1. Basic information (the title of the meeting, dates, organiser, venue, etc.)

Title: Modeling development and disease with human tissue organoids
Dates: Feb 6-9, 2023
Organizers:

Carol Schuurmans, Sunnybrook Research Institute, Toronto, Canada
Orly Reiner, Weizmann Institute of Science, Rehovot, Israel
Bhavana Muralidharan, Institute for Stem Cell Science and Regenerative Medicine (InStem)Bangalore, India
Shubha Tole, Tata Institute of Fundamental Research (TIFR), Mumbai, India

Venue: Institute for Stem Cell Science and Regenerative Medicine (InStem)
GKVK – Post, Bellary Rd
Bengaluru – 560065
Karnataka, India

2. Registration and registration fees

A website was generated with registration information
https://meetings.embo.org/event/21-organoids

Registration

- REGISTRATION DEADLINE WITH OR WITHOUT ABSTRACT
- 10 December 2022
- CHOSEN PARTICIPANTS WILL BE NOTIFIED BY
- 15 December 2022
- PAYMENT DEADLINE
- 20 December 2022

- INDIAN STUDENT/POSTDOCSINR 12,000
- INTERNATIONAL STUDENT/POSTDOCSEUR 150
- ACADEMICEUR 300
- INDUSTRYEUR 700

3. Program

https://meetings.embo.org/event/21-organoids

Day 1 | 6 February 2023

13:00-16:00
Registration
15:00-16:00
Opening Welcome Reception
16:00-16:15

Welcome Address and Acknowledgements (EMBO, ISN)
Dr. Bhavana Muralidharan & Dr. Shubha Tole
Session 1: Cerebral organoids to study neurodevelopment
Chair: Dr. Carol Schuurmans
16:15-16:45
Brain organoids for modeling brain malformations: clues from the progenitors
Dr. Orly Reiner
16:45-17:15
Engineered human cortical spheroids for dissecting molecular determinants of neurodevelopment
Dr. Debojyoti Chakraborty
17:15-17:30
Dissecting the genetic determinants of cortical interneuron migration in human forebrain assembloids
Riya Rauthan
17:30-17:45
Short Break
Session 2: Biomedical Ethics
Chair: Dr. Shubha Tole
17:45-18:15
Foregrounding Equity, Justice and Inclusion as Determinants of Access to Precision Medicine: An Ethical Case Study of Patient-Derived Tissue Organoids
Dr. Ubaka Ogbogu
18:15-18:45
Ethical and social considerations of multi-system organoids: Need of interdisciplinary approaches
Dr. Kazuto Kato
18:45-19:30
Panel Discussion
Dr. Maneesha Inamdar, Dr. Ubaka Ogbogu, Dr. Kazuto Kato
19:30
Dinner

Day 2 | 7 February 2023

8:00-9:00
Breakfast
Session 3: iPSC-derived 2D and 3D systems to model CNS disorders
Chair: Dr. Orly Reiner
09:00-09:30
Modelling neurodevelopmental disorders using iPSC-derived 2D neuronal cultures and 3D cerebral organoids
Dr. Bhavana Muralidharan
09:30-10:00
Patient-derived brain organoids to characterize epileptic Dravet syndrome
Dr. Deborah Kurrasch
10:00-10:30

Creating functional human cortical circuits in vivo using stem cells and implications for modeling neurodevelopmental disorders"
Dr. Omer Revah
10:30-11:00
Coffee break
11:00-11:30
Modeling neurodegenerative diseases using iPSC-derived neuronal and glial cells
Dr. Stefano Stifani
11:30-12:00
Understanding eye development and disease using patient-specific iPSCs and iPSC-derived organoids
Dr. Indumathi Mariappan
12:00-13:00
Poster Blitz
Dr. Orly Reiner
13:00-14:00
Lunch
Poster Session 1
14:00-16:00
Coffee break
Session 4: Mentoring Session
Chair: Dr. Shubha Tole
16:00-16:30
Navigating graduate school
Dr. Shubha Tole
16:30-17:00
How to choose a postdoc
Dr. Deborah Kurrasch
17:00-17:30
Work-life balance and mental health
Dr. Isabelle Aubert
17:30-18:00
Diversity and Inclusion
Dr. Shalini Arya
18:00-18:30
Stepwise: from a small town in India to a successful career (virtual)
Dr. Nandini Trivedi
18:30-19:30
Open Panel Discussion
Session speakers
19:30
Dinner and continued round table discussion
Dinner
21:00
Cultural Music Program

Day 3 | 8 February 2023

8:00-9:00
Breakfast
Session 5: Organoid Bioengineering
Chair: Dr. Bhavana Muralidharan
9:00-9:30
Using machine learning and bioengineering to build robust human organoids
Dr. Sharad Ramanathan
09:30-10:00
Sensor-embedded 3D human organoids for drug development
Dr. Yaakov Nahmias
10:00-10:15
Efficient expansion of iPSC-derived human lung epithelium as adherent cultures and 3D organoids using defined, serum free medium for disease modelling and cell therapy
Swathi Narasimhaiah
10:15-10:30
MicroRNA-135 drives human neural stem cell fate determination: Employing induced pluripotent stem cells (iPSCs) derived 2D neural stem cells (NSCs)
Yogita Adlakha
10:30-11:00
Coffee break
11:00-11:30
A human stem-cell model of neural tube folding morphogenesis
Dr. Eyal Karzbrun
11:30-12:00
From personalized blood-brain-barrier (BBB)-on-Chip to pre-clinical BBB targeted gene therapy
Dr. Gad Vatine
12:00-12:15
How LIS1 is Involved in the Regulation of the Extracellular Matrix
Maayan Karlinski
12:15-13:15
Poster Blitz
Dr. Orly Reiner
13:15-14:15
Lunch
Poster Session 2
14:15-16:15
Coffee break
17:00-17:30
Departure Gala Dinner
18:00-21:00
Gala Dinner
21:00
Return to hotel

Day 4 | 9 February 2023

8:00-9:00
Breakfast
Session 6: Other tissue organoids
Chair: Dr. Debojyoti Chakraborti
9:00-9:30
Engineering organoids to understand human development and disease
Dr. Nuria Montserrat
09:30-10:00
Human organoid models of kidney disease and regeneration
Dr. Benjamin Freedman
10:00-10:15
Exploiting Intestinal Organoid Model to interrogate Shigella pathogenesis
Nidhi Kamboj
10:15-10:30
Establishing 3D multicellular spheroid to imitate tumor microenvironment for chemotherapeutic drug efficacy modulation in cancer
Khushwant Singh
10:30-11:00
Coffee break
11:00-11:30
Inherited pancreatic disorders illuminated by pluripotent stem cells
Dr. Markus Breunig
11:30-12:00
Modeling atrophy and metabolic disease using skeletal muscle organoids
Dr. Arvind Ramanathan
12:00-12:30
Organs-on-a-Chip: A new tool for studying physiology
Dr. Ben Maoz
12:30-12:45
Constitutive activation of canonical Wnt signaling disrupts choroid plexus epithelial fate
Arpan Parichha
12:45-13:00
Unravelling the role of the ciliary protein CEP290 in neural development by generation of human 2D and 3D iPSC-derived neuronal models for the ciliopathy Joubert Syndrome
Melanie Eschment
13:00-14:00
Lunch
Session 7: Modeling disease and neurodevelopment with cerebral organoids
Chair: Dr. Indumathi Mariappan
14:00-14:30
Modeling neurodevelopmental diseases and cancer using cerebral organoids (virtual)
Dr. Pavithra Chavali
14:30-15:00
Using brain organoids to interrogate proneural gene function

Dr. Carol Schuurmans
15:00-15:30
Modeling human brain development and disease: the role of primary cilia
Dr. Christina Kyrousi
15:30-15:45
Adrenomedullin promotes interneuron migration in a human forebrain assembloid for hypoxic interneuronopathy of prematurity
Dhriti Nagar
15:45-16:00
Dissecting the involvement of acid sphingomyelinase inhibition in GBA-dependent Parkinson's disease
Silvia Breviario
Closing and Awards
16:00-16:30
Closing Remarks and Awards
Dr. Shubha Tole & Dr. Bhavana Muralidharan
16:30-18:00
High Tea & Departure

4. Speakers

Number	Name	Institute	Country
1	Arvind Ramanathan	Institute for Stem Cell Science and Regenerative Medicine, Bangalore	India
2	Markus Breunig	Universitaksklinikum Ulm	Germany
3	Benjamin Freedman	University of Washington, Seattle	USA
4	Bhavana Muralidharan	Institute for Stem Cell Science and Regenerative Medicine, Bangalore	India
5	Carol Schuurmans	Sunnybrook Research Institute, Toronto	Canada
6	Debojyoti Chakraborty	Institute of Genomics and Integrative Biology, New Dehli	India
7	Deborah Kurrasch	University of Calgary, Calgary	Canada
8	Eyal Karzbrun	SAGE Center, University of California, Santa Barbara	USA
9	Gad Vatine	Ben-Gurion University of the Negev, Beer Sheva	Israel
10	Indumathi Mariappan	LV Prasad Eye Institute, Hyerbad	India
11	Isabelle Aubert	Sunnybrook Research Institute, Toronto	Canada
12	Ben Maoz	Tel Aviv University, Tel Aviv	Israel
13	Nandini Trivedi	Ohio State University, Columbus	USA
14	Nuria Montserrat	Institute for Bioengineering of Catalonia, Barcelona	Spain
15	Orly Reiner	Weizmann Institute of Science, Rehovot	Israel
16	Pavithra Chavali	Centre for Cellular and Molecular Biology, Telangana	India
17	Shalini Arya	Institute of Chemical Technology, Mumbai	India
18	Sharad Ramanathan	Harvard University, Cambridge	USA
19	Shubha Tole	Tata Institute of Fundamental Research, Mumbai	India
20	Stefano Stifani	Montreal Neurological Institute Hospital, McGill University, Montreal	Canada
21	Ubaka Ogbogu	University of Alberta, Edmonton	Canada
22	Yaakov Nahmias	The Hebrew University of Jerusalem, Jerusalem	Israel
23	Maneesha Inamadar	Institute for Stem Cell Science and Regenerative Medicine, Bangalore	India
24.	Kazuto Kato	Osaka University, Osaka	Japan
25.	Omer Revah	The Hebrew University of Jerusalem, Jerusalem	Israel
26	Christina Kyrousi	University Mental Health Research Institute, Athens	Greece

5. The highlights of the meeting

In addition to the world-class science presented at the conference, a major highlight of our event was the inclusion of a symposium on biomedical ethics that involved three leading experts from Canada (Dr. Ubaka Ogbogu), India (Dr. Maneesha Inamdar)and Japan (Dr. Kazuto Kato), all of whom have been involved together in World Health Organization panels. The purpose of this session was not only to highlight ethical issues associated with human stem cell and organoid work, but also to highlight the importance of finding healthcare solutions that will have global reach and access.

Another major highlight of our meeting was the Mentoring session, a special session focused on career guidance, diversity, inclusion, and work-life balance, followed by a round table discussion. This session was put together by our co-organizer, Dr. Shubha Tole (India), who discussed how to navigate the PhD with our trainee participants. A unique Indian perspective was brought by Dr. Shalini Arya on Diversity and Inclusion, who has overcome adversity to a successful career, and R. Nandini Trivedi, highlighting her steps from a small town in India to academic success in the USA. Dr. Isabelle Aubert and Dr. Deborah Kurrasch from Canada rounded out the session with discussions of work-life balance and tips on wisely choosing a postdoc, respectively. Through these discussions, the trainee participants were encouraged to explore options while planning their careers, all while considering the important issues of work-life balance, equity, diversity and inclusion.

6. Participants

See speakers above

Trainee Participants

Trainee participants	Name	Institute	Country
1	Abhishek Teli	Institute of Bioinformatics and Biotechnology, Savitribai Phule Pune University	India
2	Abraham Peele	Birla Institute of Technology and Science	India
3	Akash Kumaran	School of Bioscience and Bioengineering, Indian Institute of Technology, Mandi	India
4	Alka Kumari	Division of Neuroscience and Ageing biology, CSIR-Central Drug Research Institute (CSIR-CDRI)	India
5	Anjan TK	Manipal Institute of Regenerative Medicine, Manipal Academy of Higher Education	India
6	Asha Channakkar	Institute for Stem Cell Science and Regenerative Medicine, Bangalore	India
7	Ashwin Dalal	Centre for DNA Fingerprinting and Diagnostics	India
8	Atanu Ghorai	(Shilpee Dutt Laboratory, Advanced Centre for Treatment, Research and Education in Cancer	India

		(ACTREC), Tata Memorial Centre, Navi Mumbai	
9	Athira Menon	Centre for Neuroscience, Department of Biotechnology, Cochin University of Science and Technology, Kochi-22	India
10	Atreyee Guria	Indian Institute of Science Education and Research, Bhopal	India
11	Barnali Biswas	Department of Innate Immunity, ICMR-National Institute for Research in Reproductive and Child Health, Mumbai	India
12	Bidisha Bhattacharya	Departments of Molecular Genetics and Molecular Neuroscience, Weizmann Institute of Science, Rehovot	Israel
13	Chen Chongtham	National Institute of Immunology	India
14	Chiara Cimmaruta	Institut Pasteur, Molecular Mechanisms of Pathological and Physiological Ageing, Paris	France
15	Dhanya SK	Institute for Stem Cell Science and Regenerative Medicine, Bangalore	India
16	Divya Khanna	Institute of Genomics and Integrative Biology, New Delhi	India
17	Ekta Gupta	Laboratory of Chromatin Biology & Epigenetics, Indian Institute of Science Education and Research, Pune	India
18	Elizabeth talker	Tata Memorial Hospital, Mumbai	India
19	Gaurav Kansagara	IFOM-inStem Joint Research Laboratory, Centre for Inflammation and Tissue Homeostasis, Institute for Stem Cell Science and Regenerative Medicine (inStem), Bangalore	India
20	Gaurav Samuel	Department of Neurological Sciences Christian Medical College-Vellore, Tamil Nadu	India
21	Gurpreet Kaur Grewal	Department of Molecular Biology and Genetic Engineering, School of Bioengineering and Biosciences, Lovely Professional University, Phagwara, Punjab - 144402,	India
22	I. A. Shaikh	Christian Medical College, Vellore	India
23	Jhilik Dey	Cell biology and Physiology Division, CSIR-Indian Institute of Chemical Biology (CSIR- IICB), Jadavpur, Kolkata -700032	India

24	Juhi Vaishnav	The Maharaja Sayajirao University of Baroda, Vadodara, Gujarat	India
25	Lakshmy Vasan	Sunnybrook Research Institute, University of Toronto	Canada
26	Silvia Breviario	University of Milan, Milan	Italy
27	Mayank Jain	Department of Thoracic Surgery, King George's Medical University, Lucknow, UP	India
28	Meghali Aich	CSIR-Institute of Genomics and Integrative Biology, New Delhi	India
29	Nasera Rizwana	Manipal Institute of Regenerative Medicine, Manipal Academy of Higher Education, GKVK, Allalsandra, Yellahanka, Bangalore	India
30	Neha Yadav	Indian Institute of Science Education and Research Berhampur	India
31	Nikayla Batohi	Synthetic Nanobiotechnology and Biomachines, Centre for Synthetic Biology and Precision Medicine, Council for Scientific and Industrial Research, Pretoria	South Africa
32	Nikhil gandasi	Department of Molecular Reproduction, Development and Genetics, Division of Biological Sciences, Indian Institute of Science (IISc), Bangalore	India
33	Niraikulam Ayyadurai	CSIR Central Leather Research Institute	India
34	Nusrat Nabi	Laboratory for Cancer Biology and Cell Signaling, Department of Biochemistry, University of Kashmir, Srinagar	India
35	Pallavi Gupta	Indian Institute of Technology (IIT), Delhi	India
36	Parvathi Satheesh	Brain Development and Disease Mechanisms, Institute for Stem Cell Science and Regenerative Medicine, Bangalore	India
37	Parveen Shagufta	Manipal Institute of Regenerative Medicine Manipal Academy of Higher Education	India
38	Poonam Yadav	Department of Research, Sir Ganga Ram Hospital, New Delhi	India
39	Pradip Paul	Molecular Genetics Laboratory, and ADBS lab, Department of Psychiatry, National Institute of Mental Health and Neurosciences, Bangalore	India

40	Dhriti nagar	Stanford University, Stanford	USA
41	Preethika Nair	Indian Institute of Technology Jodhpur	India
42	Pretty Garg	University Medical Center, Goettingen, Germany	Germany
43	Raghav Gurunathan	SRMIST – SRM Institute of Science and Technology, Chennai	India
44	Raghava Reddy	University of Washington Medical Center	USA
45	Rahul Sharma	Indian Institute of Science Education and Research Thiruvananthapuram, Kerala	India
46	Raja Sundari Meenakshi Sundaram	Department of Regenerative Medicine and Research, Chennai	India
47	Rajiv Dixit	Brain and Mind Research Institute, Weill Cornell Medicine, Laboratory of Neurogenetics and Development, New York	USA
48	Rambhadur Subedi	ICMR-NIRRCH, National Institute for Research In Reproductive and Child Health, Mumbai	India
49	Ritu Varshney	Indian Institute of Technology, Gandhinagar	India
50	Sandhya Anand	ICMR-National Institute for Research in Reproductive and Child Health	India
51	Saumya Sharma	CSIR- Institute of Genomics and Integrative Biology, New Delhi	India
52	Secunda Rupert	Department of Regenerative Medicine and Research, Chennai	India
53	Sharon abraham	Birla Institute of Technology & Science (BITS), Hyderabad Campus	India
54	Bipin Raj Shekhar	ICMR-National Institute for Research in Reproductive and Child Health, Parel, Mumbai	India
55	Shiffali Khurana	Department of Research, Sir Ganga Ram Hospital | Bhaskaracharya College of Applied Sciences, University of Delhi	India
56	Shreya Kandpal	Tata Institute for Fundamental Research, Mumbai	India
57	SNM Ashitha	Accelerator program for Discovery in Brain disorders using Stem cells (ADBS), Department of Psychiatry, National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore	India
58	Soumita Goswami	CSIR-IICB (Indian Institute of	India

