Cryo-Electron Microscopy, Network Analysis

Adaptation to the environment constitutes one of the hallmarks of all living systems. A crucial aspect of these adaptations is the internal biological clock, regulating a host of cellular responses to the environment. This internal clock is synchronized to twenty-four hours solar cycle in almost all living organisms and is referred to as circadian clock1. In mammals, the circadian clock comprises feedback and feed-forward loops involving complex interactions between transcription factors, period proteins, cryptochromes, kinases, phosphatases and several other associated factors2. Cryptochromes are quintessential clock proteins and in mammals they exist in two forms. The two CRY proteins in mammals (CRY1 and CRY2) have high sequence and structure similarity but show crucial differences in transcriptional repression and period length in single Cry1 or Cry2 null mutant mice. In this work we have explored the structure and dynamics of mammalian cryptochromes to gain insight into the mechanism of regulation of circadian rhythm. Using molecular dynamics simulations, we have evinced structural and dynamical aspects of this functional difference. The results indicate that subtle difference in the sequence between CRY1 and CRY2 causes difference in flexibility of functionally important regions of CRY1 and CRY2. We further observed that this difference in flexibility affects the binding of CRYs to their target protein CLOCK. This differential binding emanating from the difference in the flexibility of the CLOCK binding pocket on CRYs could be responsible for functional divergence in terms of transcriptional repression and period regulation observed in vivo.



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PDF 07

Pancreatic Progenitor Cells Plasticity is Restricted by DNA Methylation

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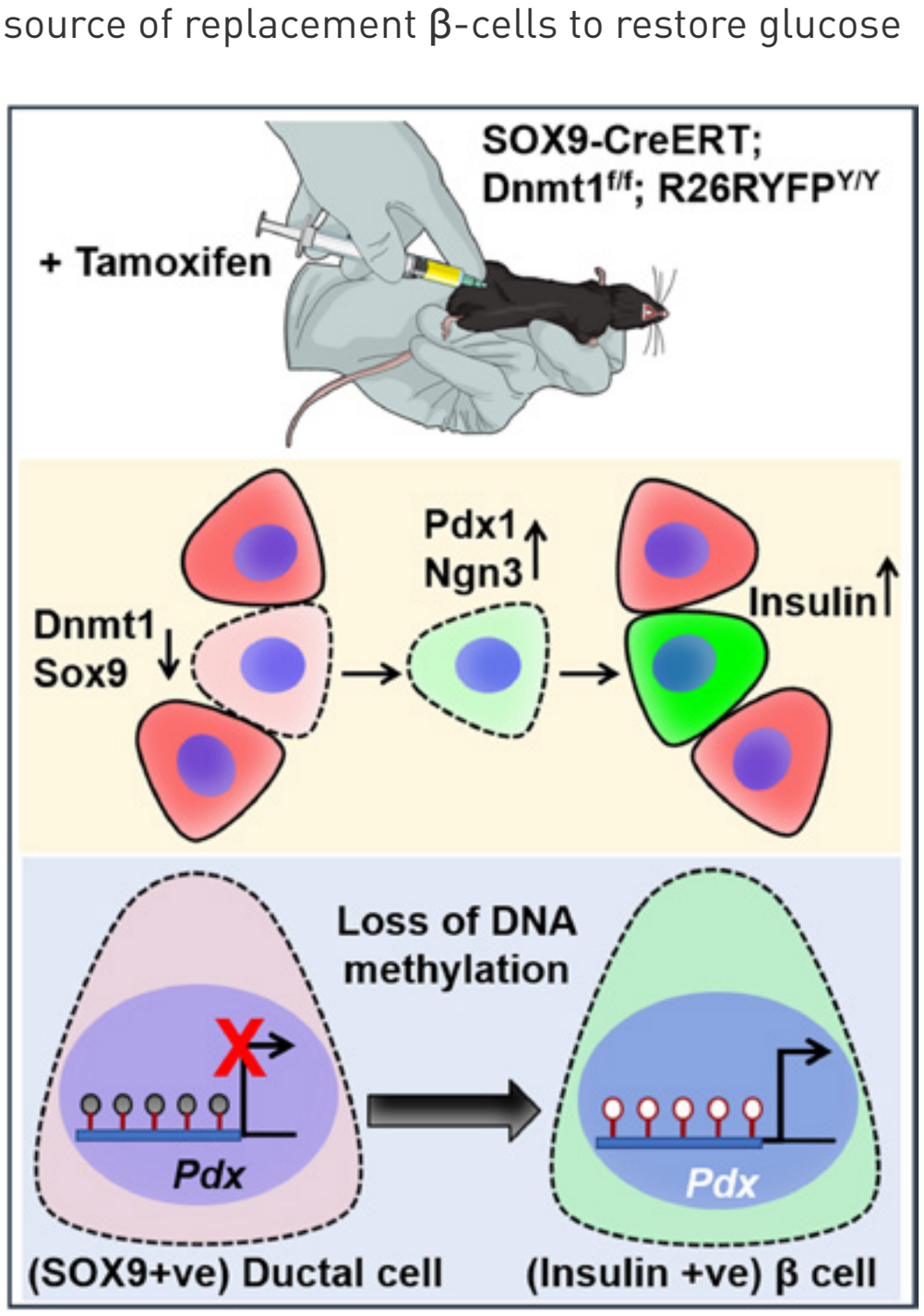
Stem Cells, Cell Signaling, Regenerative Medicine, Organoids, Diabetes

India is considered as the diabetes capital of the world with as many as 50 million cases in 2017 and presents a serious health challenge. The pathology of type 1 diabetes (T1D) involves autoimmune destruction of insulin-secreting pancreatic β-cells. Recent data suggest that deficiency of functional β-cell is also an important contributor to type 2 diabetes. Therefore, β-cell regeneration is considered as a holy grail in the treatment of diabetes. Tissue-specific resident stem/progenitor cells offer the possibility of a renewable source of replacement β-cells to restore glucose homeostasis. During organogenesis, multipotent progenitors in developing pancreas reside in ducts but lose their multipotency as organogenesis proceeds. This raises questions about how and why these progenitors lose their multipotency and what regulates ductal cell identity. The temporal and spatial control of genomic information to restrict cellular identity can be regulated at the epigenetic level. DNA methylation is an important epigenetic mediator of transcriptional repression. DNA methylation patterns are maintained during cell self-renewal by the enzyme DNMT1. Our lab investigates the processes that govern β-cell differentiation, self-renewal and have shown deletion of DNMT1 results in beta-to-alpha cell reprogramming due to misexpression of alpha-cell identity genes. This study establishes that DNA methylation represses the expression of lineage-related cellular identity genes in closely related cell types. We hypothesize that ductal cell identity is restricted by DNMT1-mediated propagation of DNA methylation patterns. We generated Sox9CreER(T2)DNMT1-knockout mice that eliminate DNMT1 in Sox9 cells upon administration of tamoxifen. DNMT1 deletion resulted in increased proliferation of ductal progenitors. Ductal cells were hypomethylated and showed abnormal ductal morphology. DNMT1 deletion in Sox9+ progenitors gives rise to insulin-producing cells in the duct. This study thus provides evidence that SOX9+ progenitors may serve as a postnatal source of β-cell regeneration and an open avenue for therapeutic intervention in diabetes.



PDF 08

Genetic and Antigenic Evolution of Swine Influenza A Viruses and Pandemic Risk

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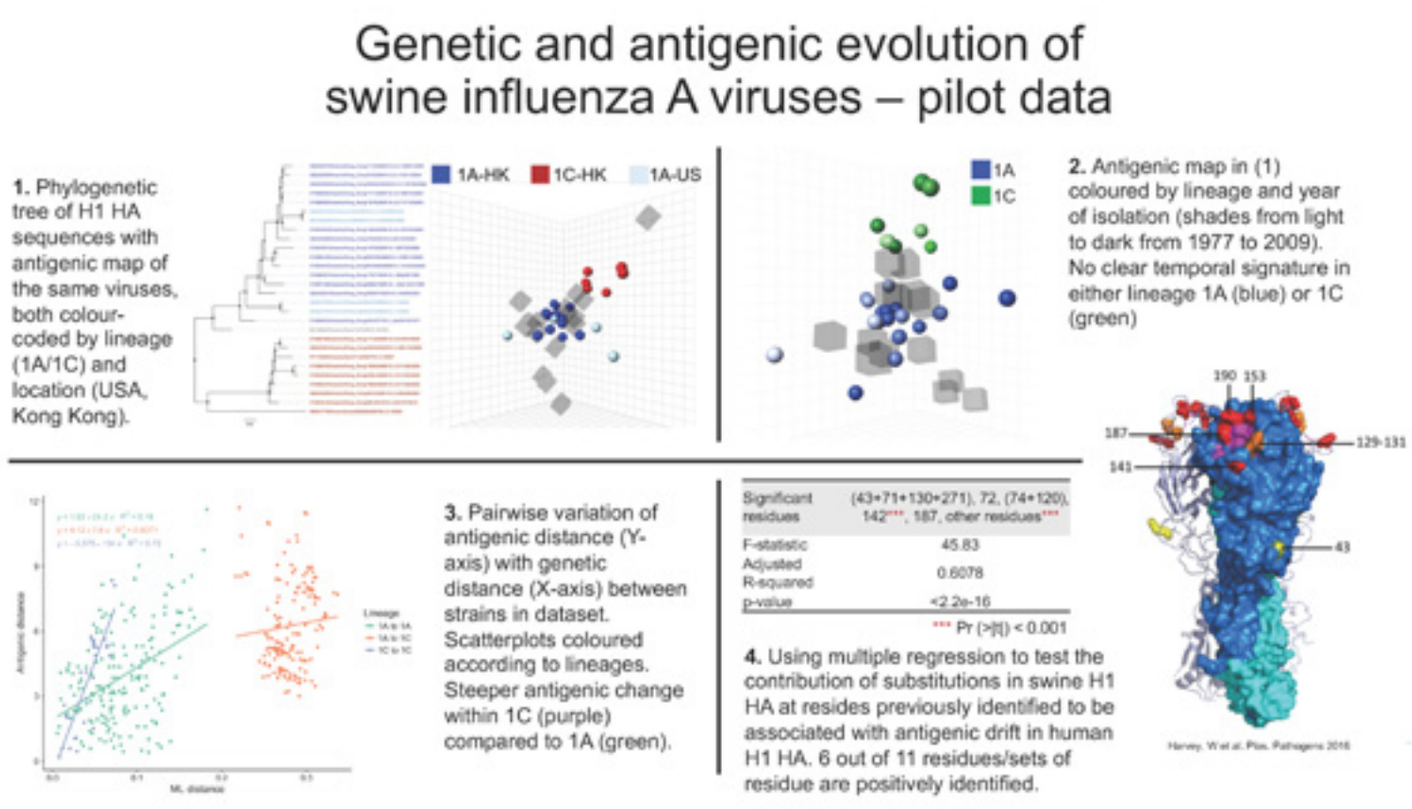
Sphingolipids, Axo-Dendritic Protein Sorting

Swine influenza presents a substantial disease burden for pig populations worldwide. The first pandemic of the 21st century was caused by a strain of influenza A virus (IAV) that was transmitted from pigs into humans, highlighting the importance of swine as reservoirs for pandemic viruses. There have also been several instances of reverse movement of human IAV into swine. H1N1, H1N2 and H3N2 are the main subtypes of swine IAV. Phylogenetic analyses of the HA gene have identified three broad genetic lineages in currently circulating swine H1 strains which reflect multiple introductions from human (1A, 1B) and avian (1C) sources.

For each HA lineage, we chose a range of viruses that best represented the available genetic diversity during the period from 2013-2018. Using hemagglutination inhibition (HI) assays, we measured cross-reactivity between chosen the swine strains and human seasonal IAV vaccine strains. The HI data was used to calculate antigenic distances between viruses using antigenic cartography, where 1 antigenic unit (AU) is equivalent to a 2-fold loss in HI cross-reactivity.

In contrast to human H3 IAV, we find no clear temporal clustering of swine IAV HAs, but strains in antigenic maps do cluster according to genetic lineage. Different swine lineages show varying rates of antigenic change and different cross reactivity with current vaccine strains, mainly based on time of introduction into swine, and substitutions and deletions. Some (but not all) residues associated with antigenic change in swine HAs are similar to those previously defined in swine H3 and human H3 and H1 lineages. Continued circulation in pigs may maintain antigens to which previously un-exposed humans may be susceptible. We are testing a subset of the swine viruses with age-stratified human sera used as indicators of human population immunity, to assess the risk of swine-to-human transmission potential."



PDF 09

Understanding the Stressed Proteome: A Ribosomal Perspective

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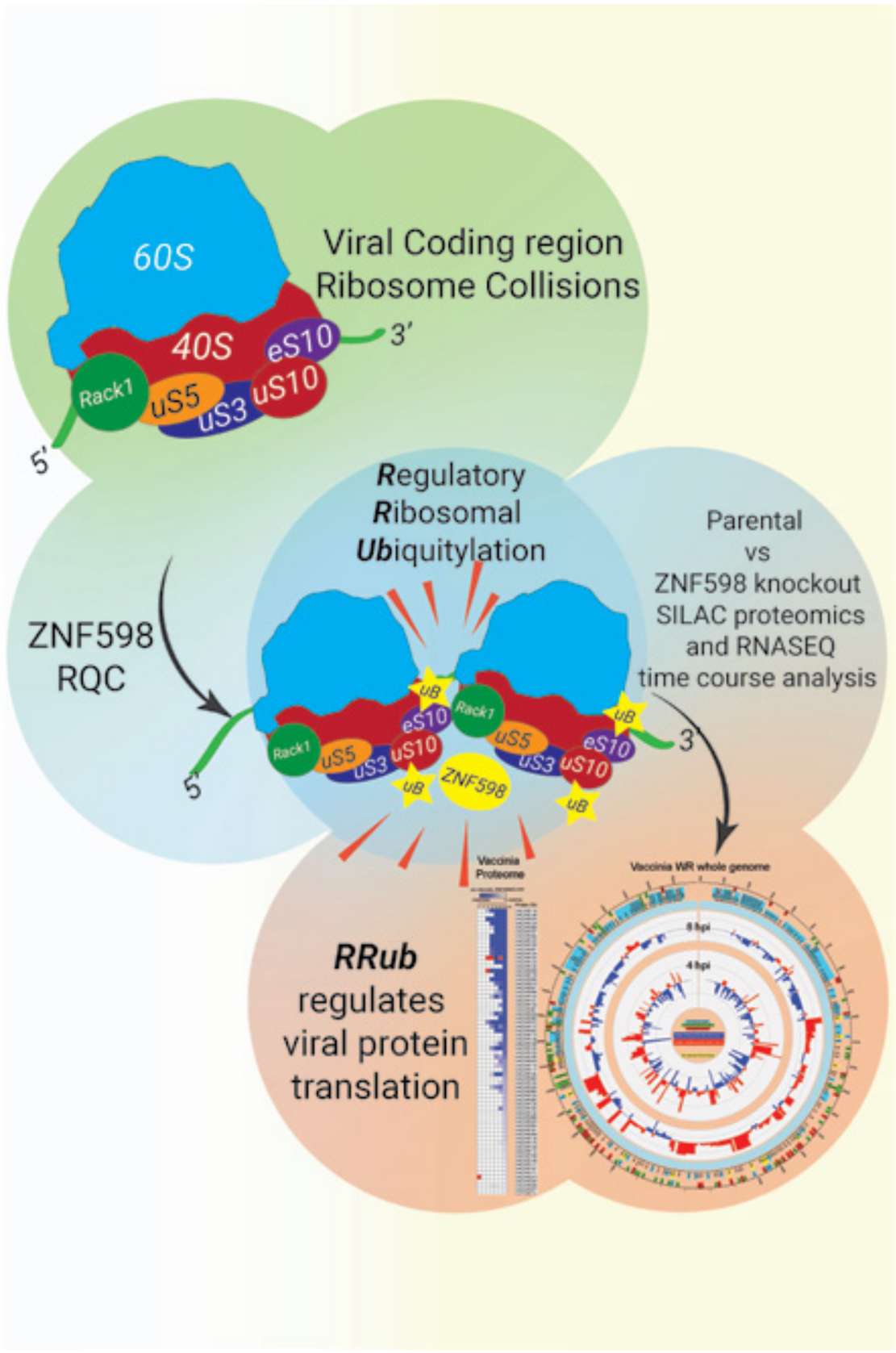
Protein Homeostasis, Ribosome, Ubiquitylation, Telomeres, DNA-Damage

Protein homeostasis or proteostasis is defined as the healthy balanced proteome required for high fidelity signaling events1. The network of proteins constituted by, but not limited to the ribosome, chaperones and the proteasome, buffers, and balances the dynamic proteome, referred to as the proteostasis network2. Translation is not an error-free process and results in the production of misfolded, truncated, or otherwise non-functional versions of the intended protein product3. The protein quality control (PQC) pathway must triage, tag, and destroy erroneous translation products4. Defects in the cellular pathways that limit the abundance or facilitate the removal of these potentially toxic defective proteins have been linked to decreased overall longevity in a variety of model organisms3. We have recently identified and characterized an evolutionarily conserved pathway that acts on ribosomes themselves when they stall in response to defective mRNA5. Our work, utilizing un-biased mass spectrometry based ubiquitin proteomics has identified a novel regulatory role for ubiquitin in regulating translation. Our recent work has uncovered how this signaling pathway is crucial for protein production during stress such as viral infections.



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PDF 10

Sphingolipid Dependent Protein Sorting in Developing Neurons: Insights into Human Genetic Disorder Hereditary Sensory and Autonomic Neuropathy Type-1 (HSAN-1)

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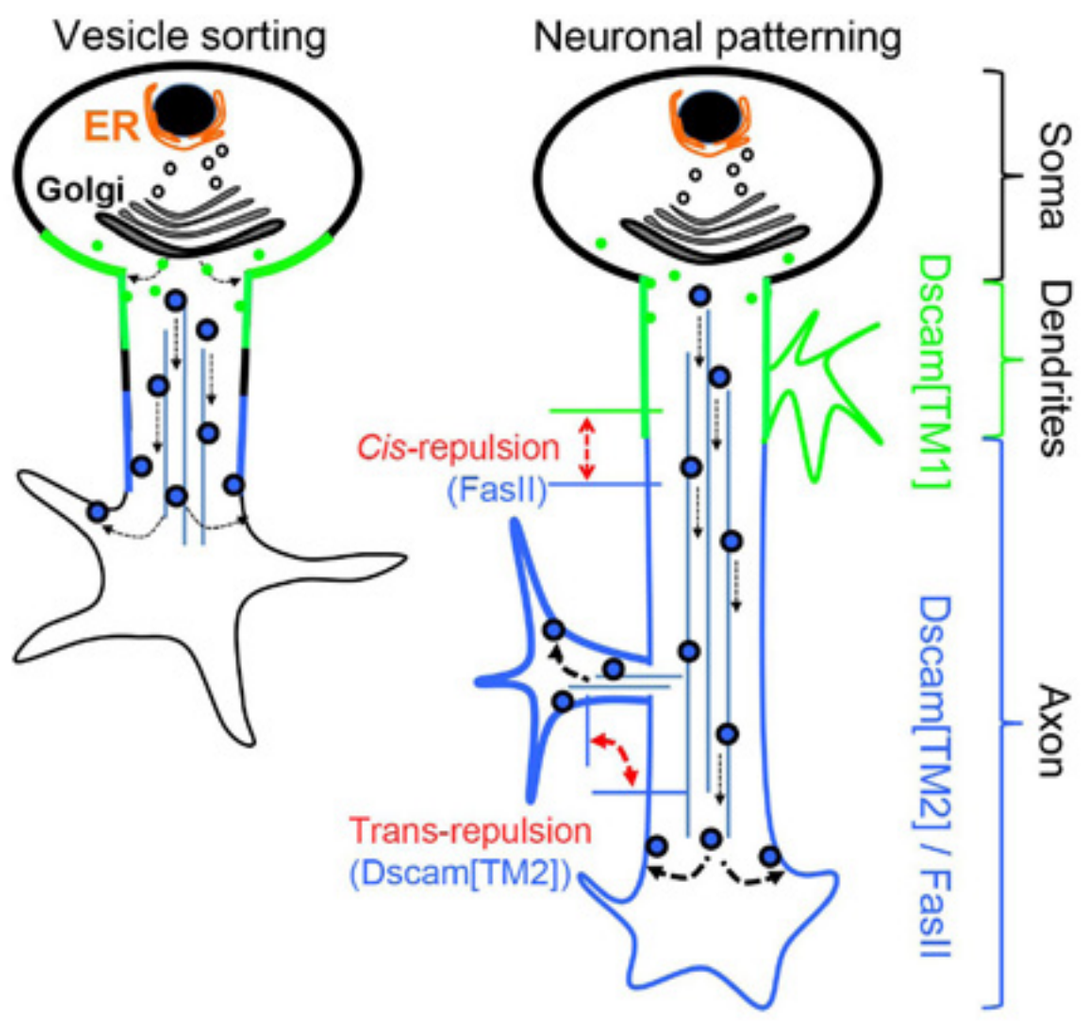
Developmental and Cellular Neurobiology, Stem Cell Biology, Genetics, High resolution developmental imaging

HSANs are rare genetic disorders (1:25,000) predominantly affecting peripheral nerve development and survival. HSAN-1 is caused due to dominant mutations in the first enzyme of Sphingolipid biosynthesis pathway, SPT-I, leading to loss of peripheral limb sensations, ulsers, shooting pains and sensory neuron loss. On analyzing Drosophila mutants for SPT-I, we found early neuronal developmental defects in the central nervous system (CNS) in addition to previously reported peripheral sensory neurons. Reduced SPT-I enzymatic activity leads to defective sorting of axon vs. dendritic proteins, formation of protein aggregates in the neuronal soma, which in turn leads to axonal morphology defects. These protein aggregates do not undergo normal protein turnover, possibly because of their altered conformation. Thus my experiments highlighted a previously unknown role of sphingolipids in neuronal development, providing novel insights into the pathogenesis of HSAN-1.



PDF 11

Establishment of Adult CNS Neurons: Applications in Modeling Hyperglycemia

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Retinal Neurodegeneration, Diabetic Retinopathy, Cell Adhesion Molecules, Hyperglycemia, Adult Neurons

Culture of adult neurons of the central nervous system (CNS) can provide a unique model system to explore neurodegenerative diseases. The CNS includes neurons and glia of the brain, spinal cord and retina. Neurons in the retina have the advantage of being the most accessible cells of the CNS, and can serve as a reliable mirror to the brain. Typically, primary cultures utilize fetal rodent neurons, but very rarely adult neurons from larger mammals. Here, we cultured primary retinal neurons isolated from adult goat and established an in vitro model of high and low glucose for performing morphological and molecular characterization studies. Immunofluorescence staining was performed to identify percentage of cultured cells expressing neuronal and glial markers. Next, we examined the relative expression of cell adhesion molecules (CAMs) in adult goat brain and retina. We also studied the effect of different glucose concentrations and media composition on the growth and expression of CAMs in cultured retinal neurons. Hyperglycemia markedly affects the length of neuronal projections in adult retinal neurons in culture. Expression of specific CAMs is significantly downregulated in the presence of high glucose. Collectively, our study demonstrates that metabolic environment affects the expression of prominent CAMs in adult retinal neurons in culture. The effect of hyperglycemia on CAM interactions, as well as related changes in intracellular signaling pathways in adult retinal neurons warrants further investigation.

PDF 12

How Ubiquitination Affects Substrate Processing by Different Proteasomes?

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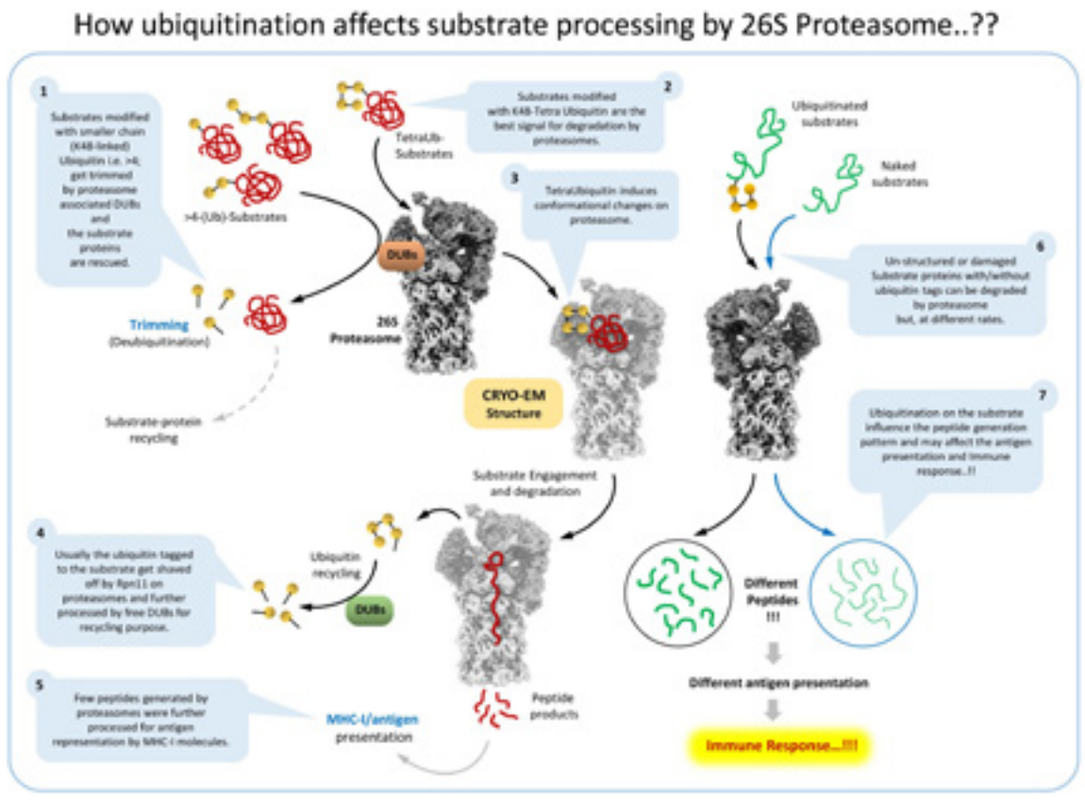
Ubiquitin Proteasome System, Protein Degradation, Deubiquitinases, Cancer Biology, Neuronal Development and Neurodisorders

In Ubiquitin-dependent proteasome degradation pathway the targeted proteins are mostly conjugated with ubiquitin; preferably via K48-linked polyubiquitin chains. The 19S regulatory-complex of 26S proteasomes mediates recognition, binding, and unfolding of the ubiquitinated substrates; and the 20S core-complex proteolytically cleaves the substrates into peptides. In contrast, in Ubiquitin-independent degradation pathway the unstructured or disordered protein substrates can be processed directly by 20S proteasomes. Recently we have shown how ubiquitination affect the substrate recognition and binding to 26S proteasomes. However, it is still unclear how ubiquitination affects substrate processivity by different proteasome species (26S & 20S), which is the main focus of our study.



By choosing an unstructured protein as target substrate, we could compare proteolytic outcome of chemically synthesized, highly homogenous non-ubiquitinated and ubiquitinated conjugates. We found that a non-ubiquitinated substrate was degraded more efficiently by 20S proteasome than by 26S proteasome both in vitro and ex vivo conditions. In contrast, ubiquitination slowed down the rate of degradation of the same substrate by 20S while enhanced degradation by 26S. Moreover, from MS/MS analysis of the in vitro proteasome-generated peptides and intracellular-peptidome we elucidated the contribution of ubiquitination to cleavage specificity, peptide-size and distribution. We have recapitulated this phenomenon in cellular model that mimic pathological conditions under hypoxia and human failing heart. In conclusion, we demonstrated parameters that could influence cleavage specificity by proteasomes and their implications in the production of antigenic peptides for various immune responses.

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PDF 13

Architecture of Human TAF11/TAF13/TBP Complex Suggests Novel Mode of TATA-box Binding

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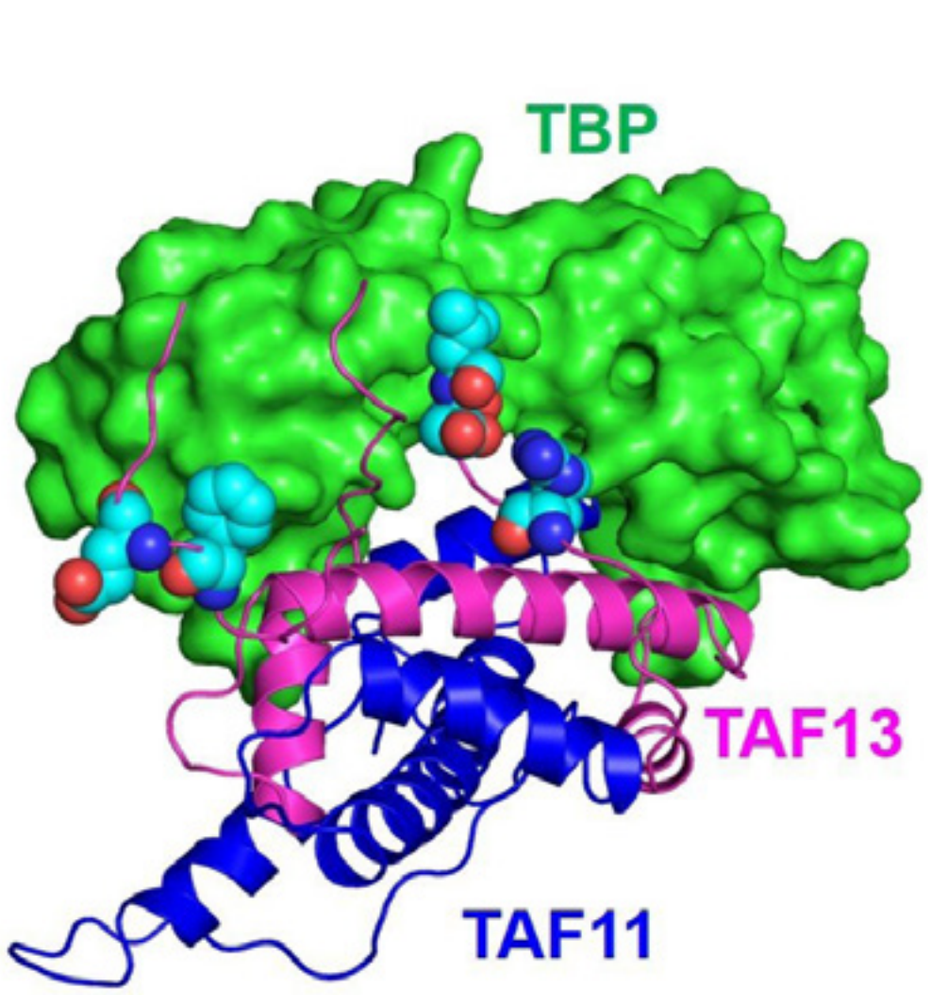
Transcription Regulation, Multi-Protein Complexes, Structural Biology Biophysics and Biochemistry, Insect Cell Expression

During Class II gene transcription a Preinitiation Complex (PIC) formation is formed by RNA polymerase II (RNA pol II) and a multicomponent transcription machinery including General Transcription Factors (GTFs)- TFIIA, -B, -D, -E, -F, -H, coactivators and repressors. GTF TFIID is key to PIC formation and consists of TATA box binding protein (TBP) and 13-14 TBP associated factors (TAFs). TBP recognizes the TATA-box in core promoter DNA in the context of PIC. In isolation, TBP was shown to heterodimerize, with two copies of TBP associating via the TATA-DNA binding interface, and a regulatory role for this dimerization has been proposed. The TAF1 subunit of TFIID, via N-terminal domains, was also shown to bind to this DNA binding interface of TBP, mimicking TATA-box DNA. TAF11 and TAF13 forms histone-fold (HF) dimer via their HF domains. We identified a ternary complex formed by TBP and TAF11/TAF13. We demonstrated the competition between TAF11/TAF13, TATA-box DNA and N-terminal domain of TAF1 for TBP binding. We determined the architecture of TAF11/TAF13/TBP complex, in an integrative approach combining crystal coordinates, biochemical analyses, and data from cross-linking mass-spectrometry (CLMS), revealing TAF11/TAF13 interaction with the DNA binding surface of TBP. We also identified a highly conserved C-terminal TBP-interaction domain (CTID) in TAF13, which is essential for supporting cell growth. All these results together suggest that the interaction between TAF11/TAF13 and TBP have implications for cellular TFIID assembly.



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PDF 14

Genetic Associations at Multi-Level Regulatory Data Improve Fine-Mapping of Causal Variants for Twelve Autoimmune Immune-Mediated Diseases

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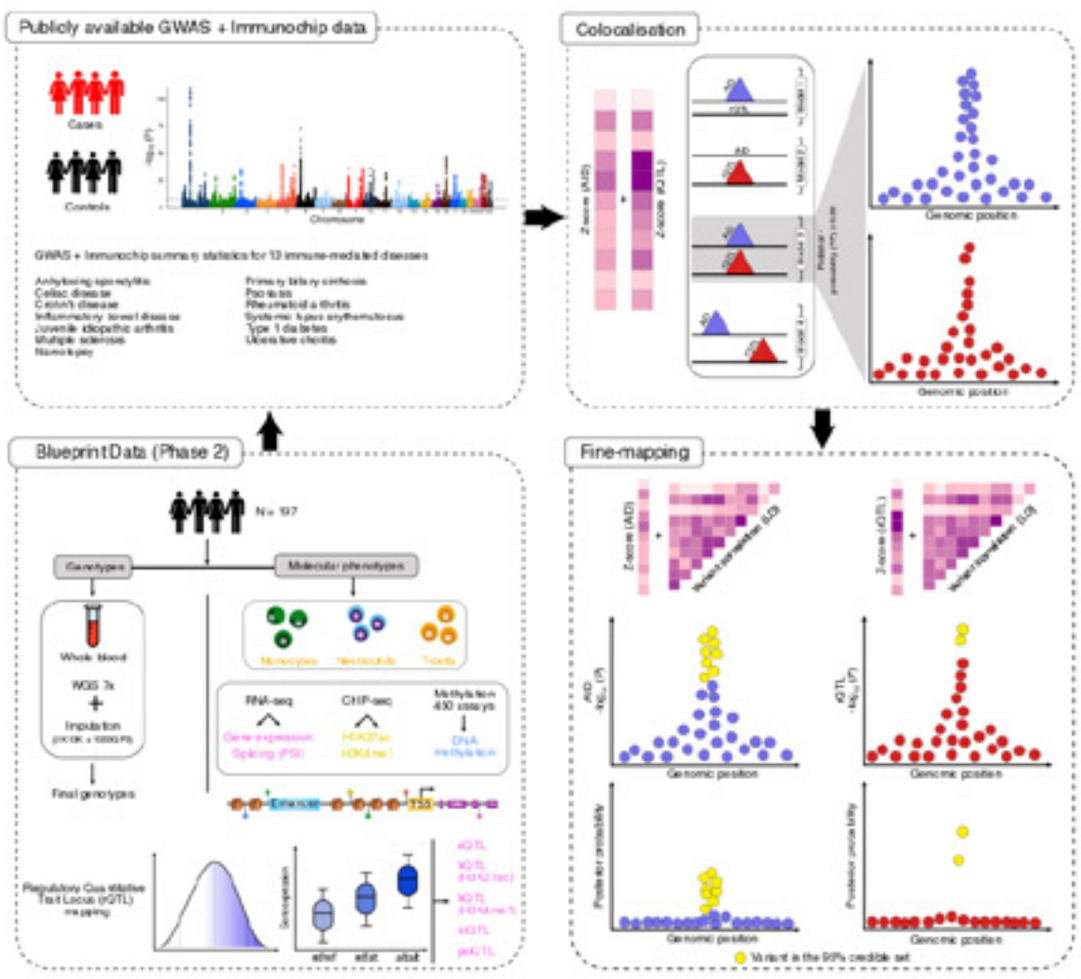
Human Genetics, Genetic Variants , Common and Rare Diseases, Population Specific Diseases, Drug Targets

Genome-wide association studies (GWAS) have identified more than a thousand genetic loci that are associated with various immune-mediated diseases. Characterising the causal genetic variants, putative effector genes and molecular mechanisms underpinning these associations is the necessary next step to harness the power of these genetic discoveries. Here we extend the evaluation of molecular quantitative trait loci (QTLs) generated as part of the BLUEPRINT project to systematically map molecular mechanisms and causal genetic variants at 12 different immune-mediated diseases. We first computed molecular QTLs in three primary human immune cell types (i.e., monocyte, neutrophil, and T-cell) using a denser genotype map. We then used colocalisation analysis to identify shared genetic effects between each molecular and disease trait, and showed 175 unique, non-HLA disease loci achieved high posterior probability of colocalisation (PP«0.99). We next sought to test the relative resolution of disease and molecular QTLs for defining credible sets of causal variants at colocalised loci. We optimized a Bayesian fine-mapping framework for analysis of disease and molecular QTL summary statistics and applied it to fine-map associations at 338 independent disease-QTL colocalised loci. We show that fine-mapping of molecular traits systematically improves resolution of causal variants compared to disease summary statistics alone. We were able to resolve causal credible sets to less than 20 variants for 67% of loci using molecular QTLs, compared to 47% based on disease GWAS alone. For example, fine mapping of the ITGA4 locus associated with inflammatory bowel disease yields smaller credible sets for expression (n=2) variants QTLs compared to use of disease GWAS alone (n=11), and highlights a putative role for one promoter variant affecting CEBPB binding. Overall, our analysis clearly demonstrates how the use of molecular data empowers the interpretation of disease associations.



PDF 15

Fabrication of Piezoelectric Contact Lens Based Pressure Sensor for Early Detection and Management of Glaucoma

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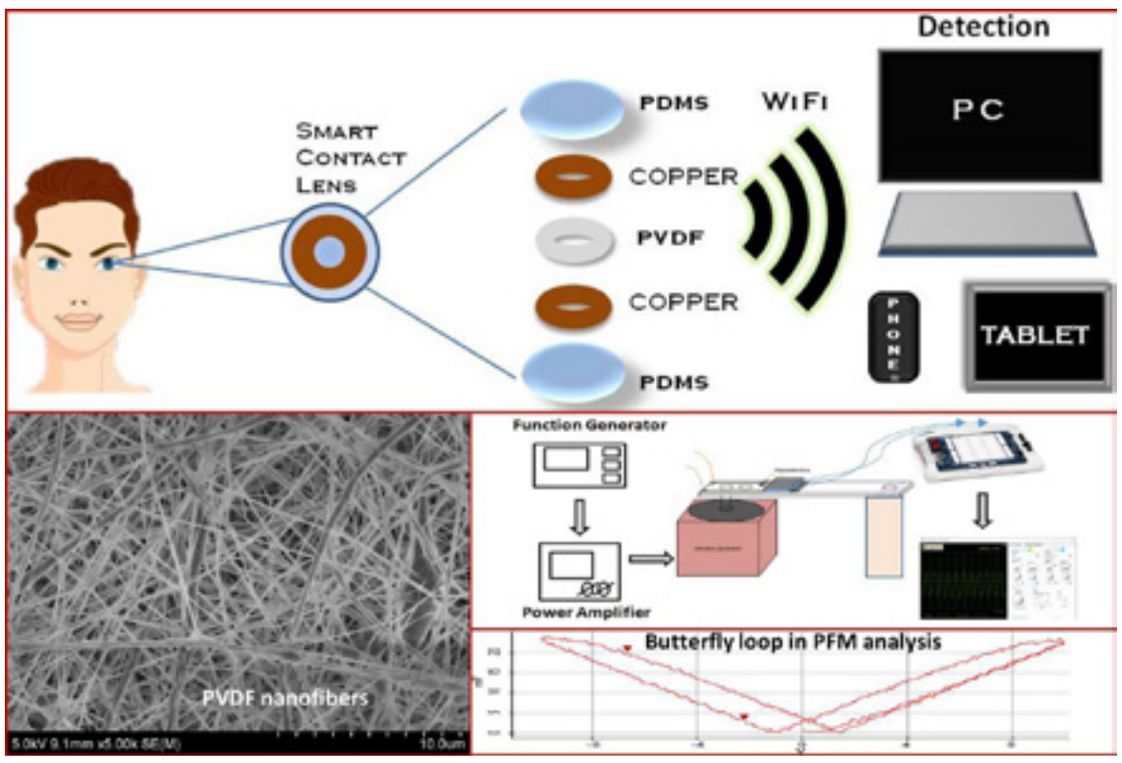
Nanobiotechnology, Point-of-care Devices, Wearable Electronic, Microbiology, Microfluidics

Glaucoma is a group of eye conditions that leads to irreversible blindness if not detected and managed at an early stage. It is caused due to excess accumulation of fluid in the anterior chamber of eye which leads to an increase in intraocular pressure (IOP). As IOP is dynamic in nature and keeps fluctuating based on many factors, there is a need to continuously monitor these changes by means of a point-of-care device.

To fabricate a piezoelectric contact lens type of pressure sensor, polyvinylidene fluoride (PVDF) was subjected to electrospinning to obtain nanofiber films with high beta phase content that exhibit superior piezoelectric property. A solution of 12 wt% concentration of PVDF in dimethylformamide and acetone was prepared and subjected to electrospinning at a voltage of 10 kV, using needle tip to collector distance of 10 cm and feeding rate of 0.3 mL/hr. The average nanofiber diameter obtained from HR-SEM was 163 nm. XRD and FTIR spectra exhibited featured peaks corresponding to polar beta phase and the amount of beta phase content was calculated to be 84%. A voltage of 1.739 V was generated at a frequency of 22.287 Hz on subjecting the film to mechanical vibration.