		Chemical Biology, Kolkata)	
59	Melanie Eschment	University of Zurich, Zurich	Switzerland
60	Subashika Govindan	Indian Institute of Technology (IIT) Madras	India
61	Sudip Sen	Department of Biochemistry, All India Institute of Medical Sciences, New Delhi	India
62	Swati Sharma	School of Medical Sciences, University of Manchester	UK
63	Trinath Jamma	Department of Biological Sciences, BITS-Pilani Hyderabad Campus	India
64	Trupti Agarwal	Center for Ocular Regeneration, Prof. Brien Holden Eye Research Centre, Hyderabad Eye Research Foundation, L.V. Prasad Eye Institute, Hyderabad	India
65	Tungadri Bose	TCS Research, Tata Consultancy Services Ltd., 54B Hadapsar Industrial Estate, Pune	India
66	Vadde Sudhakar Reddy	Biochemistry Division, ICMR-National Institute of Nutrition, Tarnaka, Hyderabad	India
67	Vaishali Saini	Infection Bioengineering Group, Department of Biosciences and Biomedical Engineering, Indian Institute of Technology Indore	India
68	Varshiny G	Indian Institute of Technology, Madras	India
69	Vinithra Ponnusamy	Molecular Physiology Laboratory, Bharathiar University, Coimbatore	India
70	Vorapin Chinchalongporn	Sunnybrook Research Institute, University of Toronto	Canada
71	Yogesh Sardana	Central University of Punjab	India
72	Zandile Nxumalo	CSIR- Synthetic Nanobiotechnology and Biomachines, Centre for Synthetic Biology and Precision Medicine, Council for Scientific and Industrial Research, Pretoria	South Africa
73	Abrar Rizvi	Institute for Stem Cell Science and Regenerative Medicine (InStem), Bangalore	India
74	Arpan Parichha	Tata Institute of Fundamental Research (TIFR), Mumbai	India
75	Atharv Athavale	National Institute of Virology, Pune	India

76	Maayan Karllinski	Weizmann Institute of Science, Rehovot	Israel
77	Swathi Narasimhaiah	Centre for Cellular And Molecular Platforms (C-CAMP), Bangalore	India
78	Nidhi Kamboj	Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh	India
79	Riya Rauthan	Institute of Genomics and Integrative Biology (CSIR-IGIB), Delhi	India
80	Khushwant Singh	All India Institute of Medical Sciences (AIIMS), New Delhi	India
81	Yogita Adlakha	Amity University, Noida	India
82	Alisha Lal	Indian Institute of Science Education and Research Thiruvananthapuram (IISER TVM)	India
83	Madhuri Chaurasia	Weizmann Institute of Science, Israel	Israel
84	Angeline Vaisika. P	SRM Arts and Science College, India	India
85	Ankita Bhattacharya	Indian Institute of Technology, Kanpur, India	India
86	Anurag Tandon	University of Toronto, Canada	Canada
87	Harsh Srivastava	Uttar Pradesh University of Medical Sciences, India	India
88	Khusbhoo gandhi	ACTREC, India	India
89	Mansi Srivastava	CSIR-CCMB, India	India
90	Masum Saini	Regional Centre for Biotechnology, India	India
91	Mythri SV	National Institute of Mental Health and Neurosciences, Bangalore	India
92	Nisa Shah	Indian Institute of Science, India	India
93	Prasanna Srinivasan	Stanley Hospital, Chennai, India	India
94	Reeteka Sud	NIMHANS, India	India
95	Saran Kumar	Kusuma School of Biological Sciences, India	India

96	Silpa Sivan	Amrita School of Biotechnology, Kerala, India	India
97	Vasavi Nallur Srinivasaraghavan	National Institute of Mental Health and Neurosciences, Bangalore, India	India
98	Vikrant Singh	Sir Gangaram Hospital, Delhi, India	India

7. Material distribution

Conference bag, notebook, pen, coffee mug, access badge

8. Social events

We had a sitar concert from the very talented Dr. Debojyoti Chakraborty, a professional sitar player!

We had a gala dinner at the Byg Brewski Brewing Company. Some twitter feed from the event! https://twitter.com/shubhatole/status/1623925446365814784?s=20&t=aKR0tY4NyJKSVdoF4J-wQA

And some gala dinner photos…

9. Travel awards and subsidies for Invited speakers

- 10 international travel awards with ISN funding and 1 international speaker

ISN funding was used to cover the travel costs for 10 trainees and one invited speaker from Canada.

Trainee travel awards	Name	Institution	City, Country	Amount (USD)
1	Chinchalongporn, Vorapin	Sunnybrook Research Institute	Toronto, Canada	$1500
2	Vasan, Lakshmy	Sunnybrook Research Institute	Toronto, Canada	$1500
3	Garg, Pretty	Heinrich Heine University	Dusseldorf, Germany	$800
4	Bhattacharya, Bidisha	Weizmann Institute of Science	Rehovot, Israel	$800
5	Nxumalo, Zandile	Council for Scientific and Industrial Research (CSIR)	Pretoria, South Africa	$800
6	Dixit, Rajiv	Cornell University	New York, USA	$1500
7	Sharma, Swati	University of Manchester	Manchester, UK	$800
8	Breviario, Silvia	University of Milan	Segrate, Italy	$800
9	Nagar, Dhriti	Stanford University	Stanford, USA	$1500
10	Eschment, Melanie	University of Zurich	Zurich, Switzerland	$800
SUBTOTAL			$10,800	

Speaker travel	Dr. Ubaka Ogbogu	University of Alberta	Edmonton, Canada	$3,200
GRAND TOTAL			$14,000	

Other awards given with additional funds:

- **5 additional trainee travel awards**

Khushwant Singh	All India Institute of Medical Sciences (AIIMS), New Delhi	New Dehli, India
Nidhi Kamboj	Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh	Chandigarh, India
Nikayla Batohi	Synthetic Nanobiotechnology and Biomachines, Centre for Synthetic Biology and Precision Medicine, Council for Scientific and Industrial Research, Pretoria	Pretoria, South Africa
Riya Rauthan	Institute of Genomics and Integrative Biology (CSIR-IGIB), Delhi	New Dehli, India
Yogita Adlakha	Amity University, Noida	Noida, India

- **7 childcare grants**

Barnali Biswas

Gurpreet kaur Grewal

Khusbhoo Gandhi

Maayan Karlinski

Madhuri Chaurasia

Nasera Rizwana
Poonam Yadav

- **50 registration waivers**

Abhishek Teli

Abraham Peele
Abrar Rizvi

Alka Kumari

Anurag Tandon

Asha Channakkar

Atanu Ghorai

Athira Menon

Bidish Bhattacharya
Chinnathambi, Subashchandrabose

Dhanya SK

Dhriti nagar

Divya Khanna

Gaurav Kansagara
Grewal, Gurpreet Kaur
I. A. Shaikh
Jain, Mayank
JHILIK Dey
Khushwant SINGH
Lakshmy vasan
Meghali Aich
Melanie Eschment
Neha Yadav
Nidhi Kamboj
Nikhil gandasi
Nusrat Nabi
Parvathi Satheesh
Parveen Shagufta
Ponnusamy, Vinithra
Pradip Paul
Preethika Nair
Riya rauthan
Samuel, Gaurav
Sandhya Anand
Saumya Sahrma
Sharma, Rahul
Sharon abraham
Shekar Bipin
Shreya Kandpal
Silvia Breviario
SNM Ashitha
Soumita Goswami
Subedi, Rambhadur
Swathi Narasimhaiah
Trinath Jamma
TRUPTI Agarwal
Vadde Sudhakar Reddy
Vaishali Saini
Vorapin Chinchalongporn
Yogita Adlakha

10. Sponsorship

- EMBO
- India Alliance DBT wellcome
- International Society for Neurochemistry (ISN)
- International Society for Developmental Neuroscience (ISDN)

11. General budget; detailed ISN budget, how the ISN funds were utilised (euro)

FINANCIAL STATEMENT

Event Title:

Total EMBO Funding Awarded	33,200.00

				AMOUNT
1st payment received from EMBO prior to event				**26560**
Other contributions (sponsors)	**NAME**			**AMOUNT**
Sponsor 1	Media Analytik			1250
Sponsor 2	Invitrogen			1225
Sponsor 3	Bi Biotech			625
Sponsor 4	India Alliance			6875
Sponsor 5	ISN			13053
Sponsor 6	ISDN			9323
Sponsor 7				
Sponsor 8		0		
Total sponsorship received to date				**58911**
Registration fees	**RATE**	**number of registrants**		**AMOUNT**
Academic, full rate	300	5		1500
Academic, reduced (student)	150	43		6450
Industry				0
total income from registration fees				**7950**
The above rates include		**PLEASE SELECT**		
accomodation		Yes		
catering		Yes		
EXPENSES				
Travel to be covered by organizers				**AMOUNT**
Speakers / Lecturers local				2500
Speakers / Lecturers Europe				19000
Speakers / Lecturers East Coast USA				2500
Speakers / Lecturers World and West Coast USA				22376
Scientific Organisers / Tutors				0
Other *(specify if over 1000 Euro)*				0
total travel expenses				**46376**
Accommodation to be covered by organizers				**AMOUNT**
Speakers / Lecturers				500
Students / Postdocs (if applicable)				2000
Organisers / Tutors				0
total accommodation expenses				**2500**
Catering				**AMOUNT**
Lunch, dinner, breaks, etc				5340
Social events (limit €3000 from EMBO the rest from industry sponsors				6000
total catering expenses				**11340**
Location expenses				**AMOUNT**
Venue (room rental, etc)				1500
Audio-visual, equipment rental, technical assistance				1250
Materials/laboratory consumables (if applicable)				
Cleaning costs				600
Poster board rental				625
Other *(specify if over 1000 Euro)* Furniture				840
Local transport (e.g. shuttle busses)				2570
total location expenses				**7385**
Organisation and promotion expenses				**AMOUNT**
Office supplies, phone and mailing costs				1000
Advertisement in print and online				122
Printing of abstract book, handouts, name badges				153
Secretarial assistance (max €4000).				1300
Credit card and bank charges				625
Other promotional and organisational expenses- Poster awards and c				2800
Website and registration system*				
Design of poster*				
Meeting bags and pens*				
total organization expenses				**6000**

TOTAL Income Received		66861
Total Expenses		73601
	Final Payment Requested from EMBO	6740

* these services are available free of charge from EMBO. Costs incurred if the EMBO services are not being used will not be covered with the exception of the COMS Payment Service.

I certify that this is a true and accurate account of the finances and will store all the relevant receipts for 10 years. Date: Signature:

Detailed ISN Budget (these values are in USD)
(***please note that the accommodation was covered by the other grants for the trainee travel award winners. Also, the registration fees for these trainees were waived. The amount reimbursed covers travel only.

Trainee travel awards	Name	Institution	City, Country	Amount (USD)
1	Chinchalongporn, Vorapin	Sunnybrook Research Institute	Toronto, Canada	$1500
2	Vasan, Lakshmy	Sunnybrook Research Institute	Toronto, Canada	$1500
3	Garg, Pretty	Heinrich Heine University	Dusseldorf, Germany	$800
4	Bhattacharya, Bidisha	Weizmann Institute of Science	Rehovot, Israel	$800
5	Nxumalo, Zandile	Council for Scientific and Industrial Research (CSIR)	Pretoria, South Africa	$800
6	Dixit, Rajiv	Cornell University	New York, USA	$1500
7	Sharma, Swati	University of Manchester	Manchester, UK	$800
8	Breviario, Silvia	University of Milan	Segrate, Italy	$800
9	Nagar, Dhriti	Stanford University	Stanford, USA	$1500
10	Eschment, Melanie	University of Zurich	Zurich, Switzerland	$800
SUBTOTAL			$10,800	
Speaker travel	Dr. Ubaka Ogbogu	University of Alberta	Edmonton, Canada	$3,200
GRAND TOTAL			$14,000	

12. ISN advertising

1. Abstract book (see appendix)
2. Introductory slides (see appendix)
3. Poster (see appendix)
4. Tweets of poster
https://twitter.com/CarolSchuurmans/status/1623212495107420161

13. Photos and awards

Selected abstracts for oral presentations	Poster prizes
Arpan Parichha	Asha Channakkar
Dhriti Nagar	Atreyee Guria
Khushwant Singh	Neha Yadav
Maayan Karlinski	Ritu Varshney
Melanie Eschment	Soumita Goswami
Nidhi Kamboj	
Riya Rauthan	
Silvia Breviario	
Swathi Narasimhaiah	
Yogita Adlakha	

Registration – day one (poster with ISN support is prominent)

Kickoff -day one – welcome to the meeting! (Bhavana and Shubha, co-organizers)

Session one- some of our speakers

Audience and attendee engagement – session one (with ISN support prominent in poster)

Bioethics session panel – audience engagement!

Break time! Scientific exchanges

Poster Sessions

Group Photo!

Trainee awards!

Childcare grant awardees

Travel awards

Registration waivers

Trainee volunteers

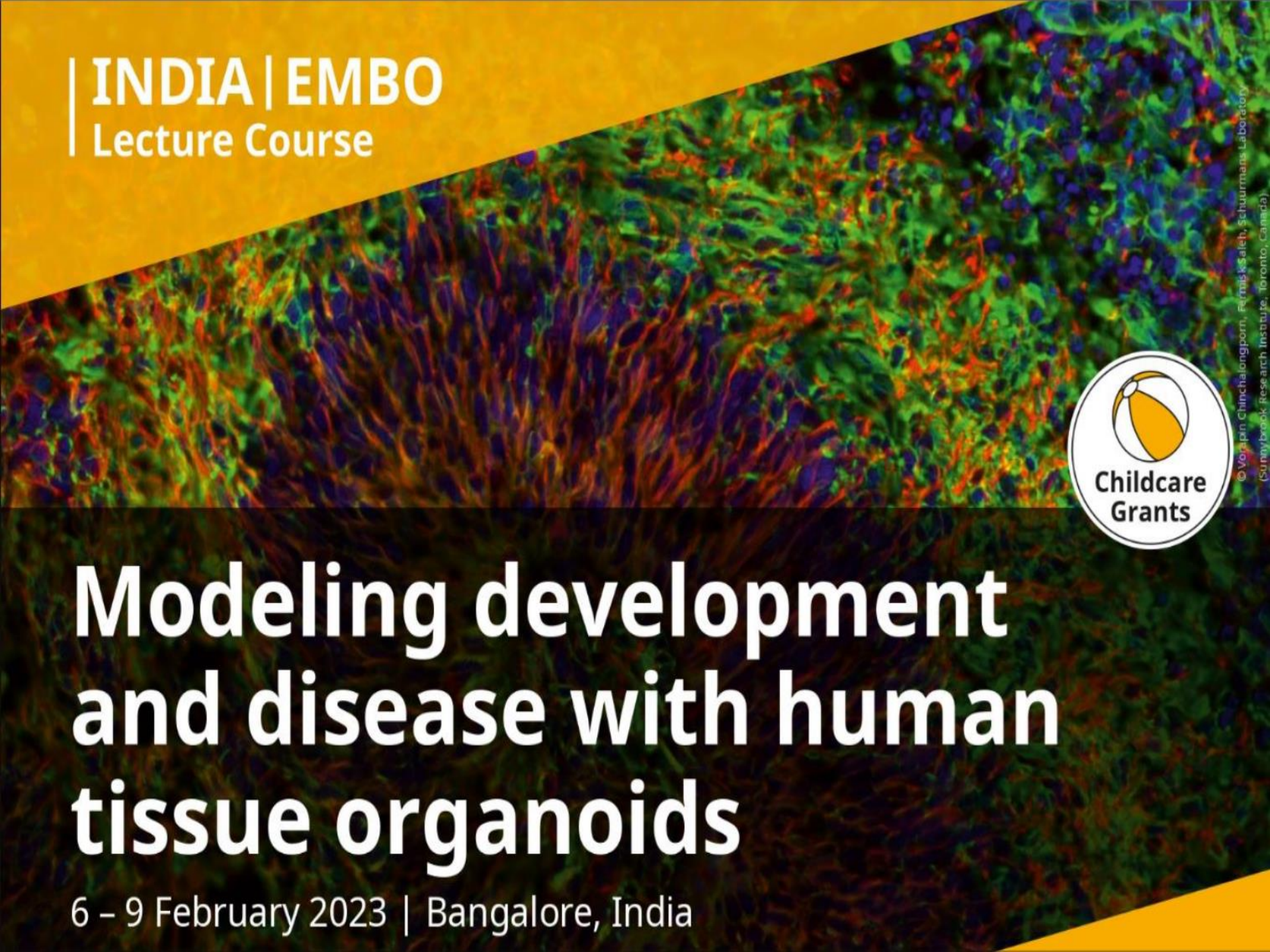
14. Comments of at least three attendants about the Meeting https://twitter.com/2023EmboOrg_IN/likes

- *Dr. Rajiv Dixit, USA*
  "It was a very interesting meeting; everyone was amazed by the way it was organised and conducted, pleased to be part of it."
- *Nikayla Batohi, South Africa*
  "It was such an honour to be a part of the organoid conference! Thank you once again for awarding me a travel bursary. "
- *Dr. Isabelle Aubert, Canada*
  "I wanted to tell you a HUGE thanks again for the opportunity to present and participate at the fantastic EMBO meeting in Bangalore. I truly appreciate this chance and I'm still 'floating' of joy at the experience and looking forward to connect with you again."
- *Dr. Kazuto Kato, Japan*

"Congratulations again on the big success of the Organoid meeting last week!"

- *Dr. Ben Maoz, Israel*
  "I would like to thank you and complement you on an amazing event!!!" "☺ it was my true pleasure ☺ "
- *Ritu Varshney, India*
  "Excited to share that I had a fantastic time at #EMBOorganoids2023 #DBT_instem. So grateful for the opportunity to learn from the leading minds and connect with amazing people in my field. And the icing on the cake? I won the best poster award"
- *Dr. Shalini Arya*
  "I am so so grateful (sp)… for giving me this wonderful opportunity to contribute a small drop in this big ocean of work.. Thank you for making me part of your team by inviting me a speaker. Your team of students is just fabulous. I learnt a lot interacting with them as well as all of you. …"Cant tell you how much I enjoyed in last three days with you all at InSTEM Niedile. Taking along a bagful of treasures! One does not learn only technical things during these meetings but much more than that. Thank you once again for everything."
- *Dr. Sharad Ramanathan*
  "The science was a lot of fun too and i learned a lot. The students were amazing. It was so impressive to watch them ask so many questions and not be afraid of doing so."
- *Arpan Parichha*
  "The EMBO India organoid meeting revealed multiple aspects and opportunities in the organoid field that could benefit me in choosing my career path as a post-doctoral aspirant. Interacting with the speakers and peers over lunch tables and during coffee breaks was the best part of the meeting, which helped me learn their work in detail. The feedback I received from the broader audience during my oral presentation enabled me to improvise my current work. Above all, the EMBO Travel Grant has alleviated the financial burden of attending the conference."
- *Mansi Srivastava*
  "The EMBO Organoid meeting was tailored for an outstanding experience for early career researchers in India. The sessions covered recent advances in organoid research in understanding developmental processes, disease modelling, and developing organ-on-chip platforms. In addition to a rich scientific content, the meeting also instilled a sense of responsibilty in us by hosting sessions on Ethics and policies in Stem-cell based research. The highlight of the meeting was the mentorship session on work-life balance and navigating graduate school. Overall, the meeting was a complete and ejoyable scientific package and helped us interact and connect with a diveristy of researchers."

Appendix



INDIA | EMBO
Lecture Course

Childcare Grants

Modeling development and disease with human tissue organoids

6 – 9 February 2023 | Bangalore, India

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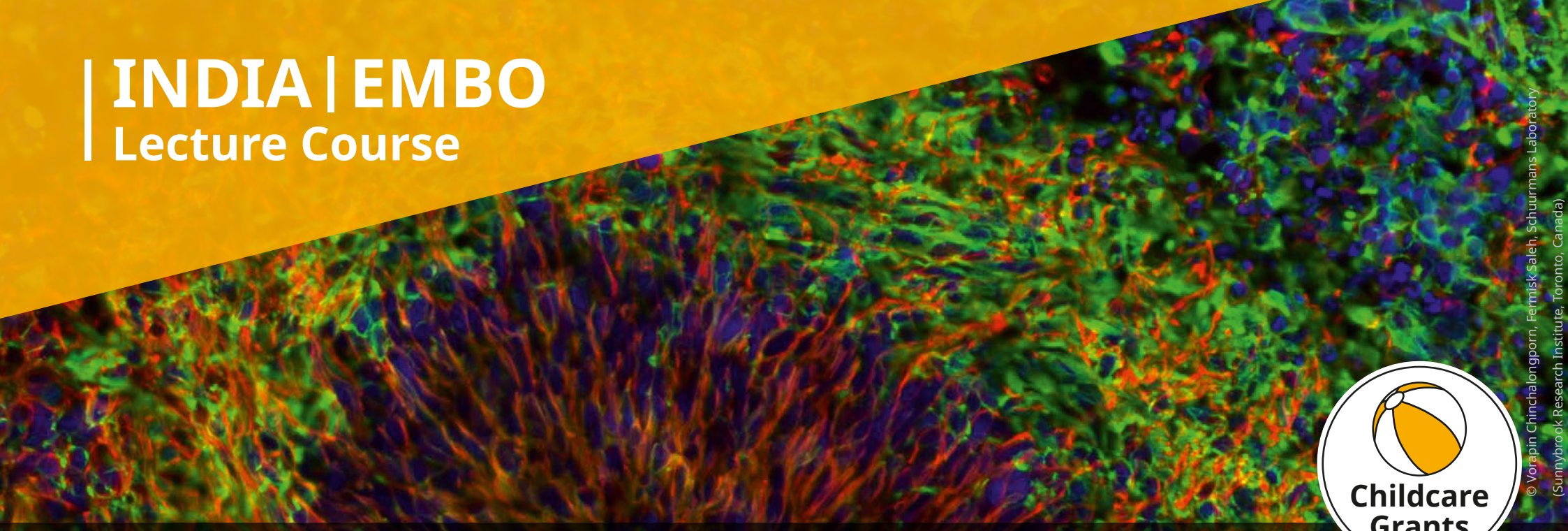

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Modeling development and disease with human tissue organoids

6 – 9 February 2023 | Bangalore, India

Organisers

Bhavana Muralidharan
Institute for Stem Cell Science and Regenerative Medicine, IN

Carol Schuurmans
Sunnybrook Research Institute, CA

Orly Reiner
Weizmann Institute of Science, IL

Shubha Tole
Tata Institute of Fundamental Research, IN

Registration

Registration deadline
10 December 2022

Indian
Students/Postdocs ..... 12,000 INR
International
Students/Postdocs ..... 150 EUR
Academic ..... 300 EUR
Industry ..... 700 EUR

Housing and meals are included in the registration fee.

Speakers

Arvind Ramanathan
Institute for Stem Cell Science and Regenerative Medicine, Bangalore, IN

Ben Maoz
Tel Aviv University, Tel Aviv, IL

Benjamin Freedman
University of Washington, Seattle, US

Bhavana Muralidharan
Institute for Stem Cell Science and Regenerative Medicine, Bangalore, IN

Carol Schuurmans
Sunnybrook Research Institute, Toronto, CA

Christina Kyrousi
University Mental Health Research Institute, Athens, GR

Debojyoti Chakraborty
Institute of Genomics and Integrative Biology, New Delhi, IN

Deborah Kurrasch
University of Calgary, Calgary, CA

Eyal Karzbrun
SAGE Center, University of California, Santa Barbara

Gad Vatine
Ben-Gurion University of the Negev, Beer Sheva, IL

Indumathi Mariappan
LV Prasad Eye Institute, Hyderbad, IN

Isabelle Aubert
Sunnybrook Research Institute, Toronto, CA

Maneesha Inamdar
Institute for Stem Cell Science and Regenerative Medicine, IN

Markus Breunig
Universitätsklinikum Ulm, Ulm, DE

Nandini Trivedi
Ohio State University, Columbus, US

Nuria Montserrat
Institute for Bioengineering of Catalonia, Barcelona, ES

Orly Reiner
Weizmann Institute of Science, Rehovot, IL

Pavithra Chavali
Centre for Cellular and Molecular Biology, Telangana, IN

Peter Loskill
Eberhard Karls University, Tübingen, DE

Shalini Arya
Institute of Chemical Technology, Mumbai, IN

Sharad Ramanathan
Harvard University, Cambridge, US

Shubha Tole
Tata Institute of Fundamental Research, Mumbai, IN

Stefano Stifani
Montreal Neurological Institute-Hospital, McGill University, Montreal, CA

Ubaka Ogbogu
University of Alberta, Edmonton, CA

Yaakov Nahmias
The Hebrew University of Jerusalem, Jerusalem, IL

Contact

india.embo.organoid.2023@gmail.com

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meetings.embo.org/event/21-organoids

EMBO | IndiaAlliance DBT wellcome | ISN International Society for Neurochemistry | ISDN International Society for Developmental Neuroscience | EMBO Molecular Medicine | EMBOpress

Abstract Book

Organisers

Bhavana Muralidharan

inStem, Bengaluru, IN

Orly Reiner

Weizmann Institute of Science, IL

Carol Schuurmans

Sunnybrook Research Institute, CA

Shubha Tole

TIFR, Mumbai, IN

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Day-1 | 6 February 2023

13:00-16:00	Registration (outside inStem 150 seater auditorium)
15:00-16:00	Opening Welcome Reception - Tea/Coffee (inStem atrium)
16:00-16:15	Welcome Address **Dr. Bhavana Muralidharan & Dr. Shubha Tole**

Session 1: Cerebral organoids to study neurodevelopment
(Chair: Dr. Carol Schuurmans)

16:15-16:45	Brain organoids for modeling brain malformations: clues from the progenitors **Dr. Orly Reiner**
16:45-17:15	Engineered human cortical spheroids for dissecting molecular determinants of neurodevelopment **Dr. Debojyoti Chakraborty**
17:15-17:30	Dissecting the genetic determinants of cortical interneuron migration in human forebrain assembloids **Riya Rauthan**
17:30-17:45	***Take a breather*** - Short Break

Session 2: Biomedical Ethics
(Chair: Dr. Shubha Tole)

17:45-18:15	Foregrounding Equity, Justice and Inclusion as Determinants of Access to Precision Medicine: An Ethical Case Study of Patient-Derived Tissue Organoids **Dr. Ubaka Ogbogu**
18:15-18:45	Ethical and social considerations of multi-system organoids: Need of interdisciplinary approaches **Dr. Kazuto Kato**
18:45-19:30	Panel Discussion **Dr. Maneesha Inamdar, Dr. Ubaka Ogbogu, Dr. Kazuto Kato**
19:30	Dinner (inStem Canteen First Floor)

Venue for all the talks will be - inStem 150 seater auditorium

Day-2 | 7 February 2023

8:00-9:00 Breakfast (NCBS Main canteen First floor)

Session 3: iPSC-derived 2D and 3D systems to model CNS disorders (Chair: Dr. Orly Reiner)

09:00-09:30 Modelling neurodevelopmental disorders using iPSC-derived 2D neuronal cultures and 3D cerebral organoids
Dr. Bhavana Muralidharan

09:30-10:00 Patient-derived brain organoids to characterize epileptic Dravet syndrome
Dr. Deborah Kurrasch

10:00-10:30 Creating functional human cortical circuits in vivo using stem cells and implications for modeling neurodevelopmental disorders"
Dr. Omer Revah

10:30-11:00 Coffee break (inStem atrium)

11:00-11:30 Modeling neurodegenerative diseases using iPSC-derived neuronal and glial cells
Dr. Stefano Stifani

11:30-12:00 Understanding eye development and disease using patient-specific iPSCs and iPSC-derived organoids
Dr. Indumathi Mariappan

12:00-13:00 Poster Blitz - ***Teasers***
Dr. Orly Reiner

13:00-14:00 Lunch (inStem Canteen First Floor)

14:00-16:00 Poster Session 1 + Coffee break (inStem atrium)
Poster session and coffee? As quintessential as tea and biscuits.

Venue for all the talks will be - inStem 150 seater auditorium

Session 4: Mentoring Session
(Chair: Dr. Shubha Tole)

16:00-16:30	Navigating graduate school **Dr. Shubha Tole**
16:30-17:00	How to choose a postdoc **Dr. Deborah Kurrasch**
17:00-17:30	Work-life balance and mental health **Dr. Isabelle Aubert**
17:30-18:00	Diversity and Inclusion **Dr. Shalini Arya**
18:00-18:30	Stepwise: from a small town in India to a successful career **Dr. Nandini Trivedi** (virtual)
18:30-19:30	Open Panel Discussion **Session speakers**
19:30	Dinner and continued round table discussion (inStem Canteen First Floor)
21:00	Cultural Music Program (inStem 150 seater auditorium) The Science and magic in Indian classical music by Dr "*Surprise*"

Venue for all the talks will be - inStem 150 seater auditorium

Day-3 | 8 February 2023

8:00-9:00	Breakfast (NCBS Main canteen First floor)

Session 5: Organoid Bioengineering
(Chair: Dr. Bhavana Muralidharan)

9:00-9:30	Using machine learning and bioengineering to build robust human organoids **Dr. Sharad Ramanathan**
09:30-10:00	Sensor-embedded 3D human organoids for drug development **Dr. Yaakov Nahmias**
10:00-10:15	Efficient expansion of iPSC-derived human lung epithelium as adherent cultures and 3D organoids using defined, serum free medium for disease modelling and cell therapy **Swathi Narasimhaiah**
10:15-10:30	MicroRNA-135 drives human neural stem cell fate determination: Employing induced pluripotent stem cells (iPSCs) derived 2D neural stem cells (NSCs) **Yogita Adlakha**
10:30-11:00	**Let's get the elixir of success - It's coffee time (inStem atrium)**
11:00-11:30	A human stem-cell model of neural tube folding morphogenesis **Dr. Eyal Karzbrun**
11:30-12:00	From personalized blood-brain-barrier (BBB)-on-Chip to pre-clinical BBB targeted gene therapy **Dr. Gad Vatine**
12:00-12:15	How LIS1 is Involved in the Regulation of the Extracellular Matrix **Maayan Karlinski**
12:15-13:15	Poster Blitz **Dr. Orly Reiner**
13:15-14:15	Lunch (inStem Canteen First Floor)
14:15-16:15	Poster Session 2 + Coffee break (inStem atrium)
17:00-17:30	**Departure Gala Dinner**
18:00-21:00	**Gala Dinner**
21:00	**Return to hotel**

Venue for all the talks will be - inStem 150 seater auditorium

Day-4 | 9 February 2023

8:00-9:00	Breakfast (NCBS Main canteen First floor)

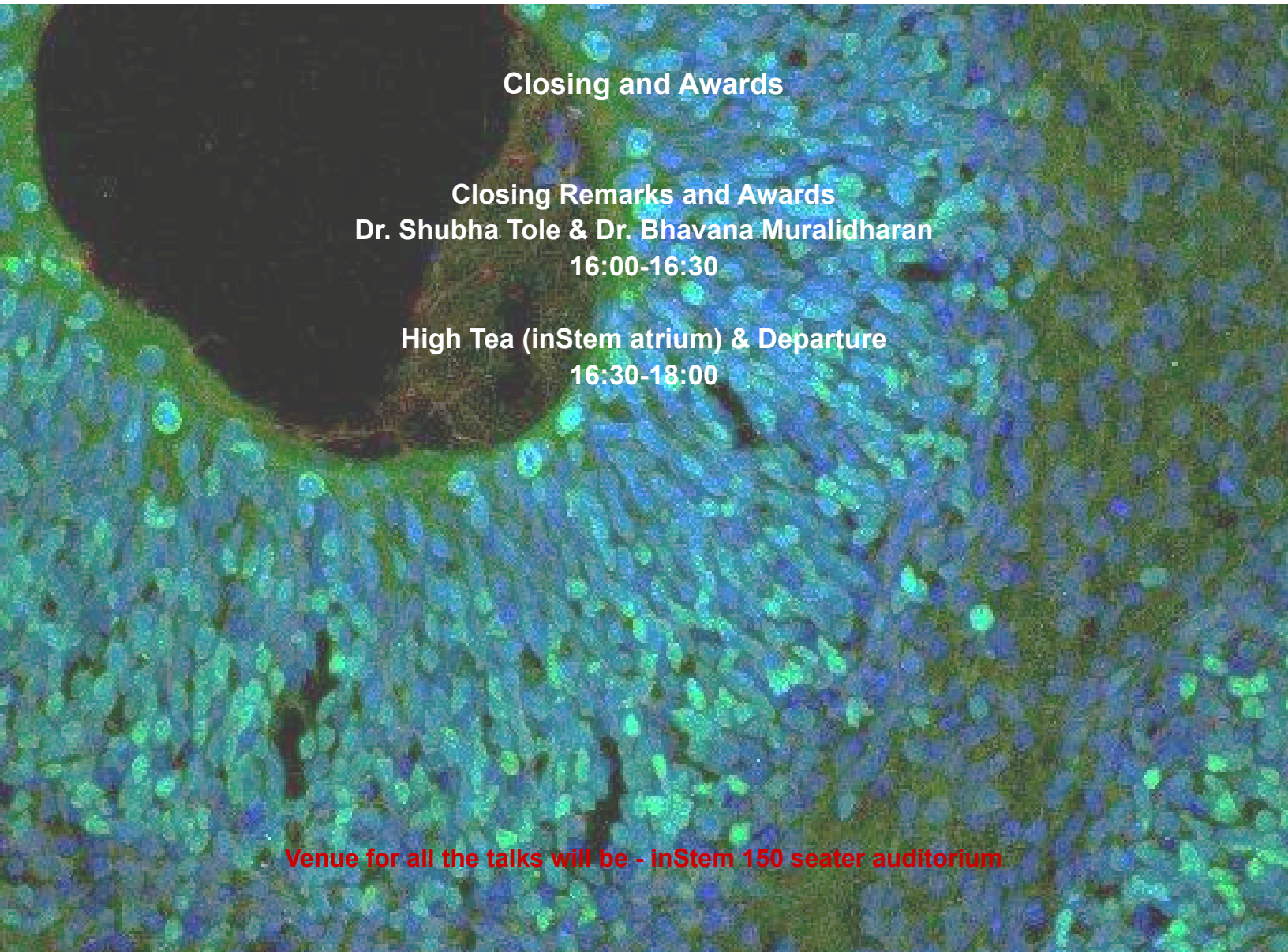
Session 6: Other tissue organoids
(Chair: Dr. Debojyoti Chakraborty)

9:00-9:30	Engineering organoids to understand human development and disease **Dr. Nuria Montserrat**
09:30-10:00	Human organoid models of kidney disease and regeneration **Dr. Benjamin Freedman**
10:00-10:15	Exploiting Intestinal Organoid Model to interrogate Shigella pathogenesis **Nidhi Kamboj**
10:15-10:30	Establishing 3D multicellular spheroid to imitate tumor microenvironment for chemotherapeutic drug efficacy modulation in cancer **Khushwant Singh**
11:00-11:30	Inherited pancreatic disorders illuminated by pluripotent stem cells **Dr. Markus Breunig**
10:30-11:00	High tea (inStem atrium)
11:30-12:00	Modeling atrophy and metabolic disease using skeletal muscle organoids **Dr. Arvind Ramanathan**
12:00-12:30	Organs-on-a-Chip: A new tool for studying physiology **Dr. Ben Maoz**
12:30-12:45	Constitutive activation of canonical Wnt signaling disrupts choroid plexus epithelial fate **Arpan Parichha**
12:45-13:00	Unravelling the role of the ciliary protein CEP290 in neural development by generation of human 2D and 3D iPSC-derived neuronal models for the ciliopathy Joubert Syndrome **Melanie Eschment**
13:00-14:00	Lunch (inStem Canteen First Floor)