Future studies consist of integration of the piezoelectric film into a PDMS (Poly-dimethylsiloxane) contact lens along with an antenna for data transmission. The advantages of this sensor are that is easily wearable and non-invasive, does not require any surgical procedure, poses minimal risk and is completely self-powered.

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PDF 16

Protein Quality Control in the Immortal Germ Lineage: Identifying Changes in Oocyte Cell Biology Triggered by Signals from Sperm

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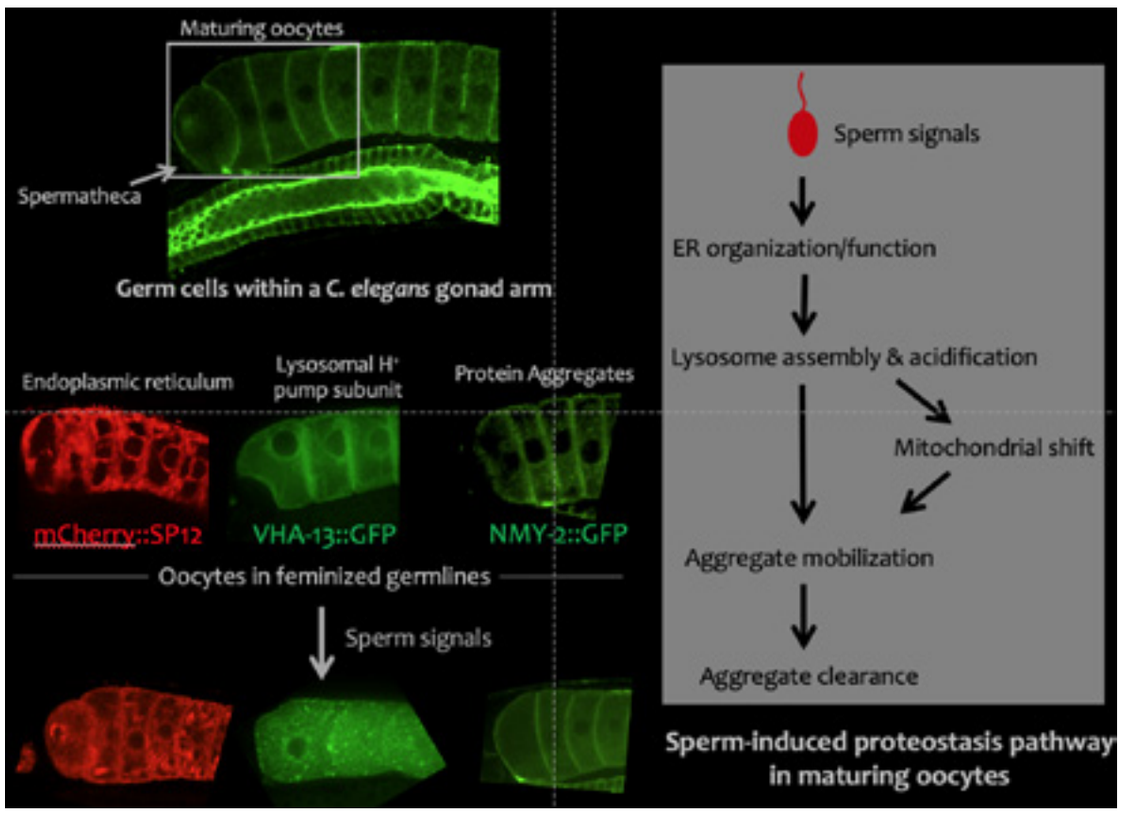
Protein Quality Control, Aging, Germline cell biology , Genome-wide Screening, Live Cell Imaging

Somatic cells age and die, yet the germ lineage is rejuvenated with each generation, ensuring germline immortality. In C. elegans, proteostasis is activated in oocytes in response to sperm-derived signals that indicate impending fertilization. Female animals lacking sperm accumulate protein aggregates in unfertilized oocytes. Our previous findings indicate that oocytes in the hermaphrodite germline activate a lysosomal switch and remove aggregates by a process resembling microautophagy. Rapid acidification of lysosomes and a shift in mitochondrial physiology are required to initiate clearance of aggregates1. We have now performed a genome-wide RNAi screen to identify additional components of this quality control switch, and to explore changes in oocyte cell biology triggered by sperm signals. By knocking down individual genes and monitoring an aggregation-prone protein within maturing oocytes, we have identified about 100 genes necessary for preventing oocyte-protein aggregation. Multiple different organelles and cellular processes are regulated by these genes. Our findings indicate that the endoplasmic reticulum (ER) and its trafficking function are required to acidify lysosomes via assembly of the lysosomal V-ATPase proton pump. Feminized animals exhibit altered oocyte ER organization and do not assemble the acidifying proton pump. Both of these phenotypes can be rapidly reversed by mating which in turn also triggers protein aggregate removal, indicating proteostasis establishment. Further, we are also investigating how other candidates identified in the screen contribute to oocyte proteostasis. Taken together, we hope that this study helps to better understand natural rejuvenation strategies of the germ lineage. The insights could potentially guide strategies for activating quality control pathways in somatic tissues during aging. In the future it will be interesting to study consequences of impaired oocyte proteostasis e.g. in aged parent worms, on the fate and health of progeny animals.



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PDF 17

Unraveling the Spatial Organization of Chromosomes by Single-Molecule Imaging

Single-molecule Biophysics, Protein-DNA Interactions, Genome Architecture, DNA Supercoiling, Super-Resolution Microscopy

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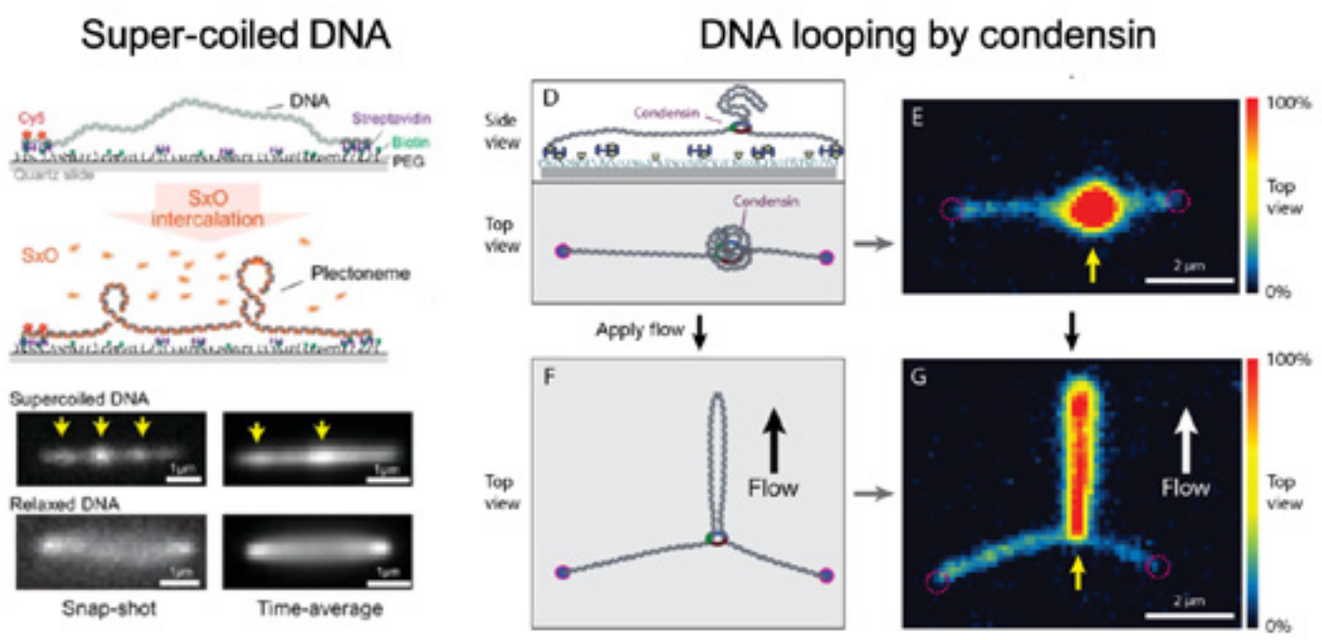
The three-dimensional organization of genome is increasingly understood to play a decisive role in vital cellular processes. In my talk, I will present two different aspects of genome organization: supercoiled DNA1and condensin mediated DNA-loop extrusion2.

(a) Sequence-structure relationship of supercoiled DNA: by using our recently developed single-molecule assay3, we visualized the plectonemes (extended intertwined DNA structures formed upon supercoiling) along supercoiled DNA. Our experiments show that the DNA sequence directly encodes the structure of supercoiled DNA by pinning plectonemes at specific sequences. We develop a physical model that predicts sequence-dependent intrinsic curvature facilitates the pinning of plectonemes. Analysis of several prokaryotic genomes indicates that plectonemes localize directly upstream of prokaryotic promoters, which we experimentally confirm for selected promoters. These findings therefore reveal a hidden code in the genome that helps to spatially organize the chromosomal DNA.

(b) DNA loop-extrusion by condensin: using the similar assay, we provide an unambiguous evidence for DNA loop-extrusion by condensin molecules by real-time imaging. A single condensin complex is able to extrude tens of kilobases of DNA at a force-dependent speed of up to 1,500 bp/sec, using the energy of ATP hydrolysis. Condensin-induced loop extrusion is strictly asymmetric, which demonstrates that condensin anchors onto DNA and reels it from only one side. These results might provide unifying mechanism for genome organization.



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PDF 18

Development of Polymer Based Antimicrobial Wound Healing Dermal Patches for Chronic and Acute Wounds

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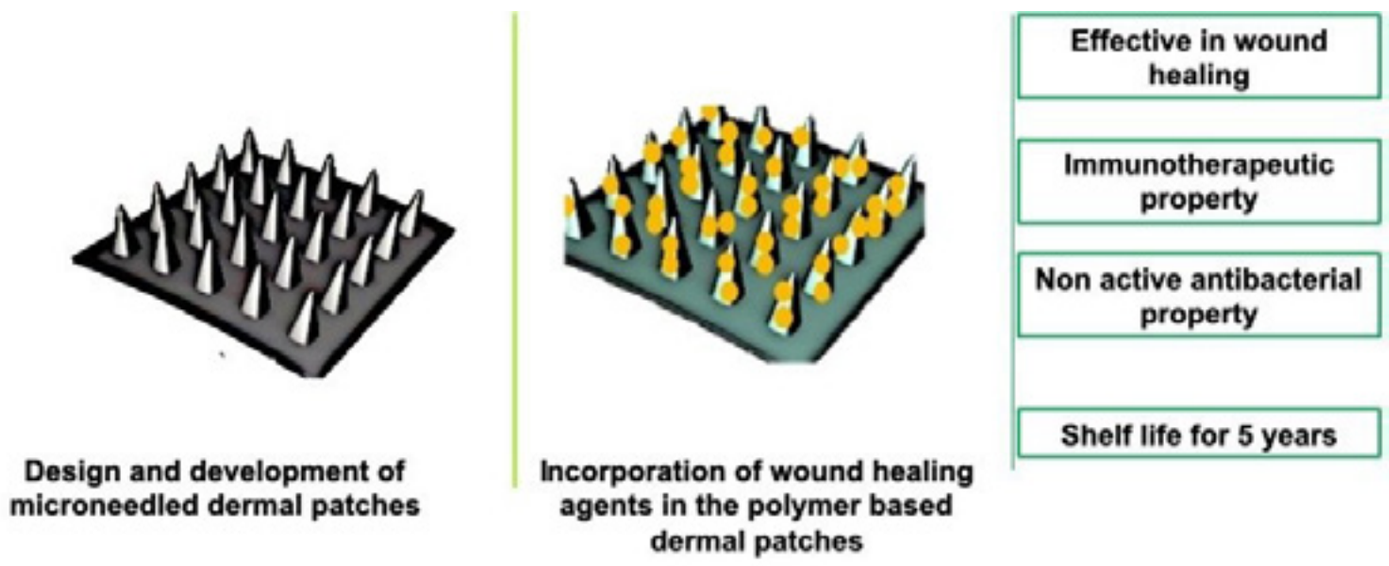
Tissue Engineering, Biomaterials, 3D Cell Culture, Regenerative Medicine, Molecular Biology

The aim of this study is to develop multilayer PCL-chitosan based wound dressings with antibacterial property and to enhance wound-healing mechanism for chronic and acute wounds. The novelty of this study is the biomaterial selection and combination of wound healing agents which helped in mimicking the skin properties such as multilayer, extracellular matrix composition, porosity, mechanical strength and flexibility. The multilayer dermal patch developed consists of different layers such as, bottom layer (furthest from the wound) with smallest pore size will prevent entry of other microbes and the top layer (closest to the wound) possess antibacterial and anti-inflammatory properties. The top layer will have microneedles made up of wound healing agent to further enhance the wound healing approach. Total thickness of the wound dressing was found to be ~ 5 mm and can be developed as sheets to cover larger surface area. The dermal patches were further characterized for its physical and biological properties such as SEM, FTIR, NMR, TEM, AFM, water vapour permeability analysis, porosity, swelling ratio, mechanical properties, biocompatibility and antibacterial property. These dermal patches showed promising results with tensile modulus of 56.7 MPa, zone of inhibition was found to be 3.2 cm for both gram positive and gram-negative bacteria and showed good biocompatibility. These results suggest its potential used in addressing issues such as wound exudate absorption and skin contracture problems.



PDF 19

Generation and Maintenance of Smooth Endoplasmic Reticulum

Membrane Proteins, Structural Biology, Biochemistry, Cellular Imaging, Shape-structure-function

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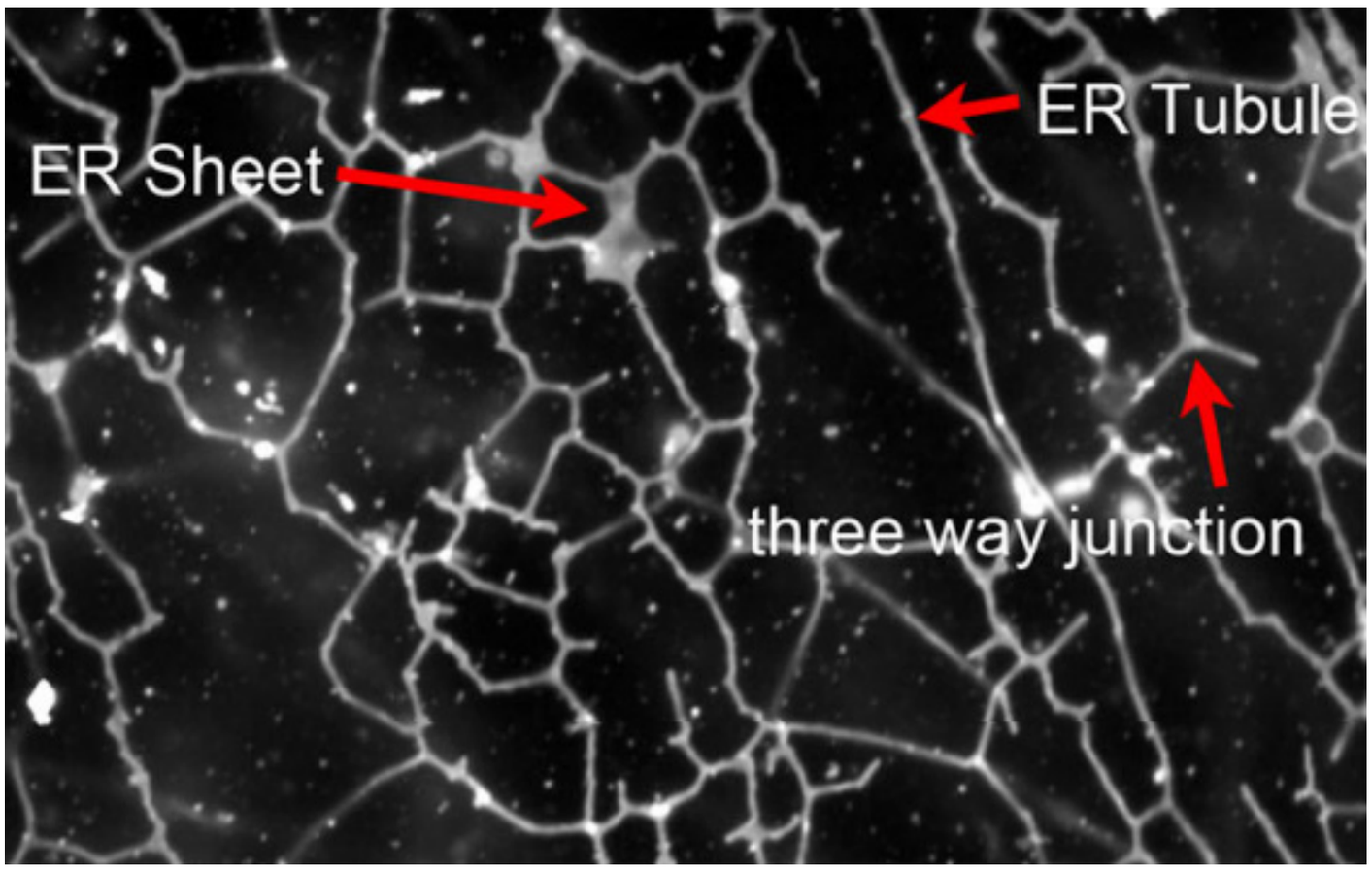
The endoplasmic reticulum (ER) is a continuous membrane system spread throughout the cell cytoplasm and regulates the various cellular processes such as protein synthesis, protein folding, protein secretion, maintaining calcium homeostasis and lipid metabolism. The ER is made up of a smooth tubular network and rough, ribosome-studded sheets, and their relative occurrence in the cells is governed by the functions undertaken by the cells. Studies have pointed out few proteins that are required for the formation and maintenance of tubules and sheets and thus, maintain their balance in the cells. Reticulons, REEPs (known to be well-conserved) and Protrudin (recently identified) have been known to be associated with the tubular network in mammalian cells and their absence shifts the balance towards ER sheets. The mechanistic details by which these proteins interact with the ER membrane lipids to induce bends in order to produce tubules is not known and thus, becomes the goal of this study, which will be addressed by structural, biochemical and cell biological approaches.



PDF 20

Structural Mechanisms of Atypical Conotoxin Modulators of the Nicotinic Acetylcholine Receptors

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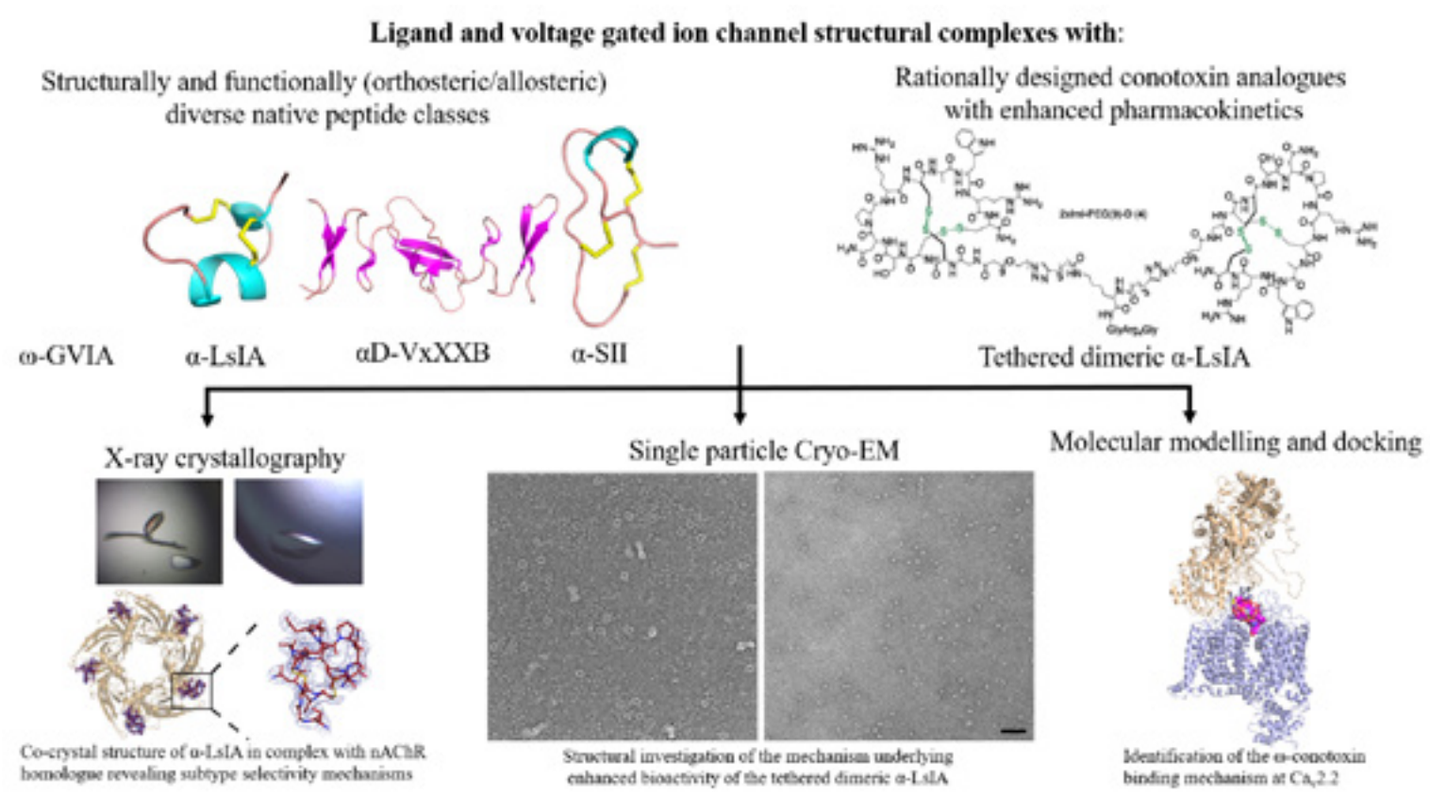
Structural Pharmacology, Membrane Proteins, Animal Toxins, Ion Channels, Neuropathic Inflammation

Cone snail venom has been the most abundant source for natural peptide modulators of the nicotinic acetylcholine receptors. α-Conotoxins from cone snail venom is the largest family of peptide inhibitors of the nAChRs. These are 17-20 amino acid long, two disulfide bonded peptides that inhibit the receptor via the endogenous ligand-binding pocket (orthosteric ligand binding site). Despite a conserved disulfide framework, three-dimensional structure and mechanism of action, α-conotoxins vary considerably in their primary sequence, which drive their distinct potency and selectivity profiles at the various nAChR subtypes. Their relative ease of synthesis, has facilitated extensive structure-activity studies, which have provided some crucial insights into the orthosteric ligand recognition properties of the nAChRs. Chemical modifications to the natural scaffold such as amino-acid substitutions, backbone cyclization, replacement of disulfide bridges with dicarba linkers and lipophilic analogues have further improved the native pharmacological properties, proteolytic resistance, synthetic yields and bioavailibitlity, making α-conotoxins amenable to therapeutic applications. In addition to α-conotoxins, the cone snail venom has proven to be a source of an array of nAChR modulators from nine superfamilies' that vary significantly in their primary sequence, structure and potentially mode of action (A, B3, D, L, M, O1, S, T and J). Demonstrating that cone snail venom can provide structurally and functionally distinct classes of peptide nAChR modulators as templates for alternate rational strategies in drug design. This project focuses on delineating the structural mechanisms underlying the mode of action of some of these atypical conotoxins targeting the nAChRs.



PDF 21

Hippocampal-Thalamo-Cortical Network for Episodic Memory

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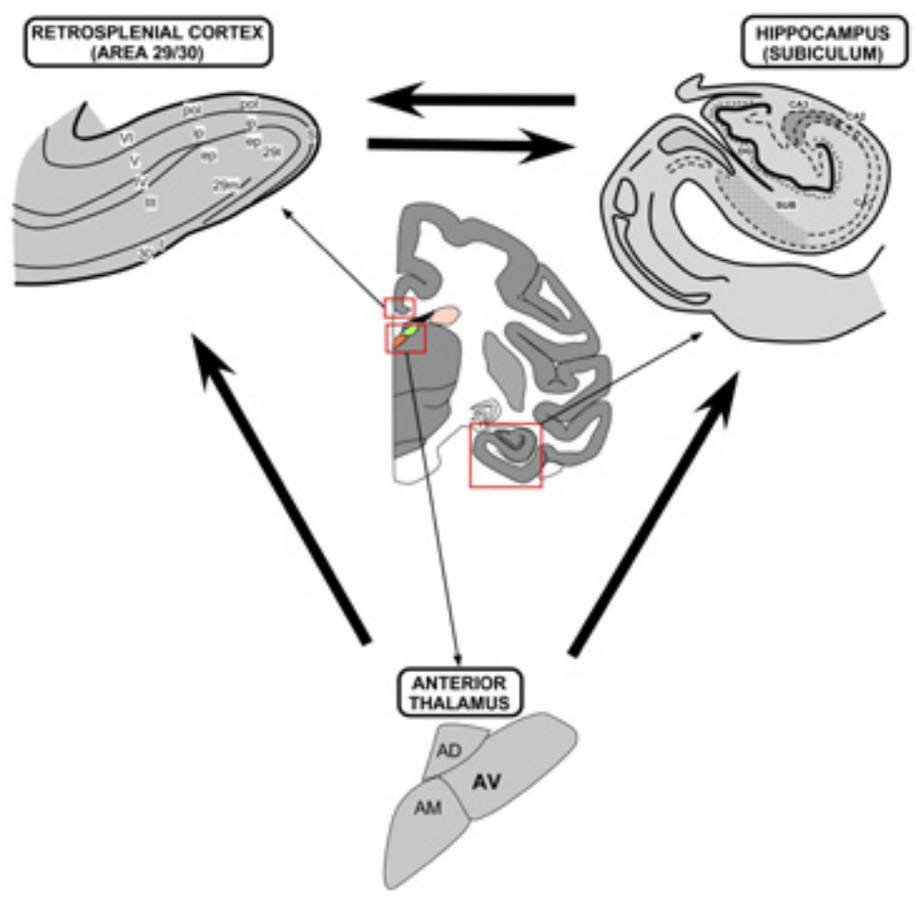
Episodic Memory, Scene, Monkey, Brain, Electrophysiology

Episodic memory refers to the ability to recollect objects, events and their contexts from one's personal past. Previous studies have shown that the hippocampus, retrosplenial cortex (RSC) and anterior thalamus (AT) form prominent nodes of interconnected brain circuit responsible for episodic memory. We hypothesized that the AT and RSC are involved in spatiotemporal binding of objects and their context and AT regulates the information flow between hippocampus and RSC.

To test our hypothesis, we simultaneously recorded spikes and local field potentials (LFP) from the AT, hippocampus and RSC of two macaques performing a visuospatial scene memory task. We used diffusion MRI to target linear microelectrode arrays to interconnected sites of this hippocampo-thalamo-cortical network, and structural MRI of electrodes in situ to confirm electrode positions.

Preliminary data show that multiple cells in AT have specific response to scene contents and different epochs after scene presentation during early learning. Further, RSC cells also showed sensitivity to scenes and their contents, and modulated their firing with time. These preliminary results from spiking activity suggest that activity in AT and RSC correlates to spatiotemporal binding of different aspects of scenes into their context.

Furthermore, our preliminary LFP results show bidirectional conditional Granger causal influences in the 5-15Hz range between hippocampus and RSC during memory retrieval. We also measured increased coherence between thalamic spikes and LFPs in both hippocampus and RSC, in the 5-15Hz range. Further, AT showed increased conditional Granger causal influences on the hippocampus and RSC in the same frequency range. These preliminary data suggest



that the anterior thalamus regulates information transmission between the hippocampus and RSC based on episodic memory demands through synchronization of activity within the hippocampus and RSC.

Overall, this study supports an important role for the anterior thalamus and retrosplenial cortex in the extended hippocampal system supporting episodic memory.

PDF 22

Dynactin Function in Dynein Driven Motion of Phagosomes

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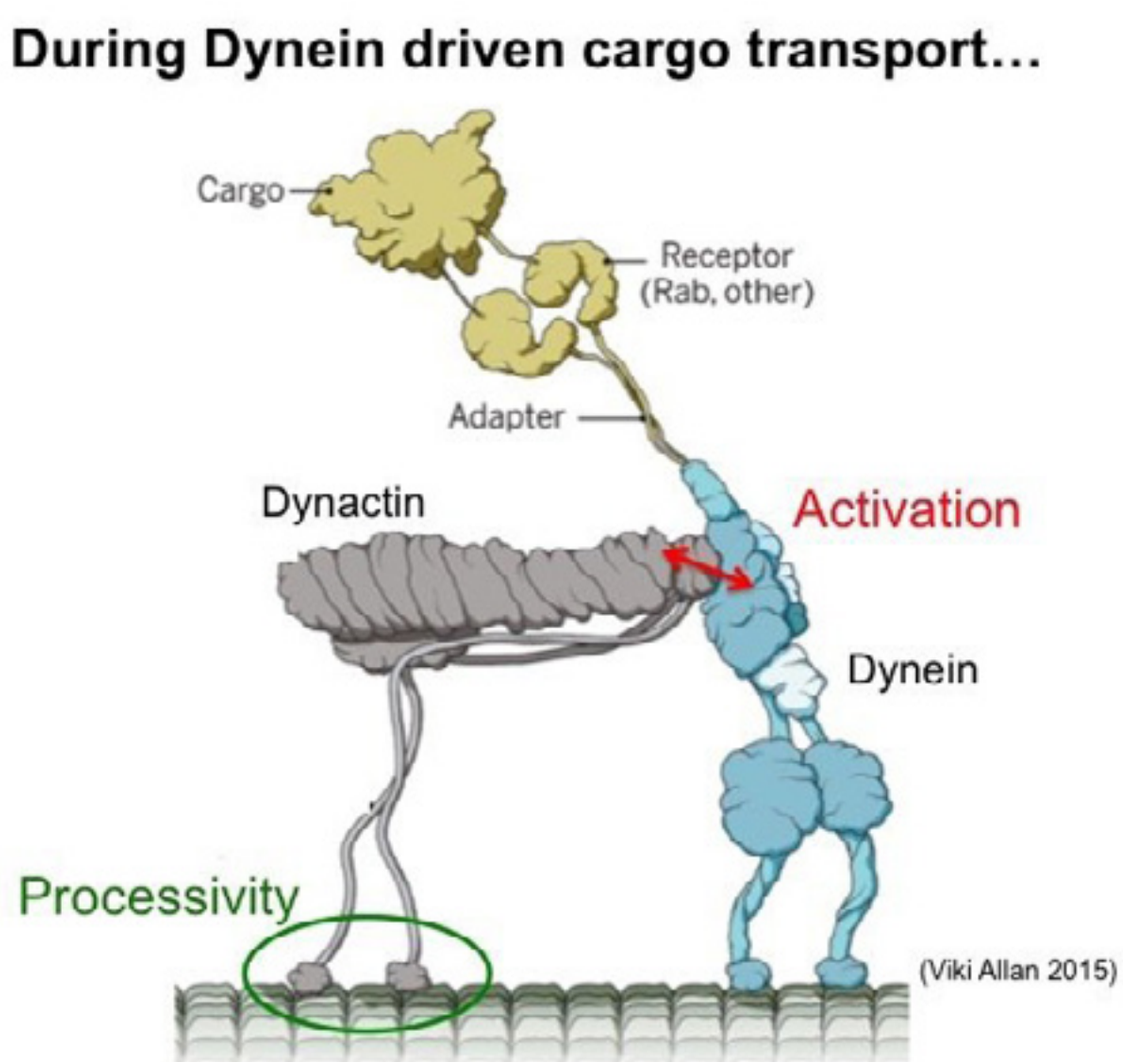
Intracellular Transport, Molecular Motors, Organellar Interaction, Cell Division, Genetics

Dynein driven transport of organelles is required for many cellular processes. It is widely known that dynein performs these functions along with its key regulator, Dynactin. Although dynactin mutations are implicated in various neurological disorders, the mechanism by which dynactin assists dynein at a molecular level remains controversial. Dynactin is a unique regulator with multiple linkages; it binds dynein, microtubules as well as cellular cargoes. We aim to understand the relevance of these interactions of dynactin with dynein, and with microtubules during cargo transport. In vitro studies show that dynactin addition increases the processivity of dynein-coated beads. However, understanding the relevance of dynactin on in vivo cargoes has been difficult because perturbing Dynactin in cells abrogates initiation of transport. To bypass these problems, we use an ex-vivo assay to study transport of native-like latex bead phagosomes extracted from Dictyostelium. Our results show that disruption of Dynein-Dynactin interaction on phagosomes leads to inactivation of the dynein motor, leading to significantly reduced initiation of transport of late phagosomes. In contrast, dynactin interaction with microtubules does not affect dynein events but is required for processive dynein motion. Thus, our studies point out the significance of these dynactin linkages to better understand how they contribute to long distance dynein motion of cellular cargoes.



PDF 23

Mitochondria and Neural Circuit Dysfunctions

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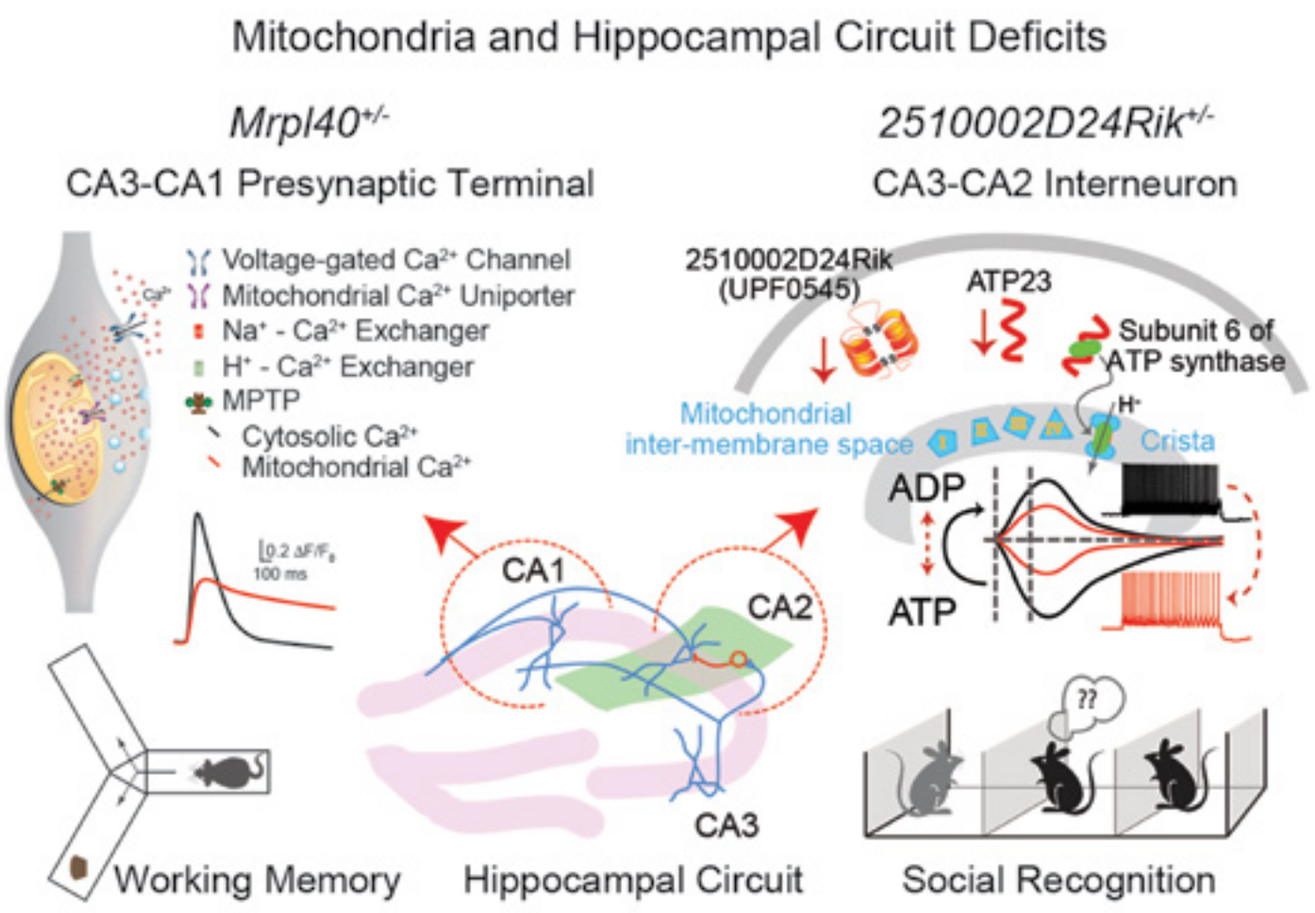
https://scholar.google.com/citations?user=03gTWRgAAAAJ&hl=en&oi=ao

Translational Neuroscience, Neural circuits, Hippocampus, Mitochondria, Synaptic Plasticity

The overarching goal of our research is to decipher the genetic, molecular, cellular, synaptic and neural circuit mechanisms of complex behaviors. Towards this end, we employ mouse models of the most common human microdeletion syndrome known as 22q11 Deletion Syndrome (22q11DS). This syndrome, caused by a hemizygous deletion of 1.5- to 3- megabase region on chromosome 22, constitutes a strong genetic risk factor for schizophrenia in adults and autism in children. In mouse models of 22q11DS, we identified that deficiency of 2 genes- Mrpl40 and 2510002D24Rik (Rik) leads to deficits in working memory and social recognition respectively. Mrpl40 encodes a protein of the mitochondrial large ribosomal subunit. Mrpl40 haploinsufficiency leads to deficits in hippocampal Short-Term Plasticity (STP) and working memory by reducing calcium extrusion through the mitochondrial permeability transition pore (MPTP). The STP deficit was rescued by overexpressing Adenine Nucleotide Translocators, which are regulators of the MPTP. Rik is a novel gene encoding a protein of the mitochondrial intermembrane space. Rik protein is enriched in the CA2 and CA3 regions of the hippocampus. Rik deficiency affects mitochondrial ATP-ADP interconversion in the CA2 interneurons but not pyramidal neurons. This molecular defect manifests in the CA2 neural circuit as a Long-Term Plasticity (LTP) deficit and behaviorally as defective social recognition. Biochemical approaches narrowed on Atp23, a protein that interacts with Rik as the most down-regulated target in Rik deficiency. The electrophysiological and behavioral abnormalities in Rik deficiency were rescued by overexpression of Atp23 in the CA2 region. Our studies on Mrpl40 and Rik identified the mitochondrial targets for hippocampus encoded memory deficits. These findings uncover new disease-causing mechanisms relevant to complex behavioral disorders such as schizophrenia and autism.



PDF 24

A Systems Biology Approach Identifies FUT8 as a Driver Of Melanoma Metastasis

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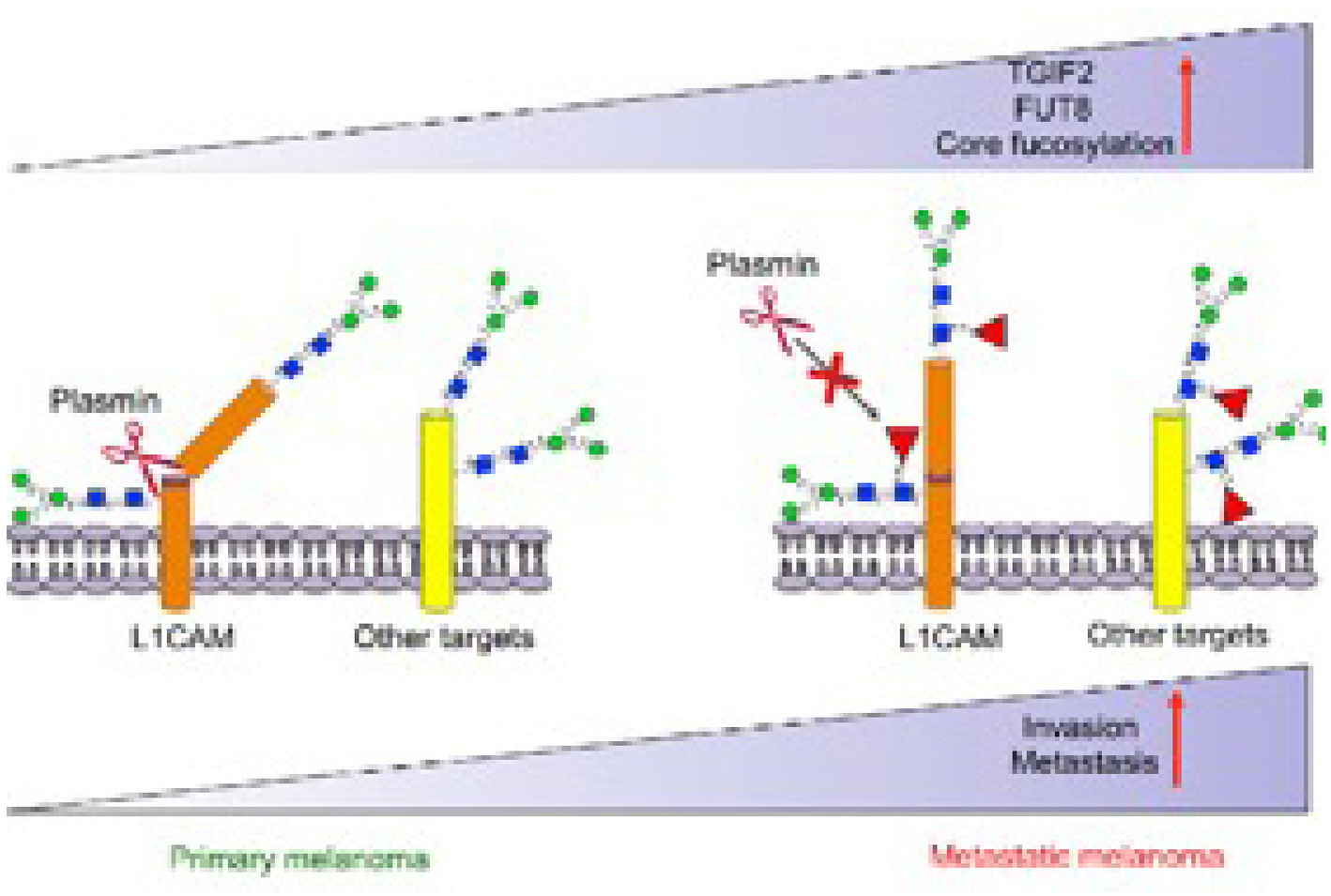
Glycosylation, Melanoma, Cancer, Metastasis, Glycogenes

Aberrant glycosylation has been previously associated with melanoma cancer progression based on studies that were mainly restricted to cell lines. Here, for the first time we have used a systematic, multi-disciplinary approach, using clinical melanoma primary and metastatic tissues to identify glycomic changes caused by glycosyltransferases (glycogenes) associated with melanoma metastasis. We utilized our innovative technology (lectin microarrays **(Agrawal et al., 2014, PNAS)**) to obtain global glycosylation patterns of patient-matched primary and metastatic melanoma specimens and identify a glycan signature characteristic of metastasis. We integrated this information with published transcriptomic profiles from patient samples to pinpoint glycosylation enzymes underlying the observed alterations. Specifically, we show that upregulation of core fucosylation by increased FUT8 expression and downregulation of α-1,2 fucosylation by decreased FUT1 and FUT2 expression are features of melanoma metastatic tissues. Functionally, depletion of FUT8 reduces in vitro cell invasion without affecting cell proliferation. Moreover, in vivo FUT8 silencing strongly suppressed tumor dissemination and metastasis. We demonstrate that upstream, FUT8 is regulated by a transcription factor TGIF2. Finally, we show those downstream FUT8 targets are core fucosylated proteins involved in cell invasion, migration or metastasis such as L1CAM. Strikingly functions of L1CAM are core fucosylation dependent. Core fucosylation impacted L1CAM cleavage and the ability of L1CAM to support melanoma invasion **(Agrawal et al., 2017, Cancer Cell)**. Thus, FUT8 and its targets represent novel therapeutic targets for prevention or treatment of melanoma metastasis.



PDF 25

Actomyosin Contractility is Essential for the Structural Integrity of the Syncytial Germline in *C. elegans*

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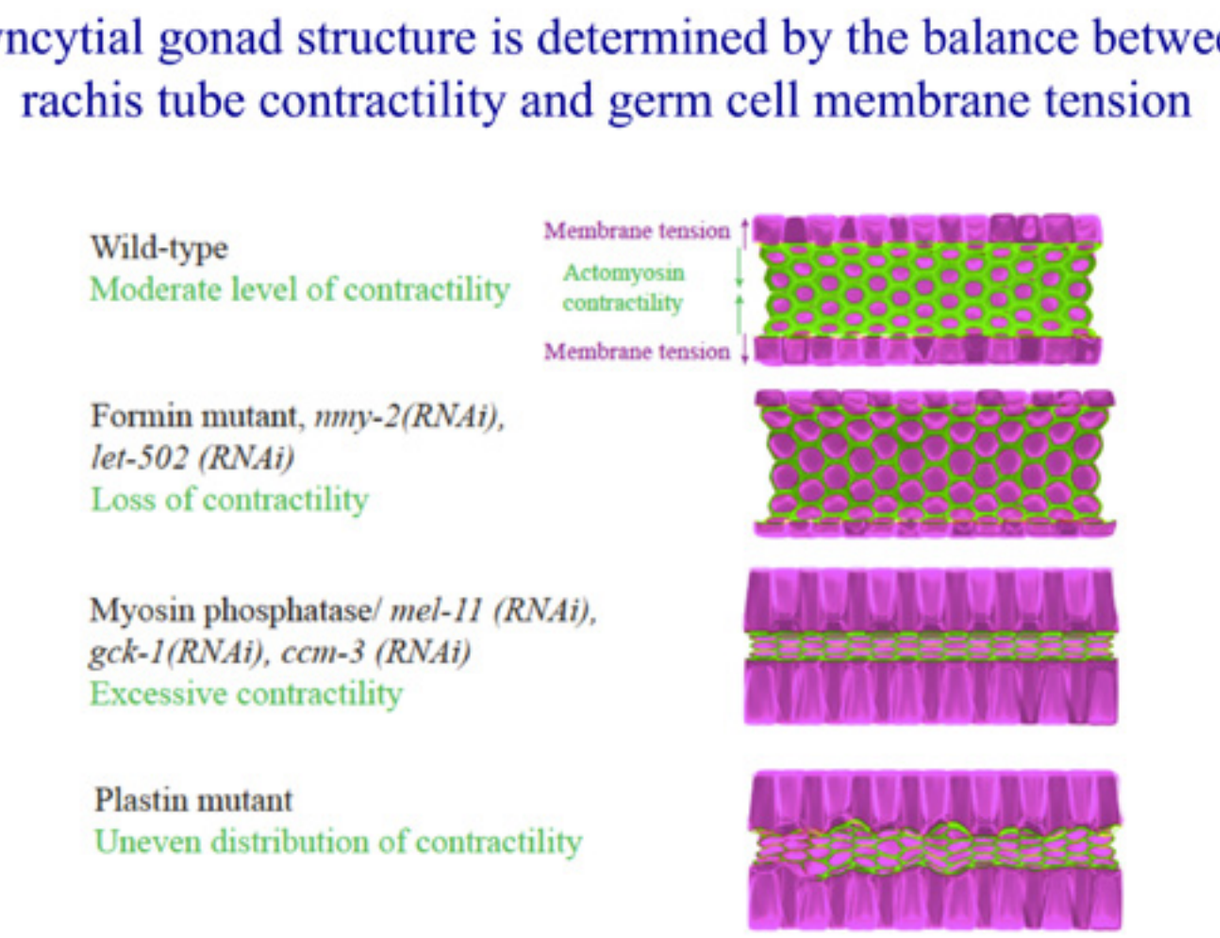
Actin, Myosin, Contractility, Development, Morphogenesis

Syncytial architecture is an evolutionary-conserved feature of the germline of many species and it plays a crucial role in their fertility. The mechanism responsible for the maintenance of syncytial organization is largely unknown. In *Caenorhabditis elegans*, multiple germ cell nuclei line the periphery of the gonad arm and remain connected to a common cytoplasm through stable openings (bridges) to a cell-free shaft called rachis and thus forming a syncytium. In the current study, we reveal that beyond the rachis bridges, actomyosin forms an inner corset-like structure within the syncytial germline, surrounding the rachis. Using a combination of mechanical, genetic and pharmacological perturbations, we showed that the inner actomyosin corset is under two-directional tension in the plane of the rachis surface and perpendicular to it, opposing membrane tension. Also, decreasing or increasing the tension affects syncytial germline structure, leading, in extreme cases, to sterility. Finally, we formulated our findings in a qualitative 3D vertex mathematical model that confirms the balance of forces within the tissue and demonstrates that changes in apical tension are sufficient to drive the changes in germline morphology we observed in vivo. Thus, our work uncovers a unique tissue-level cytoskeletal structure and establishes the critical role of actomyosin contractility in the preservation of a functional germline.



PDF 26

GCN4 Directly Controls a Methionine Mediated Anabolic Program

Genomics, Gene Regulation, Metabolism, GCN4, Microbial Evolution

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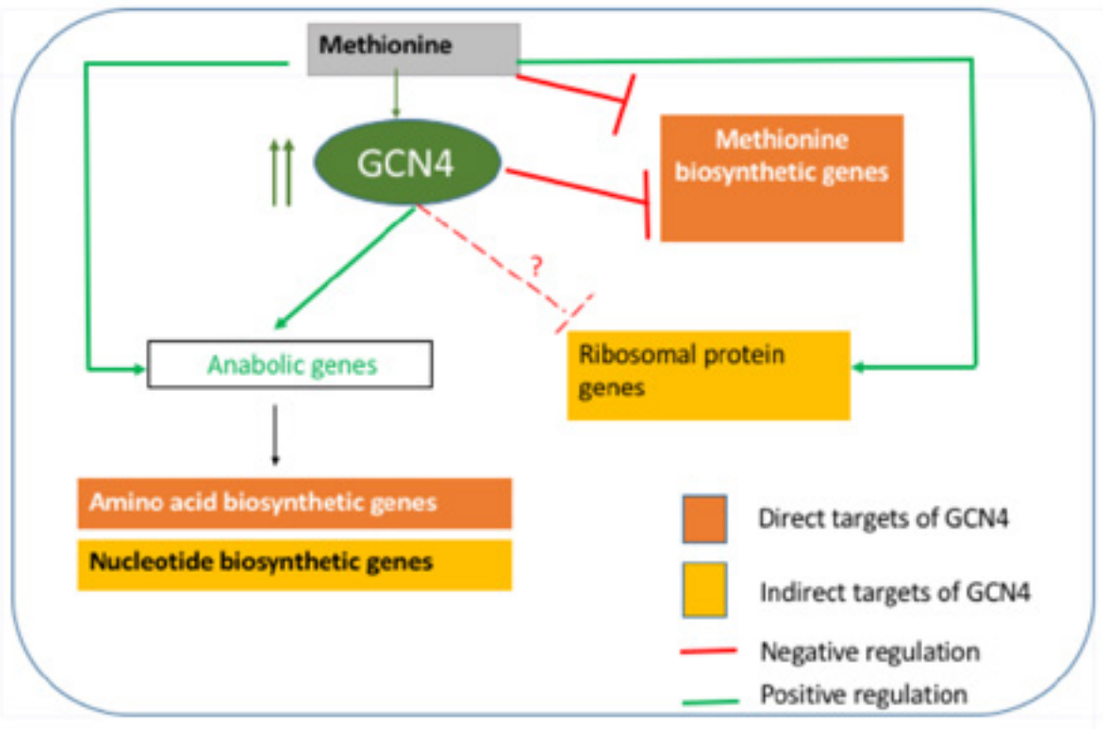
Cells respond to starvation by altering gene expression, metabolic status and so on. In this study we are exploring gene regulation in response to a sulfur amino acid- methionine. In our earlier studies, we showed that methionine supplementation in the amino acid starved cells induces anabolic response in the cells through activating specific metabolic nodes. We identified that methionine induces anabolic response by hierarchically controlling the transcription of specific nodes of metabolism such as pentose phosphate pathway, Glutamate dehydrogenase and pyridoxal-L-phosphate metabolism. These pathways are required for the synthesis of precursors and the cofactors required for the synthesis of other macromolecules. Further, this study gave us a hint about the role of a transcription factor (TF) called Gcn4, a stress responsive transcription factor in methionine dependent regulation of gene expression. My current work is to understand how much of the methionine dependent response is mediated by Gcn4. In this study, I have identified direct and indirect targets of Gcn4 in methionine dependent anabolic response. Our results shows that Gcn4 directly regulate amino acid biosynthetic genes, though regulation of nucleotide biosynthesis is also dependent on Gcn4, these genes are not regulated by direct binding of Gcn4 to its promoter. Hence, they are indirectly regulated by Gcn4. We further identified that Gcn4 directly regulates every single step in the arginine and lysine biosynthesis pathway and arginine and lysine biosynthesis is strongly reduced in the cells lacking Gcn4. We are further exploring the translational status of the proteins that are rich in arginine and lysine to understand if the protein synthesis of these genes are affected in Gcn4 dependent manner.



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PDF 27

Nanoscale Architecture of Cellular Cytoskeleton Impacts its Mechanics as Revealed by In Situ Cryo-Electron Tomography

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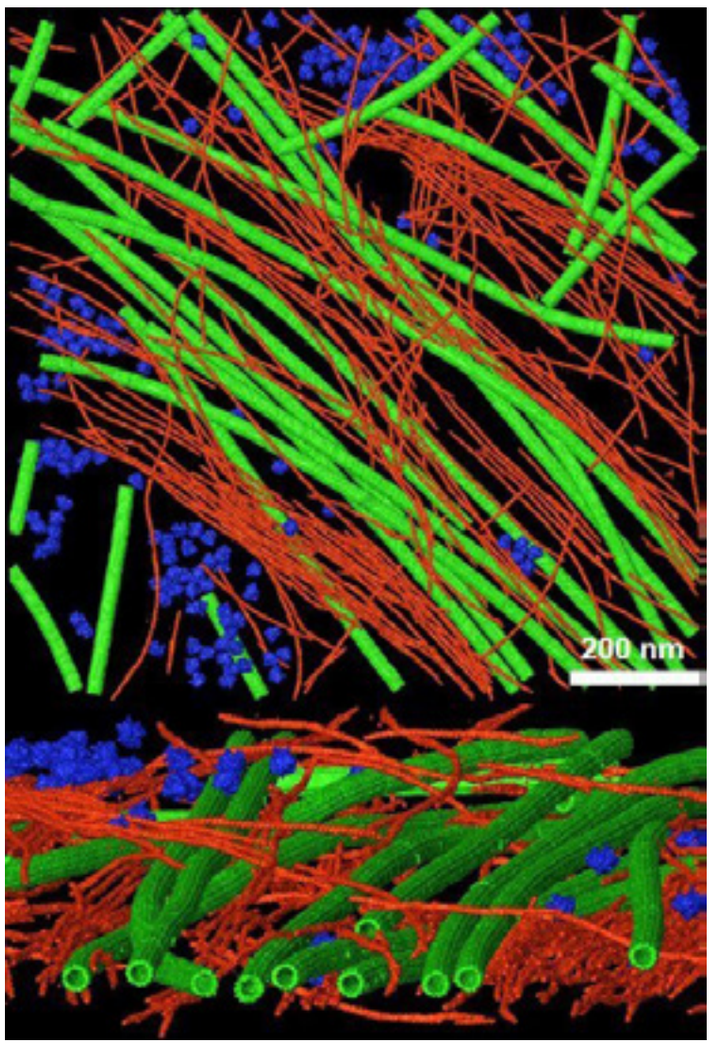
Structural Biology, RNA, Cytoskeleton, Cryo-Electron Tomography, Stress Response

Microtubules (MTs) are hollow cytoskeletal polymers that play essential roles in many cellular processes, including intracellular transport and chromosome segregation1. MTs possess a property called dynamic instability that causes MTs to switch between a stable and very dynamic states, exhibiting growth and disintegration, which allow MT ends to explore the cell volume for its targets. Such exploration often associate with higher MT curvature, frequently surpassing the limit posed by its own intrinsic material properties.



Dynamic instability induced MT curvature is thought to be regulated by MT-associated-proteins (MAPs) and posttranslational modifications of tubulins present in the MT lattice, the mechanistic bases of which are still obscure.

Recent developments in cryo-electron tomography1 enabled us to visualize subcellular ultrastructure within large eukaryotic cells by the introduction of novel sample preparation methods that include cryo-focused ion beam micro-machining, establishing correlative cryo-fluorescence for the localization of organelles inside the cell and their structural characterization via tomograms. Using these methods, we developed an assay combined with automated segmentation methods to locate and visualize MT-cytoskeleton inside mammalian cells with all the associated MAPs and determine their curvature. Remarkably, in situ curvature of cellular MTs fell clearly into distinct regimes depending on the cell cycle stages and cell types due to varied the local composition and organization of the cytoskeleton around the MTs. MTs that are co-crosslinked with the neighboring actin and intermediate filaments, tend to curve more than when MTs are more disperse or bundled. Furthermore, more curved MTs or growing MTs tend to accumulate elevated levels of lattice defects, hitherto unseen in cellular MTs. Therefore, our data showed intrinsic structure and distinct nanoscale organization of MTs impacts emerging biomechanics of cellular cytoskeleton.

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PDF 28

Ifnγ-Induced Mechanisms Restrict Intracellular Replication of the Lysosome-Adapted Bacterial Pathogen, Coxiella Burnetii

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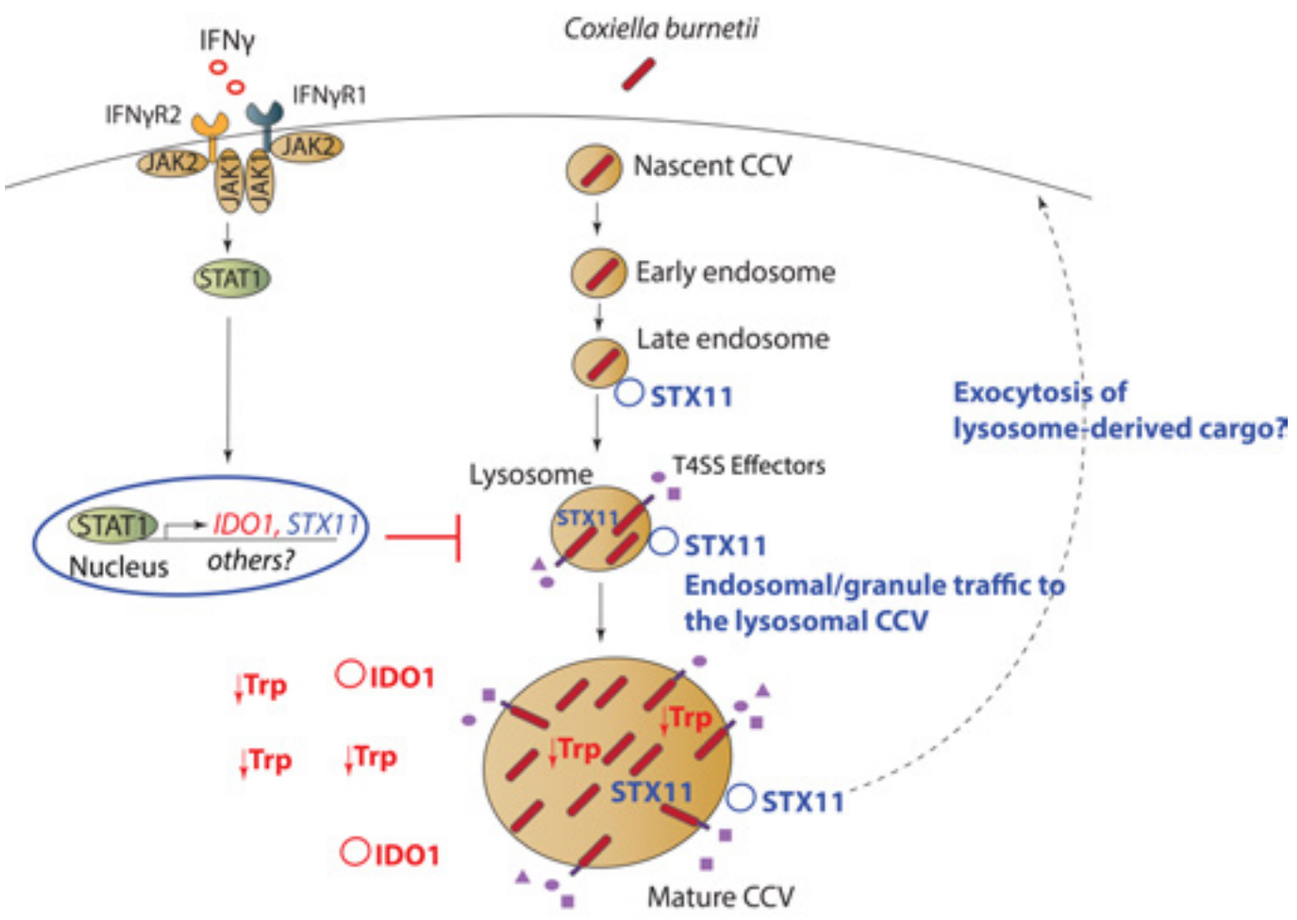
Host-Pathogen Interaction, Cell-Autonomous Immunity, Intracellular Pathogens, Innate Immunity, Vesicle-Traffic

The pro-inflammatory cytokine IFNγ promotes delivery of pathogen-occupied vacuoles to lysosomes for proteolytic degradation and pathogen clearance. While most intravacuolar pathogens prevent transit of their host-derived vacuole to the lysosome, the intracellular bacterial pathogen Coxiella burnetii requires transport to the lysosome for replication. The bacterium modulates membrane traffic to create a specialized autophagolysosomal compartment called the Coxiella-containing vacuole (CCV). Interestingly, IFNγ signaling inhibits intracellular replication of C. burnetii, raising the question of which IFN-activated genes and mechanisms might restrict replication of a lysosome-adapted pathogen. Thus, we used siRNAs to deplete IFN-induced genes in HeLa cells, monitoring replication of luciferase-expressing C. burnetii.



Our screen identified two host factors: Indoleamine dioxygenase 1 (IDO1) which catabolizes cellular tryptophan to kynurenine metabolites, and Syntaxin 11 (STX11), a SNARE protein that promotes tethering and fusion of lysosome-derived organelles with target membranes. IDO1 activity depletes tryptophan availability in cells, which suppresses replication of the tryptophan auxotroph C. burnetii. Knock-down of IDO1 or supplementing culture media with tryptophan rescued C. burnetii replication. Expression of IDO1 was also found to be sufficient to suppress C. burnetii replication in the absence of other IFNγ -induced factors. Thus, IDO1 renders the bacteria metabolically inactive by limiting an essential nutrient but this mechanism is not sufficient to kill C. burnetii. IFNγ-mediated restriction requires at least one additional factor, STX11. CCV size and bacterial replication is greater in STX11-deficient HeLa cells indicating that this protein negatively impacts infection. Fluorescence microscopy reveals STX11 on the CCV suggesting that STX11 may regulate vesicle-fusion events in the CCV. We are currently testing the hypothesis that absence of STX11 promotes retention of nutritional cargo in the CCV thereby augmenting CCV size and bacterial replication. These findings highlight the cell-autonomous defense mechanisms against pathogens that have evolved the capacity to replicate in hostile lysosomal environments.

PDF 29

Exploring the Sequence of PIWI-interacting RNAs

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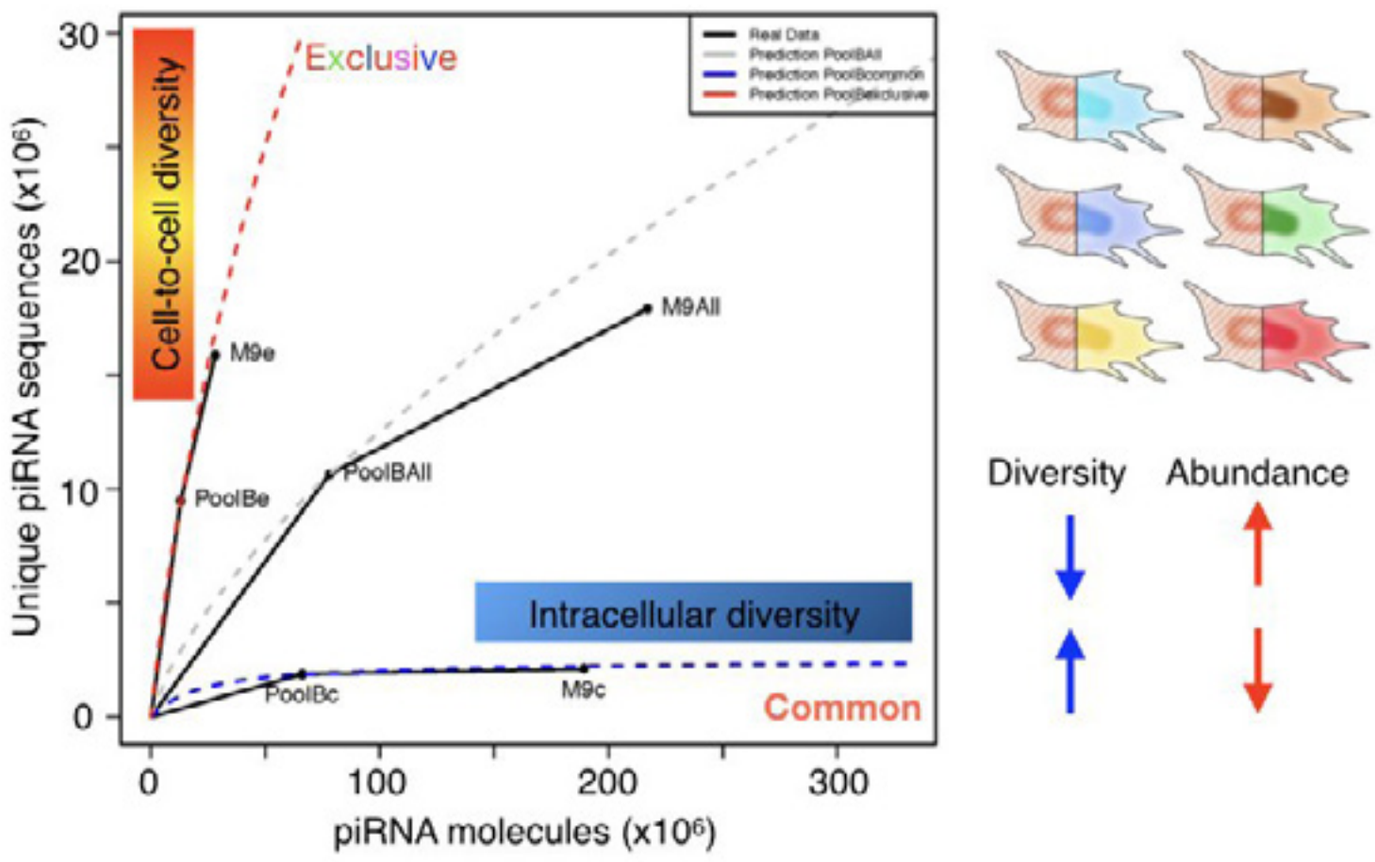
Non-Coding RNA, Transposons, Next-Generation Sequencing (NGS), Big Data Analysis, Tool and Algorithm Development

In animals, a discrete class of small RNAs, the PIWI-interacting RNAs (piRNAs), guard germ cell genomes against the deleterious activity of mobile genetic elements (transposons) that have colonized about half of our genomes1. Their ability to amplify and reinsert into novel genomic locations threatens genome integrity and must be restrained. Together with PIWI protein partners, piRNAs silence transposons at transcriptional and post-transcriptional levels. Mature piRNAs are generated from single or dual-stranded precursors that arise from discrete genomic loci, termed as piRNA clusters2. PiRNA clusters are mainly composed of transposon-derived repetitive sequences giving rise to hundreds and thousands of unique piRNA sequences, which are highly diverse in nature.

How this diverse pool of sequences is controlled to achieve specific restriction of transposons while avoiding off-target effects remains elusive. The sequence diversity of piRNAs in flies and mice has been systematically characterized. With increasing sequencing depth, we observe millions of unique piRNA sequences. This enormous diversity is only partly explained by the variability of piRNA 3´ ends and potentially reflects thousands of piRNA-generating genomic regions, piRNA clusters3. However, not every sequence seems to be required for efficient transposon restriction. Overall, our exploration of the piRNA sequence space identified subpopulations of sequences with vastly different importance for piRNA biology.



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PDF 30

Mechanism of Complement C4 Mediated Synaptic Pruning and Schizophrenia Microglia

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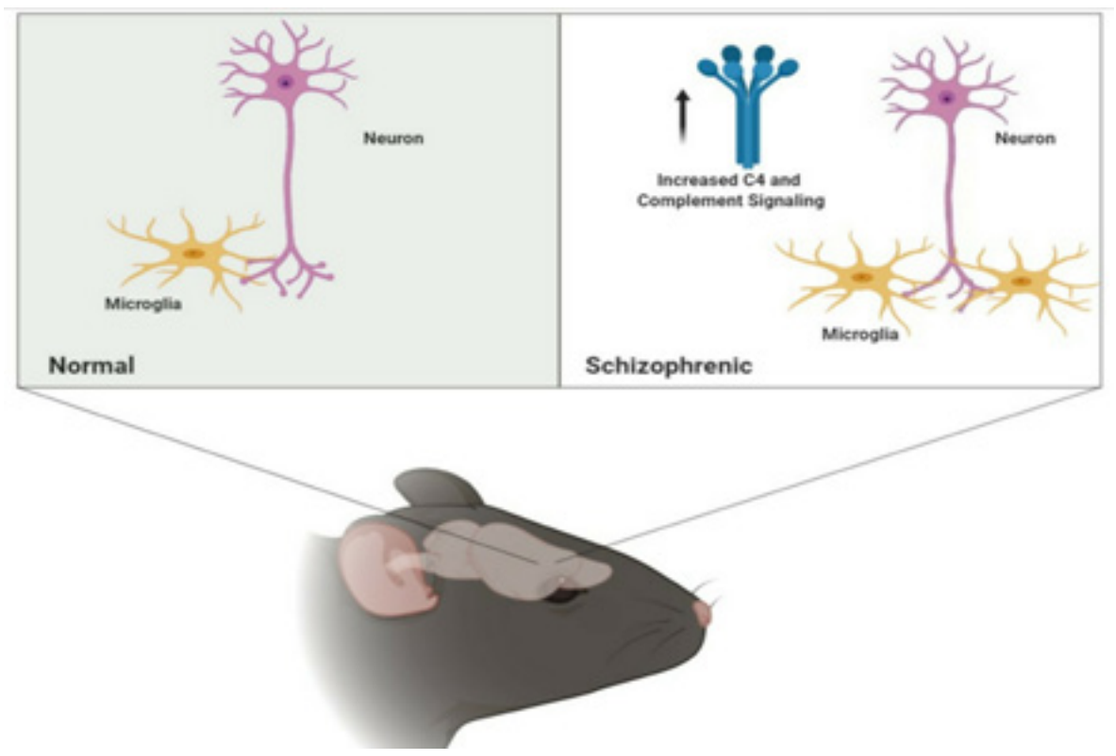
Schizophrenia, Complement Cascade, Adolescence, Synaptic Pruning

Synaptic and axonal pruning has long been recognized as a major developmental event that dramatically rewires cortical projections after birth, eliminating up to 70% of connections. It is hypothesized that defects in this process could result in psychiatric diseases like Schizophrenia. Recently this theory received a boost when a genome-wide association study1 identified copy number variants in the C4 gene as a risk factor for schizophrenia. The proteolytic cascade of complement signaling factors (C1q, C3, C4, C5) is thought to serve as an opsonization signal to promote microglia phagocytosis of synapses2. These data suggest that the C4 might act to increase microglial phagocytosis of synapses. We discovered that mice lacking Complement 3 receptor (CR3), a downstream receptor in complement cascade have a deficit in axon elimination as observed by an increased number of axons in the optic nerve. This suggests that complement cascade signaling regulates pruning of axons rather than synapses as suggested previously. In support of this hypothesis we found, using resting-state fMRI, that CR3 knockout mice have increased functional connectivity selectively in the prefrontal cortex and dorsal thalamus areas implicated in schizophrenia risk in humans. I will also discuss our results from a mouse model of C4 mediated Schizophrenia in the context of previous findings.



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PDF 31

Aberrant Activation of a Gastrointestinal Transcriptional Circuit Mediates Castration Resistance in Prostate Cancer

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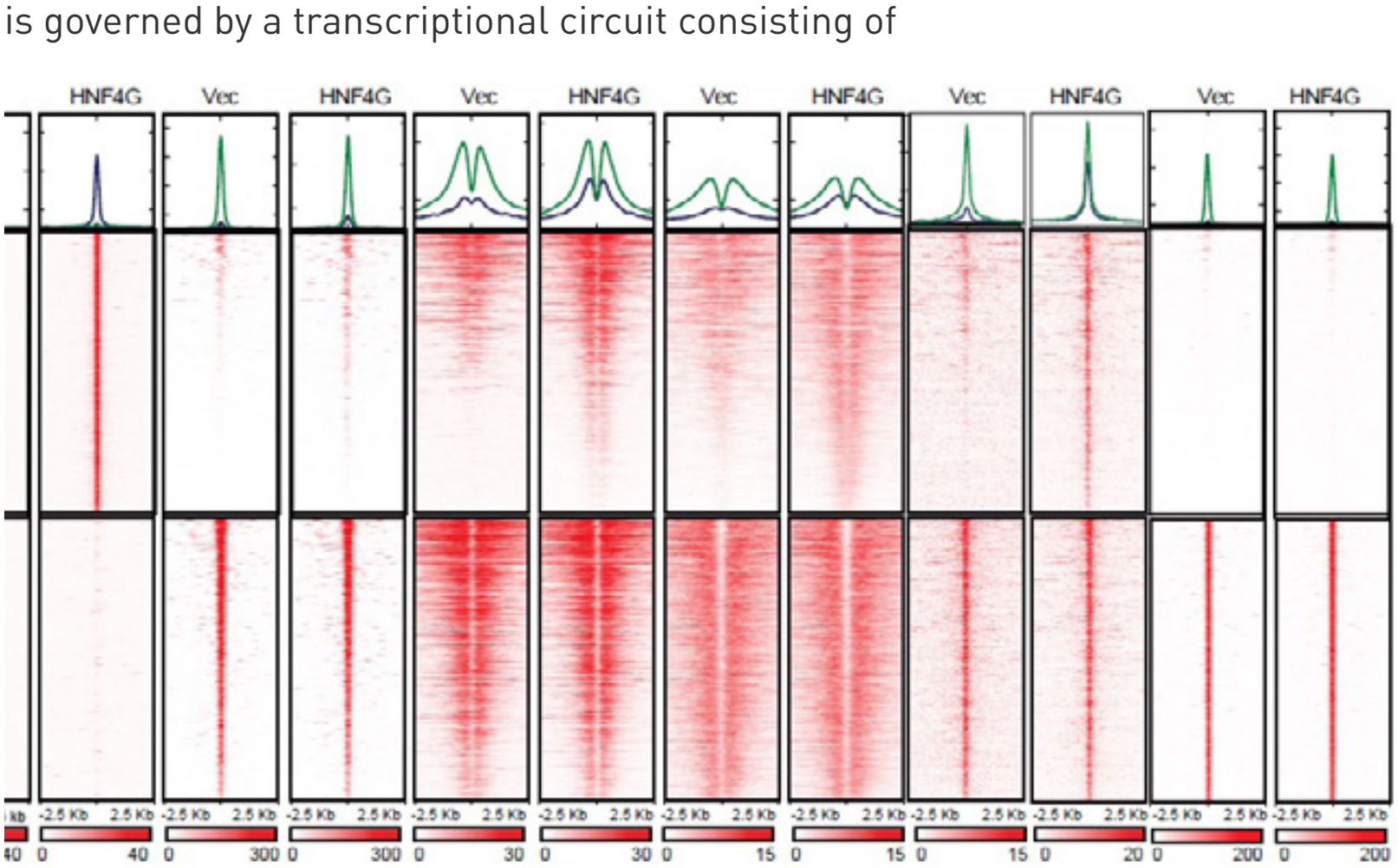
Castration Resistant Prostate Cancer, Enzalutamide Resistance, Enhancer Reprogramming, Organoid Technology, HNF4G

Prostate cancer exhibits a lineage-specific dependence on androgen signaling. Castration resistance involves reactivation of androgen signaling or activation of alternative lineage programs to bypass androgen requirement. We describe an aberrant gastrointestinal-lineage transcriptome expressed in ~5% of primary prostate cancer that is characterized by abbreviated response to androgen-deprivation therapy and in ~30% of castration-resistant prostate cancer. This program is governed by a transcriptional circuit consisting of HNF4G and HNF1A. Cistrome and chromatin analyses revealed that HNF4G is a pioneer factor that generates and maintains enhancer landscape at gastrointestinal-lineage genes, independent of androgen-receptor signaling. In HNF4G/HNF1A-double-negative prostate cancer, exogenous expression of HNF4G at physiologic levels recapitulates the gastrointestinal transcriptome, chromatin landscape, and leads to relative castration resistance.



Exogenous HNF4G expression creates new enhancer chromatin at binding sites.
Histograms (top) show the average normalized tag counts of HNF4G, FOXA1, H3K27Ac, H3K4me1, AR ChIP-seq and ATAC-signal in LNCaP cells with exogenous expression of HNF4G or vector control at top 1,000 HNF4G and AR binding sites. Heatmap shows the tag densities of HNF4G, FOXA1, H3K27Ac, H3K4me1, AR and ATAC-signal at the top 1,000 HNF4G (middle) or AR (bottom) binding sites.

PDF 32

Novel Signaling Pathway Links EBNA1 mRNA Translation Stress With Cell Proliferation

mRNA Translation, Viral Oncology, Cell Signaling, Ribosome Biogenesis, RNA Biology

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Ribosome and protein biogenesis are major metabolic events that control cellular growth and proliferation. Impairment in ribosome biogenesis pathways and mRNA translation is associated with pathologies such as cancer and developmental disorders. Processes that control global protein synthesis are regulated tightly at multiple stages by numerous factors and linked with various cellular signaling pathways. Many of these merge on the growth-promoting factor c-Myc, which induces ribosome biogenesis by stimulating Pol I, Pol II, and Pol III transcription. Interestingly, the pathway by which cells sense and respond to dysfunctional mRNA translation and how this is synchronized to cell proliferation and growth is not well understood. Epstein-Barr virus (EBV)-encoded EBNA1 carries a glycine-alanine repeat sequence (GAr), which spans over 200 residues depending on the viral strain. This repeat serves to suppress its own mRNA translation in cis thereby minimizes the production of EBNA1-derived antigenic peptides for the major histocompatibility (MHC) class I pathway and, thus, helps the virus to evade the immune system. We have shown recently that mRNA translation stress triggered by EBNA1-GAr activates c-Myc, through a specific induction of E2F1 protein synthesis via a PI3Kδ -dependent pathway. Current work addresses the molecular mechanism of this stress response pathway, with more focus on E2F1 translation regulation by an oncoprotein HDM2.

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PDF 33

Environmental Factor Effects on Tree Seedling Recruitment in a South African Humid Savanna

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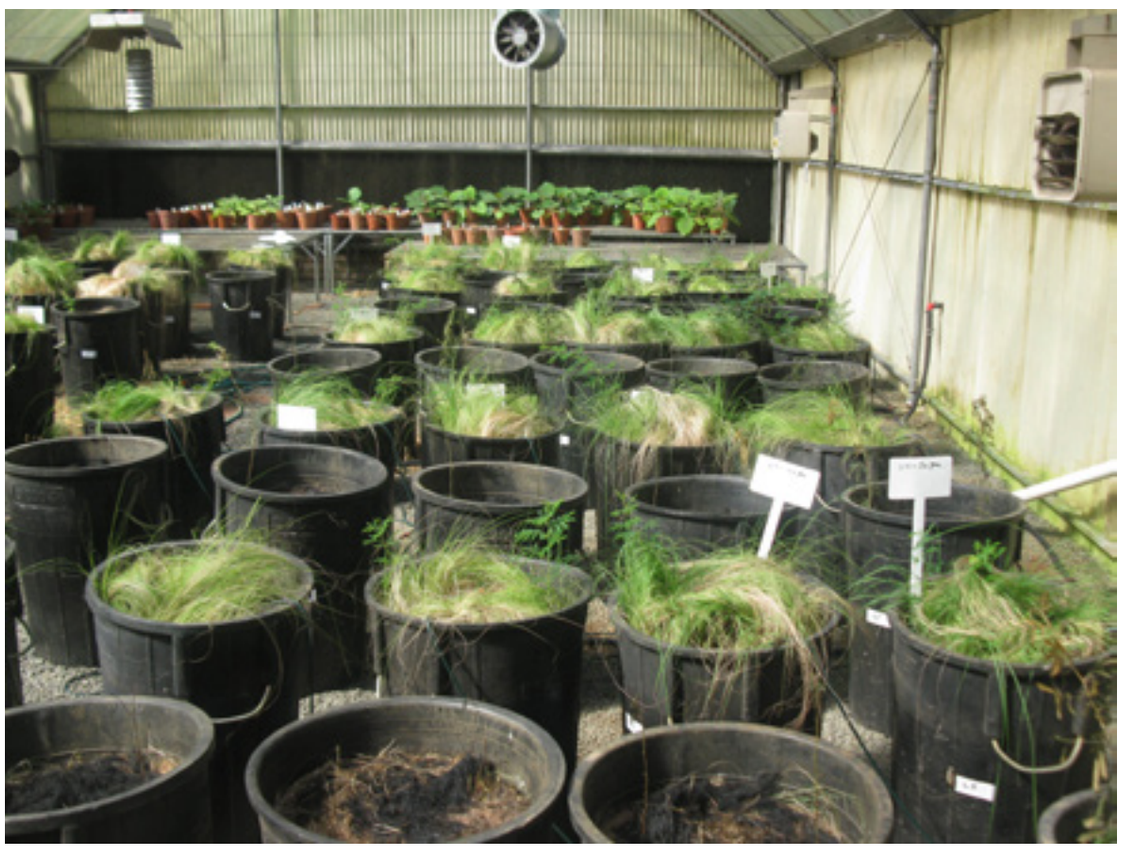
Ecosystem Structure and Dynamics, Climate Change, Plant Ecology, Indian Savannas and Forest Systems, Fire Ecology, Carbon Sequestration

Savannas are a part of major biomes of the world, occupying about 20% of global land cover and 40% of Africa. Tree invasion in savannas is an extensive problem reducing herbivore palatable grass, largely affecting rural livelihoods. However, importance of trees in carbon sequestration and human economy cannot be overlooked. Therefore tree-grass balance in savannas is crucial and it is essentially maintained through woody plant establishment in the ecosystem. Savanna trees are most vulnerable to environmental fluctuations during their seedling stage (Scholes & Archer 1997) especially in the presence of competing grasses. Therefore, tree establishment phase is a key process in maintaining savanna ecosystem structure and function (House et al. 2003; Sankaran et al. 2005).