Venue for all the talks will be - inStem 150 seater auditorium

Session 7: Modeling disease and neurodevelopment with cerebral organoids (Chair: Dr. Indumathi Mariappan)

14:00-14:30	Modeling neurodevelopmental diseases and cancer using cerebral organoids **Dr. Pavithra Chavali** (virtual)
14:30-15:00	Using brain organoids to interrogate proneural gene function **Dr. Carol Schuurmans**
15:00-15:30	Modeling human brain development and disease: the role of primary cili **Dr. Christina Kyrousi**
15:30-15:45	Adrenomedullin promotes interneuron migration in a human forebrain assembloid for hypoxic interneuronopathy of prematurity **Dhriti Nagar**
15:45-16:00	Dissecting the involvement of acid sphingomyelinase inhibition in GBA-dependent Parkinson's disease **Silvia Breviario**



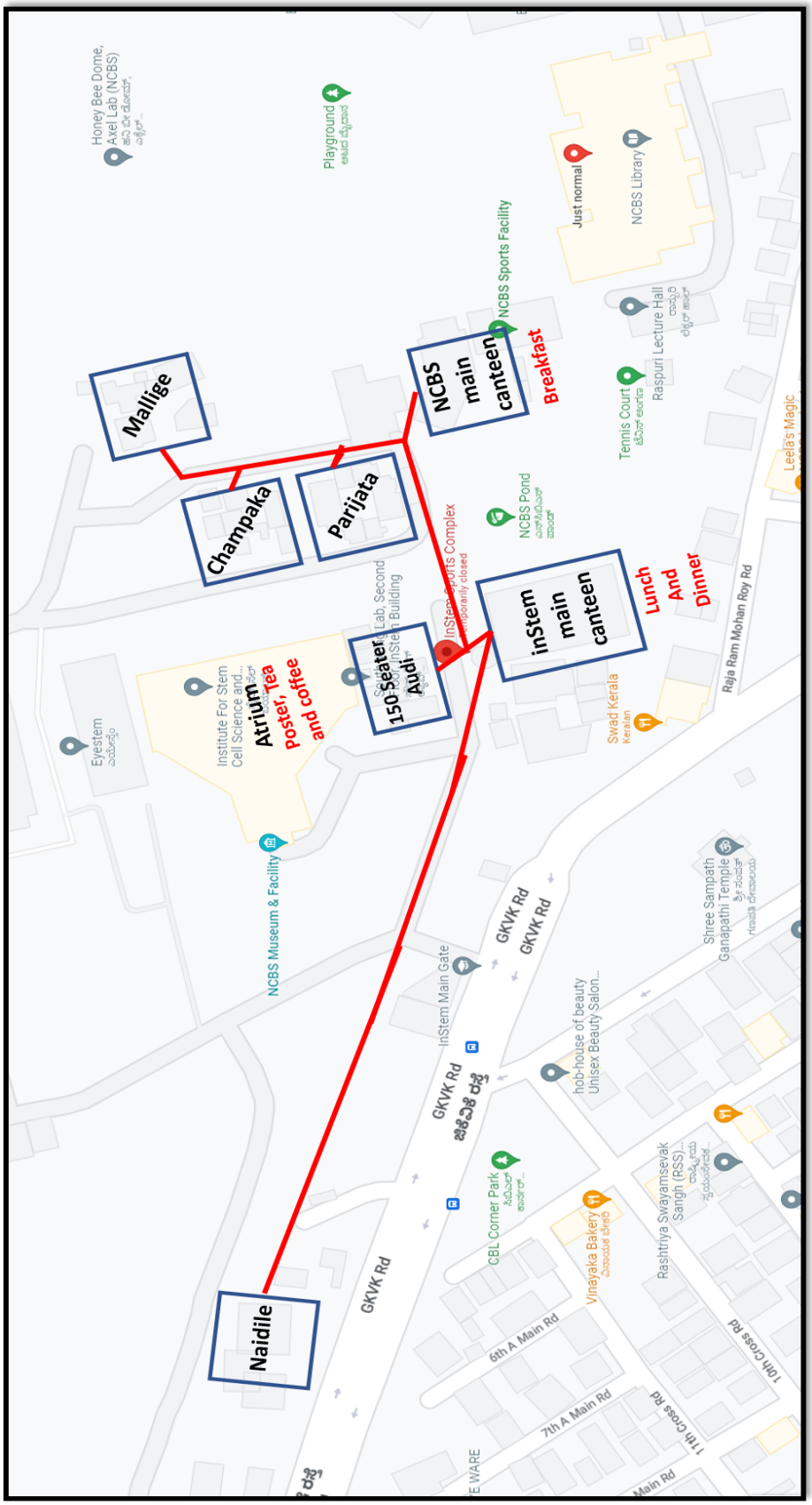
Closing and Awards

Closing Remarks and Awards
Dr. Shubha Tole & Dr. Bhavana Muralidharan
16:00-16:30

High Tea (inStem atrium) & Departure
16:30-18:00

Venue for all the talks will be - inStem 150 seater auditorium

Venue Map at inStem



Selected abstracts for oral presentation

S.No.	Presenters	Title
1	Arpan Parichha	Canonical Wnt signaling regulates choroid plexus development
2	Dhriti Nagar	Adrenomedullin promotes interneuron migration in a human forebrain assembloid for hypoxic interneuronopathy of prematurity
3	Khushwant Singh	Establishing 3D multicellular spheroid to imitate tumor microenvironment for chemotherapeutic drug efficacy modulation in cancer
4	Maayan Karlinski	How LIS1 is Involved in the Regulation of the Extracellular Matrix
5	Melanie Eschment	Unravelling the role of the ciliary protein CEP290 in neural development by generation of human 2D and 3D iPSC-derived neuronal models for the ciliopathy Joubert Syndrome
6	Nidhi Kamboj	Exploiting Intestinal Organoid Model to interrogate Shigella pathogenesis
7	Riya Rauthan	DIssecting the genetic determinants of cortical interneurons migration in human forebrain assembloids.
8	Silvia Breviario	Dissecting the involvement of acid sphingomyelinase inhibition in GBA-dependent Parkinson's disease
9	Swathi Narasimhaiah	Efficient expansion of iPSC-derived human lung epithelium as adherent cultures and 3D organoids using defined, serum free medium for disease modeling and cell therapy

10	Yogita Adlakha	MicroRNA-135 drives human neural stem cell fate determination: Employing induced pluripotent stem cells (iPSCs) derived 2D neural stem cells (NSCs)

Presenter: Arpan Parichha

Canonical Wnt signaling regulates choroid plexus development

Arpan Parichha 1, Varun Suresh 1, Mallika Chatterjee 2, Aditya Kshirsagar 3, Lihi Ben Ruven 3, Tsviya Olender 3, Velena Radosevic 4, Mihaela Bobic-Rasonja 4, Sara Trnski 4, M. Mark Taketo 5, Michael J. Holtzman 6, Nataša Jovanov-Milosevic 4, Orly Reiner 3, Shubha Tole 1
1 Tata Institute of Fundamental Research
2 Amity Institute of Neuropsychology & Neurosciences
3 Weizmann Institute of Science
4 School of Medicine University of Zagreb, Institute of Biology & Croatian Institute for Brain Research
5 School of Medicine, Kyoto University
6 Pulmonary and Critical Care Medicine, Washington University, St. Louis

The choroid plexus secretes cerebrospinal fluid and is critical for the development and function of the brain. In the telencephalon, the choroid plexus epithelium arises from the Wnt-expressing cortical hem. Canonical Wnt signaling pathway molecules such as nuclear
β-CATENIN are expressed in the mouse and human embryonic choroid plexus epithelium, indicating that this pathway is active. Point mutations in human β-CATENIN are known to result in the constitutive activation of canonical Wnt signaling. In a mouse model that
recapitulates this perturbation, we report a loss of choroid plexus epithelial identity and an apparent transformation of this tissue to a neuronal identity. Aspects of this phenomenon are recapitulated in human embryonic stem cell-derived organoids. The choroid plexus is also
disrupted when β-Catenin is conditionally inactivated. Together, our results indicate that canonical Wnt signaling is required precisely and regulated for normal choroid plexus development in the mammalian brain.

Presenter: Dhriti Nagar

Adrenomedullin promotes interneuron migration in a human forebrain assembloid for hypoxic interneuronopathy of prematurity

Wojciech Michno[1], Alyssa Puno[1], Amanda Everitt[2], Kate McKluskey[2], Li Li[1], Dhriti Nagar[1], Fikri Birey[3, 4], Jeremy Willsey[5], Anca M. Pasca, MD[1]

[1] Department of Pediatrics, Stanford University, Stanford, CA, USA
[2] Department of Psychiatry and Behavioral Sciences, UCSF Weill Institute for Neurosciences, University of California, San Francisco, San Francisco, CA, USA
[3] Department of Psychiatry and Behavioral Sciences, Stanford University, Stanford, CA, USA
[4] Stanford Brain Organogenesis, Wu Tsai Neurosciences Institute, Stanford University, Stanford, CA, USA
[5] Quantitative Biosciences Institute (QBI), University of California, San Francisco, San Francisco, CA, USA.

Extremely preterm born individuals at < 28 postconceptional weeks (PCW) are at high risk for encephalopathy of prematurity and life-long neuropsychiatric conditions. Clinical studies and animal models of preterm brain injury suggest that encephalopathy of prematurity is strongly associated with exposure to hypoxia and/or inflammation in the perinatal period. Histologic examination of postmortem brain tissue from children born preterm demonstrates decreased numbers of cortical GABAergic interneurons in the cerebral cortex. However, the cellular and molecular mechanisms underlying the decreased numbers of GABAergic interneurons in the cerebral cortex of extremely preterm individuals remain unclear. We developed a human cellular model to study hypoxia-induced interneuronopathies using human forebrain assembloids (hFA) and ex vivo human prenatal cerebral cortex at mid-gestation. The hFA are generated through the integration of region-specific neural organoids containing either dorsal forebrain (excitatory) glutamatergic neurons or ventral forebrain (inhibitory) GABAergic interneurons. We discover a substantial reduction in migration of cortical interneurons during hypoxia in both hFA and ex-vivo human prenatal cerebral cortex. We identify that this migration defect is associated with a substantial increase in the gene expression and protein levels of adrenomedullin (ADM), a member of the calcitonin gene related peptide (CGRP) family. Remarkably, supplementation with ADM during hypoxia is sufficient to restore the normal migration pattern of cortical interneurons both in hFA and ex-vivo human prenatal cerebral cortex. In summary, these findings provide insights into the cellular mechanisms contributing to cortical interneuron depletion in preterm infants and pinpoint novel molecular pathways with high translational potential for encephalopathy of prematurity.

Presenter: Khushwant singh

Establishing 3D multicellular spheroid to imitate tumor microenvironment for chemotherapeutic drug efficacy modulation in cancer

Khushwant singh, Pramod K Gautam, et al.
Department of Biochemistry, All India Institute of Medical Sciences, New Delhi-110029

The heterogeneity within tumors confers a degree of resilience to existing treatments and constraints to the deployment of ubiquitous therapeutic interventions. Chemotherapeutic drugs are proven to be effective against many malignancies when administered alone or in combination with other drugs. In the human body, malignant cancer develops as an aberrant organ, and the tumor microenvironment is heavily populated with several cell types that are crucial for cancer progression. To address this problem, we established a reproducible healthy multicellular 3D spheroid culture with macrophage infiltrates to imitate the tumor microenvironment and to modulate the efficacy of drugs on different cells present in multicellular spheroids. Utilizing human cancer cell lines CAL33 & MCF7 3D spheroids were established, while THP1 cell line was used as a source of macrophages. Cellular parameters such as health, metabolism, proliferation, spheroid compactness, protein expression, ROS, NO2, CSC, and EMT were assessed in the spheroids to ascertain the optimum conditions for multicellular 3D spheroids establishment & cancer modeling. The chemotherapeutic drug Docetaxel was used to modulate chemotherapeutic activity. We found that, in contrast to traditional monolayer culture, complex tumor microenvironments can be better represented by 3D spheroids comprising a variety of cell types, organized in several layers is a crucial factor in determining the effectiveness of chemotherapy agents. Additionally, we
found that this cancer model can be utilized to study two major problems associated with chemotherapeutics: suboptimal selectivity of chemotherapeutic agents for specific target cells and multidrug resistance driven by heterogeneity and multilayer cell arrangements in tumor microenvironment.

Presenter: Maayan Karlinski

How LIS1 is Involved in the Regulation of the Extracellular Matrix

Maayan Karlinski, Irit Sagi, Orly Reiner
Weizmann Institute of Science

Mutations in Lissencephaly 1 (LIS1) result in a range of human brain developmental diseases, such as changes in brain structure, lissencephaly, hippocampal malformation, and epilepsy. Mouse Lis1 models exhibit rather subtle cortical abnormalities compared to the human phenotype. Previous RNA-sequencing data from on-chip organoids derived from human embryonic stem cells (hESCs) revealed significant changes in the expression of extracellular matrix (ECM)-related genes in the LIS1 mutated samples. This project uses a multi-omics approach to better understand the ECM composition and regulation in human embryonic stem cells - derived mutated and control cortical organoids. We found an altered expression of multiple ECM members, several of which were altered across different expression levels in the LIS1+/- organoids. These differences were most prominent for the collagen containing ECM pathways. In addition, rheological tests indicated that the LIS1 mutated cortical organoids possess altered biomechanical properties. In the future we aim to delineate what are the ECM-related proteins that are causing the biomechanics abnormalities, and to screen for treatments that may alleviate these changes.

Presenter: Melanie Eschment

Unravelling the role of the ciliary protein CEP290 in neural development by generation of human 2D and 3D iPSC-derived neuronal models for the ciliopathy Joubert Syndrome

Melanie Eschment 1, 2, Affef Abidi-Ostorero 1, Joana Figueiro da Silva 1, Ruxandra Bachmann-Gagescu 1, 2, 3
1 Institute of medical genetics, University of Zurich
2 Clinical Research Priority Program of the University of Zurich Praeclare
3 Department of Molecular Life Sciences, University of Zurich

Ciliopathies are a group of human Mendelian disorders caused by dysfunction of primary cilia (PC), small sensory organelles protruding from the surface of most cells. Patients show various symptoms, with frequent central nervous system (CNS) involvement. Joubert Syndrome (JBTS) is a representative ciliopathy and a neurodevelopmental disorder. It is characterized by a highly specific mid-hindbrain malformation whose underlying pathomechanism remains unclear. The presence of non-structural CNS defects (f.e. seizures or intellectual disability) implies a role for PC in neuronal function beyond transmission of developmental signaling pathways. To understand these CNS malformations, we are generating iPSC-derived models. After CRISPR- knockout of the JBTS-associated gene CEP290 in hiPSCs, we apply 2D and 3D protocols to generate neuronal models. Preliminary data indicate that loss of CEP290 does not preclude cerebral organoid formation, but might affect organoid patterning. Loss of CEP290 does not alter cilia number and length in 2D neurons but affects ciliary morphologies in a subset of cells in 3D cerebral organoids. Applying different differentiation protocols to the same mutant iPSCs may identify cell-type specific functions for ciliary genes, where different neuronal cells suffer distinct consequences from their loss of function. It becomes apparent that modeling a complex genetic disease requires various models to elucidate underlying pathomechanisms.
Attending the IndiaEMBO would open great possibilities to network with peer researchers. The agenda directly relates to the research of my PhD. Learning more about organoids and advances in current brain modeling will help elaborating my research in modeling rare genetic diseases with human 3D models.

Presenter: Nidhi Kamboj

Exploiting Intestinal Organoid Model to interrogate Shigella pathogenesis

Nidhi Kamboj
Postgraduate Institute of medical education and research

Shigellosis is a dysenteric syndrome caused by Shigella, a Gram negative, enteroinvasive bacterium belonging to the family Enterobacteriaceae.This exclusively human disease is transmitted directly via the feco-oral route from an infected patient or indirectly through contaminated food and water. According to WHO vaccine development against shigellosis is a high priority considering the global burden. Shigella are highly host adaptive pathogen, humans are the only reservoirs. Therefore, no suitable animal model is available to study the relevant pathogenetic mechanisms and immune response.Human enteroids are 3-dimensional epithelial organoids obtained as primary culture system from intestinal crypts and are being used for study of normaldigestive physiology, pathology of intestinal disease and host pathogen interactions.In our study, we established this model and interrogated the differential pathogenic mechanisms evoked by different serotypes of Shigella. Our results demonstrated that different species of Shigella is able to invade human intestinal organoid model. For this, we infected human intestinal organoids with the three different species of Shigella and visualized the entry of Shigella into the human intestinal organoid and morphological changes of the organoid by phase contrast microscopy. Therefore, by using this human intestinal organoid model we were able to visualize the invasiveness of different species of Shigella and the morphologic changes of the organoids. This organoid model would be a suitable model for Shigella antigens (as vaccine) testing that exactly expresses the same immune response as in-vivo because the conditions hardly differ from the human itself. The knowledge gained will help in discovery of vaccine targets.

Presenter: Riya Rauthan

DISSECTING THE GENETIC DETERMINANTS OF CORTICAL INTERNEURON MIGRATION IN HUMAN FOREBRAIN ASSEMBLOIDS

Riya Rauthan [1, 2], Debojyoti Chakraborty [1, 2]

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Neuronal migration is a fundamental process during brain development crucial for formation of proper brain architecture and its overall function. Interneuron migration anomalies due to genetic or environmental perturbations can lead to malfunctions in the neural circuitry and are observed in case of multiple neuropsychiatric conditions. Variants in Erb-B2 Receptor Tyrosine Kinase 4 (ERBB4), a member of Tyr protein kinase family and the epidermal growth factor receptor subfamily that functions as cell surface receptor for neuregulins, have been associated with human neurodevelopment disorders such as schizophrenia, epilepsy and intellectual disability. Animal studies indicate the role of ERBB4 in neuronal migration, synaptogenesis and synaptic transmission. However, the exact mechanistic role of ERBB4 in migration of cortical GABAergic interneurons in humans is unidentified. In this study we employ CRISPR/Cas9 to knockout ERBB4 in GAD1- mClover knockin human induced pluripotent stem (hiPS) cell reporter line and report its effect on the phenotype and global gene expression upon deriving dorsal and ventral human forebrain identity cerebral organoids. GAD1/mClover exhibits distinct temporal expression in ventral forebrain organoids allowing capture of tangential migration of labelled cortical interneurons in intact fused 3D assembloids to pinpoint the role of neuregulin receptor ERBB4 in migration and function of these neurons. We also analyze change in dynamics of interneuron migration upon ERBB4 knockout on nanofiber scaffolds that mimic fibrous extracellular microenvironment. Our findings uncover the function of ERBB4 in context of human cortical interneuron migration to suggest new strategies for restoring migration deficits and rescue the associated social and cognitive behavioral abnormalities.