We studied various environmental factors affecting seedling survival and growth of savanna tree species. We conducted an experiment to assess the effects of fire and nutrient gradient on four African Acacia spp. under greenhouse conditions. In a split-plot design, we studied two level factor effects of water, shade, nutrients, grass competition, and simulated herbivory on eight savanna tree species. We measured the survival and growth of saplings of eight selected savanna tree species, and identified the factors key to their recruitment, particularly in a humid savanna system. Grass competition by far had the highest negative impact on seedling establishment. In general, it has been observed that shade under large trees in savannas provide grass free and nutrient rich conditions conducive for seedling establishment, but we found that shade has a negative influence on seedling growth. Seedling growth rate was positively influenced by fire, nutrients and regular water availability.

PDF 34

Physicochemical Properties of Ligand-Activated Enhancer Complex Determine Transcriptional Response to Signaling Programs

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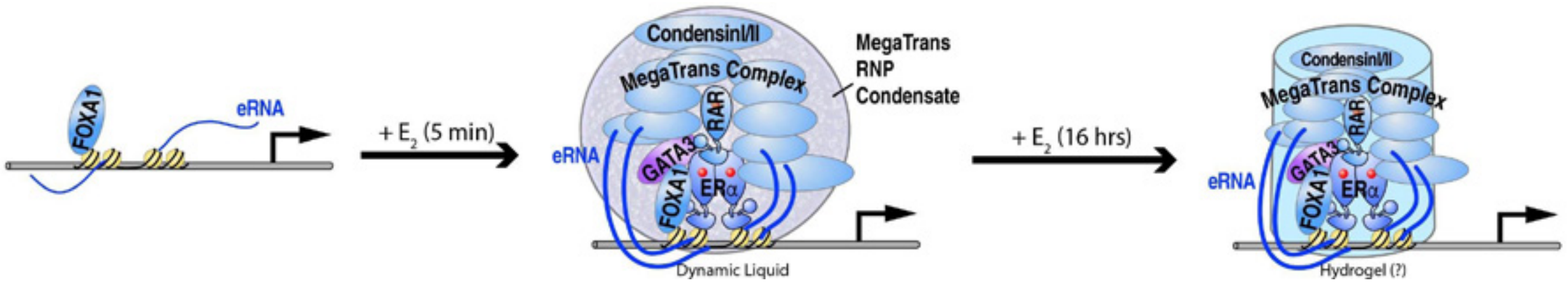
Gene Regulation, Breast Cancer, Transcription co-factors, Biomolecular Condensates, Mammary Gland Biology

A crucial feature of differentiated cells is their ability to rapidly activate large transcriptional programs in response to signals, orchestrated by signal-inducible enhancers. Enhancers are transferable DNA elements that regulate target genes within the confines of Topologically Associated Domains (TADs) through Cohesin-dependent looping. In this study, we report that 17β-estradiol (E2) rapidly increases the spatial proximity of a cohort of particularly strong E2-responsive enhancers located in widely separated TADs. These estrogen receptor ‘± (ER‘±) bound enhancers are characterized by high enhancer RNA (eRNA) induction and recruitment of mega-dalton sized multi-transcription factor complex (MegaTrans) which together function as a ribonucleoprotein complex. In order to test the hypothesis that spatial cooperation of distant enhancers is established through phase separation events on strong enhancers, we treated breast cancer cells with 1,6-Hexanediol (1,6-HD), aliphatic alcohol that disrupt phase-separated structures, followed by assessing transcriptional activity in response to E2 by Global Run-On Sequencing (GRO-Seq). Surprisingly, 1,6-HD selectively deactivated the MegaTrans bound strong ERα enhancers, not weak ERα enhancers or strong non- ERα enhancers. 1,6-HD specifically disrupts the assembly of MegaTrans on most robust ERα enhancers. Our data suggest that long-distance enhancer association and co-operativity requires E2-induced assembly of ribonucleoprotein structures composed of eRNA, Condensins and the MegaTrans complex at strong ERα bound enhancers and their co-localization with phase-separated interchromatin granules (ICGs). These findings along with other pieces of evidence that support a new model for establishment and cooperative activation of inducible enhancers following principles of liquid-liquid phase separation will be discussed.



PDF 35

Metabolic Constraints Drive Self-Organization Of Specialized Cell Groups

Microbiology, Biofilms, Metabolism, Genetics, Phenotypic Heterogeneity

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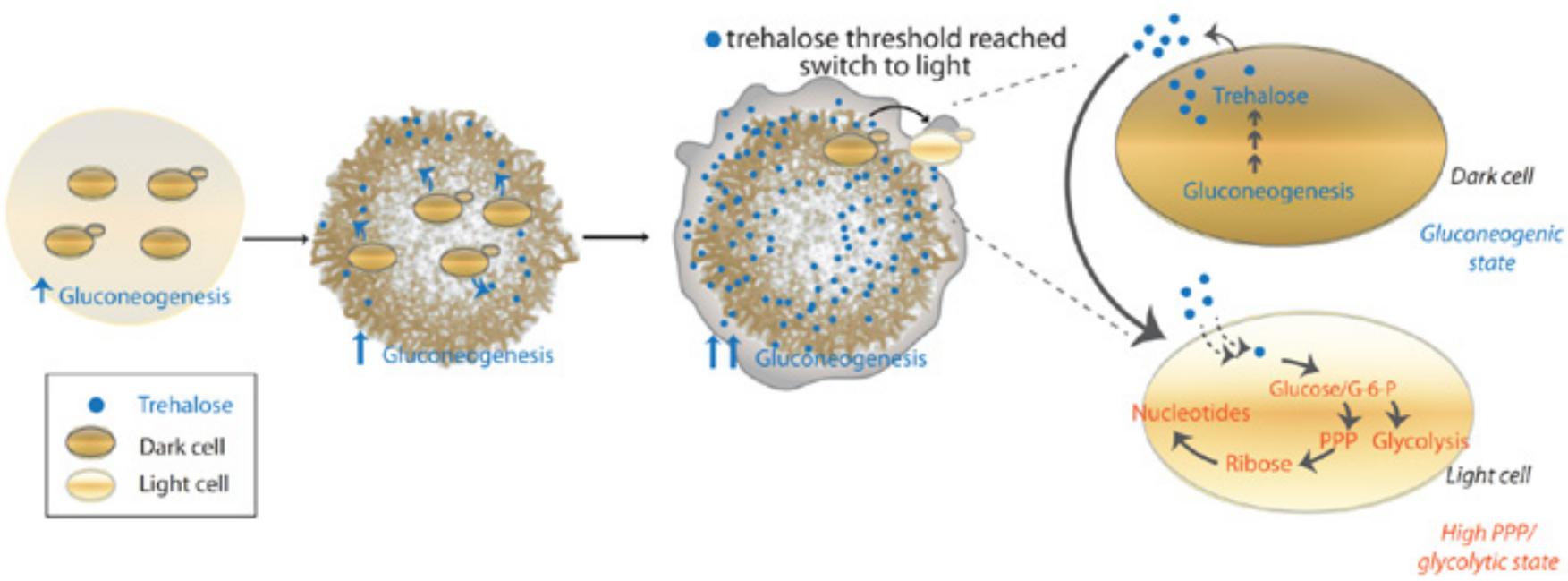
How phenotypically distinct states in isogenic cell populations appear and stably co-exist remains unresolved. We find that within a mature, clonal yeast colony developing in low glucose, cells arrange into metabolically disparate cell groups. Using this system, we model and experimentally identify metabolic constraints sufficient to drive such self-assembly. Beginning in a uniformly gluconeogenic state, cells exhibiting a contrary, high pentose phosphate pathway activity state, spontaneously appear and proliferate, in a spatially constrained manner. Gluconeogenic cells in the colony produce and provide a resource, which we identify as trehalose. Above threshold concentrations of external trehalose, cells switch to the new metabolic state and proliferate. A self-organized system establishes, where cells in this new state are sustained by trehalose consumption, which thereby restrains other cells in the trehalose producing, gluconeogenic state. Our work suggests simple physico-chemical principles that determine how isogenic cells spontaneously self-organize into structured assemblies in complimentary, specialized states.



PDF 36

Forest Tree Species Shift: Conseqeunces on Belowground Microbial Communities and Carbon Stock

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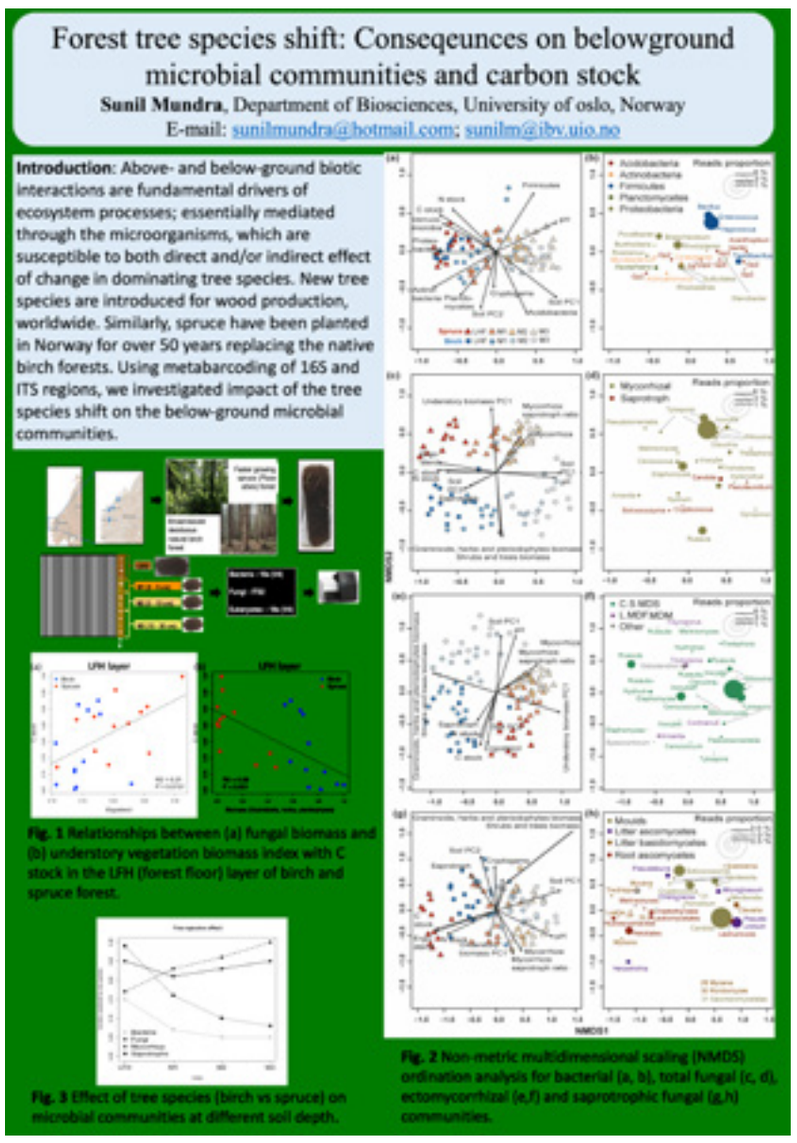
https://www.mn.uio.no/ibv/english/people/aca/sunilm/

Microbial Ecology, Metabarcoding/Metagenomics, Plant-Microbial Interactions, Climate Change: Effect on Microbiota, Forest Carbon Sequestrations

Above- and below-ground biotic interactions are fundamental drivers of ecosystem processes; essentially mediated through the microorganisms, which are susceptible to both direct and/or indirect effect of change in dominating tree species. Tree species are introduced for wood production, worldwide. Similarly, spruces have been planted in Norway for over 50 years replacing the native birch forests. Here, we hypothesised that depth-dependent variation in soil chemistry should affects the distribution and co-occurrence patterns of microbial communities; and impact of tree species change on communities should be stronger on upper organic layer and on eukaryotes compared to deeper mineral layers and free-living bacteria. We employed DNA metabarcoding in conjunction with network analyses of bacteria, fungi, as well as other micro-eukaryotes, sampled in four different soil strata in Norwegian birch and spruce forests. We observed significant influence of tree species on the microbial diversity, being lower in the spruce forests. Tree species had stronger impact on fungal communities compared to bacteria, and more pronounced in the upper leaf litter-humus layers, in comparison to the lower mineral soil layers, and patterns were related with understory vegetation. Higher C stock in upper organic layer of spruce was mediated by higher fungal biomass. Abundance of mycorrhizal fungi were relatively higher in the spruce forests and vice versa for saprotrophic fungi. Strong compositional turnover in microbial assemblages with depth was detected for all organismal groups. The proportions of copiotrophic bacteria, Arthropoda and Apicomplexa were markedly higher in the organic layer, while patterns were opposite for oligotrophic bacteria, Cercozoa, Ascomycota and ectomycorrhizal fungi. Study supports the view that different microbial groups are strongly adapted to different niches and forest soil strata, with varying level of interactions along the depth gradient, and shift in tree species is accompanied by a shift in microbial communities with tentative impacts on C stocks.



PDF 37

Integrating Neutrophil Fronts and Backs with the mTORC2 Mechanotransduction Pathway

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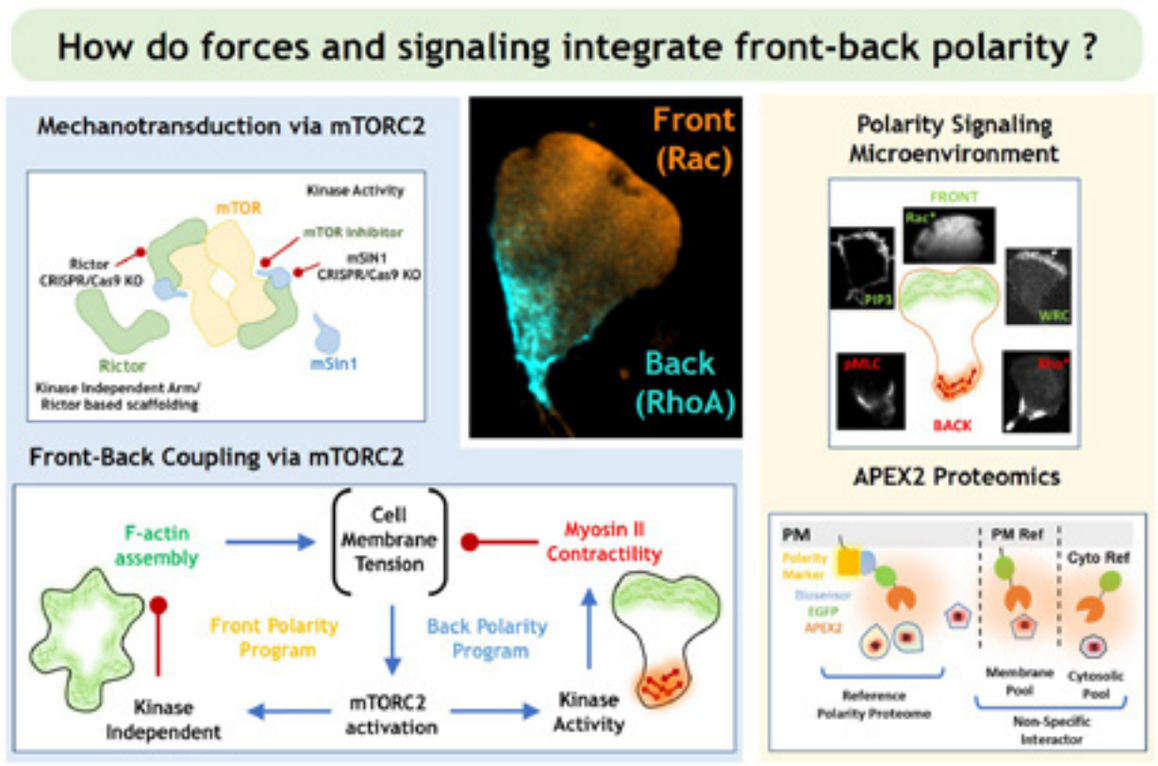
Cell Polarity and Motility, Mechanotransduction, Immune Cells, Cellular Organisation, Quantitative Live Cell Microscopy

Neutrophils leverage feedback between mechanical forces and biochemical signaling to guide their polarity and motility during immune surveillance. For efficient movement, cells need to establish a single leading edge. We recently found that tension-based communication between actin protrusions (relayed by the PLD2/ mTORC2 pathway) are responsible for long-range competition between protrusions for proper control of polarity and movement. mTORC2 is an evolutionarily conserved regulator of cellular growth, proliferation and metabolism. Surprisingly, this signaling node has been co-opted for mechanochemical regulation of membrane homeostasis and cellular polarity or motility in systems ranging from yeast to Dictyostelium to neutrophils. Here we probe the molecular logic of how mTORC2 regulates the motility machinery.



The kinase activity of mTORC2 is the most well-characterized route of regulating downstream effectors, but the complex is also thought to scaffold recruitment of some effectors in a kinase- independent fashion. Which of these activities links mTORC2 to the motility machinery is not well understood. Here we investigate this question using a combination of genetic and pharmacological approaches to selectively impair the kinase-dependent versus independent signaling roles of the complex. We find that the tension-based inhibition of Rac activity that enables competition between protrusions is gated by the kinase-independent role of the complex, whereas the mTORC2 kinase arm is essential for regulation of Myosin II activity at the trailing edge. With live cell imaging of Rac/Rho biosensors, we show the necessity of both of these branches of mTORC2 signaling for leading and trailing edge organization, cell polarity, movement, and guidance. Our results show how physical forces activate the kinase dependent and independent arms of mTORC2 to integrate both the front (Rac) and back (Rho) polarity programs during neutrophil motility. Finally, we are using APEX2 proximity-biotinylation proteomics to interrogate the proximal signaling environment at the front and back of neutrophils.

PDF 38

Cellular Heterogeneity Underlying Poly-Functional Drosophila Fat Body Tissue

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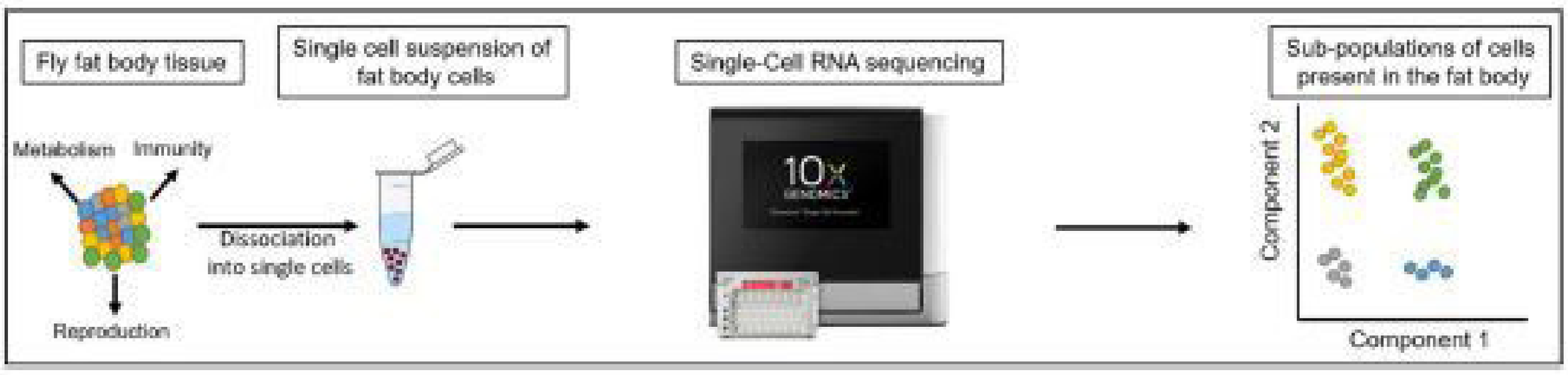
Immunity, Evolution, Drosophila, Trade-offs, Genetics

The insect fat body is a multifunctional tissue that can serve as a generic model for how poly-functional organs achieve diversified tasks, including management of immune response to infection. Fat body functions span those of at least three vertebrate organs: immune system, adipose tissue, and liver. The fat body is the primary systemic immune organ in insects, but also serves as the metabolic control organ responsible for storage and release of lipids and other nutrients and produces most of the yolk used to provision developing eggs. This is analogous to vertebrate adipose tissue, which is a cellularly heterogeneous tissue that stores lipids and also produces cytokines and inflammatory reactions in response to infection. We hypothesize that cellular heterogeneity in the fat body allows subsets of cells to specialize in each function, collectively resulting in tissue with highly varied capabilities. We further hypothesize that stimuli such as bacterial infection alter either the number or identity of sub-functionalized cells, resulting in quantitatively dynamic responses at the tissue level. We are using single-cell RNA sequencing (scRNAseq) on the 10X platform to test the hypothesis of cellular heterogeneity in Drosophila melanogaster (fruit fly) fat body. We are using flies which remain either challenged or unchallenged with a gram-negative bacteria Providencia rettgeri, both while actively engaged in egg development and in the absence of reproductive investment. We identify cells subpopulations within the fat body which are responsible for specific functions. We are further identifying plasticity in the fat body tissue under different physiological environments. We will use the data to understand how poly-functional tissues balance competing physiological functions, providing a mechanistic understanding for the classical life history tradeoff between immunity and reproduction.



PDF 39

Long-Range Control Of Striatal Interneuron Network Development

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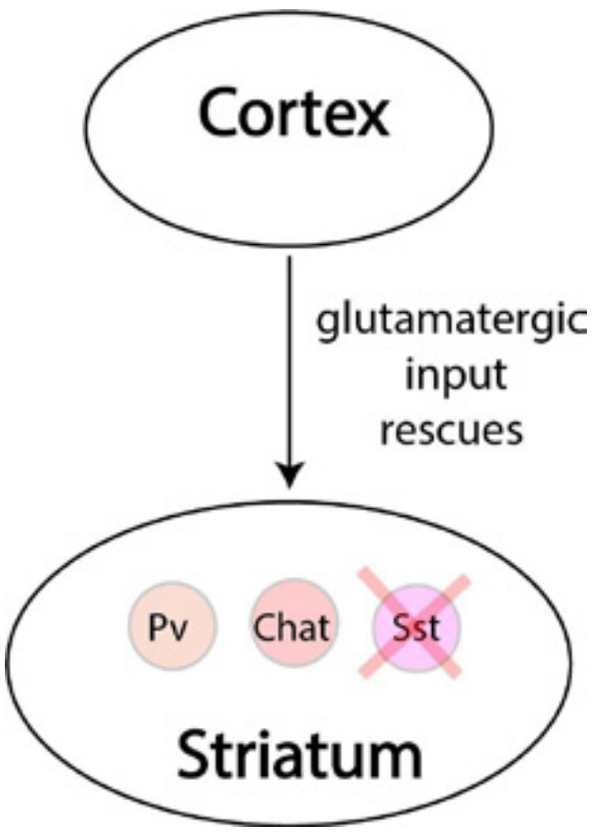
Motor Control, Sensorimotor Transformation, Cortex, Striatum, Interneurons

Complex neuronal circuits have evolved as balanced networks of excitation and inhibition. In the neocortex, this balance is achieved through programmed cell death of cortical excitatory neurons between postnatal days 2-5 (P2-P5), followed by the death of MGE derived interneurons between P6-P101. Rescuing excitatory neurons from cell death, through the removal of the pro-apoptotic BCL2 family proteins BAX and BAK, leads to a concomitant rescue of MGE interneurons while increasing cortical activity also rescues MGE interneurons1. The striatum also contains MGE derived interneurons that undergo programmed cell death between P6-P10 but the mechanisms governing the establishment of appropriate numbers of MGE interneurons remains poorly understood. Here we demonstrate an important role for neocortex in establishing appropriate numbers of striatal interneurons. Rescuing excitatory neurons in the neocortex, through Cre dependant removal of BAX and BAK, led to a rescue of parvalbumin expressing (PV+) but not cholinergic (Chat+) and somatostatin expressing (SST+) interneurons. Increasing cortical activity, through Cre dependant expression of the activating DREADD hM3Dq, rescued PV+ and Chat+ but not SST+ interneurons. Eliminating cortico-striatal neurons through the Cre dependant removal of STXBP1 led to a reduction in the number of striatal MGE neurons. Blocking cortico-striatal excitatory neurotransmission through Cre dependant expression of Tetanus toxin led to a reduction in the number of striatal MGE interneurons. Taken together, our data points to a key role for cortical glutamatergic synaptic transmission in regulating the striatal interneuron network during early postnatal development.



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PDF 40

Osteocalcin Dependent Uptake of Abeta42 by Astrocytes and Subsequent Degradation: a Means to Manage Alzheimer's Disease

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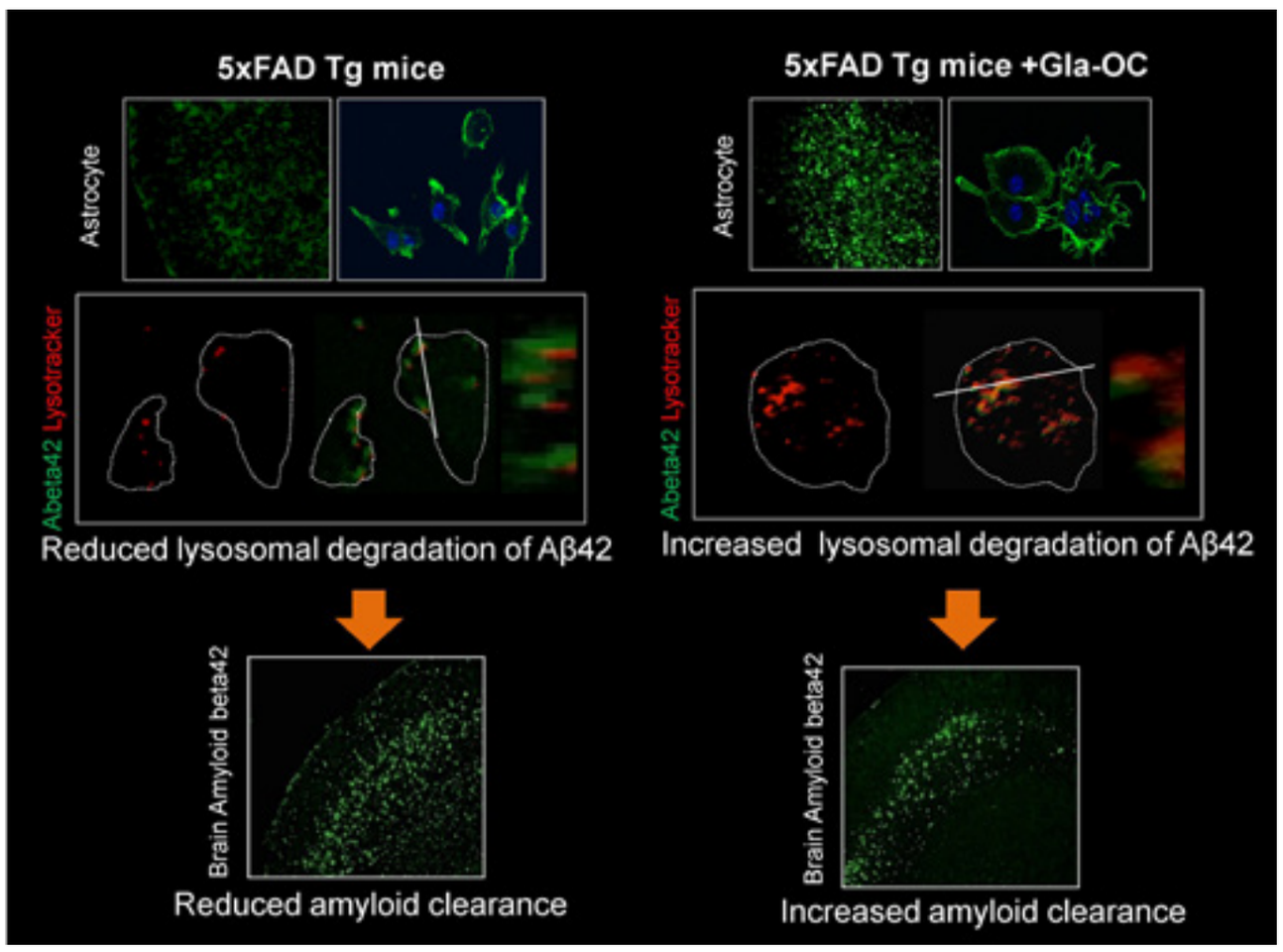
Glial biology, Amyloidopathy, Lysosome biogenesis, Osteoimmunology, Microvesicles

Alzheimer's disease (AD), a devastating disease that affects the elderly population is at an alarming rise in India. This disorder is normally characterised by amyloid deposition, neuronal loss and cognitive decline. As of now there is no cure for AD. Moreover the repeated failures in clinical trials which aims at targeting some of the critical known pathways of AD pathogenesis clearly shows an urgency to identify actual cause(s) for AD initiation so that the disease may be curbed at the preliminary stage itself. Here in this study carboxylated osteocalcin (Gla-OC), a protein imperative for bone mineralization is highlighted for its role in preventing AD progression. It was identified that familial mouse models of AD like APPswe/PS1 and familial (5xFAD) transgenic mice display osteocalcin deficit in bone with AD progression. When Gla-OC was administered to 5xFAD transgenic mice after the onset of amyloid deposition via sc injection, there was improvement in behavioural deficits, substantial reduction in amyloid deposition in cerebral cortex and decrease in oxidative stress and inflammation in brain. Importantly, the population of astrocytes, an important set of immune-competent cells of brain was increased in cerebral cortex of transgenic mice treated upon Gla-OC treatment. To determine the role of these cells in amyloid clearance associated with Gla-OC, EAAT+CD11b- astrocytes from transgenic mice were isolated and exposed to Gla-OC. Gla-OC stimulated extracellular uptake of amyloid beta42 and lysosomal activation evidenced by nuclear translocation of transcription factor EB, cathepsin D cleavage and activity and reduction in intracellular level of amyloid beta42. To sum up, these findings demonstrate the novel immunomodulatory role of Gla-OC to reduce amyloid deposition in brain and thereby holds promise as a therapeutic agent for AD.



Young Investigators

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N-Acetyl Cysteine Prevents Cigarette Smoke Induced Defective Phagocytosis

YI 02 AMIT LAHIRI

Mitochondrial Dynamics and Gut Bacteria Crosstalk In Inflammatory Bowel Disease Pathogenesis

YI 03 AMITA BARIK

Depicter: A Center for Predictors of Disordered Regions and Their Functions

YI 04 ARINDAM MONDAL

Molecular Signatures in the Bat Influenza Virus Polymerase -Determinant Of Host Tropism

YI 05 ATUL KUMAR

Molecular Insights into Parkinson's Disease

YI 06 CIBIN TR

TGFβ2 Mediated Epithelial to Mesenchymal Transition: Role of AGE-RAGE Interaction

YI 07 DHANESWAR PRUSTY

Understanding the Biochemical Features of Apicoplast RNA Polymerase of Plasmodium falciparum and its Implication for Antimalarial Drug Development

YI 08 DHAVAL PATEL

Molecular Characterization of Isoprenoid Pathway Protein (PaDXR) from P. aeruginosa

YI 09 HIMANSHU SHEKHAR

Harnessing ultrasound and Microbubbles for Next Generation Imaging and Therapy

YI 10 JAGADIS GUPTA KAPUGANTI

Novel Role of Mitochondrial Alternative Oxidase Under Hypoxia to Drive Energy Production via Phytoglobin-Nitric Oxide Cycle

YI 11 JALAJ GUPTA

Coordinated mTOR Activation and BMP Inhibition Preserve Tumor Cell Survival and Stemness Upon Loss Of LGR5+ Cells in Colorectal Tumors

YI 12 KARLA PATRICIA MERCADO-SHEKHAR

Quantitative Ultrasound Imaging Techniques for Tissue Characterization

YI 13 KRISHNA SWAMY

Proteotoxic Stress Due to Loss of Interaction Partners Induces Reproductive Isolation in Yeast Hybrids

YI 14 MANISH TIWARI

Unravelling the Role of miRNAs in Light Signalling for the Divergent Plant Responses to Vegetation Proximity

YI 15 MANJARI KIRAN

Identification of Synthetic Lethal Gene Interaction in Cancer

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Catechewing Coli: Genetically Engineering Bacteria to Remove the Color of Paan Stains

YI 17 MEGHA KUMAR

Role of Dynein Light Intermediate Chains in Embryonic Divisions and Vertebrate Embryogenesis

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Weaker Plant-enemy Interactions Decrease Tree Seedling Diversity with Edge-Effects in a Fragmented Tropical Forest

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Accurate Prediction of Protein Dynamics from Markov Models: Long vs. Short Trajectories

YI 20 **MOHIT KUMAR JOLLY**

Identifying Inhibitors of Epithelial-Mesenchymal Plasticity through a Network Topology Based Approach

YI 21 **N AYYADURAI**

Genetically Encoded L-3,4-Dihydroxyphenylalanine in Glycoside Hydrolases alter the Structural Helical Propensity and Catalytic Chemistry Enabled Expeditious Skin Fibre Opening

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Mangrove Community Resilience and Succession After Subsidence Inflicted Sea Level Rise in Car Nicobar Islands, India: Implications for Mangrove Conservation

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Diabetes Induces Pathological Changes in the Lung through Activation of TGF-β Signaling Pathways

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Gene Editing Mediated Gene Therapy for β-Hemoglobinopathies

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Elucidating the Role of Intrinsically Disordered Regions in Regulation of Function of Eukaryotic Transcription Factors

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Understanding the Heterogeneity in Nuclear Morphology of Adherent Cells

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An Integrated and Multidisciplinary Approach to the Development of Ocular Theranostic Solutions

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mTORC2-Mediated Regulation of Sphingolipid Biosynthesis is Involved in Breast Cancer Progression

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YI 38 **VANDAN NAGAR**

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YI 39 **VELMURUGAN G**

Gut Microbiota in Toxicological Risk Assessment of Drugs And Chemicals: The Need of Hour

YI 40 **VIVEK BORSE**

Lateral Flow Immunosensing: Material Processing and Parameter Optimization

YI 01

N-Acetyl Cysteine Prevents Cigarette Smoke Induced Defective Phagocytosis

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Chest Research Foundation, Pune

Immuno-Metabolism, Glycolysis, Mitochondria, Oxidative Stress, Cigarette Smoke

Background- Detective phagocytosis is a defining characteristic for the development of cigarette smoke induced chronic obstructive pulmonary disease (COPD), leading to frequent respiratory infections and exacerbations. These exacerbations are responsible for more than half the cost associated with the management of COPD.

Methods- RAW 264.7 cells were exposed to cigarette smoke condensate (CSC) generated from 4 cigarettes for 1hr. Cell viability was measured using MTT reduction assay and the increase in cellular reactive oxygen species (ROS) was measured was measured using dihydroethidium (DHE) or 2', 7'-dichlorofluorescin diacetate (DCFDA). Phagocytosis was measured using fluorescently labeled Streptococcus pneumoniae or Haemophilus influenza or using the pH rodo labelled Staphylococcus aureus.

Results- A dose-dependent decrease in cell viability was observed with CSC exposure in RAW 264.7 cells. CSC exposure also lead to a dose-dependent increase in ROS levels measured using DHE and DCFDA. A significant dose dependent decrease in phagocytosis was observed after CSC exposure as measured by internalization and the maturation of the phagolysosome. 10mM NAC supplement was supplementation was able to rescue the CS- induced decrease in cell viability, increase in ROS and the defective phagocytosis.

Conclusion- NAC is able to rescue the defective phagocytosis observed in COPD.

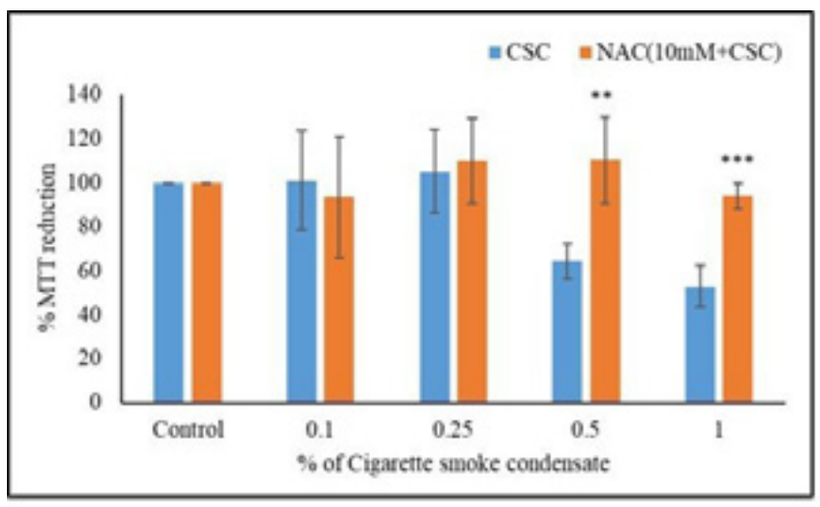

Fig. 1 – Effect of 1h CSC exposure on ability of RAW264.7 cells to reduce MTT with or without NAC (10mM) pre-treatment.

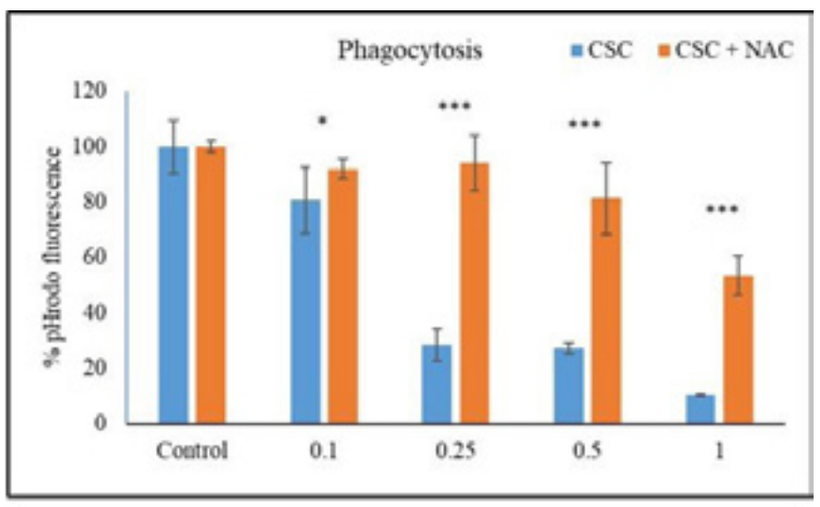

Fig. 2 - Effect of 1h CSC exposure on ability of RAW264.7 cells to phagocytose fluorescently labelled bacteria with or without NAC (10mM) pre-treatment.

YI 02

Mitochondrial Dynamics and Gut Bacteria Crosstalk In Inflammatory Bowel Disease Pathogenesis

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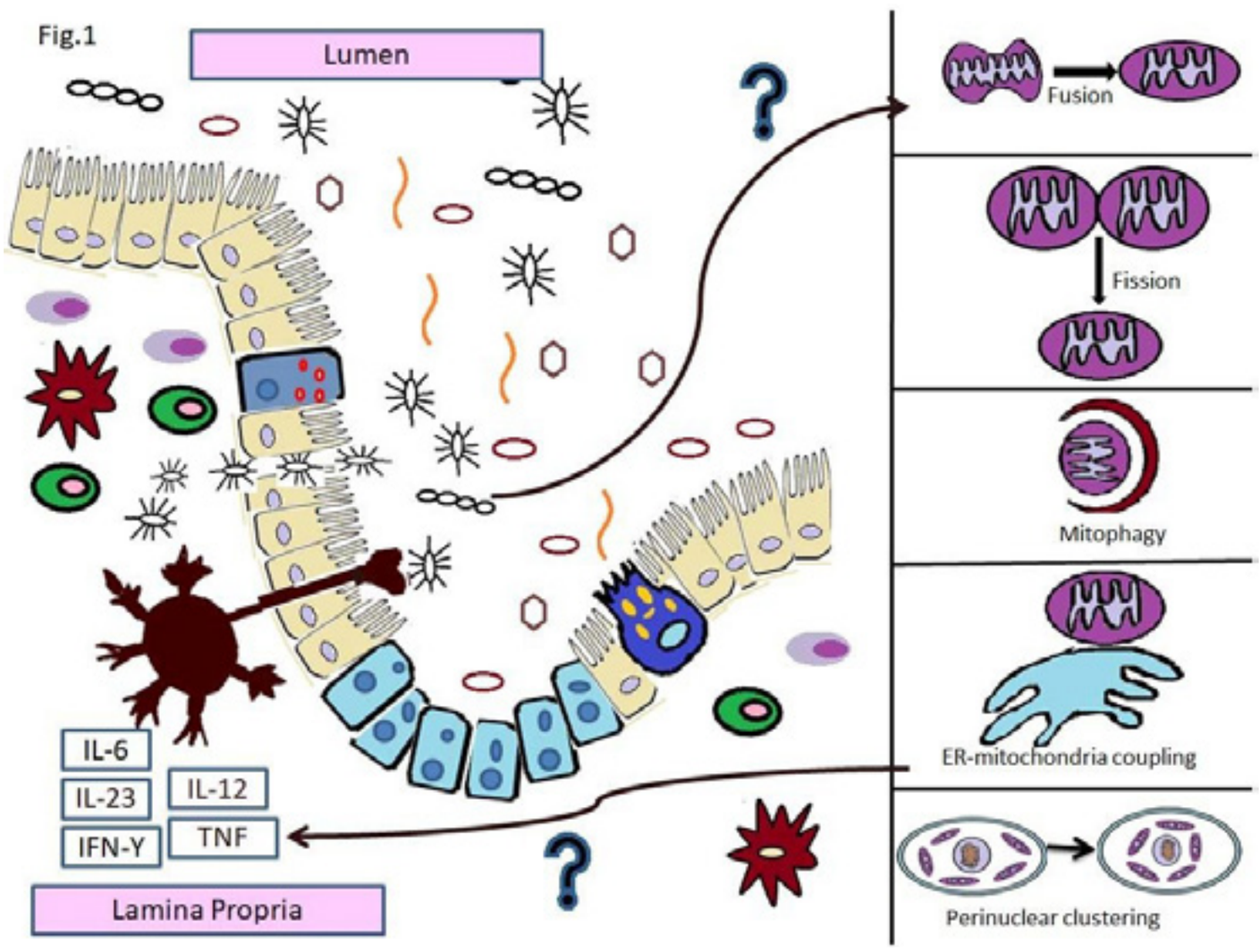
Inflammatory Bowel Disease, Mucosal Immunology, Cytokine, Mitochondrial Dynamics, Gut Microbiome

Crohn's disease (CD) and ulcerative colitis (UC), the main clinical pathologies of inflammatory bowel disease (IBD), arise due to the inter-play of genes that regulate immune function. In the susceptible host, an altered gut flora leads to an unbalanced cytokine production and tight junction dysfunction resulting in chronic inflammation and pain in the intestine. Mitochondria have recently emerged as important organelles that regulate antibacterial and antiviral immune pathways and these functions are intimately linked to their morphology. Cellular mitochondria constantly undergo fusion, fission, directed movement in the cell and mitophagy mediated clearance- collectively termed as 'mitochondrial dynamics'.

There are multiple proteins like clustered mitochondria protein homolog (Cluh, KIAA0664) that coordinate to regulate the mitochondrial dynamics. Cluh is a RNA binding protein and decides mitochondrial localization and function. We hypothesized that gut microbiota mediated host mitochondrial dynamics alteration will decide cytokine production from the inflamed intestinal tissues. Mitochondrial morphology/position on the other hand will crosstalk and shape the gut microbiota composition.



We observe that Cluh regulates proinflammatory cytokine secretion, autophagy and ROS in the LPS-stimulated BMDMs. Cluh over-expression reduces pro-inflammatory cytokine secretion while enhancing autophagy in the LPS-stimulated HeLa cells. Reducing Cluh expression leads to worse outcome during DSS colitis induction in the animal model. Collectively, we find that altering mitochondrial dynamics regulates cytokine production both in vitro and in vivo and thereby alters IBD pathogenesis. Cluh thus might be an in important target for novel IBD therapy.

YI 03

Depicter: A Center for Predictors of Disordered Regions and Their Functions

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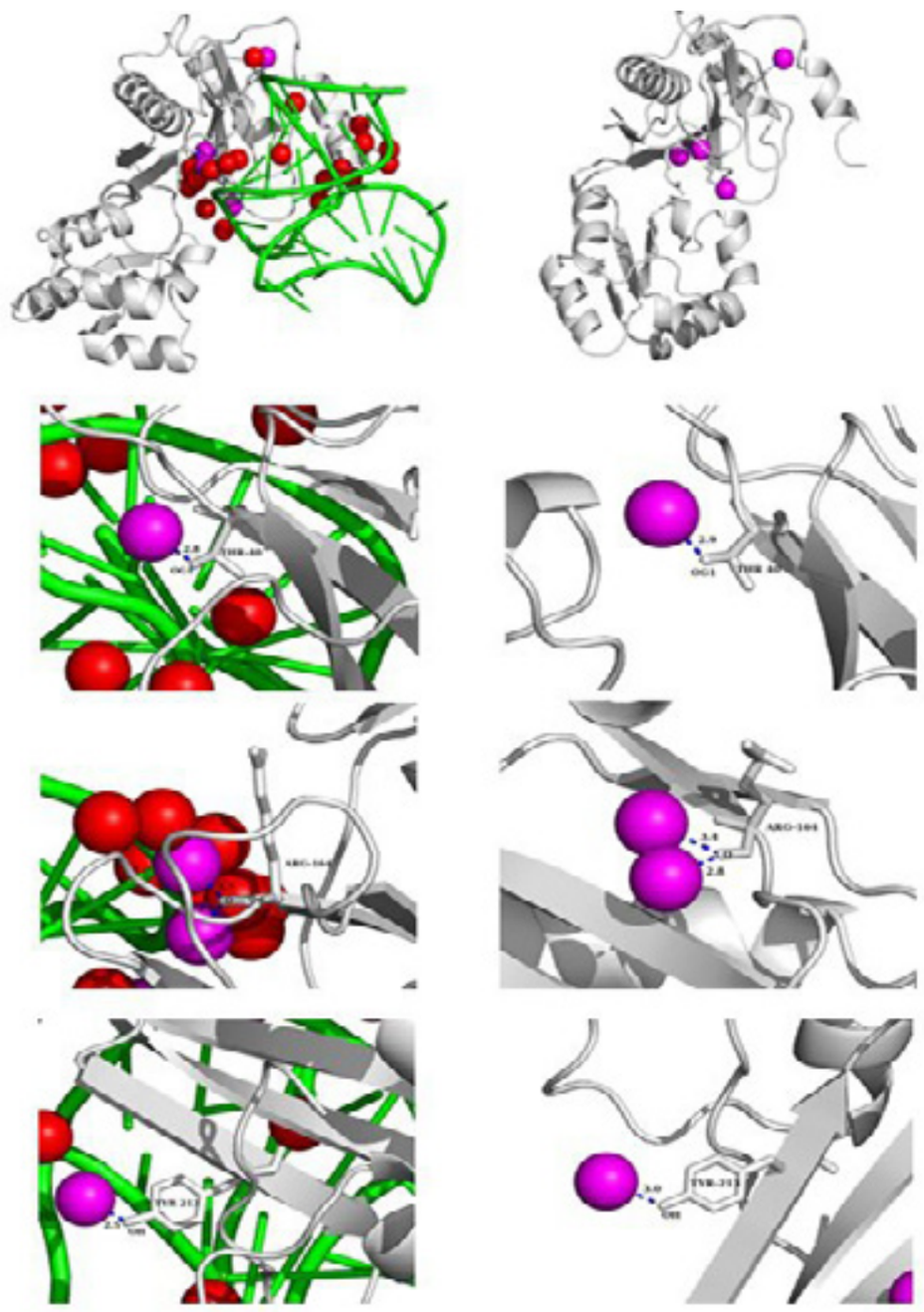
Computational Algorithms, Macromolecular interactions, Intrinsically Disordered Proteins/regions(IDPs/IDRs), Non-coding RNAs (ncRNAs), Machine Learning

Intrinsically disordered proteins (IDPs) although lack a stable three-dimensional structure, play an important role in many biological processes. Many computational programs have been developed in recent past for prediction of intrinsically disordered regions (IDRs) and their functions. Here, we attempt to include the best performing disordered protein predictors in one platform so that the user can get all outputs in one page. We have developed a web server named as DEPICTER (DisorderEd PredictIon CenTER) that includes some of the best performing predictors for IDPs such as IUPRED2A, SPOT-disorder, fMoRFpred, DisoRDPbind, ANCHOR2, DFLpred and DMRpred. The performance of DEPICTER was calculated using a training dataset of disordered proteins curated from DIPROT database and structured proteins taken from Protein Data Bank. To make an unbiased prediction, we excluded the Disprot proteins that were previously used in above mentioned predictors. Users have the options to choose from a set of predictors and accordingly the results will be displayed and emailed. Unlike the individual servers, where results are shown in text format, the outputs in DEPICTER can be also be visualized along with the text formatted outputs. The text results provide both the propensity scores and the binary values for each individual residue of the submitted protein sequence. Also, if more than one predictor is chosen, a consensus result will also be provided to the users in the results section.



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YI 04

Molecular Signatures in the Bat Influenza Virus Polymerase -Determinant Of Host Tropism

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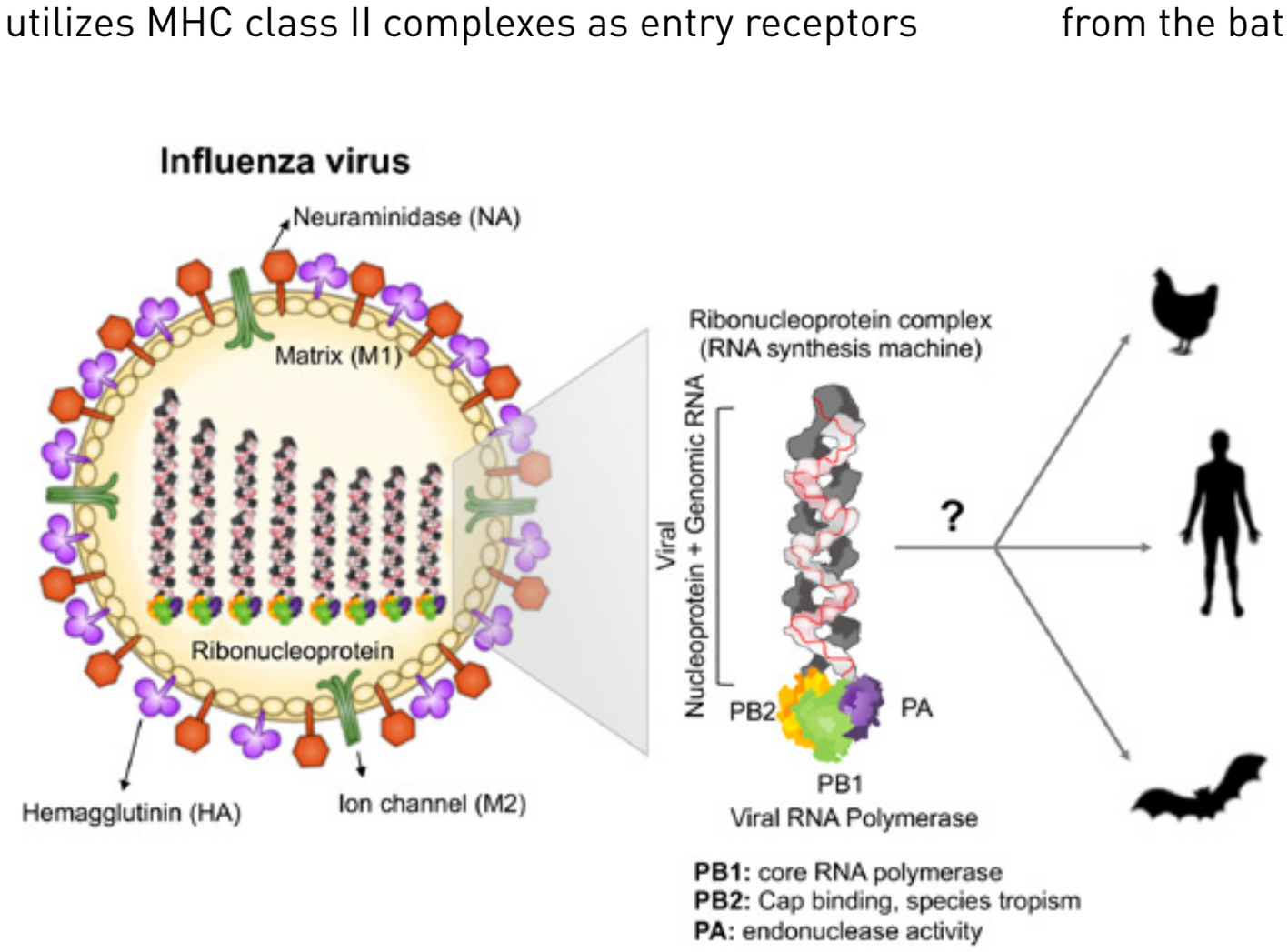
Rna Virus, Influenza Virus, RNA Polymerase, Virus-Host Interaction, Host Tropism

Influenza viruses are notorious for their ability to rapidly alter their genetic architecture through antigenic drift and shift. This results in frequent generation of novel influenza virus strains and subtypes that cause seasonal epidemics and occasional pandemics. Several new subtypes of influenza A virus (H17N10, H18N11) have been isolated from bats in recent past (1, 2). Based upon the phylogenetic analysis these influenza A viruses have been categorized as completely different lineage, which utilizes MHC class II complexes as entry receptors instead of sialic acid moieties that other influenza viruses do (3). However, the replication ability of the bat influenza viruses in other host species (human or bird) is yet to be characterized. This work deals with the identification of the molecular signatures present in the RNA dependent RNA polymerase from the bat and other influenza viruses that may be different, and hence could be a major determinant of host tropism. We have identified specific amino acid differences in the influenza virus RNA polymerase isolated from the bat and other host species, which confers additional fitness to its RNA synthesis ability in corresponding host species. Introduction of bat virus specific residues in the polymerase of human infecting virus makes the polymerase defective in human cells; suggesting that, bat influenza viruses may face restriction towards transmission in the human host. Elucidating the molecular mechanism behind this restriction would greatly improve our understanding about the transmissibility and pathogenicity of bat influenza viruses towards humans, birds and other host species.



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YI 05

Molecular Insights into Parkinson's Disease

Parkinson's, Parkin, PINK1, Ubiquitination, Phosphorylation

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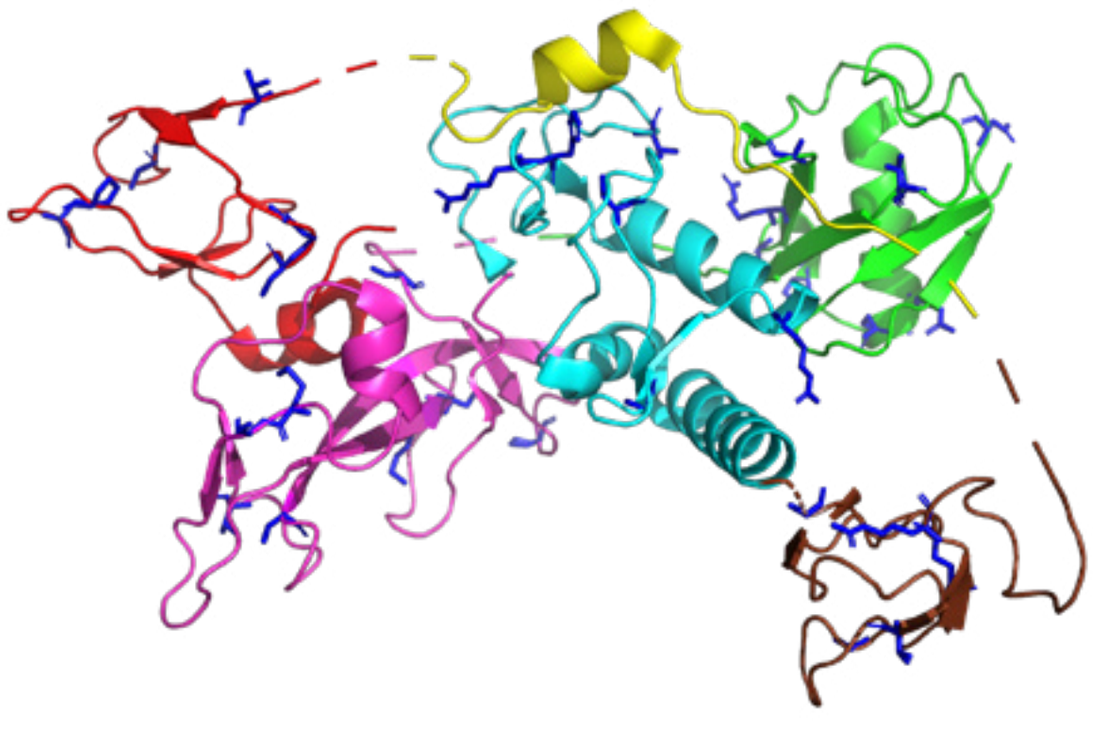
Mutations on two key enzymes PINK1 kinase and Parkin E3 ubiquitin E3 ligase cause more than 50% cases of autosomal recessive juvenile Parkinson's. The underlying molecular mechanism of PINK1-Parkin pathway is not well established except that PINK1 phosphorylates ubiquitin and ubiquitin-like (UBL) domain of Parkin, which activates E3 ubiquitin ligase activity of Parkin. I have solved various structures of human Parkin (including apo Parkin and in complex with phospho-ubiquitin), which has enhanced our understanding about Parkin autoinhibition mechanism, and its activation upon phosphorylation by PINK1. My work has also revealed the intriguing mechanism of RBR (RING-BETWEEN-RING) family E3 ligases where a donor-ubiquitin binding pocket is created on these enzymes, which is essential for their activation. My work revealed how several disease mutations on Parkin affect its activity. I have also solved first ever crystal structure of PINK1 kinase, which revealed the molecular mechanism of PINK1 kinase. My work on PINK1 identified unique insertion (INS3) in the kinase domain of PINK1, which specifically recognize ubiquitin or ubiquitin-like (UBL) domain of Parkin. I also discovered that an auto-phosphorylation site S205 on PINK1 makes crucial interactions with INS3 which is required to keep PINK1 in its active state. My work on PINK1 explained the molecular rationale of disease mutations on PINK1. Together my research on PINK1 and Parkin has provided framework for future research to develop therapeutics and understand the detailed regulatory mechanism of Parkin.



YI 06

TGFβ2 Mediated Epithelial to Mesenchymal Transition: Role of AGE-RAGE Interaction

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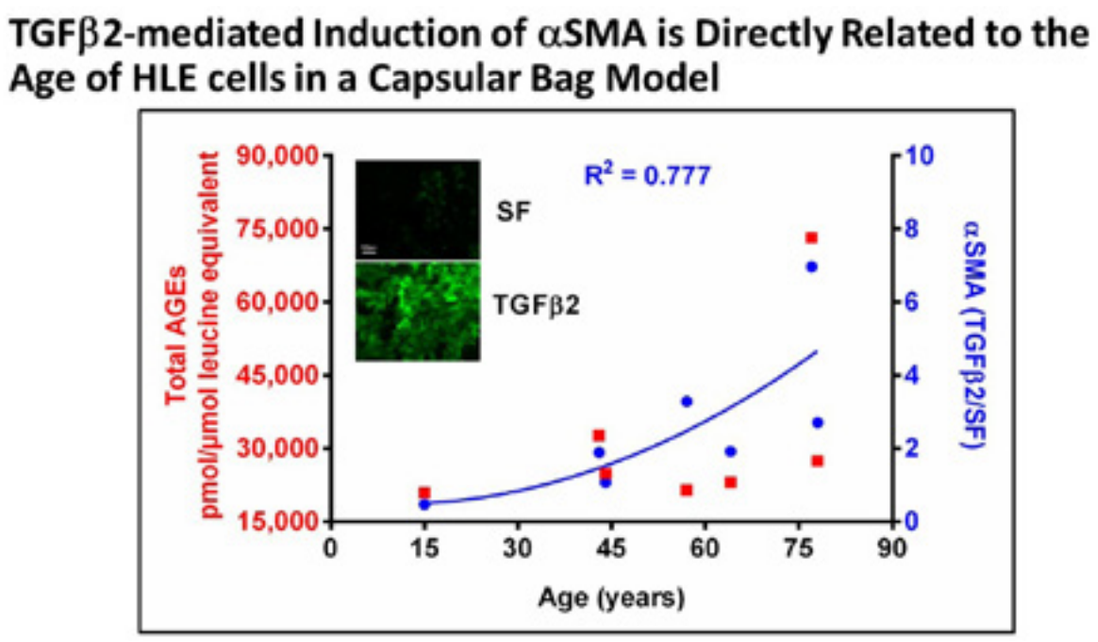
Advanced Glycation Endproducts, Basement Membrane modifications, Glycation, Glycotoxins, Receptor for Advanced Glycation Endproducts

Purpose: Proteins in the basement membrane accumulate chemical modifications with age. One such modification is glycation, which results in the formation of advanced glycation endproducts (AGEs). Previous studies have shown that AGEs in human lens capsule promote TGFβ2 mediated epithelial to mesenchymal transition (EMT) of lens epithelial cells. In this study we have investigated the role of receptor for advanced glycation endproducts (RAGE), a multi-ligand receptor, in TGFβ2 mediated EMT of lens epithelial cells.

Method: Tissue culture plates were coated with a basement membrane extract (BME; 50mg/ml) overnight and AGE-modified with glycating mixture (Ascorbate, glucose and methylglyoxal) for 7 days at 37°C. Lens epithelial cells (FHL124) were cultured on AGE-modified or unmodified BME treated with TGFβ2 for 24h. RNA was isolated, cDNA generated and real time PCR analysis was carried out for EMT-associated proteins. RAGE overexpression studies were carried out by transient transfection of GFP-RAGE. Effect of RAGE blockage on TGFβ2 mediated EMT was studied using RAGE antibody and EN-RAGE, an endogenous ligand for RAGE.

Results: FHL124 cells showed an enhanced EMT response upon TGFβ2 treatment when cultured on AGE-modified BME than on unmodified BME. RAGE was detected in these cells and its levels were unaltered in cells grown either native or AGE-modified BME or upon treatment with TGFβ2. However, RAGE overexpression in FHL124 cells amplified the TGFβ2-mediated EMT response. Moreover, blockage of RAGE with an antibody or EN-RAGE followed by TGFβ2 treatment resulted in significant reduction of EMT response.

Conclusions: These results imply that the interaction matrix AGEs with RAGE plays an important role in TGFβ2-mediated EMT of lens epithelial cells and suggest that RAGE blockage could be strategy to prevent AGE associated conditions."



YI 07

Understanding the Biochemical Features of Apicoplast RNA Polymerase of *Plasmodium falciparum* and its Implication for Antimalarial Drug Development

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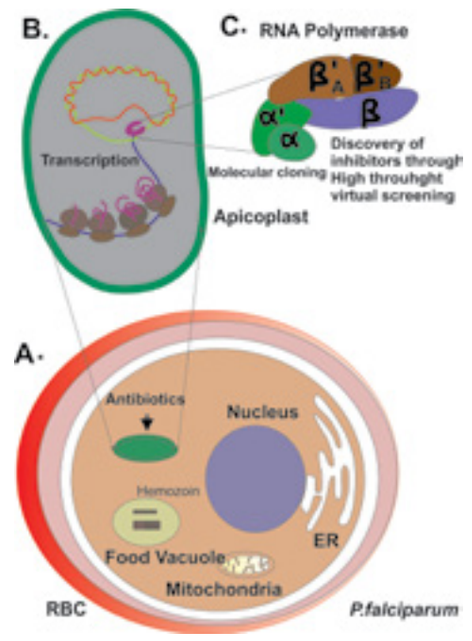
P. falciparum, *Apicoplast, RNA polymerase, Rifampicin*

P. falciparum, the leading cause of malaria-related morbidity and mortality, exclusively harbors a non-photosynthetic plastid like organelle termed as apicoplast. Apicoplast is essential for the parasite survival. All the familiar DNA metabolic processes such as DNA replication, transcription, and translation of the apicoplast genome are of prokaryotic and potential drug targets as they differ to the host processes1. Among different antibiotics used against malaria parasite in culture, rifampicin, the inhibitor of β subunit of bacterial RNA polymerase, has been reported to be the fast acting and most potent1 and a better partner in designing of combination therapy to treat malaria2. The apicoplast genome transcribes genes for tRNA, rRNA, apicoplast RNA polymerase subunits and other proteins3, 4, 5. Lack of convincing evidence of the apicoplast RNA polymerase complex at protein level builds the rationale for a comprehensive approach of biochemical investigation of the apicoplast RNA polymerase complex.

The apicoplast genome of *P. falciparum* encodes different RNA polymerase subunits such as β (PF3D7_API04400) and β` (PF3D7_API04400) subunits (RpoB and RpoC), β` subunit is further split into two parts (β`A and β`B). These subunits supposed to combine with two nuclear encoded apicoplast targeted RNA polymerase β subunits (PF3D7_1307600 and PF3D7_1472700) to compose a bacterial-type RNA polymerase [3]. In a recent high-throughput transposon insertional mutagenesis approach it was shown that both the β subunits are essential for parasite survival [6]. In the direction of biochemical characterization of different subunits of apicoplast RNA polymerase, we have successfully expressed the full length protein of one of the β subunits in heterologous bacterial expression system. In a high throughput virtual screening approach out of 2975 rifampicin scaffold based compounds, 29 ligands were sorted having a docking score of -8.6 to -6.6 compared to rifampicin (-3.428) indicating high binding affinity. Thus, our docking analysis comes out with more potent inhibitors of Pf Polβ as compared to the existing rifampicin and these inhibitors needs their experimental validation using in vitro and in vivo approaches.



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YI 08

Molecular Characterization of Isoprenoid Pathway Protein (PaDXR) from *P. aeruginosa*

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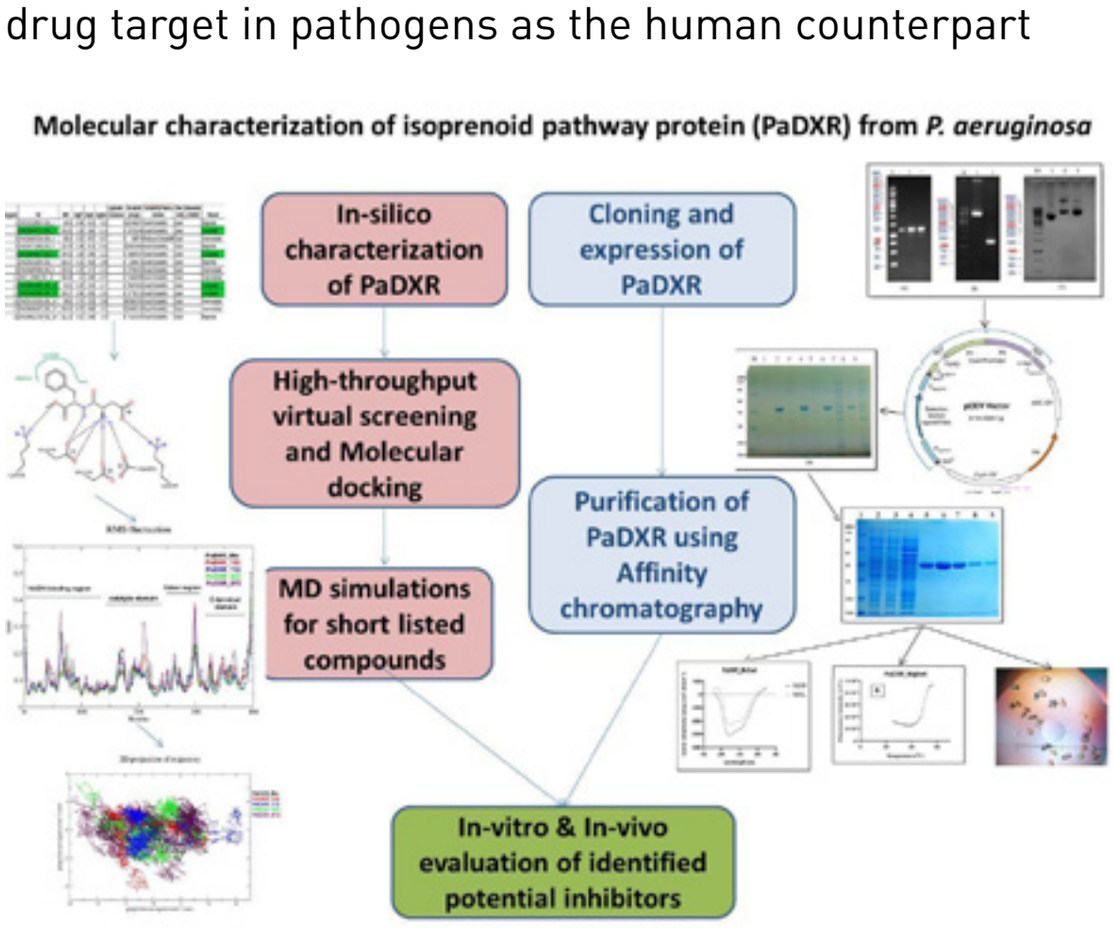
Pseudomonas aeruginosa has evolved antimicrobial resistance, making it difficult to treat limiting our therapeutic options and is a growing threat to global public health. Multidrug resistance amongst P. aeruginosa has enlisted it in the ESKAPE organisms- is of particular concern because they are responsible for many serious infections in hospitals (WHO, 2017). The MEP pathway enzymes are responsible for isoprenoid syntheses, which are an excellent drug target in pathogens as the human counterpart completely lacks these enzymes1,2. In this study, we are exploring DXR protein from the MEP pathway from *P. aeruginosa* (PaDXR) for biochemical and structural characterization. The DXR gene was cloned and the recombinant protein was expressed as ~45kDa in heterologous E. Coli Rosetta (DE3) strain. Recombinant protein PaDXR was further purified using affinity chromatography and used for downstream processes. CD spectroscopy data also performed to confirm the secondary structure of PaDXR and PaDXR with Mg and Mn ions. Thermal shift assay was also carried out to assess the temperature stability of protein and protein with metal ions. Also, for identification of putative inhibitors, a virtual screening approach using a pharmacophore model against ZINCDB was undertaken for PaDXR followed by MD simulations for assessing the binding affinity. The purified protein & identified compounds will be further used to assess the protein-ligand binding parameters as well as structural changes associated with it using biophysical techniques. If successful, further *in-vivo* studies against the pathogenic *Pseudomonas* strains will be performed.



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YI 09

Harnessing ultrasound and Microbubbles for Next Generation Imaging and Therapy

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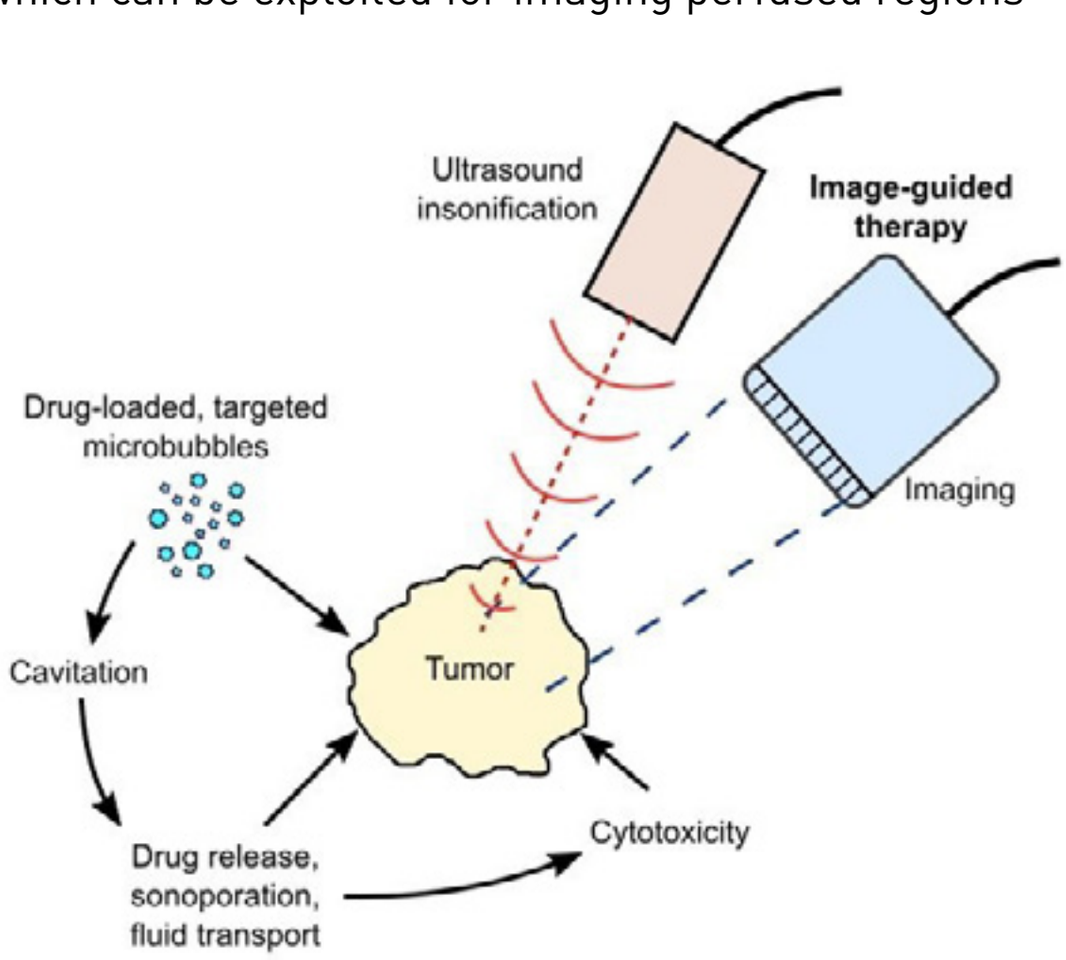
Ultrasound Molecular Imaging, Therapeutic Ultrasound, Microbubbles, Theranostics, Medical Devices

Ultrasound is a diagnostic as well as a therapeutic modality that is versatile, portable, widely accessible and relatively inexpensive. Encapsulated microbubbles stabilized with lipid, protein, or polymer coating are approved for clinical use as ultrasound contrast agents. In response to ultrasound exposure at moderate acoustic pressures, microbubbles undergo volumetric oscillations and produce nonlinear acoustic emissions, which can be exploited for imaging perfused regions in vivo with high sensitivity and specificity. The microbubble shell can be functionalized for molecular targeting of sites that express specific biomarkers. Molecular imaging with ultrasound holds promise in the early detection of pathology or monitoring response to therapy. In addition, microbubbles can be used for ultrasound-enhanced drug delivery. Loading drugs into microbubbles has been shown to minimize rapid degradation of drugs in the blood circulation, enhance bioavailability, and enable ultrasound-mediated drug release at the treatment site. Microbubbles serve as cavitation nuclei and can be harnessed to promote drug delivery through sonoporation and improved fluid transport. In this poster, I will discuss representative examples of a) physicochemical characterization of microbubbles for use in imaging and therapy, b) nonlinear and molecular imaging using microbubbles, and c) the mechanisms involved in contrast-enhanced imaging and therapy. Next, the applications of ultrasound for lysing thrombi and site-specific delivery of neuroprotective agents will be discussed. I will conclude by sharing preliminary results of ongoing work on ultrasound-mediated therapy for anticancer applications in my laboratory at IIT Gandhinagar.



YI 10

Novel Role of Mitochondrial Alternative Oxidase Under Hypoxia to Drive Energy Production via Phytoglobin-Nitric Oxide Cycle

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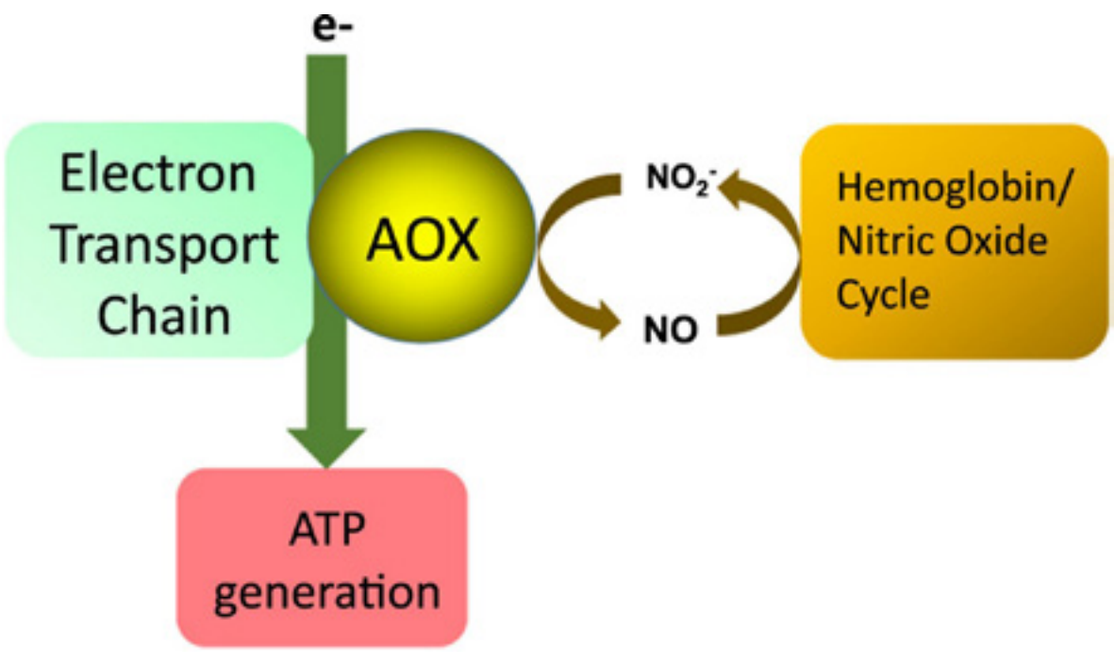
Mitochondria, Nitric Oxide, Reactive Oxygen Species, Nitrooxidative Stress, Signaling

Mitochondria generate most of the energy in the form of ATP using proton motive force generated via electron transport chain (ETC) during the transfer of electrons from reducing equivalents to oxygen. As well as the usual terminal oxidase, cytochrome c oxidase (COX), plant mitochondria also contain an alternative oxidase (AOX). This protein accepts electrons from ubiquinone pool and thus bypasses the later proton pumping steps in the electron transport chain, leading to reduced generation of ATP. Electron transfer via AOX can reduce deleterious levels of ROS, contributing to the prevention of oxidative stress. Recent evidence suggest that AOX can prevent reactive oxygen species (ROS) and nitric oxide (NO) production



under non-stressed, normoxic conditions. Here we assessed the roles of AOX by imposing stress under normoxia in comparison to hypoxic conditions using AOX over expressing (AOX OE) and anti-sense (AOX AS) transgenic Arabidopsis seedlings and roots. Under normoxic conditions reactive nitrogen species stress was induced with the defence elicitor flagellin (flg22). AOX OE reduced NO production whilst this was increased in AOX AS. Moreover AOX AS also exhibited an increase in superoxide and therefore peroxynitrite, tyrosine nitration suggesting that scavenging of NO by AOX can nitrooxidative stress under normoxia. In contrast, during hypoxia interestingly we found that AOX is a generator of NO using nitrite as electron acceptor. NO produced during hypoxia, was enhanced in AOX OE and suppressed in AOX AS. The enhanced levels of NO correlated with expression of non-symbiotic haemoglobin, increased NR activity and ATP production. The ATP generation was suppressed in nia1,2 mutant and non symbiotic haemoglobin antisense line treated with SHAM. Taken together our results suggesting that hypoxic NO generation mediated by AOX feed into the haemoglobin-NO cycle to drive energy efficiency under conditions of low oxygen tension.

YI 11

Coordinated mTOR Activation and BMP Inhibition Preserve Tumor Cell Survival and Stemness Upon Loss Of LGR5+ Cells in Colorectal Tumors

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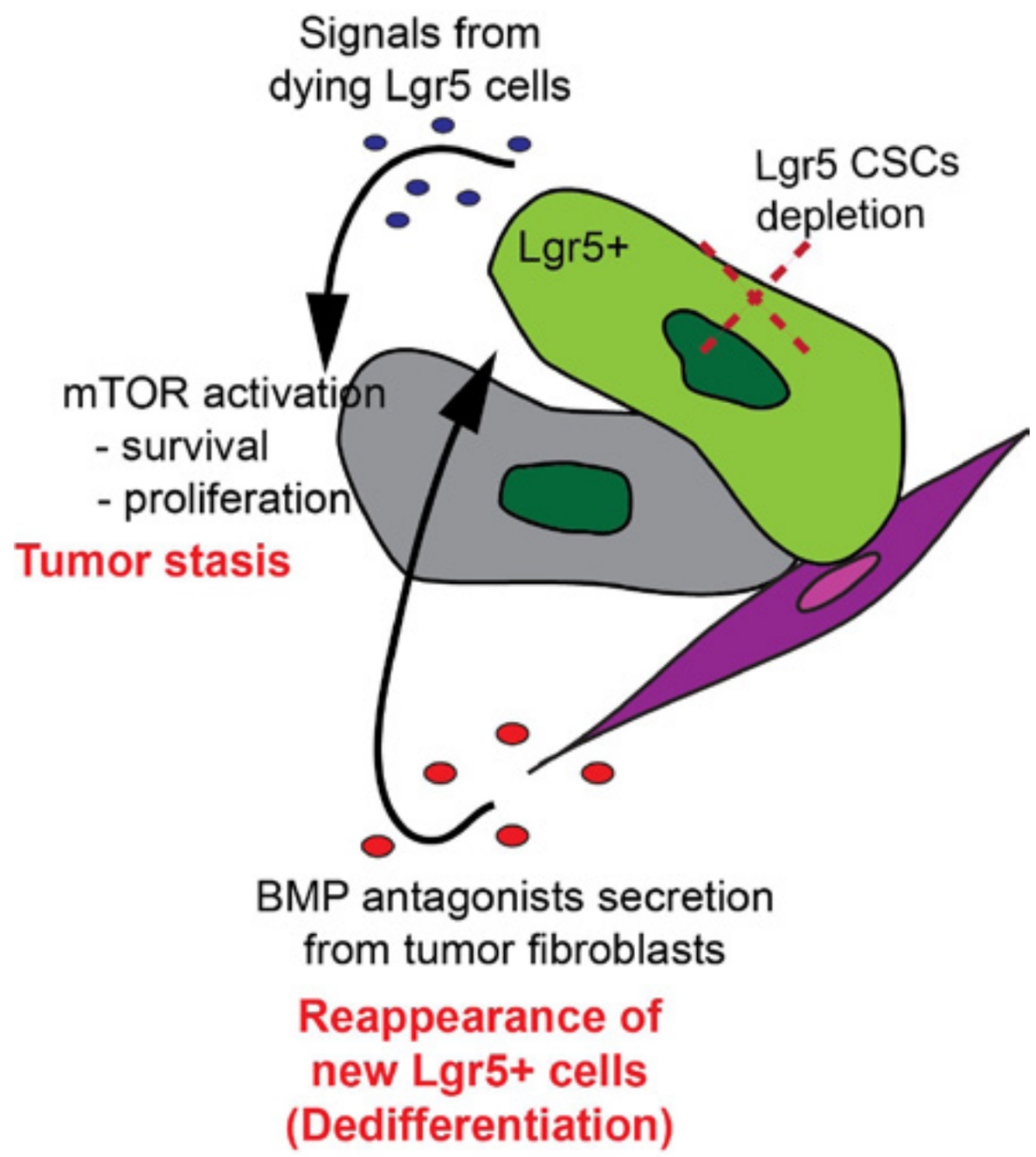
Cancer Stem Cells, Dedifferentiation, Mouse Models, Cancer Therapy, Tissue Regeneration

Cancer stem cells (CSCs) represent the core of the tumor with infinite self-renewing capacity, thus elimination of CSCs holds a widespread clinical implications. However, recent data suggest that specific ablation of LGR5+ CSCs in primary colorectal tumors does not lead to tumor regression, instead `tumor stasis' is maintained by proliferative Lgr5- tumor cells that have capacity to generate new Lgr5+ CSCs upon cessation of CSCs depleting treatments, demonstrating enormous plasticity of tumor cells. Here, we show that Lgr5- tumor cells rapidly activate mTOR signaling through paracrine factors released by dying Lgr5+ CSCs to maintain proliferation and thereby tumor stasis. Inhibition of mTOR pathway in combination with Lgr5+ CSCs depletion results in rapid regression of colon tumors. However, rapidly activated mTOR signaling does not contribute to regeneration of new Lgr5+ CSCs pool. Instead, CAFs secrete BMP antagonists which act on remaining tumor cells to inhibit BMP pathway to induce stemness and reversibility to Lgr5+ CSCs. Our data provide molecular insights into the plasticity of CSCs which opens new therapeutic avenue for the successful elimination of Lgr5+ CSCs pool.