Presenter: Silvia Breviario

Dissecting the involvement of acid sphingomyelinase inhibition in GBA-dependent Parkinson's disease

Silvia Breviario[1], Emma Veronica Carsana[1], Giulia Lunghi[1], Emanuele Frattini[2], Alessio Di Fonzo[2], Massimo Aureli[1]

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Heterozygous mutations in the GBA gene, encoding for the lysosomal enzyme beta glucocerebrosidase (GCase), represent one of the major genetic risk factors for the development of Parkinson's disease (PD). However, not all the GBA-mutated carriers develop this neurodegenerative disorder.
Recent data reported in literature obtained in different GCase-inhibited models link the deficiency in the lysosomal enzyme acid sphingomyelinase (ASM) with an improvement of the pathological phenotype.
Starting from this evidence, we evaluated whether the ASM inhibition could ameliorate the pathological phenotype in a neuronal model of GBA-PD using human iPSC-derived dopaminergic neurons, treated with Conduritol-B-Epoxide (CBE), a pharmacological inhibitor of GCase. To evaluate the effect of ASM inhibition, before the end point of the incubation with CBE, we also administered amitriptyline, a functional inhibitor of ASM, for 24 hours and 7 days.
CBE-treated neurons showed accumulation of glucosylceramide and neurodegeneration. Interestingly, after both the acute and chronic treatment with amitriptyline we found an amelioration of the neurodegenerative phenotype, a reduction of glucosylceramide content and an increase in the activity of the non-lysosomal glucocerebrosidase (NLGase).
These results suggest that the inhibition of ASM could represent a strategy to ameliorate the neurodegenerative phenotype in GBA-PD, by increasing the NLGase activity acting as a possible counteracting mechanism against glucosylceramide accumulation. Now we are evaluating whether the effect of ASM inhibition is maintained also in midbrain organoids from GD-PD patients, so attending this workshop could be very useful for me for increasing my knowledge in this field and for ameliorating our experimental model.

Presenter: Swathi Narasimhaiah

Efficient expansion of iPSC-derived human lung epithelium as adherent cultures and 3D organoids using defined, serum free medium for disease modelling and cell therapy

Swathi Narasimhaiah, Ravindra Zirmire, Harshini Surendran, Rajarshi Pal *Eyestem, CCAMP*

Cell replacement therapy is an attractive therapeutic option for pulmonary disorders leading to fibrosis. Emerging evidence from ongoing clinical trials suggest that an average human lung requires at least 1 million cells per kg of body-mass. Scaling up bonafide target cells ex vivo is one key challenge in cell therapy which we are addressing in this study. Our lab has extensive experience differentiating human induced pluripotent stem cells (iPSC) into distal alveolar and proximal airway cells via temporal regulation of WNT signaling. Using PneumaCultTM, we successfully expanded the lung epithelial cells for 10 passages thereby generating more than 1 billion cells from a starting population of 1 million. The cultures primarily comprise type II alveolar cells (SP-C+) and airway cells (FOXJ1+). Interestingly, these cells coexpress lung stem cell markers SCGB1A1, KRT8 with Ki67 highlighting their reparative potential. In parallel, self-assembling 3D lung organoids cultured in suspension for more than 60 days mimics in vivo tissue architecture and lamination. Immunohistochemistry on organoid sections indicated the presence of type II alveolar- (SP-C, SOX-9), airway- (SOX-2, FOXJ1), basal- (KRT5/8), multiciliated- (acetylated tubulin), and secretory cells (MUC5AC) arranged in different layers. This 2D/3D model can serve as a promising investigational platform to study the efficacy as well as mechanism of action of drugs for lung diseases.

Presenter: Yogita Adlakha

MicroRNA-135 drives human neural stem cell fate determination: Employing induced pluripotent stem cells (iPSCs) derived 2D neural stem cells (NSCs)

Yogita Adlakha
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Human brain development is an exceptionally complex phenomenon. Our understanding of human brain development is scarce due to the limited accessibility of the human brain. MicroRNAs (miR), the small non- coding RNAs, refine gene expression and are also enriched in the brain. How they modulate neural development remains elusive. Recently, we have investigated the role of miR-135 in neural stem cell fate determination. We employed human neural stem cells (hiNSCs) derived from induced pluripotent stem cells (iPSCs). The iPSCs were derived from human peripheral blood. Overexpression of miR-135 in hiNSCs reduced proliferation while accelerated the neuronal differentiation as revealed by reduced expression of neural stem cell marker, Nestin, and increased expression of neuronal marker, Tuj1. MiR-135 also suppressed the pluripotency transcription factors, OCT4 and SOX2 in hiNSCs. Since, neurons are metabolically highly active cells and depend on mitochondria to satisfy their energy needs, hence we hypothesized that miR-135 might be modulating mitochondrial dynamics to enhance neuronal differentiation. Ectopic expression of miR-135 enhanced mitochondrial biogenesis by upregulating transcription factor A of mitochondria (TFAM) and Sirtuin 1.
Additionally, the genes implicated in mitochondrial fusion displayed an increasing trend of OPA1 and MFN2. In- silico analysis predicted wingless-type MMTV integration site family member 3 (WNT3) as a target of miR-135. Thus, by downregulating a gene which is implicated in primordial germ cell specification and brain development, miR-135 promotes neuronal differentiation. Our study provides novel molecular insights into how miR-135 modulates mitochondrial dynamics to boost neural development. This may potentiate the design of treatments for neurodegenerative diseases.

Selected abstracts for poster presentation

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2	Abraham Peele Karlapudi	Virtual screening of cyclooxygenase inhibitors from Tinospora cordifolia using the machine learning tool
3	Akash Kumaran	3D cellular models for molecular analysis of novel ALS-associated gene
4	Kumari Alka	Nuclear receptor Nurr1 activation exert neuroprotective effect in rat model of Parkinson's disease by improving mitochondrial dysfunction
5	Anjan	Generation of Blastocyst-like structures using Extended pluripotent stem cells.
6	Asha Channakkar	Chromatin regulation of human neural stem cells by putative causative of intellectual disability-LSD1
7	Ashwin Dalal	Finding novel genes for rare genetic diseases in Indian population
8	Atanu Ghorai	Prolonged replication stress maintains radiation-induced senescence in therapy-resistant residual glioblastoma disease cells
9	Athira M Menon	Tumoroid models to study the role of neurons in the metastatic tumor microenvironment
10	Atreyee Guria	Understanding the role of Collective Cell Migration in Colorectal Adenocarcinomas
11	Barnali Biswas	Membrane proteomics unravels roles of Golgi N-glycans in Spermatogenesis and Male fertility

12	Bidisha Bhattacharya	Studying ROTATIN (RTTN) Gene Mutations Using Human Brain Organoids
13	Chen Chongtham	Milk based high fat diet ameliorates DSS induced colitis
14	Chiara Cimmaruta	Oxidative/nitrosative stress and neurological defects in progeroid Cockayne syndrome modeled by iPSCs patient-derived cerebral organoids
15	Sreeja Dhanya	Elucidate the role of RBBP4 in regulating neocortical development and its neuropathological role in autism spectrum disorder
16	Divya Khanna	Patient derived organoids – models for drug screening
17	Ekta Gupta	Regulation of pluripotency factors by SATB family chromatin organizer proteins in colorectal cancer
18	Elizabeth Talker	Cohort analysis of Hormone receptor positive, HER2 negative breast cancer patients progressed on endocrine hormone therapy
19	Gaurav Kansagara	The Matricellular Protein Mindin Induces Pro-Inflammatory Response in Fibroblasts to Manifest Dermal Fibrosis
20	Gaurav Samuel	Human 3D brain organoid development for altered cellular signalling mechanisms
21	Gurpreet Kaur Grewal	In Vitro investigation of role of antiepileptic drugs in oxidative stress and ABCC2 activity
22	Atif I. A. Shaikh	Studying pathogenesis of Parkinson's disease using organoid models derived from patients with various genetic mutations leading to clinical presentation.
23	Jhilik Dey	POTENTIAL ROLE OF ENDOGENOUS NEURAL PROGENITORS IN REGENERATION OF HIPPOCAMPAL PYRAMIDAL NEURONS FOLLOWING NEURODEGENERATION.

24	Juhi Vaishnav	Investigating the role of thyroid hormones in ventral wall closure during embryonic development of domestic chick.
25	Lakshmy Vasan	L3mbtl3 is a novel gatekeeper of neurogenic gene expression and mRNA processing during neocortical neurogenesis
26	Madhuri Chaurasia	Characterizing the role of TECPR2 in iPSCs derived neuronal systems
27	Mayank Jain	Yogic intervention improves the level of TNF-α, IFN-γ, MDA, and NO in breast cancer patients undergoing treatment
28	Meghali Aich	TOBF1 modulates mouse embryonic stem cell fate by regulating alternative splicing in a cell cycle dependent manner
29	Nasera Rizwana	3D Bio-printing of Decellularized Dental Pulp tissue derived extracellular matrix in Peripheral Nerve Regeneration.
30	Neha Yadav	Advanced Neuroimaging and Event Based Modelling of Brain Structure and Microstructures :Development of Imaging Based artificial intelligence platform of Cognitive status
31	Nikayla Batohi	Precision medicine using drug repurposing platform – the way forward in applying novel drug combinations for Ovarian Cancer treatment
32	Nikhil Gandasi	Subcellular view of islets to understand type-2 diabetes – Islet organoids might provide novel insights
33	Niraikulam Ayyadurai	Biosynthesis of Next Generation Biomaterials through Genetic Code Expansion
34	Nusrat Nabi	FAK, Src and PCTAIRE1: Novel targets for anti-cancer therapy
35	Pallavi Gupta	Elucidating the extent of coordinated splicing of exons in the mammalian brain
36	Parvathi Satheesh	Identification and molecular analysis of altered neurodevelopmental pathways that lead to

		neuropsychiatric disorders
37	Shagufta Parveen	Modelling Folic acid Deficiency associated Neural Tube Defects using iPSC derived 3D Neural Cysts and OrganoidS
38	Poonam Yadav	Apoptotic Effect of Interferon (IFN) and Tumor Necrosis Factor (TNF) Induced Wharton's Jelly Mesenchymal Stem Cells (WJMSC) on Pancreatic Ductal Adenocarcinoma cells (PDAC) -A Cell based Model.
39	Pradip Paul	Three-Dimensional organoid model of the human forebrain to study neuropsychiatric disorders.
40	Pragyan Acharya	Upregulation of ELANE, MPO and CD177 genes in Acute-on-Chronic Liver Failure Derived Granulocytes
41	Preethika Nair	3D multicellular, patient-derived glioblastoma spheroids for personalized therapeutics
42	Pretty Garg	The secret to faster differentiation of serum-free, mature human astrocytes for disease modelling
43	Raghav Gurunathan	Chitosan-based Nanocarriers for Non-coding RNA Delivery in Biomedical applications
44	Raghava Reddy	Modeling nephropathic cystinosis with human kidney organoids
45	Rahul Sharma	CARP2 regulates the Golgi dynamics upon EGF stimulation
46	Raja Sundari Meenakshi Sundaram	Immunomodulatory profiling of Human Mesenchymal Stem Cells derived from various sources under in vitro inflammatory conditions
47	Rajiv Dixit	Modeling and Deciphering the Molecular Mechanism of Polyglutamine Neurodegenerative Diseases
48	Rambhadur Subedi	Recombinant fragment of human Surfactant Protein D (rfhSP-D) inhibits metastasis of PC3 and LNCaP prostate cancer cells: A potential immunotherapeutic mechanism

49	Ritu Varshney	Development of isogenic stable tagged cell models using CRISPaint Technology for autophagy and neurodegenerative studies
50	Sandhya Anand	Development of an in vitro model system reflecting early trophoblast development using human embryonic stem cells
51	Saumya Sharma	Development and characterization of cellular models for the study of megalencephalic leukoencephalopathy with subcortical cysts
52	Secunda Rupert	Mesenchymal Stem Cell Derived Exosomes as Therapeutic Option for Liver Disease
53	Sharon Mariam Abraham	Explore glutamate receptor subunit dysfunction in cell and animal based model of schizophrenia (SCZ)
54	Bipin Raj Shekhar	Exome analysis in familial schizophrenia: identification of a shared pathway and modelling with induced pluripotent stem cells
55	Shiffali Khurana	Neuronal ExomiRNA-6988-5p regulates neurotransmission in Amyotrophic lateral sclerosis
56	Shreya Kandpal	Role of nutrients in shaping epithelial architecture
57	Ashitha SNM	Investigating Immune Functions of neuronal genes burdening Autism Spectrum Disorder: An integrated gene expression and mutation analysis
58	Soumita Goswami	Microglia Secreted ICAM-1 reduces Amyloid Beta (Aβ) mediated neuroinflammation by targeting ERK pathway and improves synaptic health in 5xFAD mice
59	Subashchandrabose Chinnathambi	Purinergic receptor P2Y12 involves in Tau oligomers-induced microglial phagocytosis and endocytic trafficking via filopodia associated actin remodelling
60	Subhashika Govindan	Neuro-toxicogenomic mapping of TMT induced neurotoxicity using human minibrain reveals

		associated adverse molecular events
61	Sudip Sen	Using human fetal neural stem cells to develop a disease model for cerebral palsy
62	Swati Sharma	Investigating retinal cellular dynamics in eye disorders using Zebrafish embryos and retinal organoids
63	Trinath Jamma	Host gut microbial metabolites regulate activated immune cell-driven EMT in intestinal epithelial cells
64	Trupti Agarwal	Retinal commitment of RB1 null induced pluripotent stem cells is independent of pRB expression
65	Tungadri Bose	One Size Doesn't Fit All - Towards Personalized Probiotics
66	Vadde Sudhakar Reddy	Neuroprotective role of vitamin B12 in Streptozotocin-induced diabetic rat brain
67	Vaishali Saini	Understanding EBV-induced Alzheimer's disease using cerebral organoid models
68	Vinithra Ponnusamy	Obesity and tongue papillae density-What organoids could do?
69	Vorapin Chinchalongporn	MR spectroscopy reveals a maturing neurochemical profile of human cerebral organoids imaged at different developmental stages
70	Yogesh Sardana	Comparing Protective Effects of Melatonin and Quercetin in Swiss Mice on Modulation of Mitochondrial Dysfunction during Lead Induced Neurotoxicity.
71	Zandile Nxumalo	Using various 2 Dimensional (2D) cancer cell lines to screen for anti-cancer drugs for applications in the development of a predictive high throughput (HTS) drug screening platform.

Presenter: Abhishek Teli **Poster number: 1**

Spheroids & Organoids as Appliances to Reiterate Tumor-Associated Macrophage- Tumor Crosstalk

Abhishek Teli, Tuli Dey

Institute of Bioinformatics and Biotechnology, Savitribai Phule Pune University

Immunosuppressive microenvironment of solid tumors is a major cause behind the unfulfilled success of current immunotherapies. Crosstalk between cancer cells and immune cells causes Immune-editing and activation of immunosuppressive functions in immune cells. To study this crosstalk, human-relevant model system which is amenable to experimental manipulations & which can recapitulate the complex cellular interactions is need of the hour. Therefore, in the following study, we used breast cancer spheroids to study early-stage breast tumor-macrophage crosstalk and potential therapeutic targets. Spheroids were used to mimic early-stage avascular tumors. Co-culture with macrophages resulted in their polarization towards TAM-like phenotype. Analysis of this crosstalk will shed light on novel potential therapeutic targets involved in chemotactic recruitment and repolarization of TAMs towards anti-tumor phenotype. The study further involves the use of patient-derived tumoroids and organoids to assess the clinical relevance of findings.

Development and use of organoids as human-relevant tumor model faces several hurdles such as ethical permissions, it also requires expertise in clinical specimen handling, careful selection of precisely defined medium, and so on. These variables contribute to success of development and establishment of organoids, cost effectiveness, and reproducibility. Moreover, only few reports have shown successful, reproducible development of breast organoids. Several subtypes and cell types of origin add up to the challenge. Therefore, information about subtype-specific defined mediums and growth factors required is limited. Attending talks of pioneers and exchange of ideas with peers will provide deeper insights into the research topic as well as the discussions will help in troubleshooting technical challenges.

Presenter: Abraham Peele Karlapudi **Poster Number: 2**

Virtual screening of cyclooxygenase inhibitors from Tinospora cordifolia using the machine learning tool

Abraham Peele Karlapudi, Siva kumar Samudrala, Indira Mikkili, , Krupanidhi Srirama*, Venkateswarulu T.C*
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Tinospora cordifolia have a variety of compounds and some of these compounds may have anti- inflammatory and antioxidant properties. In the present study, we identified the compounds in leaf extract of Tinospora cordifolia through Gas Chromatography-Mass Spectrometry (GC-MS) analysis and found the various metabolites. The compounds are screened virtually using a machine learning model, followed by molecular docking and simulation study for the identification of top hit compounds as inhibitors of cyclooxygenase (COX). The molecular docking revealed that the compound 7,9-Di-tert-butyl-1-oxaspiro (4,5) deca-6,9-diene-2,8-dione (CID:545303) exhibited the lowest binding energies of −7.1 and -6.8 kcal/mol against cox-1 and cox-2 respectively. The interactions are favored by hydrogen bonding and hydrophobic interaction inside the binding pocket. The 100ns MD simulation study for these compounds was performed to know the stability and found the RMSD around 2Å and, around 1.0 Å with minimal fluctuations indicating a stable complex throughout the simulation of 100 ns. Based on these findings, we proposed 7,9-Di-tert-butyl-1-oxaspiro (4,5) deca-6,9-diene-2,8-dione could be used as a dual inhibitor of COX enzymes and a drug-like a molecule for treating inflammation after evaluation of their biological properties. The web-based platform developed using Streamlit for large scale prediction of cyclooxygenase inhibitors was deployed using the Heroku cloud application platform.