YI 12

Quantitative Ultrasound Imaging Techniques for Tissue Characterization

Ultrasound Tissue Characterization, Ultrasound Elastography, Quantitative Ultrasound, Point-of-care Imaging, Medical Devices

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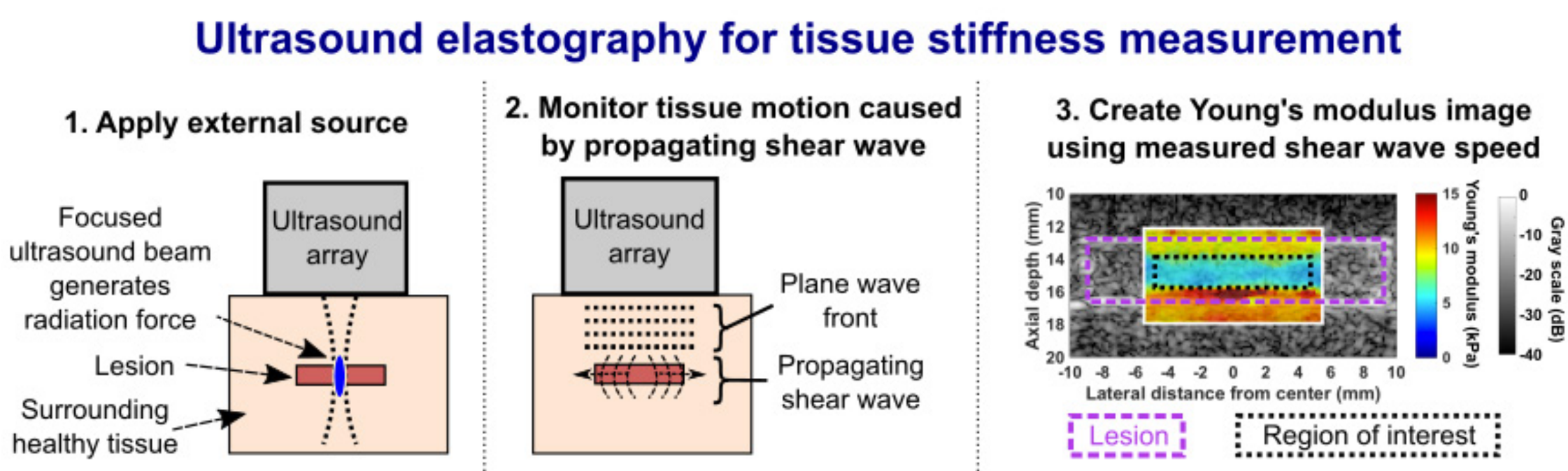
Ultrasound is an affordable, non-ionizing and point-of-care medical imaging modality that can improve access to cutting-edge healthcare. However, conventional ultrasound provides limited information about tissue stiffness and structure, which are valuable for enabling objective diagnosis. Quantitative ultrasound is an emerging set of technologies that can extract structural and mechanical properties nondestructively and aid tissue characterization and diagnosis of pathologies. Integrated backscatter imaging compensates for system-dependent and physical parameters such as ultrasound beam diffraction, gain, and acoustic attenuation, to obtain features based on the intrinsic backscatter from tissue. Further, shear wave elastography exploits the shear wave generated by an ultrasound beam and extracts tissue stiffness parameters based on the measured shear wave velocity. I will discuss research efforts focused on using Integrated Backscatter Imaging and Shear wave Elastography to assess the structure of 3-D tissue-engineered constructs, aimed at guiding their fabrication. Specifically, I will demonstrate the feasibility of estimating cell concentration and detecting spatial variations in collagen hydrogel structure using integrated backscatter imaging, and measuring hydrogel stiffness using shear wave elastography. Next, I will discuss the in vitro evaluation of shear wave elastography for predicting thrombolytic susceptibility, which is relevant in multiple diseases including stroke and deep vein thrombosis. Finally, I will highlight innovative potential applications of backscatter imaging and shear wave elastography for diagnosing pathological conditions such as cancer and fatty liver disease.



YI 13

Proteotoxic Stress Due to Loss of Interaction Partners Induces Reproductive Isolation in Yeast Hybrids

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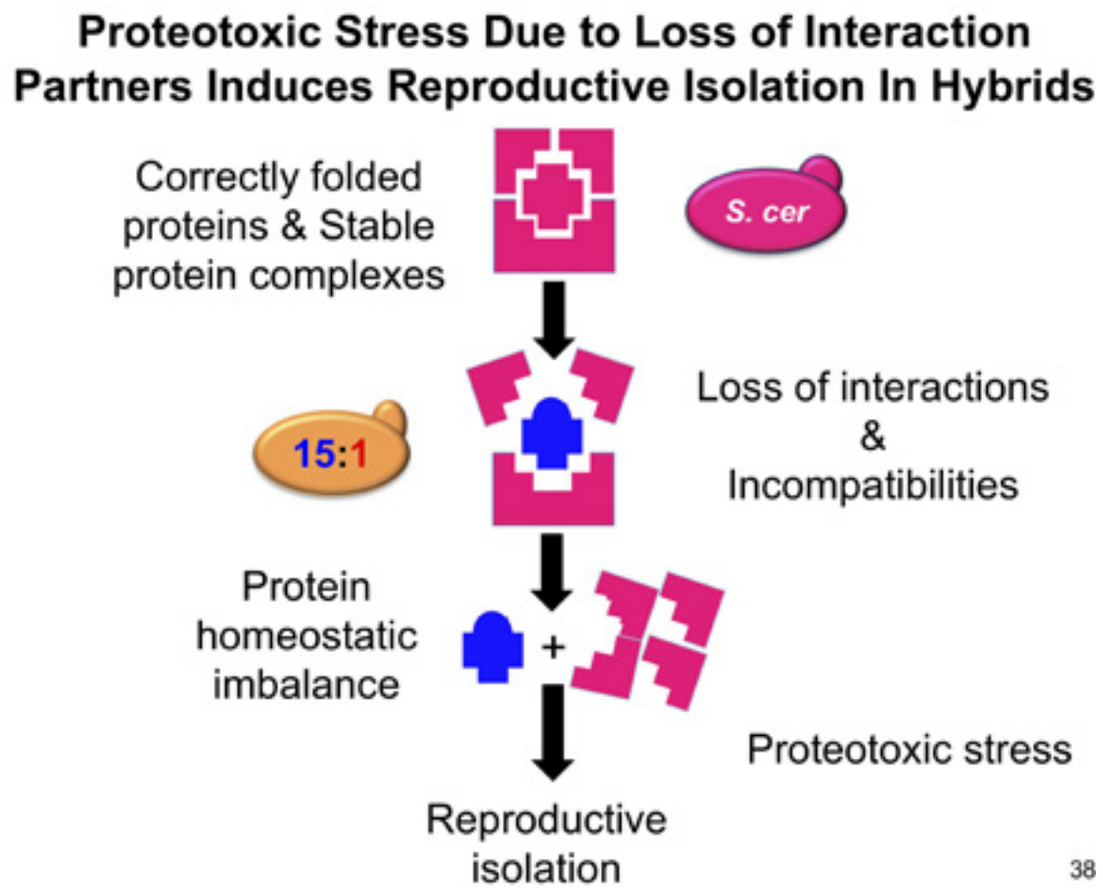
Molecular mechanisms in evolution, Speciation, Complex traits, Evolvability and robustness, Systems biology

Dobzhansky-Muller incompatibilities represent reciprocal-sign epistasis between inter-specific alleles and are widely accepted as a major driver of postzygotic reproductive isolation. Although complex epistasis involving multiple incompatibility loci with weak effects have been frequently observed in experimental crosses, the underlying mechanistic evidence has remained elusive. Here, we find multiple S. cerevisiae lines (rep-lines) introgressed with one or two chromosomes from its closely related species S. bayanus suffer from proteotoxic stress caused by complex epistasis, which has dire consequences on their fitness and sporulation rate. Accordingly, rep-lines harbor significantly higher levels of endogenous protein aggregates compared to wild-type S. cerevisiae and the observed proteotoxic stress can be alleviated or aggravated by up- or down-regulating ubiquitin-proteasome degradation machinery. Using proteomic approaches, we detect several destabilized multi-protein complexes in the most defective rep-line, suggesting that proteotoxicity is due to improper or failed interactions between components encoded by different genome. These



impaired complexes are involved in some basic cellular functions, including RNA transcription, protein translation, and mitochondrial biogenesis. Together, we show that complex epistasis caused by impaired multi-protein complex assembly results in imbalanced protein homoeostasis and represents a general source of hybrid breakdown.

YI 14

Unravelling the Role of miRNAs in Light Signalling for the Divergent Plant Responses to Vegetation Proximity

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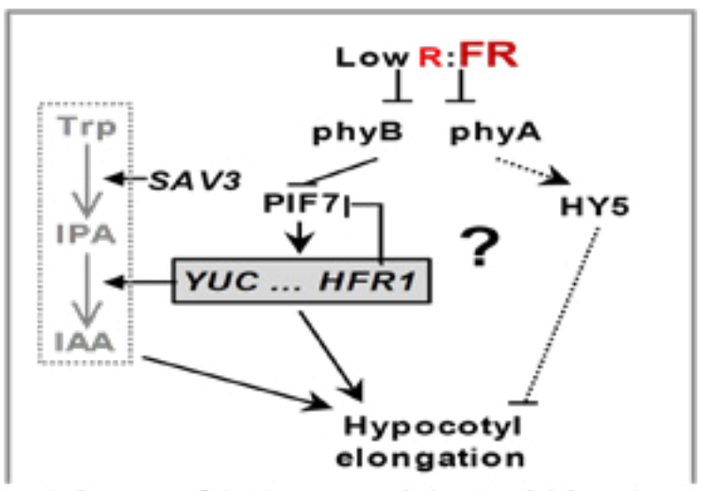
www.nbri.res.in

Light Signaling, Shade Avoidance, Phytochrome, Plant Growth, Arabidopsis

Plants sense the presence of competing neighboring vegetation as a change in light quality (i.e., a reduced ratio of red to far-red light, R:FR), a signal perceived by the phytochrome photoreceptors, which act as light-inducible molecular switches. The perception of low R:FR ratio by the phytochrome photoreceptors triggers the shade avoidance syndrome (SAS) responses, which include elongation of hypocotyls or stems, and changes in leaf surface and/or plant architecture (Casal JJ 2012). Overall, SAS comprises a set of morphological adjustments aimed to adapt optimally to the vegetation proximity; for instance, enhanced elongation of the stem or petioles result in vertical growth that allows plants to orient their leaves in favorable position to get a better light conditions. In general, shade avoidance responses are detrimental for the crop yield as the major carbon resources are shifted to the stem or petiole growth instead of grain filling. When low R:FR is perceived, shade-tolerant species lack the characteristic stem or hypocotyl elongation response to escape from shaded conditions. This particular trait has much agronomical importance as it may allow growers to increase plant density in an effort to increase harvest index of crops. However, to this date there is very little information available regarding molecular and genetic regulation of shade tolerance. Herein, the contribution of miRNAs for determining or overcoming the SAS response is investigated.

Study of the missing links of light signalling



Scheme of SAS network in Arabidopsis

YI 15

Identification of Synthetic Lethal Gene Interaction in Cancer

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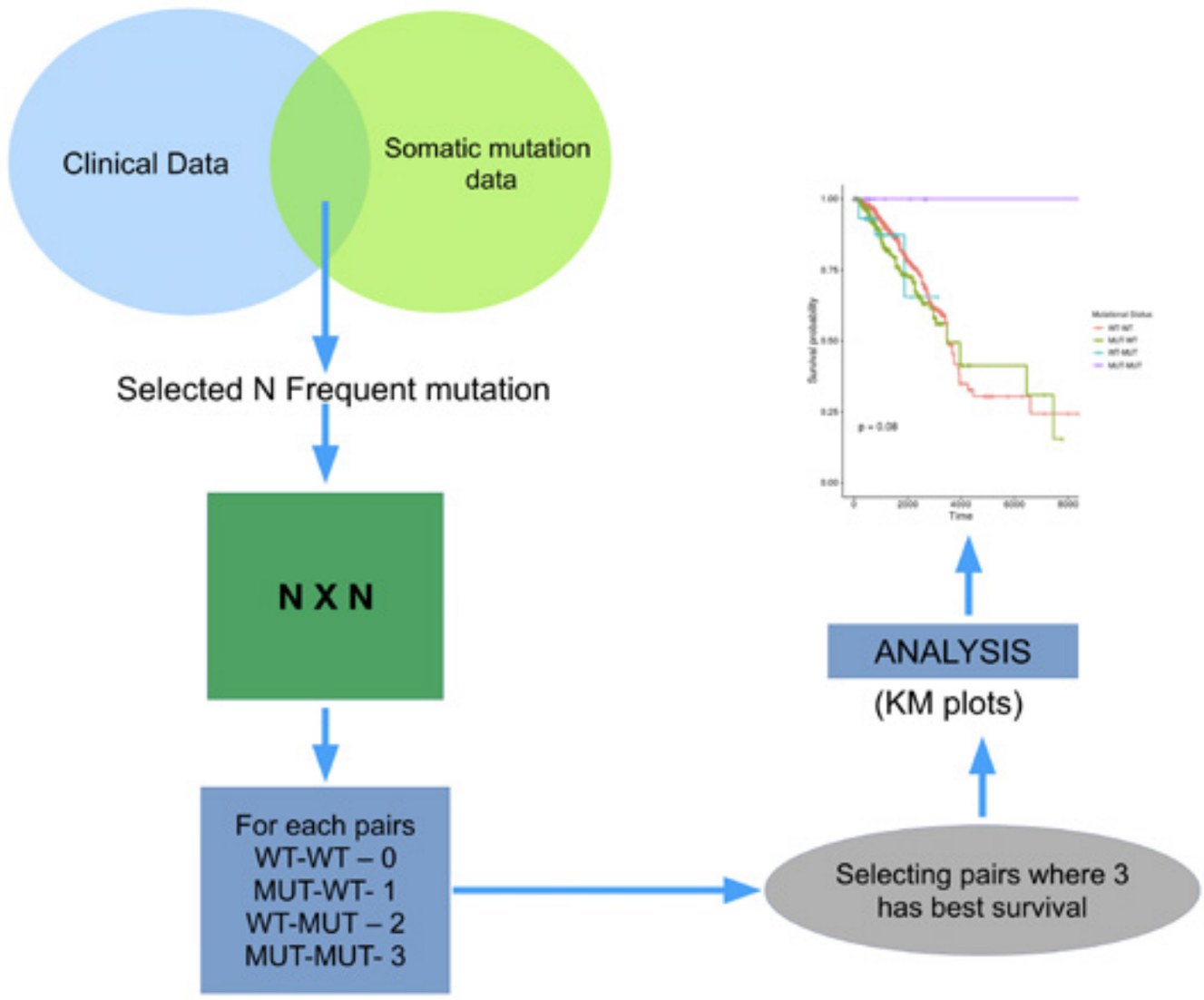
Cancer, Genomics, Network, Drugs, Computational

In cancer, tumour growth and survival depends largely upon kind of mutation harboured by the tumour cells. Synthetic Lethal gene pairs can be a good target for anti-cancer therapy and are promising candidates to develop drug therapy with increased therapeutic window. Experimental methods of finding synthetic lethality is limited due to the amount of gene interactions to be analyzed manually.

The present study focuses on developing a genomic data driven approach to find new possible synthetic lethal gene pairs by using mutation data and patients' survival information from acute myeloid leukemia and breast cancer patients. Various possible synthetic lethal gene interactions are found and reported in this study. This resource will aid clinicians to find better therapies for context-driven therapeutic targeting of specific tumours.



YI 16

Catechewing Coli: Genetically Engineering Bacteria to Remove the Color of Paan Stains

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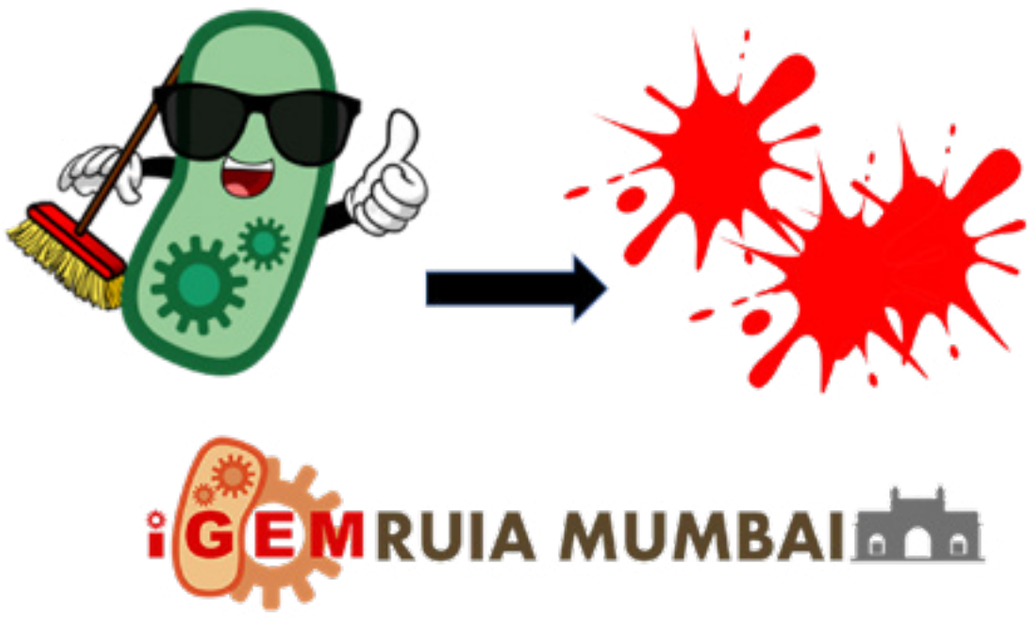
Chromatin, Epigenetics, Genome Engineering, Synthetic Biology, Yeast Biology

Indiscriminate spitting of red-colored catechu (Paan-) based products is a common practice in much of southeast Asia. Paan stains tarnish public places and historical monuments in the country. Although a considerable amount of resources are invested in cleaning these stubborn red-stains, existing methods are ineffective in removing them. We took a two-pronged approach to design a system that would remove Paan stains more efficiently. We identified natural isolates that would breakdown the red colour of Paan. We also used a rationale enzyme search to identify enzymes that are predicted to target these stains. We were able to clone these enzymes and show that the resulting cell lysates decolourised the Paan stains to a considerable degree. Given the enormity of this social issue, we also took a holistic approach to actively engage our community and learn from industry experts, users, cleaners, and policy makers how to effectively remove existing stains as well as prevent new ones.



YI 17

Role of Dynein Light Intermediate Chains in Embryonic Divisions and Vertebrate Embryogenesis

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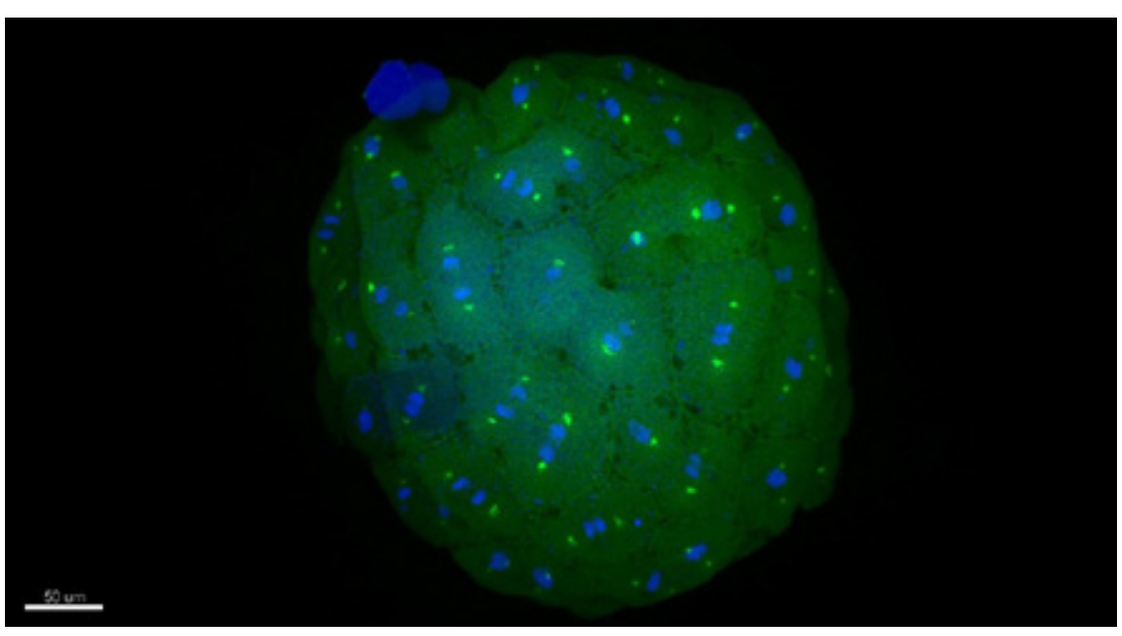
Developmental Biology, Cell Biology, Cell Divisions , Mitosis Associated Congenital Disorders, Human Embryology

The regulation of somatic cell division (mitosis) forms the basis for key morphogenetic processes during early embryogenesis. We are studying the role of the multifunctional molecular motor cytoplasmic dynein in embryonic development. Dyneins have been shown to perform a variety of functions during mitosis. The Light Intermediate Chain subunits of dynein, LIC1 and LIC2, present in mutually exclusive dynein complexes, asymmetrically distribute several mitotic functions and are hypothesized to be cargo-binding adaptors that enable the diversity of dynein functions. The aim of this study is to determine the functions and mechanistic roles of the dynein LIC subunits during vertebrate embryonic development. We hypothesize that zebrafish LICs are required for these functions and that loss of or defects in these subunits impair proper spindle formation and orientation, leading to developmental defects. We used a gene knockdown approach to understand the functional role of the LICs in the developing zebrafish embryo. The LIC depleted embryos show distinct mitotic defects such as increased spindle length, spindle pole focusing defects and chromosome congression defects. The LIC morphants also show gross developmental defects, suggesting that these subunits mediate key mitotic functions to regulate normal embryonic development. Further studies will focus on the mechanisms regulating the function of these important members of the dynein motor.



YI 18

Weaker Plant-enemy Interactions Decrease Tree Seedling Diversity with Edge-Effects in a Fragmented Tropical Forest

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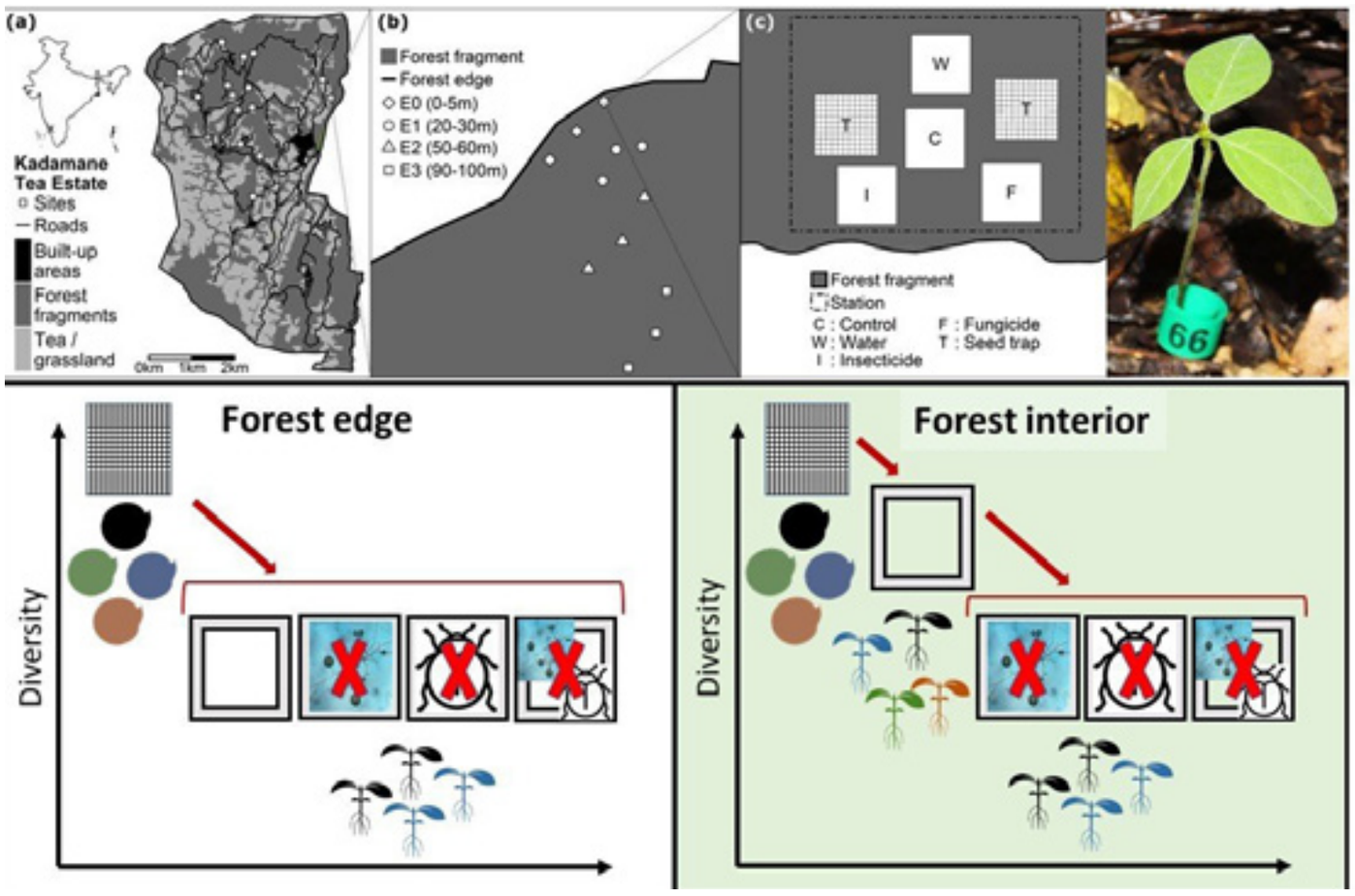
Community Ecology, Species Coexistence, Community Assembly, Forest Dynamics, Plant Functional Traits, Seedling Regeneration

In fragmented forests, tree diversity declines near edges1,2 but the ecological processes underlying this loss of diversity remain poorly understood3. Theory predicts that top-down regulation of seedling recruitment by insect herbivores and fungal pathogens contributes to maintaining tree diversity in forests4,5, but it is unknown whether proximity to forest edges compromises these diversity-enhancing biotic interactions. Here we experimentally demonstrate that weakened activity of fungal pathogens and insect herbivores reduced seedling diversity, despite similar diversity of seed rain, during recruitment near forest edges in a human-modified tropical landscape. Only at sites farthest from forest edges (90-100 m) did the application of pesticides, to suppress fungi and insects, lower seedling diversity relative to control plots. Notably, lower seedling diversity corresponded with weaker density-dependent mortality attributable to insects and fungi during the seed-to-seedling transition, but only at sites closest to edges. Our results suggest that the role of natural enemies in mediating plant diversity weakens near forest edges. We provide mechanistic evidence that edge effects can manifest as cryptic losses of crucial biotic interactions that maintain diversity.



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YI 19

Accurate Prediction of Protein Dynamics from Markov Models: Long vs. Short Trajectories

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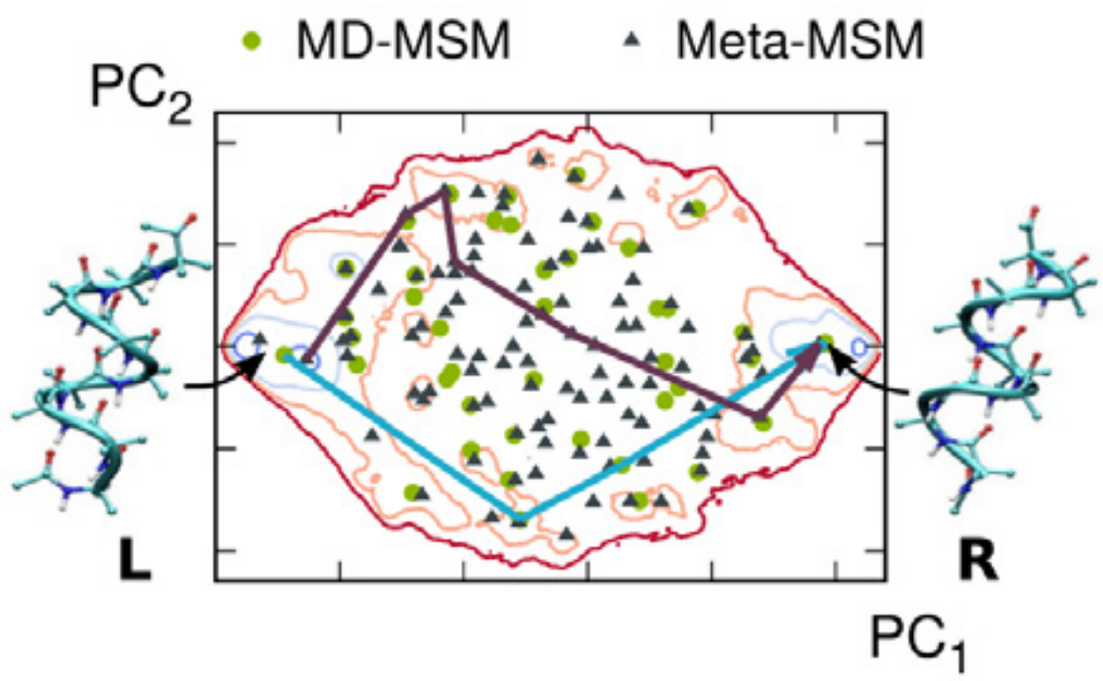
Computational Biophysics, Protein Folding, Markov Models, Photoregulation, Crowding

Markov state models (MSMs) can predict long time scale protein dynamics using data from molecular dynamic (MD) simulations. An essential feature of MSMs is that one does not need a long continuous MD trajectory. Instead an ensemble of short trajectories can be employed, which can be run in parallel. However, it is not clear in what practical aspects a MSM based on ultra long MD trajectory differs from that based on short trajectories. Here we investigate this issue for conformational transition of a model peptide helix (Aib) by constructing and comparing MSMs based on a single long trajectory and ensemble of short MD trajectories. The results indicate that the long MD simulations cannot provide the correct equilibrium populations of the metastable states or qualitative features of pathway distributions of the peptide.



YI 20

Identifying Inhibitors of Epithelial-Mesenchymal Plasticity through a Network Topology Based Approach

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Cancer Metastasis, Cellular Plasticity, Systems Biology, Mathematical Modeling, Non-genetic Heterogeneity

Metastasis still remains a major clinical burden and the cause of more than 90% of cancer-related deaths. A hallmark of cells undergoing metastasis is Epithelial-Mesenchymal Plasticity (EMP)- the bidirectional transitions between epithelial, mesenchymal, and one or more hybrid epithelial/mesenchymal (E/M) phenotypes. EMP is implicated in tumor-initiation potential (stemness), immune evasion, drug resistance, and associates with patient outcome. Various preclinical and clinical efforts have attempted to block EMT (Epithelial Mesenchymal Transition)- one of the arms of EMP- but such efforts may even facilitate MET- the other aspect of EMP, thus possibly even increasing metastasis. Thus, to curb metastatic load, EMP needs to be blocked bi-directionally, i.e. preventing interconversions among all cell phenotypes- E, M and E/M. Mathematical models have played a key role in identifying the dynamics of EMP and associated cellular traits, and suggested network motifs that may stabilize these three phenotypes. However, whether these phenotypes can be stabilized simultaneously, thus preventing EMP, remains to be yet established.

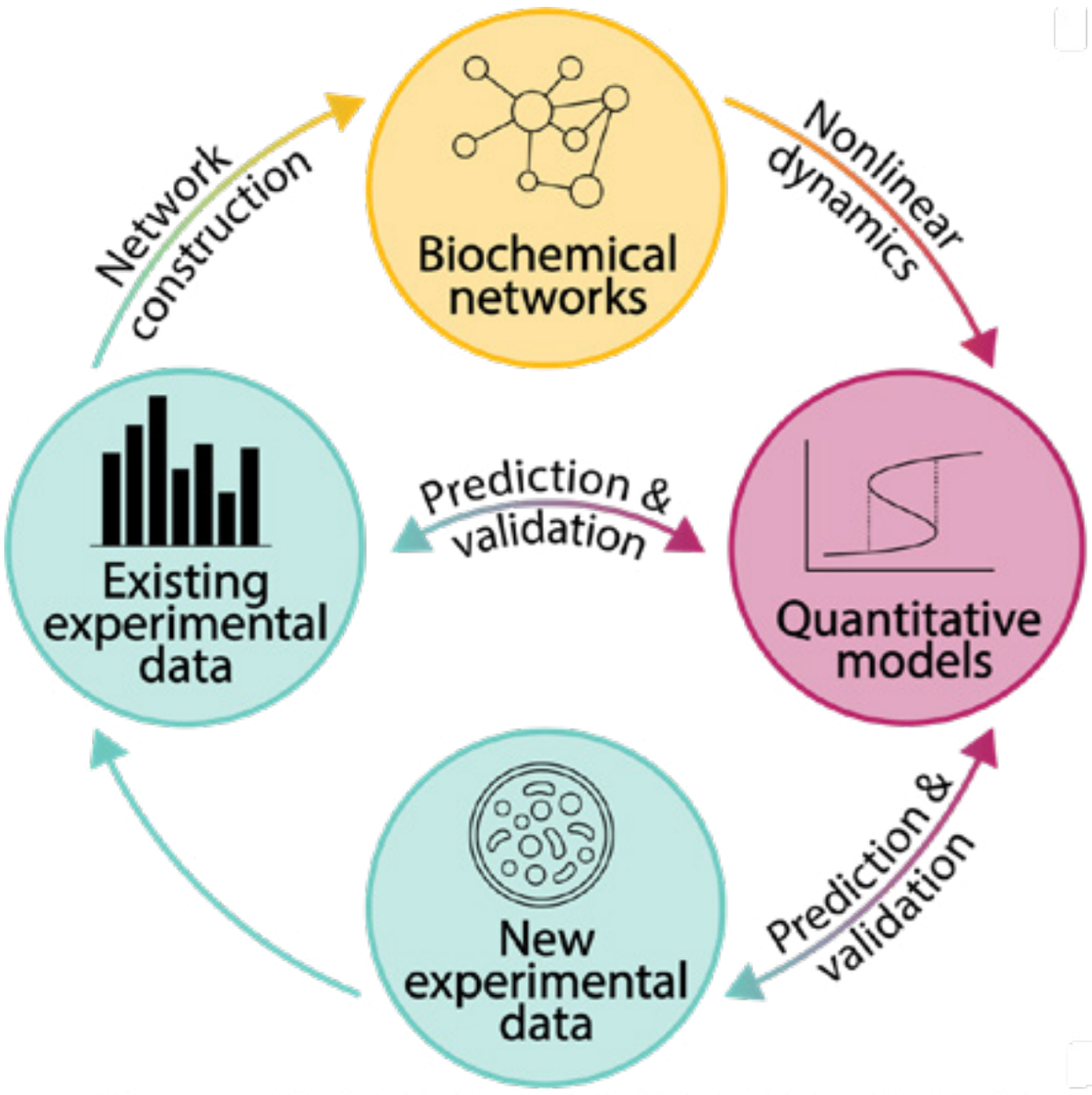

Image courtesy: Maya Sheth (Jolly *et al.* Pharmacol Therap 2018)

Here, using mathematical models of various networks implicated in EMP, we identify and rank various network perturbations that curb EMP in both directions, i.e. prevent transitions among E, M, and E/M states. Intriguingly, these network perturbations have a topological signature, i.e. perturbing these network motifs in a specific manner can significantly prevent phenotypic plasticity. These perturbations reveal underlying design principles for the multi-scale networks driving EMT/MET, and provide a rational network-based platform for identifying therapeutic targets to curb EMP and consequent metastatic load.

YI 21

Genetically Encoded L-3,4-Dihydroxyphenylalanine in Glycoside Hydrolases alter the Structural Helical Propensity and Catalytic Chemistry Enabled Expeditious Skin Fibre Opening

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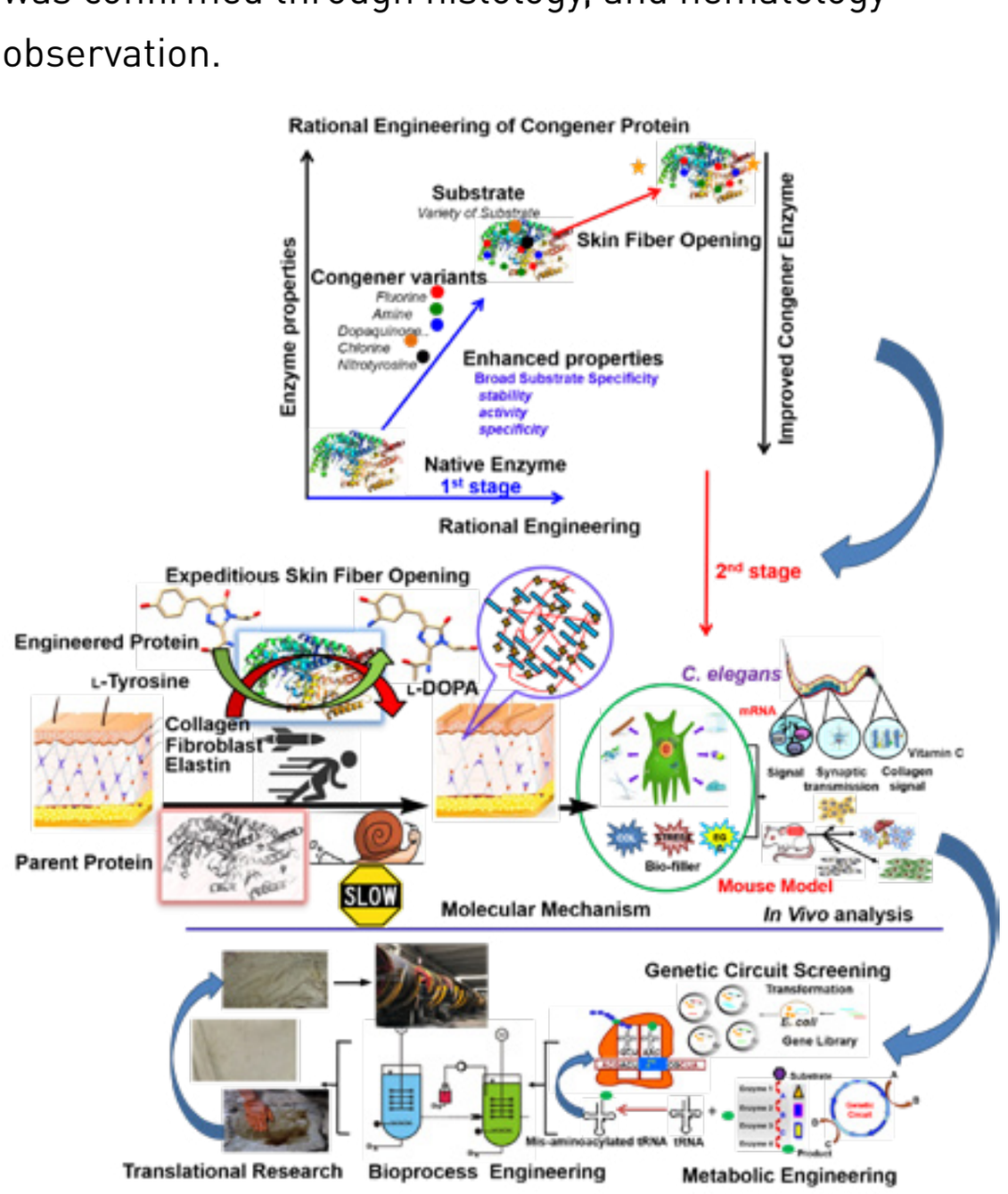
Xenobiology, Expanding and Engineering the Genetic Code, Protein Engineering, Recombinant Biomaterials, Enzyme Engineering

Self-administrative, painless, targeted delivery of macromolecules through the skin is of paramount important for treating aging based on regenerative medicine. Here, we address this challenge through genetically encoded L-3,4-dihydroxyphenylalanine in α-1,4-glycosidic hydrolase. The next-generation rational engineering of α-1,4-glycosidic hydrolase resulted in a novel xenobiocatalyst with an additional hydroxyl group in the protein core remarkably enhanced the catalytic efficiency (up to 120-fold higher than that of the wild-type) and turnover rate with chondroitin sulfate, a predominant glycosaminoglycan present in the extracellular matrix of skin, resulting in expeditious skin fiber opening (10 min) without damaging the network. The evolved biocatalyst also significantly reduced the chemical oxygen demand, and the total solid effluent load was found to be 8.5 and 22 kg t^{-1} as compared to the traditional chemical method (13 and 53 kg t^{-1}). Biophysical investigation revealed that the genetic incorporation of noncanonical side chain remodeled the molecular interaction of catalytic pocket with chondroitin sulfate resulted in the high binding. The ability of various macromolecular transport was tested as well as the role for skin regeneration explored in mammalian cells, *Caenorhabditis elegans*, and animal models. The results of biocompatibility was confirmed through histology, and hematology observation.