Presenter: Akash Kumaran **Poster Number: 3**

3D cellular models for molecular analysis of novel ALS-associated gene

Akash Kumaran, Baskar Bakthavachalu
Indian Institute of Technology, Mandi

The most common underlying cause of ALS is genetic mutations. With the rapidly evolving genomic technologies, large sets of ALS genome data are available for analysis. At the same time, new studies have reported several potential ALS-associated mutations (~690) in the non-coding regions of the human genome using computational tools along with machine learning-based approaches. We intend to study the effect of a few selected gene candidates from these available lists in iPSC-derived neurons. In parallel, we also have designed a novel genome-wide screen strategy to identify genetic modifiers of ALS using suppressor and activator CRISPR screens in iPSC-derived neurons. We anticipate identifying several ALS modifier genes that will be further used for detailed mechanistic studies. With initial studies on 2D models, we intend to use the 3D brain organoids to study the pathological features of neurodegenerative diseases with respect to the identified genetic modifiers and explore the possibilities of targeting these genes for therapeutic applications.

Presenter: Kumari Alka **Poster Number: 4**

Nuclear receptor Nurr1 activation exert neuroprotective effect in rat model of Parkinson's disease by improving mitochondrial dysfunction

Kumari Alka, Parul ., Shubha Shukla

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The orphan nuclear receptor Nurr1 plays an important role in the maintenance and differentiation of midbrain dopaminergic neurons. Recent evidences have indicated that reduced expression of Nurr1 is associated with several dopamine-related CNS disorders. Similar research has advised that Nurr1 also control expression of several mitochondrial associated genes, that are important for regulation of mitochondrial respiratory chain. Parkinson's disease (PD), the second most common neurodegenerative disorder is associated with mitochondrial dysfunction along with selective and progressive loss of dopaminergic neurons in substantia nigra pars compacta (SNpc) region of mid brain. In this study, we administered Nurr1 agonist, Amodiaquine (AQ) at the dose of 20 mg/kg, (i.p.) in 6-OHDA lesioned rat model of Parkinson's disease for 21 days. Our results have demonstrated that Nurr1 activation improved motor functions, as well as nonmotor functions. At molecular level, effect of AQ treatment on mitochondrial health (in terms of expression of apoptosis related signalling proteins, mitochondrial membrane potential (MMP) and mitochondrial biogenesis associated cascade), was assesed in substantia nigra pars compacta (SNpc) region of brain.

In conclusion, our data suggest that pharmacological activation of Nurr1 was able to reverse behavioral deficits both motor and non-motor symptoms in 6-OHDA lesioned rat model of Parkinson's disease. Thus, transcription factor Nurr1 could be a promising therapeutic target for management of PD associated pathology.

Neural organoid as a model can be used to explore expression of Nurr1 transcription factor at different stages during development of mesencephalic dopaminergic neuron. This course will be highly helpful for our work plan.

Presenter: Anjan TK **Poster Number: 5**

Generation of Blastocyst-like structures using Extended pluripotent stem cells.

Anjan TK, Pallavi, Shagufta Parveen
Manipal Institute of Regenerative Medicine, Manipal Academy of Higher Education.

Pluripotent stem cell-derived models of human blastocysts(Blastoids) and donated supernumerary embryos have been extensively used to study developmental events of self-organization, lineage specification, implantation and lumenogenesis. However, the mechanisms underlying developmental disorders remain largely unknown. Here, We attempted to model organization of aneuploid-Turners syndrome blastocysts using Extended pluripotent stem cells(TS-EPSCs) developed from iPSCs using a previously reported cocktail of chemical inhibitors(Yang et al.2017). From our previous experiments, we found out that TSEPSCs are competent towards Embryonic as well as Extra-embryonic lineages. Therefore, they can be used to create clonally-reproducible blastocyst models to investigate abnormalities in early development of Turners Syndrome(TS) conceptus. To achieve this, we aggregated TS-EPSCs on a microwell-based system(AggreWells). They self-organized into structures resembling Blastocysts in terms of Oct3/4 segregation, reminiscent of the Inner cell mass. Such 3D developmental models could help us understand fate of aneuploid cells during peri-implantation development, impairments in lineage allocation, expression profiles and the overall developmental potential of defective embryos compared to their normal counterparts.

Presenter: Asha Channakka **Poster Number: 6**

Chromatin regulation of human neural stem cells by putative causative of intellectual disability- LSD1

Asha Channakkar et al.

Institute for Stem Cell Science and Regenerative Medicine, Bangalore

The cerebral cortex is the seat of higher-order functions in the brain. Dynamic modulation of the chromatin state throughout the development regulates progenitor proliferation, differentiation, and cell-fate decisions providing cell type specificity and diversity found in the brain. LSD1 is a Lysine Specific Demethylase that erases methyl groups from specific lysines on Histone 3. It is a part of the chromatin remodeler complex NuRD. Patients with de novo mutations in LSD1 are presented with developmental delay and intellectual disability. LSD1 has been reported to function differentially between mice and humans, it positively regulates progenitor proliferation in mice, whereas, it promotes neuronal differentiation in humans.

We have performed LSD1 ChIP-seq and RNA-seq upon its inhibition in human neural stem cells to ascertain its genome-wide targets. Our study has revealed that LSD1 regulates the genes crucial for forebrain development, neuron generation, and synapse organization. We report that LSD1 binding modulates expression of genes involved in signal transduction, ECM homeostasis, and cell adhesion in a human-specific manner. Transition from Neuroepithelial cells to Radial Glia cells is dependent on Notch signaling. This signaling is also essential for progenitor pool maintenance. On LSD1 inhibition, Notch signaling genes such as TLE1 and HES6 are repressed. Overexpression of these genes in NSCs phenocopies LSD1 inhibition phenotype. Our study reveals novel downstream effector functions of LSD1 in regulating human neuronal development. This conference may help me gather recent updates in organoids field and provide insights into how we can integrate organoids to move this project forward.

Presenter: Ashwin Dalal **Poster Number: 7**

Finding novel genes for rare genetic diseases in Indian population

Ashwin Dalal
Centre for DNA Fingerprinting and Diagnostics

Monogenic disorders are rare diseases individually, but collectively they are important cause of morbidity and mortality in humans. To date ~ 5000 rare diseases have been documented and new rare diseases are being reported regularly. The identification of candidate gene for single gene disorder has importance, not only in prenatal diagnosis and genetic counselling but also in basic understanding of gene function and pathophysiology of disease. The classical methods of gene identification such as chromosomal mapping, linkage analysis and homozygosity mapping have led to identification of a number of novel genes but these methods have certain limitations. These have been overcome by new sequencing technology of massively parallel sequencing. We have identified novel candidate gene/variants for number of rare single gene disorders using exome sequencing. We have identified novel phenotype to gene association in a case of Complex- camptosynpolydactyly, a rare disorder described in an Indian family. The p.E74L pathogenic variation in basic DNA binding domain of transcription factor BHLHA9 was found to lead to interference with its function. We have also identified a novel gene ARMC9 for ID (intellectual disability) with ptosis and polydactyly in a family. The pathogenic variant c.879G>A in ARMC9 is a synonymous variant but was predicted to cause splicing defect.
Functional characterization using pCAS minigene system revealed that this variant leads to skipping of exon9 of ARMC9. In-silico modelling revealed that the deletion of 33 aa is likely to lead to structural alteration in ARM domain and may lead to impairment of protein-protein interactions.

Presenter: Atanu Ghorai **Poster Number: 8**

Prolonged replication stress maintains radiation-induced senescence in therapy-resistant residual glioblastoma disease cells

Atanu Ghorai [1, 3], Bhawna Singh [1, 2], Shilpee Dutt [1, 2]

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Glioblastoma multiforme (GBM, WHO grade 4) is the most common and aggressive primary brain tumor in humans having a dismal outcome with median survival of approximately 15 months despite multimodal therapy. There is a need for efficient and clinically relevant experimental model system to study therapy resistance in GBM. Therapy-induced senescence (TIS) and recovery from TIS, have been recently attributed as one of the reasons for therapy resistance and recurrence in cancers including GBM by us. But, how such TIS is manifested is still obscure. In this current study using cell biological and biochemical approaches, we have shown that replication stress (RS) is one of the crucial factors for TIS in GBM cell lines. Interestingly, we have found a 'biphasic' mode of DNA damage after radiation treatment as detected by γH2AX and comet assay. We established that the second phase of DNA damage originated in the S- phase of irradiated cells experiencing RS as confirmed by DNA fiber assay. Importantly, such RS precedes the induction of senescence as found in the β-gal assay.

Mechanistically, we find persistent ATR activation during the second phase of DNA damage. Genetic ablation and pharmacological inhibition of ATR result reduction in TIS, leading to apoptosis. Interestingly, ATR inhibition further sensitizes PARP1 inhibitor induced enhanced TIS to the cell death pathway. Together, our results demonstrate that RS plays a crucial role to maintain the TIS in residual disease cells in GBM and targeting ATR will be an effective strategy to eliminate TIS for better treatment outcomes.

Presenter: Athira M Menon **Poster Number: 9**

Tumoroid models to study the role of neurons in the metastatic tumor microenvironment

Athira M Menon

Centre for Neuroscience, Department of Biotechnology, Cochin University of Science and Technology, Kochi-22

Unravelling the essential roles of the tumour microenvironment in cancer has paved the way for an emerging field of study, “Cancer neuroscience.” It deciphers the key signalling molecules involved in cancer–nervous system crosstalk. A solid tumor is highly equipped with peripheral nerve endings. Studies have shown that discrete neuron types, including adrenergic, cholinergic and many more, boost the proliferation and metastasis of cancer cells. However, the origin and mechanism of their innervation in the tumor microenvironment are unknown. In our study, we aim to construct a 3D co-culture system constituting different compartments of cancer and neural cells in collagen/fibrin matrix, along with integrated cell adhesion molecules, to study role of neurons in the primary and metastatic tumor niche. The preliminary work have shown that cancer cell lines' remarkable capability to form tumoroids in collagen type I matrix. Co-cultured models of prostate cancer cells and primary neural stem cells from Sub-Ventricular Zone (SVZ) of the brain’s lateral ventricle (in the layer composed of fibrin matrix over the top of collagen matrix) have shown mutual connections and increased gene expressions of extracellular matrix proteins and metalloproteases. The cellular morphology and viability were also investigated by microscopic imaging, histological staining, and fluorescently labelled cell tracking. We would further aim to construct a three-compartment model, including supporting stromal cells that would closely mimic the in vivo conditions of the disease. Further analysis will aim at the transcriptomics and molecular levels of the modulators involved that could be exploited as targets for improved anticancer therapies.

Presenter: Atreyee Guria **Poster Number: 10**

Understanding the role of Collective Cell Migration in Colorectal Adenocarcinomas

Atreyee Guria, Amrita Khamari, Sunando Datta
Indian Institute of Science Education and Research, Bhopal

Invasion and metastasis are major hallmarks of cancer, involving ECM remodeling by invadopodia and cancer cell migration to distant organs.
Recently, our lab has shown that PLP2 associates with ZO1 to promote collective cell migration (CCM) in SW480 colorectal adenocarcinomas. During the initial hours, PLP2-ZO1 is predominantly localized to lamellipodia like umbrella-shaped protrusions at the leading edge of cells. Their association facilitated Rac1 activation leading to cytoskeletal remodeling at the wound front [1]. Currently, through differential proteomics, we are trying to understand time-dependent intermediate molecular interactors of PLP2 that are linked to polarized CCM and Rac1 activation. We are also exploring the role of the Hippo-signaling pathway effector YAP, in differential gene expression during CCM of colorectal adenocarcinomas. Additionally, we are investigating the polarized trafficking of MT1-MMP in response to HGF and the role of HGF receptor cMET in tumor invasion.
We, presently use 2D-cell culture assays to study invasion and migration. Compared to cell lines, organoids promise a more accurate physiological in-vitro representation of organs. Through this workshop, I hope to gain a better understanding of current techniques and research for utilizing organoids to model disease conditions.
This will enable us to extend the expertise to the benefit of the lab and employ organoids as an alternative model for cancer research.

Presenter: Barnali Biswas **Poster Number: 11**

Membrane proteomics unravels roles of Golgi N-glycans in Spermatogenesis and Male fertility

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ICMR-NIRRCH, MUMBAI

A defect in the glycosylation machinery may impair the functions of glycoproteins and lead to a congenital disorder of glycosylation (CDG). Spermatogenesis in the male is tightly regulated differentiation events leading to production of functional gametes. Male infertility presents a significant public health problem globally. The potential effects of mutations in corresponding glycosylation genes of humans is investigated to understand the consequences to fertility. Insights into roles for glycans in sperm production are obtained from mutant mice following deletion or inactivation of genes that encode enzymes involved in the glycosylation activity. We previously reported conditional knock out of a key glycosyltransferase (Mgat1) causes block in spermatogenesis and infertility. N-glycosylation of membrane proteins is important for a wide variety of cellular processes. Proteomics analyses of Chinese Hamster Ovary (CHO) cells having point mutation in either of the genes encoding for N-glycosylation pathway enzymes Mgat1 (Lec1 cells) or Mgat5 (Lec4 cells) showed significantly dysregulated membrane expression of insulin like growth factor -1 receptor (IGF-1R) and GTPase activating protein (IQGAP-1). To understand the complex physiological process underlying mouse testis in response to N-glycosylation inhibition (tunicamycin), we characterised the changes in the membrane proteome of co-cultured mouse Spermatogonial cells and Sertoli cells. Results revealed tunicamycin not only affects the expression of glycosylated proteins but also alters an extended scale of proteins. Functional annotation of altered proteins revealed majority of the proteins are related to ER stress and junctional proteins. Future studies are ongoing to validate these findings in a enzymatically modified testicular organoid model.

Presenter: Bidisha Bhattacharya **Poster Number: 12**

Studying ROTATIN (RTTN) Gene Mutations Using Human Brain Organoids

Adva Hadar 1, Bidisha Bhattacharya 1, Kalina Draganova 2, Magdalena Goetz 2, Orly Reiner 1
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Recessive mutations in the ROTATIN (RTTN) gene result in several brain malformations, including polymicrogyria (extra brain folds) and microcephaly (small brains). The Rotatin protein contains two Armadillo- like domains mediating protein-protein interaction. It is a centrosomal protein known to be involved in cell-cycle regulation.
This study aims to understand the role of Rotatin in nucleokinesis during the interkinetic nuclear movement (INM), which is the motion of nuclei during the cell cycle in the radial glia. The nuclei are located in the rosette's superficial area (the basal surface) during S-phase when cells synthesize DNA, RNA, and proteins. During the G2 phase, the nuclei travel from the basal side to the apical surface, close to the ventricle, where the cells undergo mitosis. Post-mitosis, the daughter nuclei travel back to the basal surface during their G1 phase of the cell cycle.
On-chip brain organoids were prepared from wild-type (WT) and isogenic RTTN-mutant hESCs with a mutation in the Armadillo-domain introduced by CRISPR/Cas9 genome editing.
Using time-lapse microscopy, we analyzed the dynamic behavior of the nuclei during INM. Our results suggest that RTTN mutations may affect the activity of molecular motors involved in apical to basal motion. In conclusion, RTTN mutations affect INM. Our future experiments will explore the molecular mechanisms involved in these processes.

Presenter: Chen Chongtham **Poster Number: 13**

Milk based high fat diet ameliorates DSS induced colitis

Chen Chongtham, Aneeshkumar AG

National Institute of Immunology

The exact cause of inflammatory bowel disease (IBD) varies, but diet and gut flora are among the main triggers or aggravators of the condition. Diets enriched in fat are linked to an increased risk of inflammatory bowel disease (Li et al. 2019; Zhao et al. 2020). The composition of fat plays a significant role in the development of colitis (Haskey et al. 2022). One frequently used animal model that closely resembles the clinical and histological characteristics of IBD in humans is colitis induced by Dextran Sodium Sulfate (DSS) feeding. We investigated the effects of a brief course of treatment with a milk based, fat-rich diet (MBD) on the development of the inflammatory response induced by DSS. Surprisingly, MBD, despite having higher fat content, appears to play a protective role against DSS-induced colitis.The severity of the disease and histopathology scores were lower in the MBD group after 7 days of treatment with 1.5% DSS compared to the control group. In the MBD group, the major proinflammatory cytokines IFN-gamma, TNF alpha, IL1-beta, and IL6 levels were reduced, while anti-inflammatory cytokines IL10, TGF-beta, and IL22 levels were significantly increased. These data suggest that the milk based, fat-rich diet (MBD) diet creates a protective environment against DSS-induced colitis by inducing an anti-inflammatory milieu.

Presenter: Chiara Cimmaruta **Poster Number: 14**

Oxidative/nitrosative stress and neurological defects in progeroid Cockayne syndrome modeled by iPSCs patient-derived cerebral organoids

Chiara Cimmaruta 1, Tara Fournier 1, Frank Yates 2, Miria Ricchetti 1
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Cockayne syndrome (CS) is a rare genetic disease characterized by a defective repair of UV-induced DNA damage leading to photosensitivity, as well as dramatic precocious ageing and neurodegeneration.
Hypersensitivity to sunlight is shared with UV-sensitive syndrome (UVSS) patients who do not age rapidly and do not display neurodegeneration, despite carrying the same genetic defects as in CS (CSA or CSB mutations). Thus, the cause of the progeroid/neurodegenerative phenotype in CS is not known, and a defective DNA damage repair alone appears unable to explain it.
Several mitochondrial defects and mismanagement of oxidative/nitrosative stress (ROS/RNS) have been detected mainly in patient-derived CS fibroblasts (1, 2). These processes are typically linked to ageing and neurodegeneration, suggesting their potential involvement in CS. These defects have not been assessed in neural cells that are rich in mitochondria and are severely affected in CS.
Due to the lack of reliable animal models and confronted with the large and yet unexplained clinical heterogeneity of CS, we generated patient iPSC-derived cerebral organoids to elucidate the role of mitochondrial dysfunction and high ROS/RNS levels in neurodevelopmental/congenital defects of clinically relevant CS patients. We also aim to address whether these 3D structures respond to antioxidant and/or anti- RNS therapies, that we showed to be effective in CS fibroblasts (2).
This EMBO workshop can help me to develop more advanced cerebral organoids disease models, update with the continuous and rapid development in this field and propose our models as a pipeline for other neurodevelopmental and/or progeroid diseases.