YI 22

Mangrove Community Resilience and Succession After Subsidence Inflicted Sea Level Rise in Car Nicobar Islands, India: Implications for Mangrove Conservation

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Mangrove, Sea Level Rise, Invasive Alien Species, Restoration Ecology, Biodiversity Monitoring

The inter-specific resilience among mangrove species to sea level rise (SLR) is key to design conservation strategies for this economically and ecologically important ecosystem that is among the most vulnerable to SLR. In addition to the eustatic sea level rise, tectonic processes can also cause increase or drop in sea level, which can provide insights for the mangrove community responses to sea level change. We observed the mangrove species responses and succession after the acute SLR of c. 1 m caused by land subsidence during 2004 Sumatra-Andaman earthquake at Car Nicobar Island, India. The seaward mangrove community comprised of *Rhizophora* spp. have survived after the subsidence, whereas mass tree mortality was observed in the landward mangrove community comprised of *Bruguiera* spp., *Lumnitzera* spp., and *Xylocarpus* spp. Subsequently, the *Rhizophora* spp. (mainly *R. mucronata*) have successfully colonized the earlier landward mangrove habitats, whereas the landward mangroves are found seldom in the new inter tidal habitats that were coconut plantation before the subsidence. Seed source availability may be the major influencing factor for the varying rates of landward and seaward mangrove colonization in the new habitats. The observed resilience of *Rhizophora* spp. can be explained by the local specific geological legacy and species specific ecological processes.
It is noteworthy that these island landscape have experienced four large frequency earthquakes (>7 Mw) and land subsidence & uplift during the past two centuries, which might have had an positive influence in the species specific resilience for sea level change. The observed resilience of *Rhizophora* spp. indicates their potentiality for the mangrove restoration activities targeted towards mitigating sea level rise and provides opportunities for further scientific enquiries on multiple aspects of mangrove response to subsidence.

YI 23

Big-Data Approach to Decipher the Role of Cis-Regulatory Variations for Local Climate Adaptation in Plants

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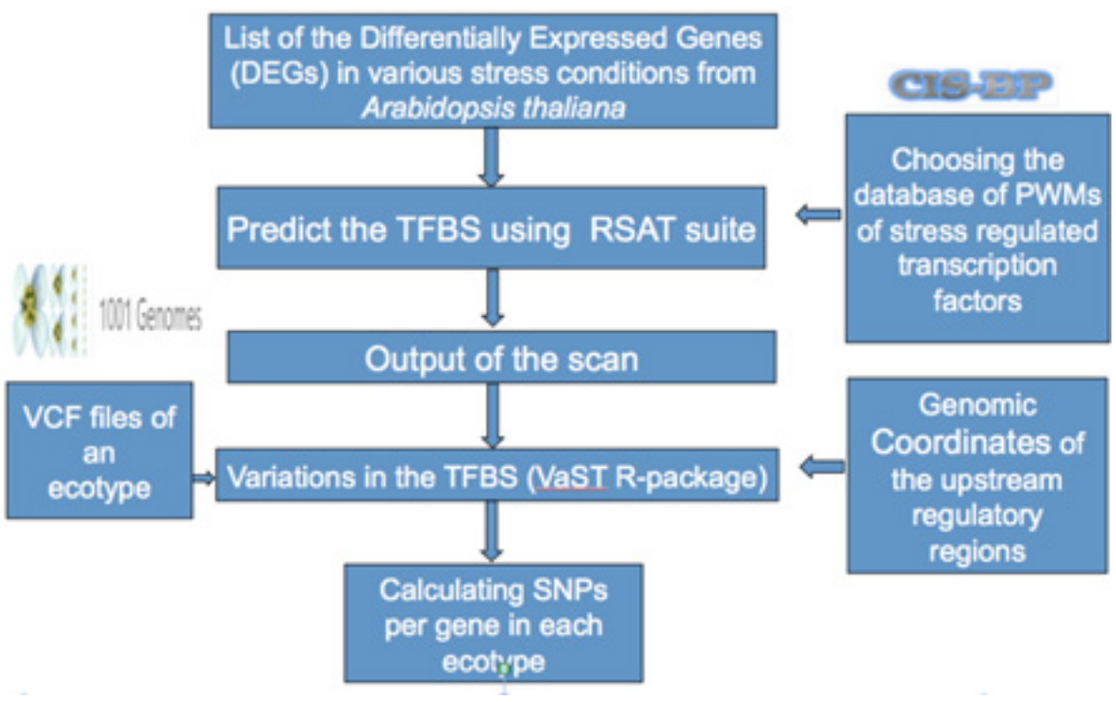
https://scholar.google.com/citations?user=03gTWRgAAAAJ&hl=en&oi=ao

Bioinformatics, Systems Biology, Next Generation Sequencing, Big Data, Genome evolution

Non-coding cis-regulatory sequences control morphogenesis, development of anatomy and physiology of living organisms by regulating gene expression. Mutations in these sequences confer intra- and inter-specific phenotypic variation. Variations in these sequences are caused by epigenetic factors, which help the organism to adapt to its local climatic conditions. Using *Arabidopsis thaliana* as model organism we have examined the potential role of cis-regulatory variations in local climate adaptation. For that we have developed an integrative computational workflow and an R package (VaST, Variation Scanner in Transcription factor binding sites) to analyze large scale genome sequence from more than 1000 ecotypes of A. thaliana and experimentally determined Transcription Factor Binding Sites (TFBS) data available from the cis-BP database. We have collected differentially regulated genes (DEGs) of *A. thaliana* in various stress conditions and scanned them with TFs motif model. We have identified significantly enriched TBFS in the 5' UTR regions (1 kb) of the stress regulated DEGs. Homo and heterotypic clustering patterns of TFBS have indicated the combinatorial nature of transcriptional regulation, and suggested the potential role of the homotypic clusters of TFBS towards maintaining transcriptional robustness against cis-regulatory mutations to facilitate the preservation of key stress response processes. We have observed that the variations in the TFBS of the stress regulated DEGs are correlated with the local climatic factors among the ecotypes. Our preliminary results and developed methods have established the basis for extending the analysis to other plant genomes for a comparative analysis. Our method has been benchmarked on desktop workstations as well as on high performance computing servers for parallel processing. Currently we are working to implement the workflow in graphics processing unit (GPU) environment using open source tools. Such big-data analysis approach will enable us for better understanding the role of cis-regulatory variations in local climate adaptation in plants.



YI 24

Tuning of Iron Oxide Nanoparticles by Albumin Coating Towards Induction of Protective Immune Response

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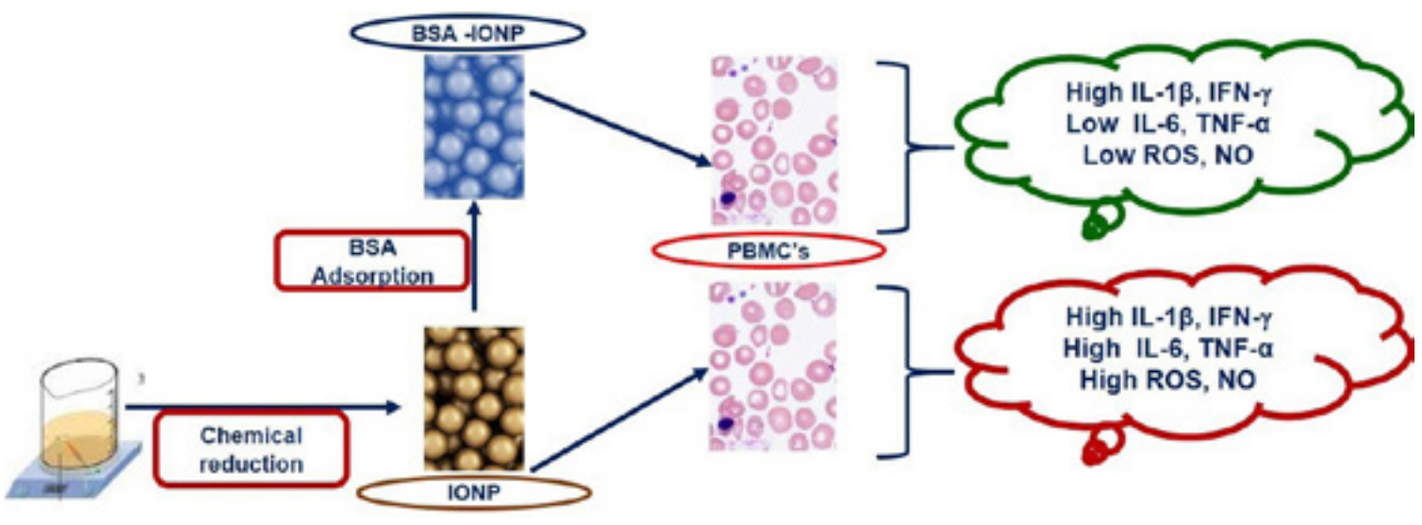
Immunomodulation, Nanodrug Delivery System, Mesoporous Bioglass, Bio-Nano Interface, Cancer therapeutics

Strategies to enhance the efficacy of vaccine for boosting immunogenicity, particularly inducing cell-mediated immune responses to cytotoxic damage, are of great interest. Iron oxide nanoparticles (IONP) are reported to elicit cellular immune response. However, when injected into blood, there will be adsorption of protein on the particle, which might modulate/inhibit its capacity to activate immune cells. In this regard, we investigated the efficacy of albumin (BSA) coated IONP (BSA-IONP) on eliciting immune response in peripheral blood mononuclear cells (PBMC). IONP were synthesised by chemical reduction method and to obtain BSA-IONP, adsorption method was utilised. The nanoparticles were characterised for phase, identity, size, and morphology by employing XRD, FTIR, DLS, SEM techniques. Later, we assessed the influence of BSA-IONP on the polarization of the immune response in peripheral blood mononuclear cells (PBMC). There was significant increase in IL-1β and IFN-γ with both IONPs whereas IL-6 levels and TNF-α level were increased only with native IONP. Also, naive IONP induced significant increase in reactive oxygen species (ROS) and nitric oxide (NO) but BSA-IONP failed to so. These in vitro data reveal that coating of protein on IONP may be beneficial in inducing a protective immune response. Future investigation will unravel the mechanism of this differential activation by protein coated IONP.



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YI 25

The Story of the Lost Twins: Decoding the Genetic Identities of the Kumhar and Kurcha Populations from the Indian Subcontinent

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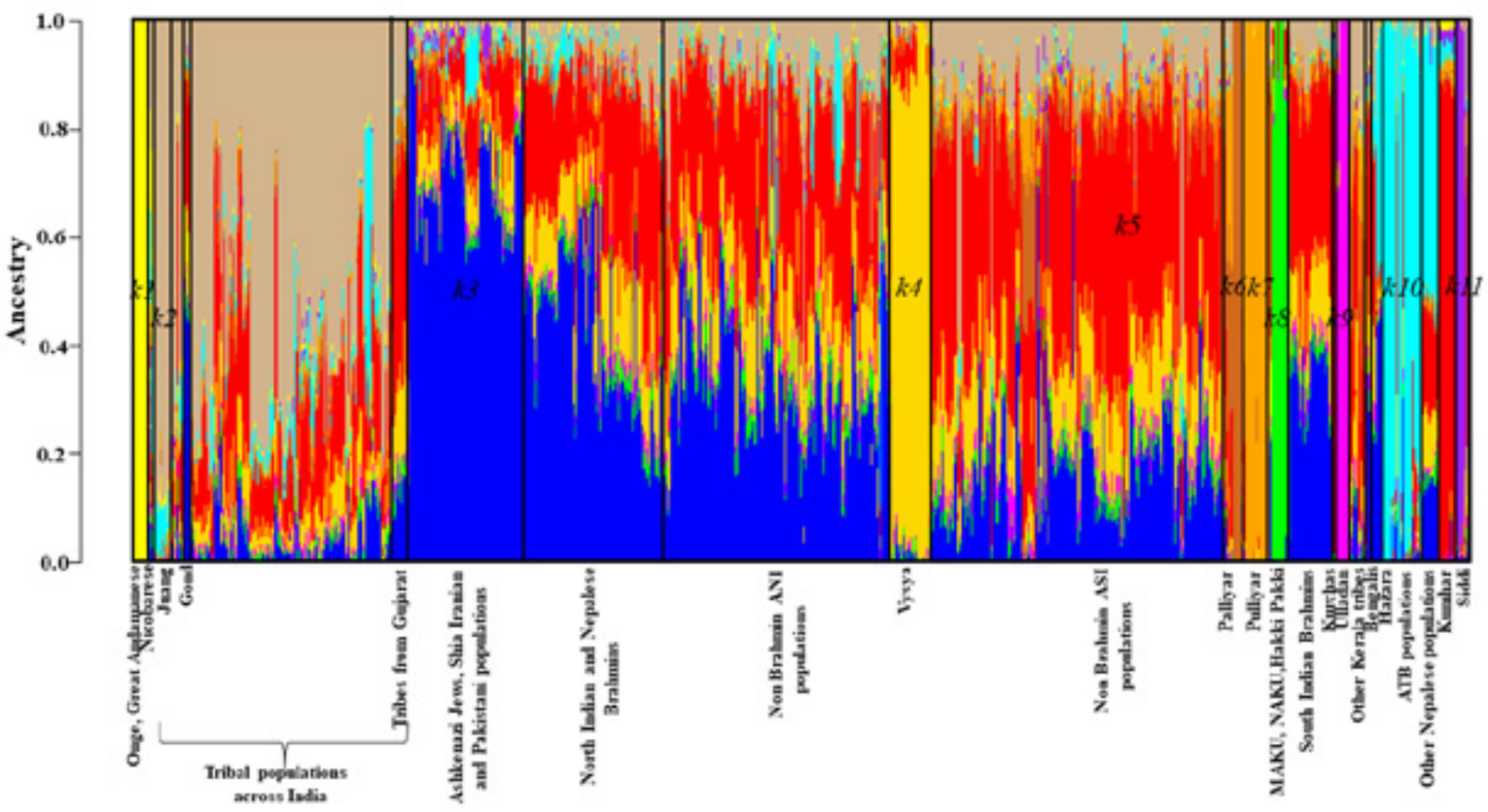
Ancestry, Ancestry Informative Markers (AIMs), Geo-localization of individuals with unknown ancestral origin, Employing AIMs for preservation of wild fauna, Population genetics of South Asians

The population structure of the Indian subcontinent is a tapestry of extraordinary diversity characterized by the amalgamation of autochthonous and immigrant ancestries and rigid enforcement of sociocultural stratification. Here we investigated the genetic origin and population history of the Kumhars, a group of people who inhabit large parts of northern India. We compared 27 previously published Kumhar genomes sampled from Uttar Pradesh in north India to various modern day and ancient populations. Various approaches such as Principal Component Analysis (PCA), Admixture, TreeMix concurred that Kumhars have high ASI ancestry, minimal Steppe component and high genomic proximity to the Kurchas, a small and relatively little known population found ~ 2500 km away in Kerala, south India. Given the same, biogeographical mapping using Geographic Population Structure (GPS) assigned most Kumhar genomes in areas neighboring to those where Kurchas are found in south India. We hypothesize that the significant genomic similarity between two apparently distinct modern day Indian populations that inhabit well separated geographical areas with no known overlapping history or links, likely alludes to their common origin during or post the decline of the Indus Valley Civilization (estimated by ALDER). Thereafter, while they dispersed towards opposite ends of the Indian subcontinent, their genomic integrity and likeness remained preserved due to endogamous social practices. Our findings illuminate the genomic history of two Indian populations, allowing a glimpse into one or few of numerous of human migrations that likely occurred across the Indian subcontinent and contributed to shape its varied and vibrant evolutionary past.



YI 26

Diabetes Induces Pathological Changes in the Lung through Activation of TGF-ß Signaling Pathways.

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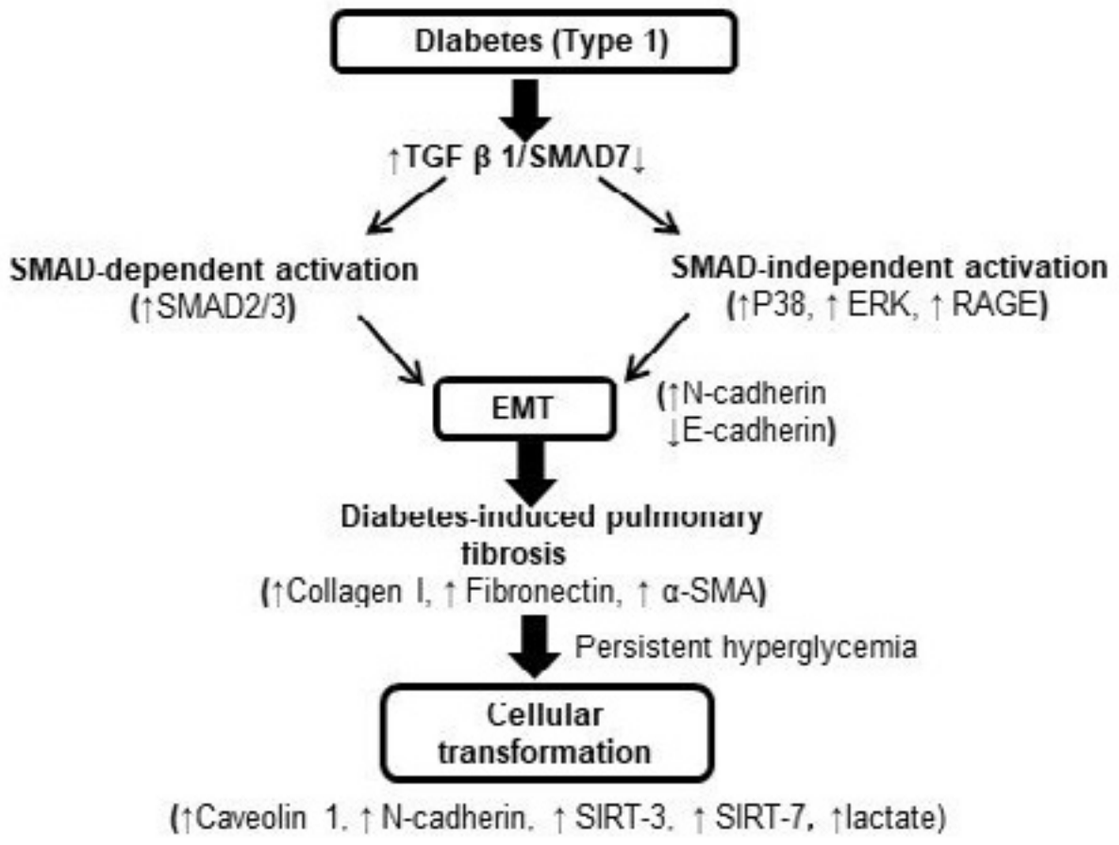
Diabetes, Sports Nutrition, Nutrigenomics.

Diabetes profoundly affects multiple organs in the body, such as kidney, heart, brain, liver, and eyes in the long term. The gradual loss of function in these vital organs contributes to mortality. Nonetheless, the effects of diabetes on the lung are not well characterized. Our studies demonstrate that diabetes induces inflammatory and fibrotic changes in the lung. These changes are mediated through the TGF-β activated epithelial to mesenchymal transition (EMT) through the involvement of both SMAD-dependent and -independent signaling pathways. Our studies also revealed that diabetes-induced TGF-β activation is observed first in the kidney, followed by the liver and the lung. The delayed effect of diabetes in the lung compared to the liver and the kidney was due to higher levels SMAD7, a negative regulator of TGF-β signaling.

Further, our results also revealed that glucose restriction promoted the mesenchymal to epithelial transition (MET), and substantially reduced the inflammatory and fibrotic changes suggesting that EMT was mediated by the durable effect of elevated glucose levels. Taken together, the study suggests that diabetes induces pathological changes in the lung in part by TGF-β activated EMT pathways. The glucose restriction can ameliorate above pathological changes.



YI 27

Is Direct cell-to-cell Transfer of Amyloid-β in Tunnelling Nanotubes the Consequences of Oligomer Induced Membrane Damage?

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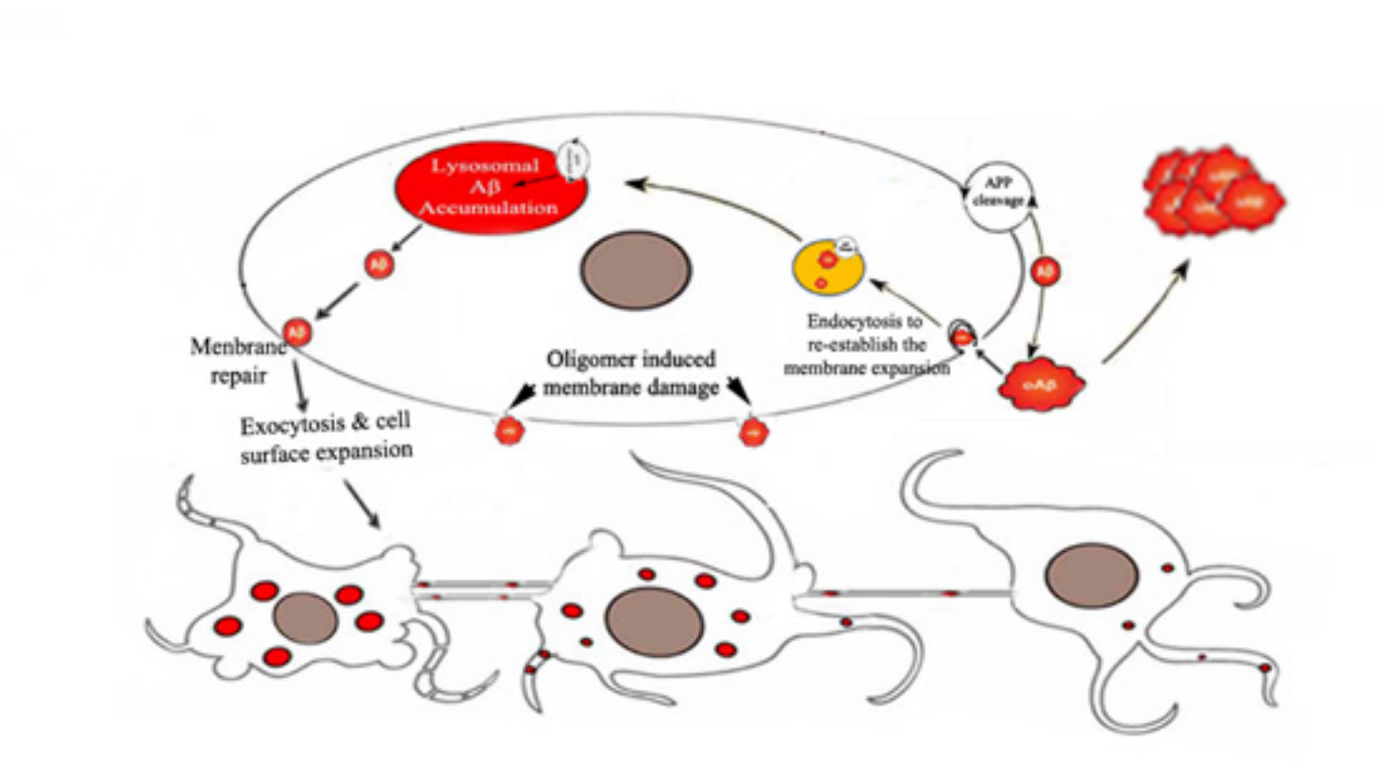
Neurodegenerative Diseases, Cell-To-Cell Direct Transfer, Tunnelling Nanotubes, Endo-Lysosomal Pathway, Exocytosis, Membrane, Biophysics, Single Molecule Imaging, Super-Resolution Microscopy

Background: Alzheimer's disease (AD) pathology progresses gradually through the anatomically connected brain in a strict spatiotemporal pattern. The progressive pathology development is due to transfer of non-degradable soluble oligomers of amyloid-β 1-42 (oAβ) between connected neurons (Nath et al., J Neurosci. 2012). However, the mechanism of transfer is not revealed yet. Results: Here we show that internalization of toxic oligomers of oAβ in SH-SY5Y cells, causes cellular stress detected as significant membrane surface expansion. Subsequently, protrusions in the form of tunnelling nanotubes (TNTs) appear towards neighbouring cells. The phenomenon is independent of differentiation stages of neuronal cells. The (TNTs) mediate direct cell-to-cell transfer of oAβ and oAβ is co-localized with lysosomes and organelles. Preceding the formation of TNTs, we detect oAβ-induced plasma membrane damage and repair through lysosomal exocytosis. The repair process is finalized by endocytosis to re-establish the plasma membrane. Eventually, the internalized and transferred oligomers end up to lysosomes. Conclusion: Direct transfer of PrPSc, β-synuclein, Aβ, tau and polyQ via TNTs has recently been suggested as means of pathology spreading in neurodegenerative diseases. However, molecular basis of TNTs formation is unexplored.



The present study gives insight that the formation of TNTs might derive as the consequences of plasma membrane damage and perturbed membrane repair process in the oAβ accumulated stressed cells, probably to maintain cell surface expansion and/or membrane tension in equilibrium. The study is also revealing the involvement of oAβ-induced TNTs in direct neuron-to-neuron transfer of amyloid pathology in AD progression.

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YI 28

Gene Editing Mediated Gene Therapy for β-Hemoglobinopathies

Gene Editing, Gene Therapy, Translational Research

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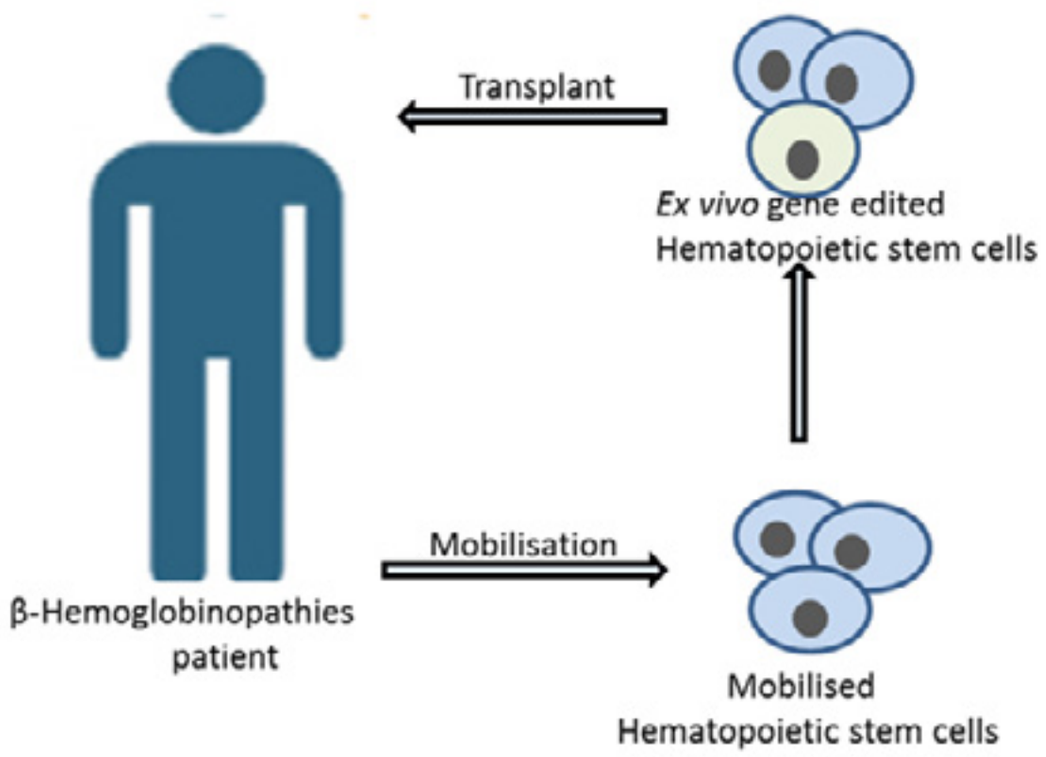
β-hemoglobinopathies namely β-Thalassemia and sickle cell disease (SCD) is the most common genetic disorders in India and a huge burden on the health care system of the country. Despite huge progress in understanding and identifying the diseases there exists only one curative treatment option of hematopoietic stem and progenitor cell (HSPC) transplantation from the human leukocyte antigen (HLA)-identical donors. However, this approach is limited to very few patients having matched donors.



Ex vivo genetic correction of patient HSCs and the transplantation of corrected HSPCs back to the patient is a potential alternative. Using CRISPR/Cas9 gene-editing system we genetically corrected the disease-causing mutation or introduced diseases alleviating beneficial mutations in the HSCs. The gene-edited HSPCs are differentiated to erythroblasts where we observed the gene-editing associated alteration in the erythropoiesis and hemoglobin production. The precision, the clinically beneficial levels of gene editing and hemoglobin production of our approach and the transplantation characterization of the gene-modified HSCs will be discussed.

YI 29

Learning the Hard Way: How Bees Handle Flowers of Complex Morphologies

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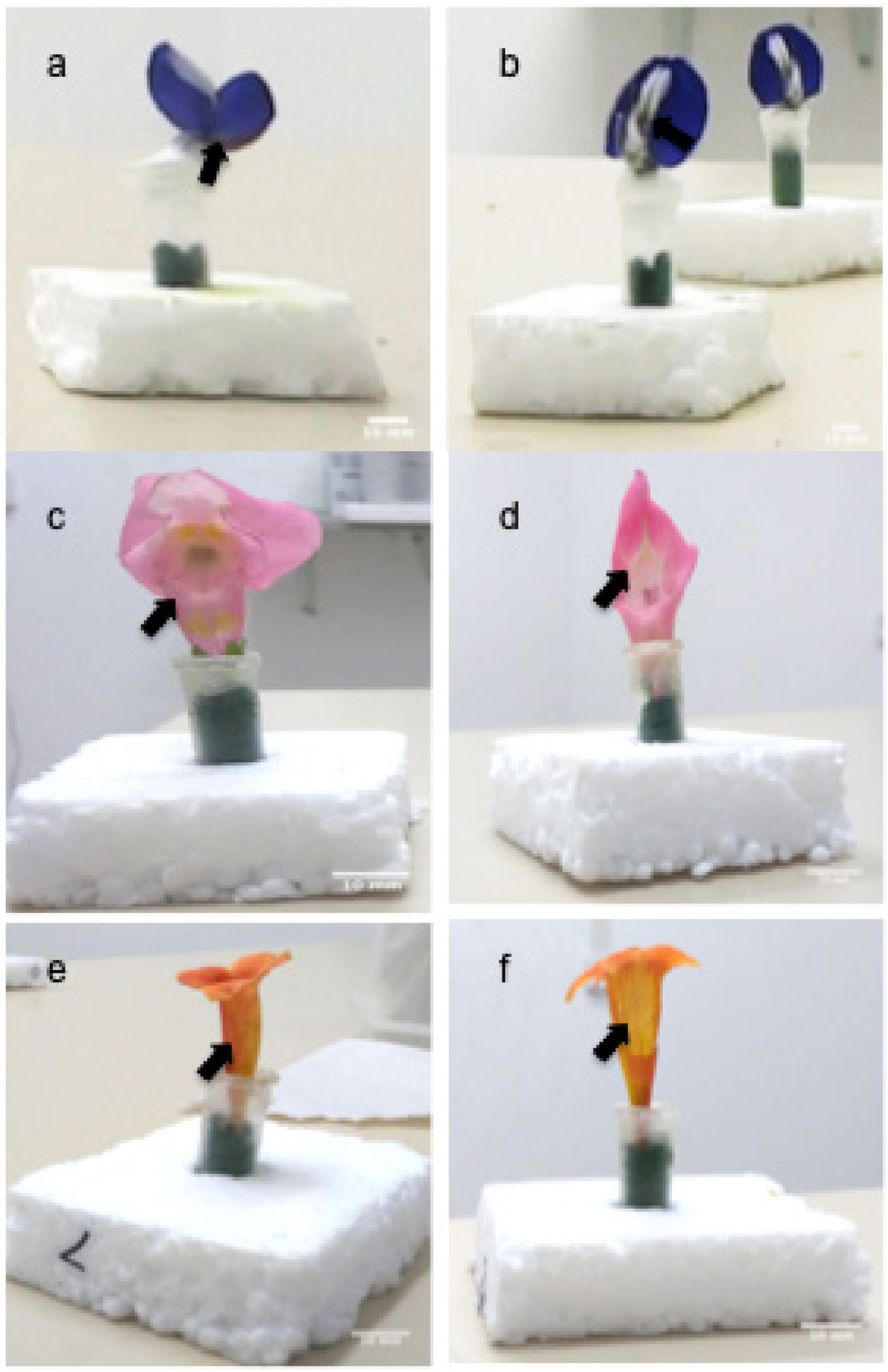
Plant-animal Interactions, Pollination, Plant Ecology, Foraging, Seed Dispersal

Foraging bees expend considerable time and energy handling flowers that are morphologically complex whilst flowers with readily available rewards bloom simultaneously in their foraging environment. How pollinators foraging choices and success vary along a floral complexity gradient and with prior experience has received less attention. Firstly, I investigated using real flowers of increasing complexity, how complex flowers are chosen and handled by naíve and experienced bumblebees when presented along with simple ones. Intact flowers of Tecoma x 'Orange Jubilee' (Bignoniaceae), *Antirrhinum majus* (Plantaginaceae) and *Lupinus pilosus* (Fabaceae) represented a gradient of increasing morphological complexity. I manipulated some flowers of each species to look simple with readily accessible and equal food reward, while keeping their color and odor unchanged in choice assays in a flight room. 60% of *naíve* Bombus *terrestris* foragers chose a complex flower on their first visit in all three flower species. Experienced bees visited complex flower types in all three species, but had lower feeding success and longer handling times in the more complex species. The bees' foraging efficiency on the complex option decreased with increasing complexity of the flowers. These results suggest that inexperienced foragers and unsuccessful feeding attempts increasingly contribute to floral pollination along the morphological complexity gradient.



YI 30

Novel Potential Natural Molecule Based Lead for Drug Discovery

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Natural Product Chemistry, Drug Discovery, Anti-cancer, Biological evaluation, Metabolomics, Proteomics

Natural products have been contributed significantly to anticancer drug discovery. The current report is focusing on medicinal chemistry of Dysoxylum binectariferum (DB). DB is phylogenetically related to the Ayurvedic plant D. malabaricum. DB is reported as rich source of rohitukine, discovery of clinical drug flavopiridol (CDK inhibitor) is based on rohitukine. Phytochemical investigation of DB yielded bulk amount of rohitukine. Minor amount of rohitukine N-oxide, and new region-isomer dysoline. A bioassay-guided isolation reported camptothecin and 9-methoxy camptothecin first time from DB. Several derivatives of rohitukine were synthesized and screened against a panel of CDK and cancer cell lines. The 2,6-dichloro-styryl derivative IIIM-290 was identified a potential lead and showed inhibition of Cdk-9/T1 (IC50 1.9 nM) kinase and Molt-4/MIAPaCa-2 cell growth (GI50 < 1.0 μM). Further studies; 71% oral bioavailability, in vivo efficacy in pancreatic, colon, and leukemia xenografts at 50 mg/kg, po. identified IIM 290 as potential lead to be developed further as anti-cancer therapeutics.

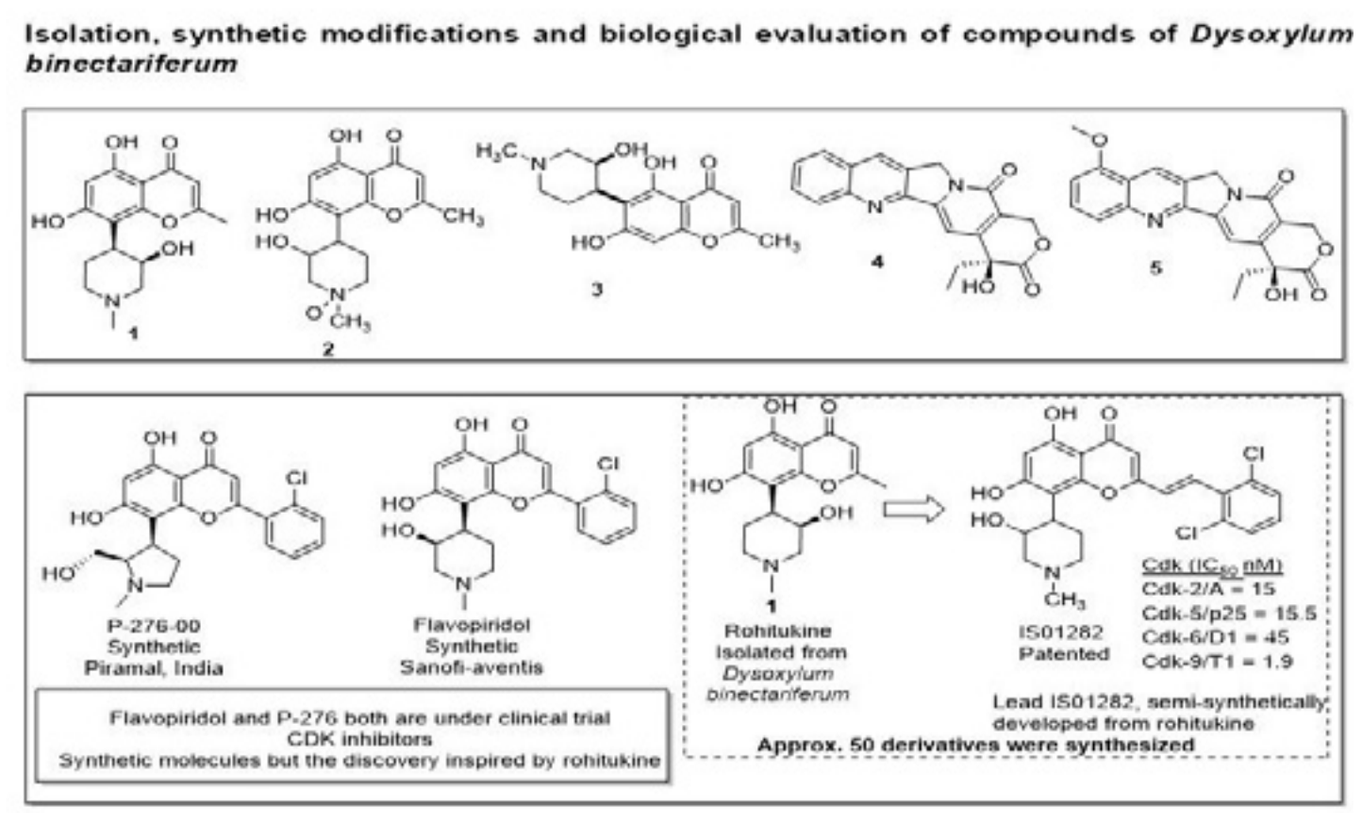

Table 1. CDK2, CDK9, cytotoxicity, PK and in-vivo anticancer results of IS01282.