Presenter: Sreeja Dhanya **Poster number: 15**

Elucidate the role of RBBP4 in regulating neocortical development and its neuropathological role in autism spectrum disorder

SREEJA DHANYA

Institute for Stem Cell Science and Regenerative Medicine

The cerebral cortex consists of diverse neuronal and glial subtypes arranged cytoarchitecturally in six layers. Dynamic interaction between chromatin modifiers drives the generation of neuronal diversity from neural progenitors. Aberrations in epigenetic modifiers result in many neurodevelopmental disorders (Stessman et al., 2017). Putative risk variants in Retinoblastoma binding protein 4 (RBBP4) which is a chromatin remodelling factor have been associated with autism spectrum disorder (Firth et al., 2009). However, the exact molecular basis by which RBBP4 functions alter the epigenetic regulation of cortical development needs to be explored. We have used a mouse model system to decipher the functional role of RBBP4 in cortical development. We isolated mouse neocortical progenitors from Embryonic day 12.5 and performed nucleofection experiments either to knock down RBBP4 or overexpress RBBP4. Our work demonstrates that loss of RBBP4 results in reduced neuronal numbers indicating the essential role of RBBP4 in maintaining the neocortical neuronal population. Interestingly, the neuronal subtype which was reduced is CTIP2 expressing layer V neurons. To further understand the epigenetic regulation of RBBP4, we performed ChIP seq in neocortical cells and identified novel RBBP4 target genes that are crucial for transcription, differentiation, signal transduction and cell cycle. The functional consequences of RBBP4 dysregulation on gene expression in the neocortex will be further investigated.

This EMBO meeting is expected to shed light on various organoid applications to further extend my research on mouse cortical organoids in characterizing the effect of the putative point mutation in altering neocortical development, thereby devising therapeutic strategies for neurological disorders.

Presenter: Divya Khanna **Poster Number: 16**

Patient derived organoids – models for drug screening

Divya Khanna, Shantanu Chowdhury
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The established heterogeneity existing in cancer tissue is regarded as the preliminary reason for the failure of conventional cancer therapy. Therefore, the need to reconstruct intra- and inter patient heterogeneity in cancer models is deemed to be crucial for better understanding of cancer biology. Patient-derived organoids (PDOs) represent an emerging approach for creating in vitro cancer models that closely recapitulate the pathophysiological features of natural tumorigenesis and metastasis. Recently, numerous studies have used PDOs in the discovery of personalized anti-cancer therapy and prognostic biomarkers. In the present study we have used breast cancer patient derived tumor tissue (snap frozen and fresh tissue) and their respective adjacent normal tissue samples to derive organoids in lab. Both adherent and submerged cultures have been standardized and characterized respectively. The organoids prepared are planned to be used to screen the G4 binding ligands for their efficacy against cancers. For pilot study a HER2+ breast cancer patient derived organoids was tested for chlorpromazine (SCHL1) G4 binding ligand. Post 48 hour treatment we were able to see disruption in organoid architecture and decrease in expression of genes. The results need further validation in more patient derived organoids as well as other breast cancer subtypes to reach out on a useful conclusion.

Presenter: EKTA GUPTA **Poster Number: 17**

Regulation of pluripotency factors by SATB family chromatin organizer proteins in colorectal cancer

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The dysregulation of intestinal stem cells (ISC) leads to the generation of cancer stem cells (CSC), causing initiation and relapse of the disease. It is widely known that the Wnt/β-catenin pathway contributes to CSC enrichment and colorectal carcinogenesis. Although SATB family proteins are key players in the Wnt pathway, their role in regulation of intestinal CSCs is unclear. The differential expression of chromatin organizers SATB1/2 is reported to be critical for the development and progression of CRC. We aim to understand the role of SATB proteins in the regulation of pluripotency factors, CSCs and CRC progression by modulating its expression in CRC cell lines as well as spheroids and organoids. Since colon organoids (colonoids) are more physiological relevant of the intestinal tissue, they could provide better insights in understanding the cancer initiation and progression of the disease. We show that SATB1/2 over-expression in colorectal cancer cell line modulates the expression of pluripotency factors. Moreover, we observe that CRC cell line derived spheroids recapitulate SATB protein expression dynamics. Further, treatment with statins, the cholesterol-reducing drug, reverses the expression profile of SATB1/2 proteins in CRC cell lines and spheroids. Interestingly, our data also indicates that statin treatment reduces expression of the pluripotency factors significantly when compared across CRC cell lines and their respective spheroids. Furthermore, statin seems to revert the EMT phenotype in spheroids. As the study would be expanded using colonoids, therefore the exposure to various national and international laboratories using relevant techniques during the EMBO course will be very useful.

Presenter: Elizabeth Talker **Poster Number: 18**

Cohort analysis of Hormone receptor positive, *HER2* negative breast cancer patients progressed on endocrine hormone therapy

Elizabeth Talker[*1,2], Pallavi Parab[*1,3,] Rasika Kadam[1,2], Riddhi Ursekar[2], Jaya Chitra[2,4], , Anushree kadam[2], Suhani Sale[2,4], Nilesh Gardi[1,2,3], Yogesh Kembhavi[1],Shalaka Joshi[2,3,4], Seema Gulia[1,3], Tanuja Shet[3,5], Khushboo Gandhi[2], Rohan Chaubal[2,3,4], Sudeep Gupta[1,2,3]

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Background**:** 1/5 hormone receptors (HR) positive, *HER2*- breast cancer (BC) patients develop endocrine hormone therapy (EHT) resistance, the ethology/mechanisms of which remain unclear. Aim: a) Establish clinical characteristics of aforementioned patients b) Identify ctDNA based biomarkers to predict onset of relapse c) Establish pre-clinical in-vivo models Methods: BC patients presenting at Tata Memorial Centre (May 2017-November 2022); positive for estrogen receptor and/or progesterone receptor, and *HER2/Neu*- on IHC with ≥two-year follow-up were eligible. Patients were recruited to either: Resistant (patients progressed ≤2 years of EHT) or sensitive (patients sensitive for ≥2 years of EHT) cohorts. Relapse tumour and normal samples were bio-banked. Diagnostic biopsies were acquired from hospital's Tumour Tissue Repository. Blood plasma was subjected to cfDNA extraction followed by quality control to establish presence of ctDNA. Results: 380/1836 screened patients were eligible (221 sensitive, 159 resistant). 153/380 (58 premenopausal, 95 postmenopausal) patients clinico-pathological variables were analysed. 70 had tumour in right breast, 67 in left and 16 had a bilateral disease. Lymph node involvement was seen in 73/153 patients. The median age at diagnosis was considerably higher in resistant than sensitive cohort (51 years vs. 57 years, p-value 0.002), indicating that BC at younger age was more likely to relapse. Plasma from blood was successfully separated from 247/292 patients (181 Sensitive, 66 resistant). 240/247 patients (174 sensitive, 66 resistant) showed presence of cfDNA. 19/174 sensitive and 66/66 resistant patients had >50% ctDNA with >20 ng of ctDNA (p-value 0.001). Tumors at relapse from 12 resistant patients were implanted orthotopically in 17 NOD-SCID mice and are currently in G_1 Generation, with one lung cancer patient xenograft having progressed to G_2 phase. Conclusion: Our clinical cohort constitutes a valuable resource for research in this very important field of cancer.

Presenter: Gaurav Kansagara **Poster Number: 19**

The Matricellular Protein Mindin Induces Pro-Inflammatory Response in Fibroblasts to Manifest Dermal Fibrosis

Gaurav Kansagara [1, 2], Sunny Kataria [1, 3], Isha Rana [1], Krithika Badarinath [1, 3], Rania Zaarour [1], Rakesh Dey [1], Akash Gulyani [4], Colin Jamora [1]

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Fibrosis is an inflammatory disease that can occur in any connective tissue of the body and can lead to loss of organ function. Fibrotic diseases contribute to 1/3rd of the deaths worldwide, yet, there is no effective cure available to combat the disease. The key player in this disease condition is activated fibroblasts(myofibroblasts), which produce excessive amounts of Extra-Cellular-Matrix(ECM) proteins that compromise tissue physiology. The entire process of fibrogenesis is multifactorial, as various secreted soluble factors mediate the persistent activation of fibroblasts. However, the etiology of the disease is not yet well understood.

Using a mouse model of skin fibrosis, we have identified a matricellular protein called Mindin that plays an indispensable role in fibrogenesis. We found that mindin increases migration, contraction, pro-inflammatory cytokine production and secretion of ECM proteins by dermal fibroblasts. Mindin specifically increases inflammatory cytokine expression and migration of the reticular fibroblasts. On the other hand, the papillary fibroblast contract in response to mindin and also adopt features of cancer-associated-fibroblasts(CAF). Our findings indicate that these differential responses to mindin is caused by selected activation of subfamily members of the Src-family of kinases and Rho-GTPases, in addition to activation of the NF-κB signalling pathway. Our studies have also demonstrated that the N-terminal domain can recapitulate the effects of full-length mindin on mouse fibroblasts. Currently, efforts are underway to discover the cognate receptor of Mindin on dermal fibroblasts. Considering the enormous public health burden of fibrotic diseases, our studies have the potential to offer novel routes for therapeutic intervention.

Presenter: Gaurav Samuel **Poster Number: 20**

Human 3D brain organoid development for altered cellular signalling mechanisms

Gaurav Samuel, Christhunesa S Christudass, Prabhakar AT, Shaik Atif Iqbalahamed

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Cognitive disorders comprising of Alzheimer's, epilepsy & relative disorders often begin subtly but progress until significantly impede the affected individual's quality of life. It is imperative to understand the molecular mechanisms underlying various cognitive disorders.

Human mesenchymal stem cells (MSCs) and neural progenitor cells represent a fundamental approach to derive 3D invitro brain organoids. Hence, MSCs promote dorsal corticoid organoid formation for disease modelling, drug screening and possibly cell therapy. There are inadequate limitations of 2D neural cultures to investigate cell signalling pathways in neurogenerative disorders. This study shall provide an understanding of specific cell types present in 3D brain spheroids, cellular localization, cytokine expression, and cell -cell interactions.

Neural progenitor cell lines will be differentiated corresponding neurons, oligodendrocytes and astrocytes. Cells will be screened for stem cell markers Nestin (ABD69, MAB353, Sox-2 (AB5603) and Mushashi (MABE268). Similar approach shall be followed for mesenchymal stem cells (MSCs) isolated from glioblastoma specimens. MSCs will be isolated from surgical specimens using mechanical dissociation for MSC isolation. Briefly, surgical specimens will be minced, dissociated in DMEM/F12 and passed through a series of cell strainer's (100-µm). Flow cytometry analysis of cultured cells for biomarkers CD105, CD45, CD73, CD90, CD31, and nerve/glial antigen 2 will be performed. qRT PCR for FGF2, VEGFA, PGE2 and TGF-ß mRNA expression. Histology sections shall be imaged using confocal microscopy.

This study shall provide fundamental characterization of human primary neural cultures when grown in 3D structure and elucidate complex cell signalling pathways.

Presenter: Gurpreet Kaur Grewal **Poster Number: 21**

In Vitro investigation of role of antiepileptic drugs in oxidative stress and ABCC2 activity

Gurpreet Kaur Grewal[1], Ritushree Kukreti[2], Shrikant Kukreti[3]

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Epilepsy is a chronic neurological disease affecting 69 million people worldwide and 6–7 million people in India. Epileptic seizures are controlled with antiepileptic drugs (AEDs) but 20–30% of patients fail to respond to pharmacotherapy. Non-responsiveness to AEDs is a major clinical problem in treatment of epilepsy and over expression of ATP binding cassette (ABC) transporters is one of the important contributing factor. As, AEDs are oral drugs and ABC transporters being present at major tissue barriers –Liver and Blood brain barrier can influence oral bioavailability and clinical efficacy of many drugs which are substrates of transporters. We demonstrated the interaction of first line AEDs carbamazepine and valproate with ABCC2-well known efflux transporter with ATPase and 5,6-carboxyfluorescein inhibition assays. Thus, altered functionality of ABCC2 can affect the disposition of administered drugs. ABCC2 transporter is also associated with cellular oxidative stress. Various studies suggest there is oxidative stress is involved in pathophysiology of epilepsy and AEDs can be important player in this role but not examined in human brain endothelial cells. We aim to investigate effect of AEDs Carbamazepine and Valproate in human brain endothelial cells and assessing oxidative stress markers and influence on ABCC2 activity. The role of nuclear receptors in ABCC2 altered expression would be evaluated. Further, we aim to assess the potential of Alpha lipoic acid as antioxidant and effect on ABCC2 transporter functional activity. In order to effectively manage epilepsies, it is important to identify mechanisms that contribute to oxidative stress and alteration in ABC transporter activity.

Presenter: Atif I. A. Shaikh **Poster Number: 22**

Studying pathogenesis of Parkinson's disease using organoid models derived from patients with various genetic mutations leading to clinical presentation.

Atif I. A. Shaikh[1], Gourav Samuel[2], Christhunesa Soundararajan[1]

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Parkinson's disease [PD} is a neurodegenerative condition, which is progressive in nature. The diagnosis is largely clinical and pathology is formation of Lewy bodies as a result of synuclein deposition in certain brain areas.

Most of PD is sporadic and is suspected to be a combination of genetic predisposition and environmental risk factors.
Our aim is to study pathogenesis of PD using data from patients with genetic PD. The mutations that are cause PD are very variable in different areas, and involve different cellular functions. Is it possible to have a unifying pathogenetic model for PD?

Over 1.5 years we have identified 31 individuals with young onset PD. Only 3 out of this have a family history. 10 patients consented for genetic screening using clinical exome or whole exome analysis with next generation sequencing. Out of these, 6 patients had a known mutation that is associated with PD either as a causative factor or a risk factor. 1 patient had MAPT mutation, that is associated with tauopathies, however she had clinical features of PD.

Future plan is to complete genetic studies in all individuals. Organoid/IPSC phenotyping derived from individuals with genetic PD may be of help in confirming causative mutation. Additionally, it will be helpful in patients who have features of young onset PD and negative genetic screen. Finally, using organoids, staging of disease, pathology and pathogenesis in association with synuclein deposition and cell dysfunction can be studied, especially looking at various mutations causing same pathogenesis and clinical manifestations.

Presenter: Jhilik Dey **Poster number: 23**

POTENTIAL ROLE OF ENDOGENOUS NEURAL PROGENITORS IN REGENERATION OF HIPPOCAMPAL PYRAMIDAL NEURONS FOLLOWING NEURODEGENERATION.

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Background: Seizure induced neurodegeneration in hippocampus provides a powerful model for investigating adult neurogenesis as a response to injury in an attempt for brain regeneration following neurodegeneration. Our present study investigates the response of endogenous neural progenitors following seizure and their roles in hippocampal regeneration. Materials and Methods: Kainic Acid was administered once intraperitoneally at dose of 30mg/kg of animal body weight following with BrdU injection at various time points at dose 100 mg/kg to mark the new-born neurons. Transcardial perfusion was performed; brain samples were fixed and processed by cryosection. Immunofluorescence was performed using routine procedure. Results: Seizure induced lesion at CA1 and CA3 regions of hippocampus were detected following KA treatment by Nissl staining. Also, TUNEL+ cells were observed at those injury sites (CA3 and CA1). Our result showed that there is massive activation, proliferation and migration of the endogenous neuronal progenitors at injury sites following KA induced neurodegeneration. Around 45 days of post KA treatment, reappearance of pyramidal neurons at the injury sites was observed. Discussions: In response to neurodegeneration following seizure, robust proliferation of endogenous neuronal progenitors in dentate gyrus of adult brain has taken place. These new born neural progenitors may in turn, have subsequently migrated at the injury sites (CA3 and CA1) to generate new neurons there. Thus, the presence of new neural progenitors at injury sites, following with gradual regeneration of hippocampus pyramidal neurons shows the endogenous repair potential of the brain to restore brain functions.

Presenter: Juhi Vaishnav **Poster Number: 24**

Investigating the role of thyroid hormones in ventral wall closure during embryonic development of domestic chick.

Juhi Vaishnav, Suresh Balakrishnan

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Thyroid hormones (TH) through their course of evolution have had diverse roles to play in different classes of organisms. In Poikilotherms like amphibians and fishes, TH induces metamorphosis and regulate development. During evolution, while transitioning from poikilothermy to homeothermy, TH developed a thermogenic role. Though, its function during development still persists, lesser mechanistic details have been elucidated yet. Current studies in our lab have shown that upon inhibition of synthesis of TH by administration of a chemical Thiourea in chick embryo, several developmental anomalies have been observed. A comprehensive morphological study has been carried out using a sub lethal concentration of thiourea and defects such as incomplete closure of ventral body wall, vasculature defects, crooked limbs, incomplete heart looping have been observed, affecting the normal mesodermal patterning. The current study aimed to understand mechanisms behind function of TH in the ventral body wall closure by studying the effects of thiourea treatment on various signaling molecules involved in mesodermal patterning, specifically the lateral plate mesoderm which derives the ventral wall. The expression patterns of crucial molecules such as Shh, Bmp4, Cdh1, Pcna, MyoD1, Caspases, Vimentin were found altered. Histological studies showed disruption of overall tissue morphology in treated groups. Our ongoing study aims to check protein expression patterns and immunolocalization of the aforementioned molecules in chick embryonic sections. The future study will focus role of TH on epigenetic regulation of these genes, and aims to study if methylation patterns are regulated by TH.