Cell line	IC_{50} (μM)	Pharmacokinetics, IS01282		% TGI in *In-vivo* anticancer IS01282, IP	
	IS01282	Oral, 10 mg/kg	IV, 1 mg/kg	Ascites Carcinoma	Ehrlich solid tumor
HL-60	0.9	Bioavalability: 70%,	-	90 mg/kg: 90%	90 mg/kg: 41%
MOLT-4	0.5	Half life: 4.6 hr	5.46 h	(Mortitity 6/7)	(No mortitity)
SW620	0.2	C_{max}: 593 ng/mL	312 ng/mL	70 mg/kg: 85%	70 mg/kg: 37%
Panc-1	3	AUC_{0-t}: 2076 ng·h/mL	242 ng·h/mL	(Mortitity 2/7)	(No mortitity)
NCIH322	1	Clearance: -	55.4 mL/min/Kg	5-FU (20 mg/kg):	50 mg/kg: 33%
HGF	18	V_d $AUC_{0-\infty}$ 2128 ng·h/mL	26.2 L/Kg	96%	(No mortitity)
HOP-92	2		301 ng·h/mL	TGI :Tumor growth Inhibition	5-FU (22 mg/kg): 58

YI 31

Covalent Magnetic Tweezers: A New Tool to See Biology

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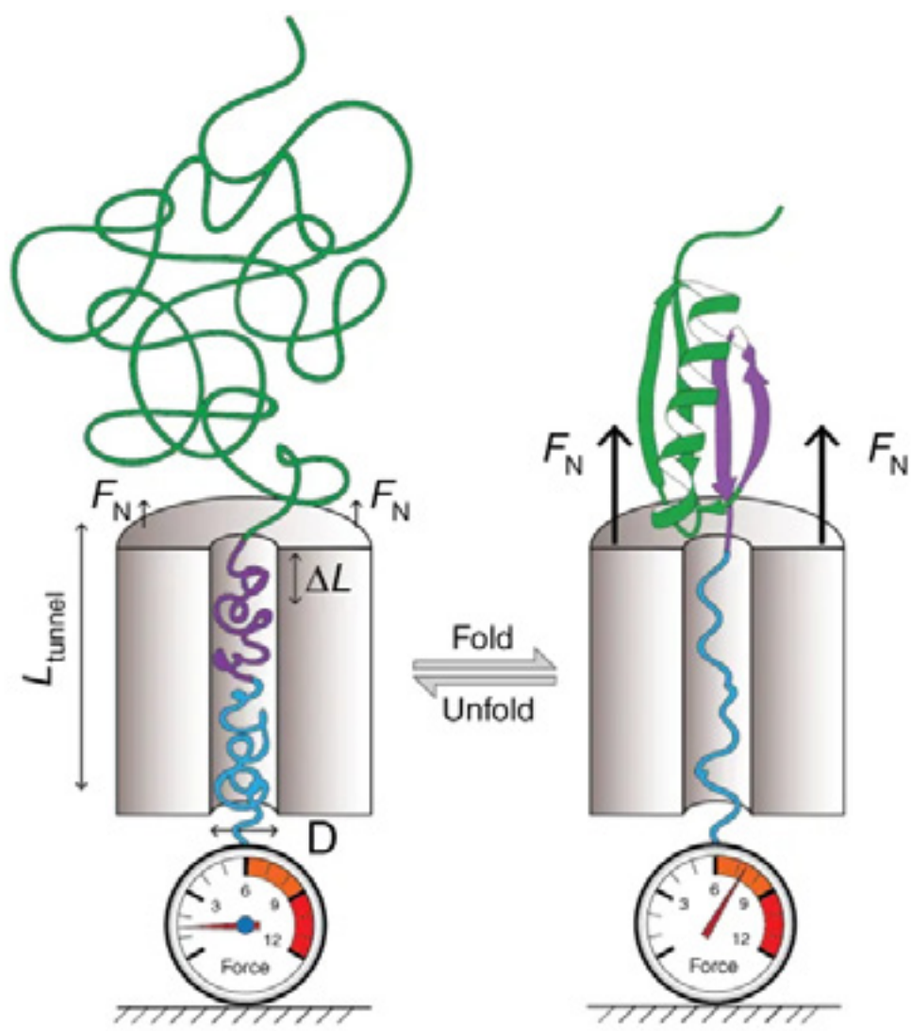
Covalent Magnetic Tweezers, Single Molecule Spectroscopy, Chaperone, Protein Folding

Proteins fold under mechanical forces in a number of biological processes, ranging from muscle contraction to co-translational folding. As force hinders folding, chaperones must play a crucial role in this scenario. Nevertheless, to date, it has not been possible to monitor the direct influence of a chaperone on a protein folding under force. Here, we introduce single molecule covalent magnetic tweezers (CMT) to study the folding dynamics of protein L in presence of the prototypical molecular chaperone Trigger Factor (TF) over the range of physiological forces (4 to 10 pN). Our results show that TF modulates folding of protein L by prominently increasing the probability of folding against the force and accelerating the refolding kinetics. Moreover, we find that the ability of TF to catalyze the folding reaction depends on the pulling force; as the force increases, higher concentrations of TF are needed for rescue folding. We propose for the first time that chaperones such as TF can work as foldases under force by restricting the entropy of the unfolded state.



YI 32

Structural Analysis of the Hsp70/Hsp40 Interactions using single molecule and bulk techniques

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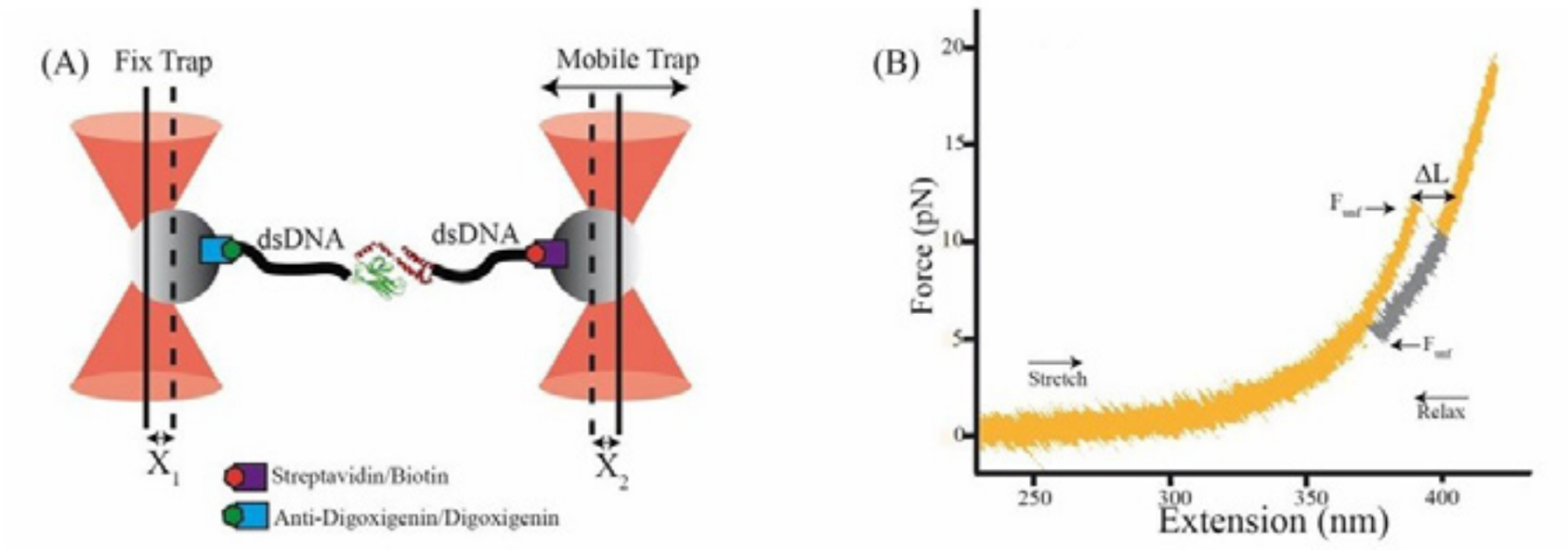
Protein Folding, Single Molecule, Heat Shock Proteins, Immunoprecipitation

The knowledge of physics associated with the functioning of macromolecules such as DNA, proteins is of significant importance to understand the functionality associated with them. The proteins can be single domain or multi domain which again influences the function it carries out in the body. Small proteins upto ~100 amino acids (aa) may fold in few milliseconds, while complication arises in the folding of larger proteins (>100 aa). The allosteric communication between the domains in a multi domain protein tends to control a variety of functions.

In a cell, misfolded or newly synthesized polypeptide chains interact with these chaperones. This interaction is associated with their conformational rearrangements, which finally converts polypeptide chains to a functionally active protein. The *E. coli* Hsp70 DnaK stabilizes the newly synthesized/unfolded polypeptide chains through a complicated DnaK cycle. This cycle is regulated by co-chaperones. DnaK consists of two subdomains, a nucleotide binding domain (NBD) and a substrate-binding domain (SBD). The NBD consists of four subdomains while SBD consists of two subdomains namely the -helical lid domain and β-sandwich domain, harboring the peptide-binding site. The nucleotide binding status of NBD along with the co-chaperones modulates conformational changes in SBD subdomain. The mechanism by which cochaperones viz., DnaJ, GrpE modulate allosteric interaction is unclear and hence raises several questions.

In this study, we use immunoprecipitation and optical tweezers (OT) assays to investigate the chaperonic action and allosteric signal transmission mechanism. The kinetic parameters were extracted from OT measurements at the level of a single molecule.



YI 33

Elucidating the Role of Intrinsically Disordered Regions in Regulation of Function of Eukaryotic Transcription Factors

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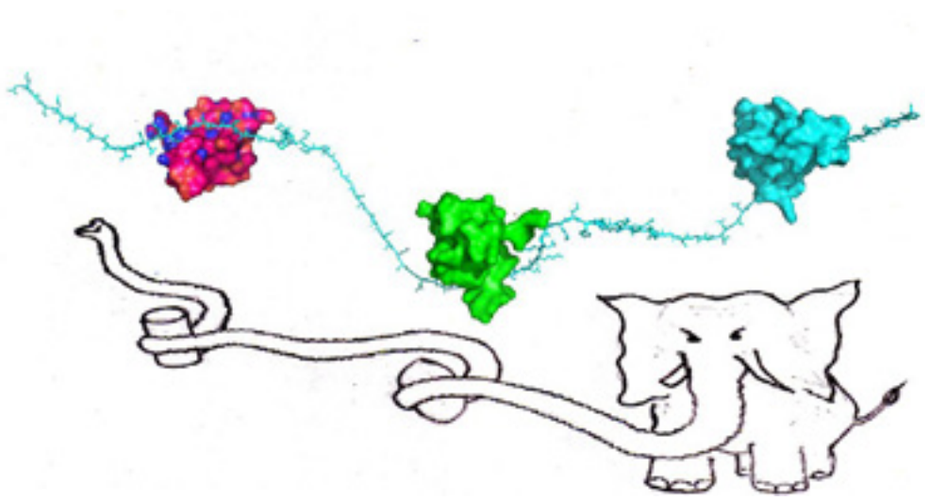
Intrinsically Disordered Region, Transcription Factors, Protein-Protein Interaction, Protein Dynamics, NMR Spectroscopy

Transcription factors (TFs) are DNA-binding proteins that regulate gene expression and play crucial roles in many biological processes. TF functions are under tight regulation, loss of which results in various diseases. Most eukaryotic TFs have long stretches of intrinsically disordered regions (IDRs), which do not form any defined 3D structure but are functionally important. IDRs regulate TF functions via post-translational modifications, interactions with partner proteins and DNA, and DNA-binding autoinhibition. These mechanisms require sequence specific interactions between IDRs and other proteins. This raises a critical question: in the absence of any defined 3D structure how do IDRs achieve specific interactions with proteins and DNA?

Recently, we have shown that IDRs have short rigid segments that are important for the function of the protein. Using NMR spectroscopy, we characterized the picosecond-nanosecond dynamics of two Drosophila HOX TFs: Deformed and Sex comb reduced. We introduced a method to measure the residue-wise rigidity of the IDRs and show that not all residues are equally flexible. IDRs consist of small stretches of residues (~5 to 7), which have significantly higher rigidity compared to the remaining IDR residues. We found one segment in the IDRs, which is also conserved in the HOX family, with significantly higher rigidity. By titration experiments we show that this rigid segment is specifically bound by a co-transcription factor Extradenticle. We propose that IDRs consist of rigid segments, which can regulate the protein function through specific interactions with other molecules.

Our overarching aim is to identify rigid segments in TFs and investigate their function in normal and diseased conditions. Currently, we are studying IDRs in several human HOX factors involved in leukemia and prostate cancer. We are establishing collaborations for in vitro and in vivo functional experiments to assess the roles of the identified rigid segments in IDRs.



YI 34

Understanding the Heterogeneity in Nuclear Morphology of Adherent Cells

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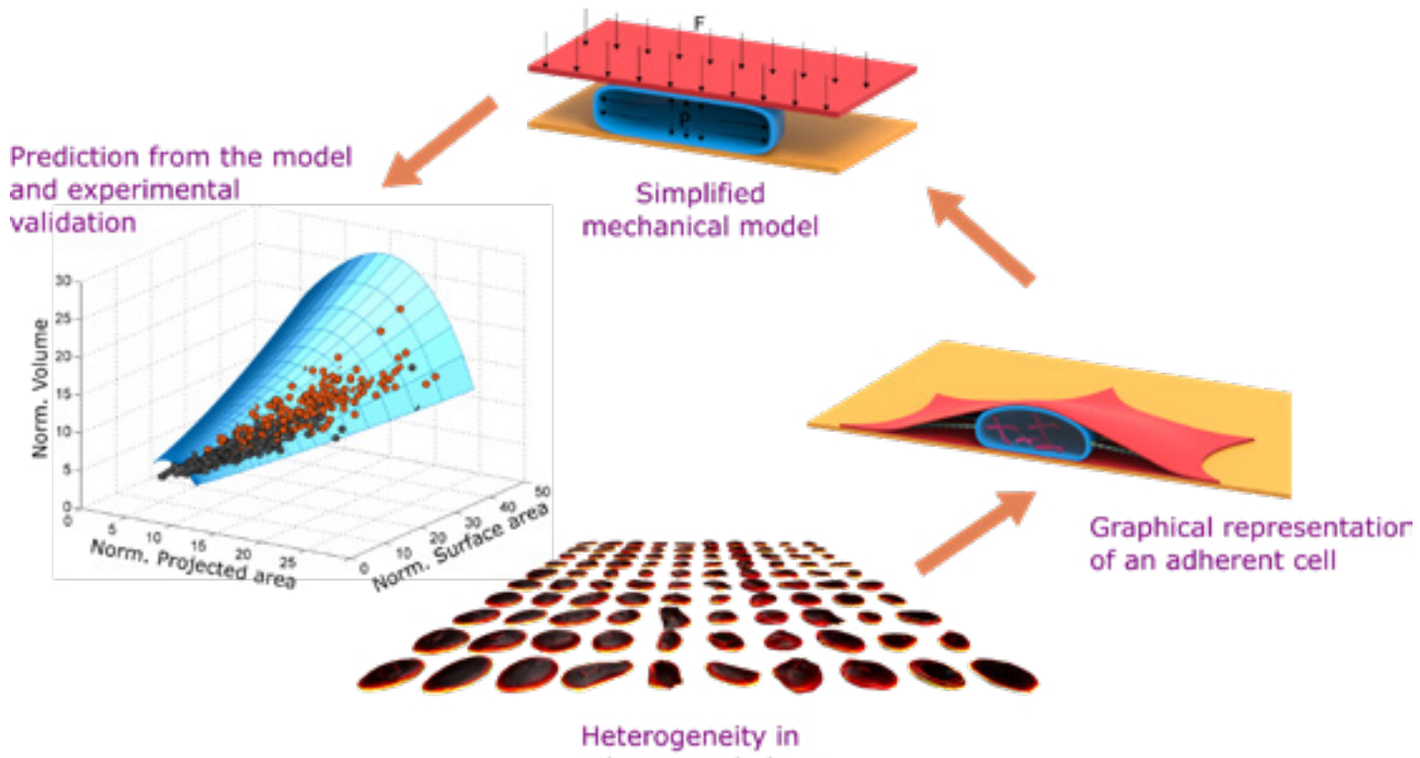
Cell Mechanics, Mechanobiology, Micromanipulation, Biomechanics, Compliant Mechanisms

Nuclear morphology of individual cells is known to exhibit large variability. Even though many factors that regulate nuclear shape are known1, there are no theories that can quantitatively explain this variability. Here, we propose a mechanical model that can explain this variability and infer molecular mechanisms by merely analyzing nuclear morphology2. Our model predicts a relationship among nuclear shape parameters such as projected area, surface area and volume, which was satisfied by individual nuclei of multiple adherent cells of varied origin such as Huh7, MCF7, MDAMB231, HEK and NIH3T3. The relationship was maintained even when these cells were perturbed using drugs that regulate the cytoskeleton and when they were cultured on a 3D substrate.

Our model defines two nondimensional parameters that can be estimated from the morphology of individual nuclei. These nondimensional parameters are a function of various mechanical parameters of the cell such as stiffness of the nuclear envelope, the compressive force on the nuclear envelope due to cortical actin and an inflating pressure on the nuclear envelope due to the difference in osmotic pressure between nucleoplasm and cytoplasm. By comparing the changes in these nondimensional parameters due to any stimuli, the molecular mechanisms responsible for the changes in nuclear mechanics due to that stimuli can be predicted. We show this in the case of Hepatitis C Virus infection in liver cells, wherein we identify the downregulation of lamin and upregulation of actin by merely analyzing the changes in nuclear shape.



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YI 35

An Integrated and Multidisciplinary Approach to the Development of Ocular Theranostic Solutions

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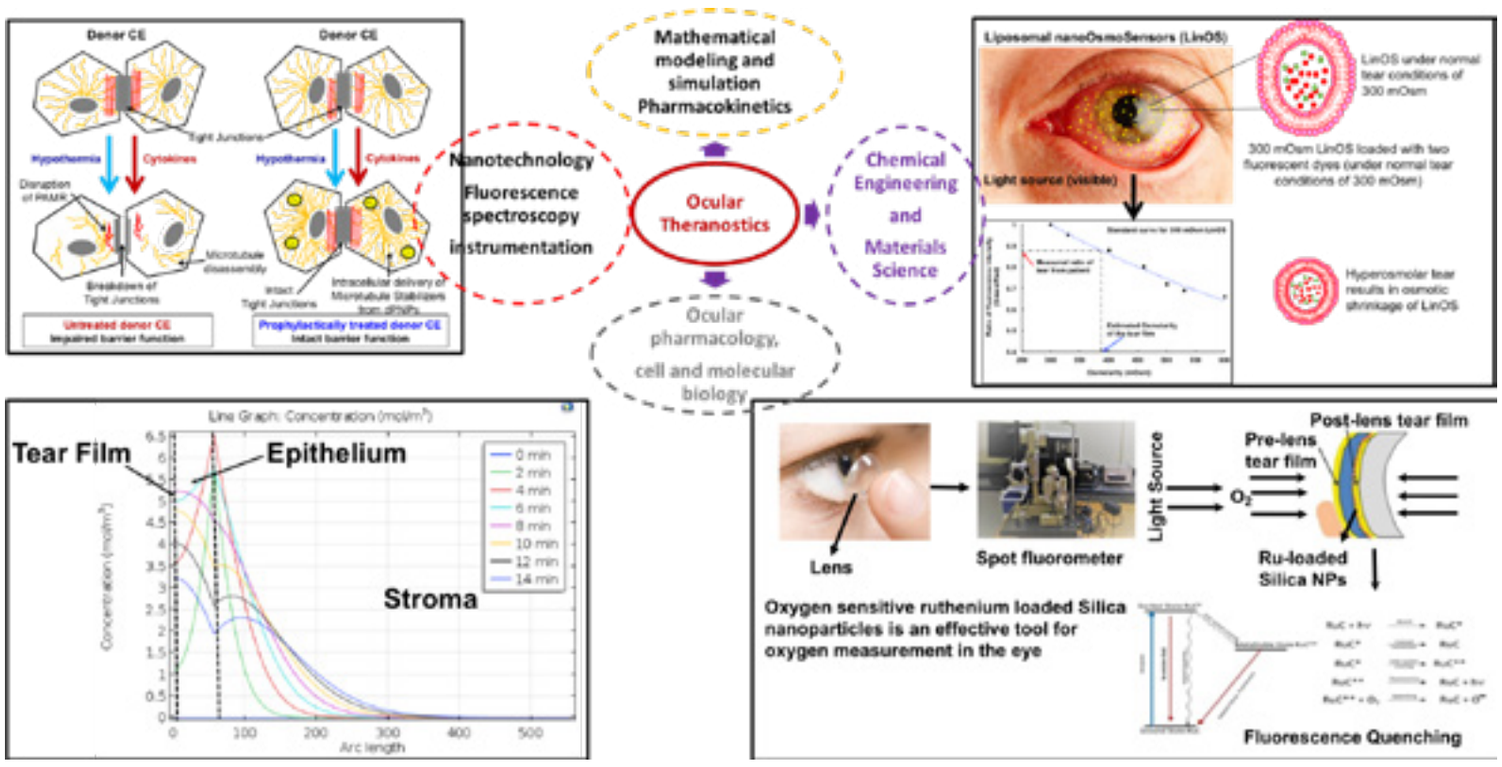
Drug Delivery, Ocular Biosensing, Bioengineering, Stem Cell Biology, Fluorescence Spectroscopy

The human eye offers many challenges, yet exciting opportunities for drug delivery. Its transparency could be harnessed to sense clinically relevant microenvironmental factors for diagnosis. We narrate here four examples of our multidisciplinary and integrated approach for developing ocular drug delivery systems and biosensors. (i) Contact lens wear affects oxygen tension (pO2) in the post-lens tear film (PLTF), and thereby, influence oxidative metabolism in the cellular layers of the cornea. Thus, it is imperative to assess pO2 in the PLTF. Measurement of phosphorescence lifetime of O2-sensitive porphyrin yields 100-1000 us at a slow sampling speed of ~ 0.1 Hz. We have prepared functionalized, Ruthenium loaded-SiO2 nanoparticles and successfully deposited on the posterior surface of hydrogel contact lenses. The nanoparticles possessed an O2-sensitive lifetime of ~6 us. Thus, we have advanced rapid measurement of pO2 dynamics in the PLTF. (ii) Accurate diagnosis of local dry spots in dry eye disease is a clinical unmet need. We are developing a highly osmosensitive liposome-based nanosensor to non-invasively measure local osmolarity in the tear film. The nanosensors are loaded with two fluorescent dyes (Calcein and Sulforhodamine), at low concentration and saturation, respectively. Using a custom-made ocular spot fluorometer, we intend to measure the local osmolarity via ratiometric fluorescence spectroscopy approach. (iii) During corneal transplantation, corneal functionality is compromised under hypothermic stress and after transplantation (cytokine stress) due to disruption of the tight junction. Hence, we are developing a nanoparticle-based prophylactic drug delivery approach to protect the barrier integrity before and after transplantation. (iv) Mathematical modelling and simulation of drug/nutrient transport across various ocular barriers is being performed. This would help us understand transport properties of drugs and design rational drug delivery devices. Validation of the models are being done using patient data. Our future goals include prototype development and subsequent clinical translation.



YI 36

mTORC2-Mediated Regulation of Sphingolipid Biosynthesis is Involved in Breast Cancer Progression

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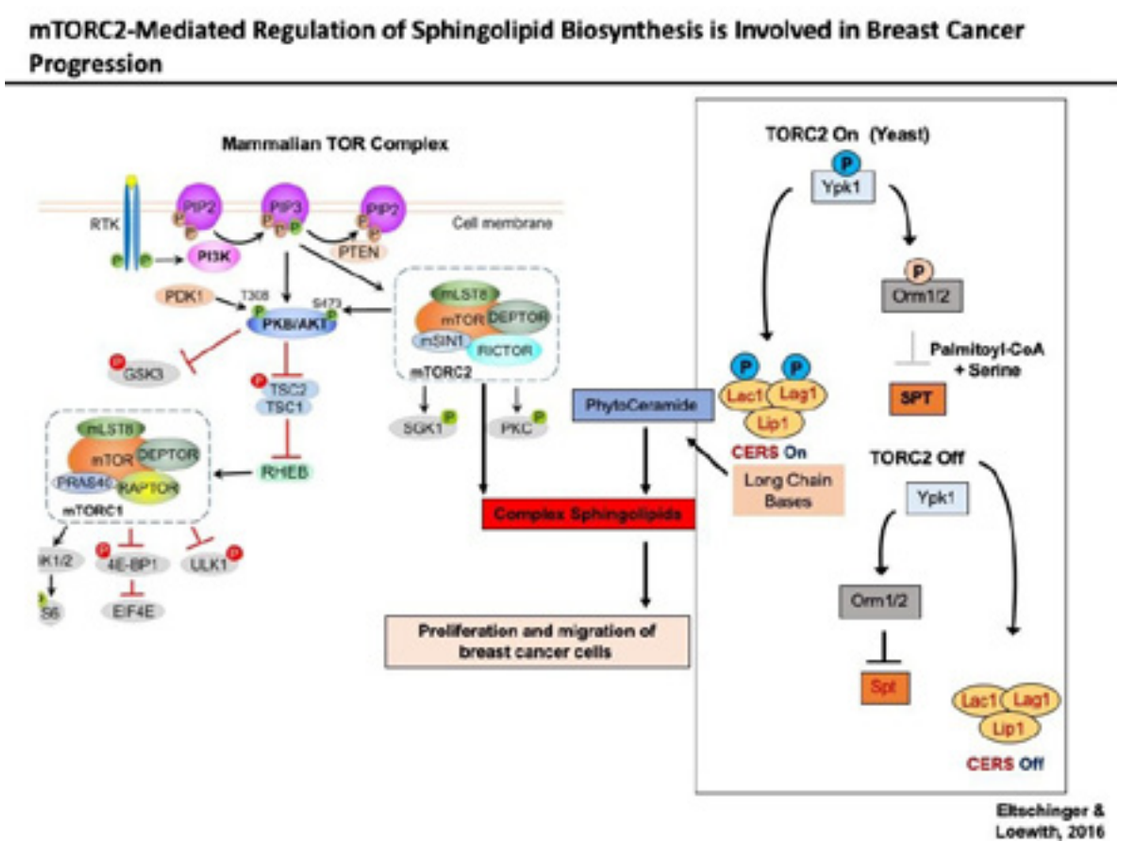
Sphingolipids, Cancer, Regulation, Signalling, Therapy

Rapamycin-resistant TOR Complex (Target of Rapamycin) component TORC2, that regulates cell proliferation, actin rearrangement, and survival shows a distinct role in cancer and has been shown to regulate the sphingolipid metabolic pathway in yeast. Sphingolipids have emerged as key regulators of cancer progression. However, regulation of sphingolipid pathway through mTORC2 complex in mammals is still unknown. We hypothesized that there may be parallels between yeast and mammals with respect to regulation of sphingolipid biosynthesis by TORC2. As sphingolipids are crucial for cancer cell proliferation and apoptosis, mTORC2 may be playing a critical role in cancer progression through sphingolipid signalling and metabolic programming.



We silenced RICTOR (regulatory subunit of mTORC2) gene expression in Estrogen receptor positive breast cancer MCF7 (Luminal A) and BT474 (Luminal B) cells by shRNA-mediated knockdown. RICTOR silenced MCF7 cells show significantly decreased cell proliferation and migration in in vitro assays. Qualitative and quantitative lipidomics showed significant alterations in the sphingolipid profile of RICTOR silenced MCF7 and BT474. Silencing of RICTOR led to downregulation of glucosylceramides and upregulation of lactosylceramides in MCF7 cells and upregulation of ceramides and lactosylceramides in BT474 cells. The alterations in the lipid levels could be correlated with corresponding changes in the gene expression that code for the respective enzymes in the pathway. Therefore, our data shows that mTORC2 signalling regulates sphingolipid biosynthesis in mammalian breast cancer cells.

Pharmacological/genetic manipulations in MCF7 cells to mimic the alterations in sphingolipids as seen on RICTOR silencing, followed by in vitro proliferation and migration assays are now in progress with the rational that targeting the mTORC2 branch of mTOR signalling pathway via modulation of sphingolipids may offer a new and distinct therapeutic approach with potentially lower side effects and/or inherent toxicities.

YI 37

Amelioration of Neurodegeneration through Modulation of Protein Quality Control Processes in Cobalamin Supplemented Diabetic Rats

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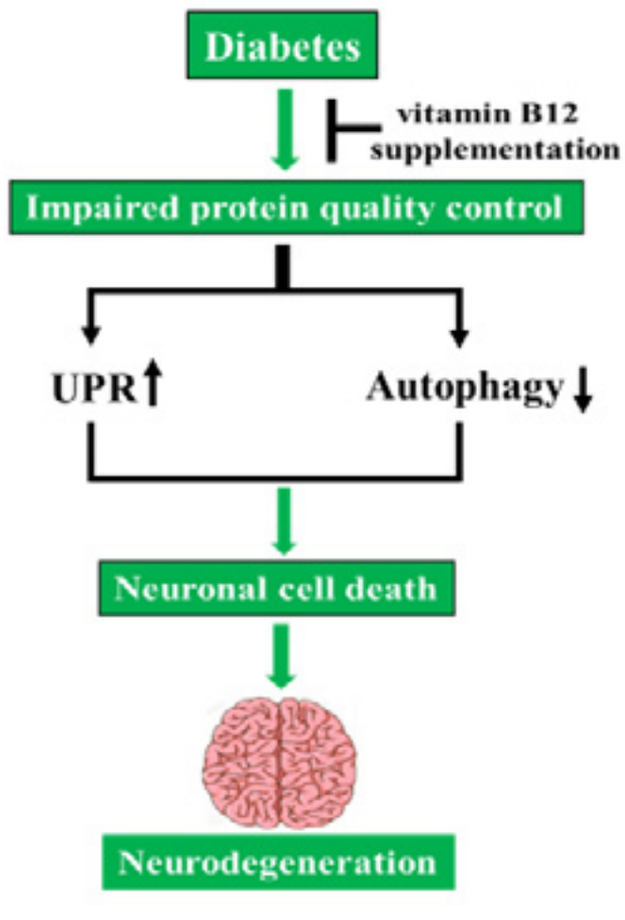
Mini-Chaperones, Heat Shock Proteins, ER Stress, Proteostasis, Diabetes

Hyperglycemia-induced ER stress, altered neurotrophic support and apoptosis in the brain contribute to neurodegeneration and cognitive deficit. Several studies have documented the increased frequency of cobalamin deficiency in patients with diabetes1. Protein quality control processes are associated with the maintenance of functional protein homeostasis. Unfolded protein response (UPR), and autophagy constitute part of proteostasis and altered in diabetes2. In this background, we aimed to investigate impact of cobalamin supplementation in diabetic neurodegeneration. We induced diabetes in WNIN rats using STZ and the animals are divided into (i) control (CN) (ii) diabetes (D) (iii) diabetic rats supplemented with the cobalamin (DS) after induction of diabetes for 4 months. Here, we show that supplementation of cobalamin increased the plasma cobalamin levels in DS group while decreased the homocysteine levels in plasma of D and DS groups. H&E, Nissl body staining showed eosinophilic degeneration, and chromatolysis of neuronal cell bodies in cerebral cortex of D group while restored upon supplementation of cobalamin. Further, cobalamin alleviated the ER stress by decreasing the expression of ER stress markers and restored the neurotrophic support and autophagy in DS group compared to diabetes. Cobalamin supplementation also reduced the cell death as analyzed by TUNEL assay and caspase-3 immunostaining. Overall, here we show that supplementation of cobalamin ameliorates the neurodegeneration by modulating ER stress, autophagy, neurotrophic support, and cell death in diabetes. This study likely to help in developing vitamin B therapy based strategies for diabetes.



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YI 38

Understanding Stress Response of Aeromonas in Food Environment and its Control

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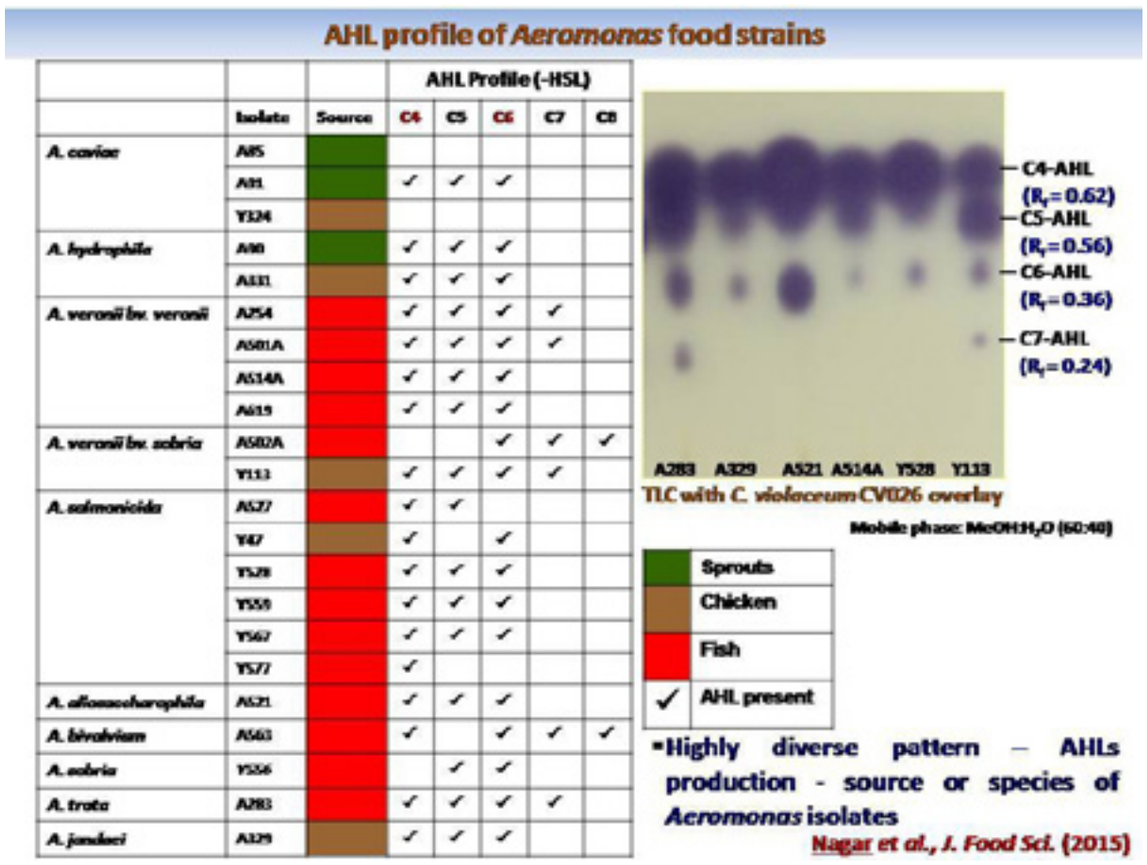
Food Microbiology, Biofilm, Quorum Sensing, Bacteriophage, Food Processing

Aeromonas are regarded as opportunistic as well as primary pathogens of humans and fish, and are associated with gastroenteritis and septicemia in humans. There is lack of information regarding quorum sensing mechanism, biofilm formation and gene expression in *Aeromonas* food strains. Moreover, there are no studies regarding the relative efficacy of gamma radiation against *Aeromonas* free-living planktonic and biofilm-associated cells. Our study showed that majority of food strains produced C4-HSL and C6-HSL as quorum sensing molecules and formed highly variable biofilms in two different media. Majority of the strains formed the highest biofilm at low temperature (10 °C) and acidic condition (pH 5), and their biofilm reduced with an increase in NaCl concentration. Food-related sub-lethal stresses invoked significant changes in the expression of important housekeeping (rpoD), general stress-response regulators (rpoS and uspA), and aerolysin (aer) genes in *A. hydrophila* strains in a strain-dependent manner. Various virulence genes and class 1 & 2 integrons were present in majority of these food isolates and thus may be potentially pathogenic. Decimal reduction (D10) doses of planktonic and glass-associated biofilm cells did not show significant difference; whereas, significant increase in the D10 values of carrot-associated biofilm cells was observed as compared to planktonic and glass-associated biofilm cells. Bacteriophages against pathogenic *Aeromonas* species have been isolated and characterized. Structure of AhyR will be further determined for high throughput screening of natural molecules from database using molecular docking studies for their inhibition of various QS-regulated phenotypes. In addition, the use of various methods (quorum quenching compounds/ enzymes/ bacteriophages) in combination will be studied for the better efficacy of removal of biofilms from the food systems.



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YI 39

Gut Microbiota in Toxicological Risk Assessment of Drugs And Chemicals: The Need of Hour

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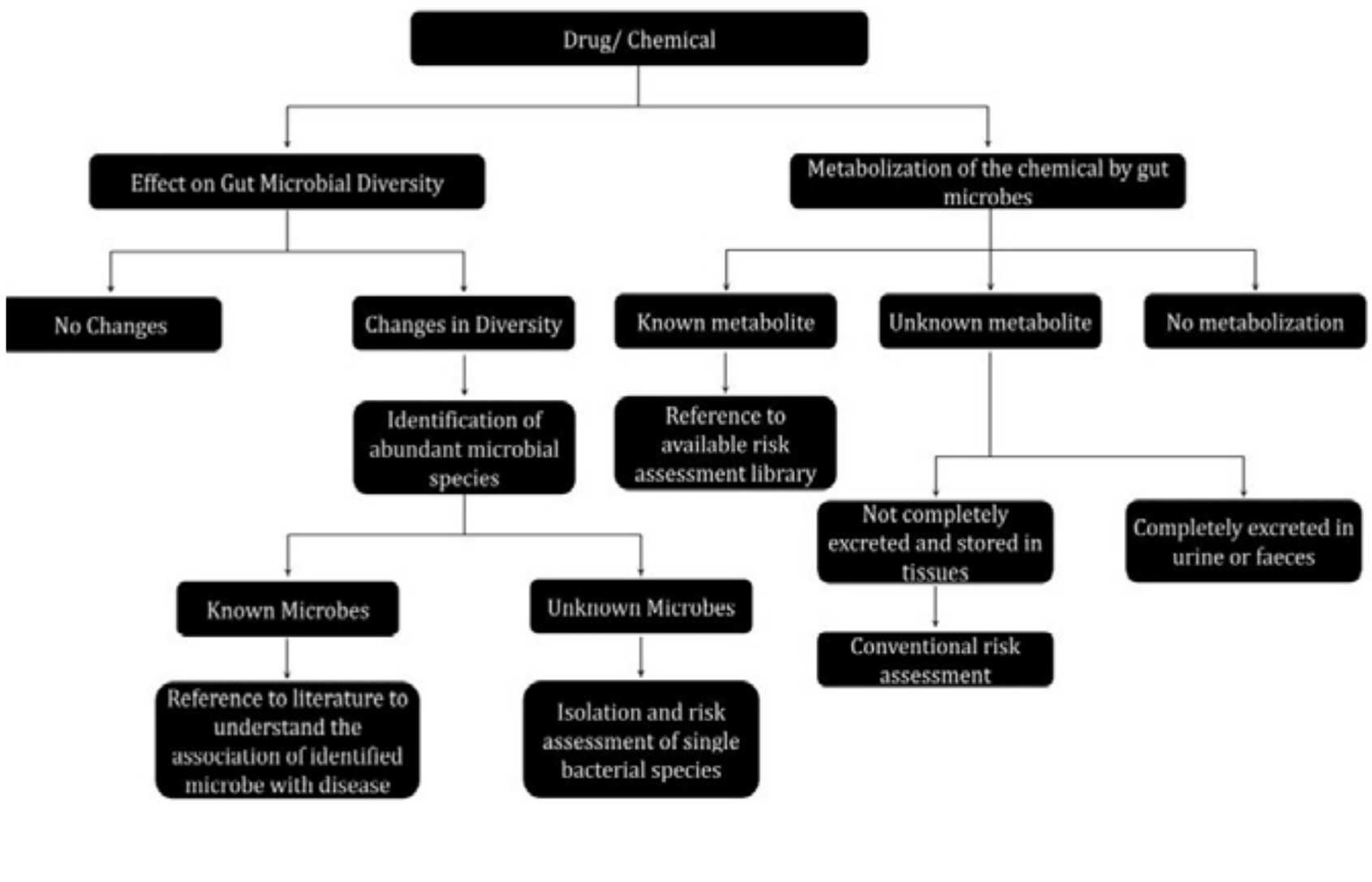
Gut Microbiota And Human Health, Endocrine-Disrupting Chemicals, Environmental Microbiology, Microbial Technologies, Chemomicrobiomics

The advent of industrial revolution caused a large inflow of synthetic chemicals for medical, agricultural, industrial and other purposes in the world. In general, these chemicals were subjected to toxicological risk assessment for human health and ecology before release for public use. But today we are witnessing a negative impact of some of these chemicals on human health and environment indicating an underestimation of toxic effects by current risk assessment protocol.

Recent studies established gut microbiota as one of the key player in intercession of toxicity of drugs and synthetic chemicals. Hence, the need of the hour is to include the assessment for microbiota specifically gut microbiota in human toxicological risk assessment protocol. Herewith we are proposing a framework for assessment of gut microbiota upon exposure to drugs or chemicals.



YI 40

Lateral Flow Immunosensing: Material Processing and Parameter Optimization

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Point-of-care NanoDiagnostics, NanoBioTehcnology, Lateral Flow Immunodiagnostics, Gold NanoBioSensors, Drug Delivery

Lateral flow immunosensing (LFIS) is a commonly used method in the field of point-of-care diagnostics. Various components such as sample pad, conjugate pad, nitrocellulose membrane (NCM), absorbent pad are assembled on the plastic backing laminate to prepare the functional LFIS strip, which is used for analyte sensing. The material used for the strip assembly is to be processed using heat and buffer treatment, which ultimately affects the physicochemical parameters of the NCM. Processing of material and technical parameters further affects the sensitivity of LFIS as the surface morphology and structure is modified. We have described various material used in the LFIS preparation and properties thereof. Procedures of material modification used in LFIS development by virtue of particular application are also included. The combinations of various assemblies that are used for the detection of various analytes are also studied with respect to the literature. Various parameters and their effect on the flow properties of fluid through NCM are described with respect to application examples. We have described optimization processes that can be considered while designing and developing the LFIS. The processes used for the amplification of the signal and improve the sensitivity of the LFIS technique are explained with examples. We expect that this study may potentially help researchers in the selection of material and process parameter optimization for the development of the LFIS based diagnostic platforms.

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