Presenter: Lakshmy Vasan **Poster Number: 25**

L3mbtl3 is a novel gatekeeper of neurogenic gene expression and mRNA processing during neocortical neurogenesis

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The six neocortical layers are generated sequentially during development. Neurog2, a proneural transcription factor, is required and sufficient to specify early-born, deep-layer and not later-born upper-layer neuronal fates, despite being expressed throughout cortical neurogenesis. Here we report that L3mbtl3, an MBT-domain protein that interacts with Rnf2, a core component of Polycomb Repressive Complex 1 (PRC1), is a novel Neurog2 interactor and regulator of cortical neurogenesis. L3mbtl3 and Neurog2 are co-expressed, along with PRC1 and PRC2 components, in cortical neural progenitor cells (NPCs). In L3mbtl3 knock-outs (KOs), fewer upper-layer neurons are generated, while cortical NPCs expand. Transcriptomic analyses revealed a marked derepression of transcriptional repressors, including Rest, Sfmbt1 and Tle4, and an associated downregulation of glutamatergic neuronal differentiation genes in L3mbtl3 KO cortices. In Drosophila, MBT domain proteins recruit PRC1 via a conserved Pho (Yy1) repressive complex. Strikingly, a gene regulatory network with Yy1 as a central hub gene was

underrepresented in L3mbtl3 KOs. Nevertheless, chromatin architecture remained unaltered in L3mbtl3 KOs. Instead, L3mbtl3 overexpression in cortical NPCs suppressed mRNA export, effectively suppressing neural marker protein translation, and preventing cortical NPC differentiation and migration. L3mbtl3 is thus an essential gatekeeper of cortical neurogenesis, repressing neurogenic transcriptional repressors and mRNA processing genes in the mouse brain. Now, to study the role of L3MBTL3 in human cortical development, we used CRISPR-Cas9 engineering to create NEUROG2-mCherry human pluripotent stem cells, from which we generated cortical organoids. L3MBTL3 overexpression studies are in progress in this system, to study how L3MBTL3 regulates NEUROG2 function and expression.

Presenter: Madhuri Chaurasia **Poster Number: 26**

Characterizing the role of TECPR2 in iPSCs derived neuronal systems

Madhuri Chaurasia[1], Milana Fraiberg[1], Bat-Chen Tamim-Yecheskel[1], Jacob H. Hanna [2], Zvulun Elazar[1]

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Tectonin β-propeller repeat-containing protein 2 (TECPR2), a novel multi-domain protein. TECPR2 is comprised of an amino-terminal WD domain, a middle unstructured region, and a carboxy-terminal TECPR repeats domain followed by a functional LIR motif. Mutations in TECPR2 have been identified as the basis of a rare autosomal recessive neurodegenerative disorder in children classified as Hereditary sensory and autonomic neuropathy 9 (HSAN9). Patients present severe intellectual disability and evolving spasticity, along with autonomic-sensory neuropathy and chronic respiratory disease. Skin fibroblasts obtained from HSAN9 patients display defects in autophagy. We have established new systems to investigate the role of TECPR2 in the neuronal system; a TECPR2 knockout mouse and induced pluripotent stem cells (iPSC) derived from HSAN9 patient fibroblasts. In our recent findings, we observed defects in autophagy, and altered mitochondrial homeostasis using biochemical approaches in both patient fibroblast derived iPSCs and in TECPR2 knockout MEF cells. We hypothesize that TECPR2 regulates selective autophagy, a process particularly important in the neuronal system. I want to participate in this lecture course to better understand and learn about troubleshooting approaches and challenges related to organoid differentiation.

Presenter: Mayank Jain **Poster number: 27**

Yogic intervention improves the level of TNF-α, IFN-γ, MDA, and NO in breast cancer patients undergoing treatment

Mayank Jain[1], Archana Mishra[1], Shailendra Kumar[1], Satyendra Kumar Mishra[2] [1] *1. Department of Thoracic Surgery, King George's Medical University, Lucknow, UP, India* [2] *2. Department of Human Consciousness and Yogic Sciences, University of Lucknow, Lucknow, UP*

Background. Inflammation is very well linked to tumor proliferation and metastasis in breast cancer. The yogic intervention had a positive impact on the patient's quality of life and fatigue. But its association with pro-inflammatory cytokines along with oxidative stress markers in breast cancer has not yet been reported. Material & methods. We randomized 96 stage II/III breast cancer patients receiving radiotherapy and/or chemotherapy. Forty-eight stage II/III breast cancer patients were divided into each group (yoga and control). The yoga group was performing yoga for 5days/week for 1-year. Serum levels of TNF-α, IFN-γ, GM-CSF, MDA, NO, SOD and catalase were measured in both the group at baseline, 4th months, 8th months, and 12th months. Results. The mean age in the control group was 47.67±11.68 and in the yoga group 43.11±9.388. A total of 42 patients in the yoga and 40 patients in the control group were analyzed for all 4-time points. Serum IFN-γ and MDA, levels decreased significantly in the yoga group vs the control group at the 8th($p<0.001$) and 12th($p<0.001$) months. Whereas reduction in the TNF-α was observed in both the groups but the difference in the control group was not significant. TNF-α decreases significantly in yoga group vs control at 8th($p<0.05$) and 12th($p<0.01$) months. However, the level of NO was upregulated in the control group but in the yoga group, no change was observed. Conclusion. Long-term yogic intervention is beneficial in reducing the level of TNF-α, IFN-γ, and MDA in the breast cancer patients going through treatment.

Presenter: Meghali Aich **Poster Number: 28**

TOBF1 modulates mouse embryonic stem cell fate by regulating alternative splicing in a cell cycle dependent manner

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Embryonic Stem cells (ESCs) are characterized by a remarkable developmental plasticity and their capacity to self-renew indefinitely under appropriate culture, opening new avenues for personalized therapy and disease modelling. The establishment of pluripotency and differentiation require an orchestrated regulatory mechanism of the cellular machinery including various signalling pathways, factors involved in transcription, translation, epigenetic modifications which are mediated by several noncoding RNAs (ncRNAs) and protein associated with them which is known as RNA Binding protein (RBPs). RBPs comprise a larger class of proteins that have very crucial role in interacting with RNA transcripts for various RNA driven processes. RBPs regulate various RNA driven processes in post-transcriptional modification such as Alternative Splicing, nuclear export and maintaining transcript stability.
In our study, we have identified a novel pluripotency regulator, TOBF1 which interacts with the lncRNA Panct1 and gets recruited to genomic sites at a specific cell cycle manner. TOBF1 a Ser/Arg (SR) protein, is a splicing factor which contributes to efficient splicing of transcripts associated with stem cell renewal and maintenance and when this RBP is modulated by overexpression or downregulation, it impacts the pluripotency and cell cycle progression. These results reveal the mechanism for TOBF1 dependant alternative splicing events indispensable for maintaining the stem cell identity. Further, we are keen on understanding the mechanistic pathways that associate with the spliceosome complex related to varied human diseases.

Presenter: Nasera Rizwana **Poster Number: 29**

3D Bio-printing of Decellularized Dental Pulp tissue derived extracellular matrix in Peripheral Nerve Regeneration.

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Peripheral nerve injury affects around 12-23 persons/lakh every year. Autografts were known to be gold standard treatment for PNI but due to donor shortage, synthetic nerve grafts have been explored. Tissue engineered tubular structures made of natural /synthetic biopolymers that are designed to have necessary mechanical and biochemical cues for neural regeneration are called nerve guide conduits. However, developing an ideal conduit with appropriate mechanical and biological properties remains a major challenge.

My research focuses on decellularizing dental pulp tissue to obtain extracellular matrix and prepare a bioink using Rat Schwann cells for fabrication of nerve conduits. The 3D bioprinted conduits are of increasing interest as they can enable rapid creation of in vivo like tissues for transplantation and also mimic highest standards of manufacturing, quality control and regulation. The printed conduits can be fabricated close to the patient or treatment facility and can be customized to the patient's requirement for better acceptance and compliance. My research will further study how the decellularized dental pulp extracellular matrix based bioprinted conduits will direct the dental pulp stem cells to form pulp like spheroids or organoids and also study how differentiation media may help to differentiate these cells towards neuronal lineage. By attending the EMBO lecture course, I would gain more knowledge about how organoids are developed and I will be able to use this experience in establishing an in vitro disease model to study neuroregeneration and also neurodegenerative diseases. This course will also help me in networking for future academic endeavors.

Presenter: Neha Yadav **Poster Number: 30**

Advanced Neuroimaging and Event Based Modelling of Brain Structure and Microstructures :Development of Imaging Based artificial intelligence platform of Cognitive status

Neha Yadav, Arkaprava Majumdar, Vivek Tiwari

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Changes in brain health with aging involve a series of brain structure, vascular and functional changes over the period. The events of brain health changes during normal aging need to be delineated from alterations which are manifestations of mild cognitive impairment. We believe that when the kinetics of structural atrophy of a definitive brain feature undergo pathological changes beyond a threshold, it would result in cognitive impairment. We have employed comprehensive MRI morphometry measurements of small vessel disease pathologies and neuroanatomic volumes. We found that a series of Neuroanatomic changes such as progressive loss in gray matter volume, reduction in cortical thickness of Parahippocampal gyrus, reduction in hippocampal volume together with accruing of periventricular and deep white matter pathologies identify with MCI and AD compared to cognitively normal subjects.This would help us to understand Alzheimer's progression with aging and differentiate it from normal aging. Currently animal models and 2D neuronal culture are used which are unable to recapitulate the complexity of human disease. 3D brain organoid model will help accurately recreate the natural physiology and mechanical forces that cells experience in the human body, and changes that occur as neurological disorders progress. We aim to develop cerebral organoids, micro physiological systems , and in vitro microfluidics blood-brain barrier chips to investigate different neurological disorders. The lecture course will refine my research skills by providing high quality knowledge and technical skills and help in developing and working on organoid and micro-physiological as a model system to address my research problems.

Presenter: Nikayla Batohi **Poster Number: 31**

Precision medicine using drug repurposing platform – the way forward in applying novel drug combinations for Ovarian Cancer treatment

Nikayla Batohi 1, 2, Greta Dreyer 2, Deepak Thimiri Govinda Raj 1, 2

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More than half of the women diagnosed with ovarian cancer ultimately succumb to death after 5 years of diagnosis. Standard platinum-based chemotherapy often results in patient relapse; thus, new therapeutic strategies are required. We aim to establish robust drug screening to pinpoint drugs and drug combinations that are effective in precision medicine for individual ovarian cancer patients. Ovarian cancer cells from 30 patients will be cultured for high-throughput drug screening against a library of clinically relevant drug combinations.

Thereafter, phospho-flow cytometry will be used to identify signalling pathway aberrations and potential biomarkers. This, together with drug screening data, will be used to create a directed phospho-flow screen on a smaller subset of drugs. The drug screening platform will be used to produce drug combination effects for selected drug screening which will be complemented by phospho-flow-based analysis used to characterise cellular heterogeneity and drug effect on ovarian cancers. The drug effects will be validated using functional bioassays and flow cytometry. With the implementation of direct drug sensitivity screening and effective drug combinations for precision cancer therapy, we are optimistic that this may provide relapsed and platinum- resistant ovarian cancer patients with individualised treatment plans.

Presenter: Nikhil Gandasi **Poster Number: 32**

Subcellular view of islets to understand type-2 diabetes – Islet organoids might provide novel insights

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A well-functioning pancreas preserves glucose homeostasis and prevents diabetes. Glucose homeostasis is maintained by secretion of insulin from pancreatic beta cells that lowers blood glucose after a meal. Although mechanisms behind secretion of insulin have been studied for years a clear subcellular view of secretion had remained elusive. My previous work was focused on elucidating the steps leading to secretion of insulin from the individual secretory granules localized in beta cells using high-resolution total internal reflection fluorescence microscopy techniques. Secretory granules localized at the plasma membrane were visualized to discover granule pools in individual beta cells responsible for secretion of insulin. Molecular determinants that include SNARE and accessory proteins which are part of secretory machinery pools were identified. The changes in the molecular determinants leading to disrupted insulin secretion in human type-2 diabetic beta cells were discovered. This discovery led to understanding the abnormalities in human type-2 diabetic islet cells affecting mechanisms of insulin secretion.

Recently there has been a larger push to make islet organoids from human tissue for the study of diabetes. Since the human islets are in short supply and many of the islets in murine tissue do not really correspond to human islets. Our work shows the importance of developing such organoids and the potential that comes with developing new anti-diabetic treatment strategies, better diagnosis and prognosis of diabetes.

Presenter: Niraikulam Ayyadurai **Poster Number: 33**

Biosynthesis of Next Generation Biomaterials through Genetic Code Expansion

Niraikulam Ayyadurai
CSIR Central Leather Research Institute

In living cells, through millions of years of evolution nature introduces amino acids (see Glossary) to the growing protein chain, favoring similar over dissimilar chemistry-encoded amino acids. Through Genetic code expansion, we are incorporating of unnatural amino acids (UNAA) directly into the active core that confers dedicated structure and functions to engineered protein. Structurally protein biomaterials are tandem repeats that intrinsically include UNAAs generated through post-translational modifications to execute assigned functions.

Though advanced, conventional genetic engineering approaches using the prokaryotic system has limited scope in the biosynthesis of functionally active biomaterials with UNAAs. On the other hand, trends in tissue engineering focus on fabricating personalized tissue constructs with anisotropic architecture, heterogeneous cells, and composite nano/biomaterials towards regenerating functional tissue. GCE extends the possibility to develop congener protein biomaterials, and growth factor mimetics that mediate cell-cell and cell-matrix interactions. The protein biomaterials are fine-tuned with appropriate viscoelasticity promise as a potential organoid, printable bio-ink for 3D bioprinting, and a cutting-edge technology to fabricate tissue-mimetic constructs for functional regeneration. Interestingly, GCE brings forth the unique possibility of exploring various bio-inspired proteins and developing their congeners to realize specific applications. Overall, our group explored the GCE as a promising tool to achieve tissue-informed, tissue-compliant tunable biomaterials.

Presenter: Nusrat Nabi **Poster Number: 34**

FAK, Src and PCTAIRE1: Novel targets for anti-cancer therapy

Nusrat Nabi 1, Syed Qaaifah Gillani 1, Misbah Un Nisa 1, Zarka Sarwar 1, Sheikh Zahoor Ahmad 2, M. Hussain Mir 2, Naveed Shah 2, Shaida Andrabi 1
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PCTAIRE1 (PCT1) is a cyclin-dependent kinase (CDK) that belongs to the family of serine-threonine kinases. It is highly expressed in terminally differentiated tissues and plays an important in neuronal cell differentiation, intercellular vesicular transport, and spermatogenesis. However, its role in cell cycle regulation, particularly mitosis, is not well understood yet. Here, we report that PCT1 is regulated by several serine-threonine and tyrosine kinases within the cell and also plays an important role in mitosis. Previously, we have screened a library of 200 serine-threonine kinases using an inducible overexpression cell line that expresses polyoma virus small T(PolST) as a tool. We identified PCT1/CDK16 and FAK as potent kinases that overcomes PolST induced mitotic arrest,thereby promoting cell survival against apoptotic stimuli. Interestingly,this survival by PCT1 and FAK was also seen when cancer cell lines were grown in presence of anti-cancer agents like paclitaxel.
Moreover, PCT1 protein levels changed steadily during the course of the cell cycle and reached their maximum during mitosis. Further, we show that the tyrosine kinases FAK and SRC1, which are well-known for their involvement in cancer, also regulate PCT1 protein levels. Interestingly, our findings also report that PCT1 and FAK1 colocalize at the spindle poles and midbody along with SRC. Interestingly, we also found that PCT1,FAK and SRC are overexpressed in ovarian tumors,thereby suggesting their importance in tumorigenesis. Together, our results show that PCT1 along with FAK is a highly expressed and regulated protein of the cell cycle and has a potential role in cancer and drug resistance.

Presenter: Pallavi Gupta **Poster Number: 35**

Elucidating the extent of coordinated splicing of exons in the mammalian brain

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The brain is a heterogenous organ with over 70 progenitor and mature cell types, distributed spatially and temporally. This diversity arises as over 40% of the genes in the brain are alternatively spliced, expanding the number of encoded proteins. Recently, it has been shown that the alternative exons combine in a non-random fashion and occur together in transcripts with a frequency different than expected by chance. The presence of mutually inclusive and exclusive exon pairs leads to a fewer number of isoforms than the theoretical value, i.e., (2^N)-1 for a gene with N alternative exons. However, the underlying mechanism at the level of splicing is not studied in-depth predominantly due to technological challenges. Unlike short-read sequencing, long reads capture full-length transcripts and can better resolve long-range interactions such as coordinated splicing. This has been demonstrated by a few studies from the mammalian brain. A larger adoption of this methodology is currently limited due to lack of computational tools that quantify such events and perform appropriate statistics. Here, we develop the first bioinformatics pipeline to identify trends in exon-exon coordination using single-molecule sequencing. We apply this tool to publicly available dataset, across species (human vs mouse), developmental time points (fetal vs adult), and brain regions (cortex vs striatum vs hippocampus). We find that coordination in splicing is more prevalent than previously reported. We hope our tool will shed light on diversification of the transcriptional code across the mammalian brain and help uncover the molecular origin of its complexity.

Presenter: Parvathi Satheesh **Poster number: 36**

Identification and molecular analysis of altered neurodevelopmental pathways that lead to neuropsychiatric disorders.

PARVATHI SATHEESH

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Neuropsychiatric disorders such as bipolar disorder (BD) and schizophrenia are considered to be neurodevelopmental in origin and can be studied in iPSC derived cerebral organoids as they replicate the patient genetic background. We analyzed a comprehensive list of genetic variants generated from the exome sequencing data from a clinically dense Indian family with a very high prevalence of BD type I of three patients and one first-degree relative family control. We further shortlisted them based on their expression in the developing brain and this analysis yielded a number of genetic variants of DNMBP, C16orf89, SLC4A3, SPEN, SIT1, CDC26 and CTBP2. Among these, SPEN is a transcriptional repressor and chromatin remodelers play a fundamental deterministic role in cortical development. Hence, we chose SPEN (frequency <0.1%) to elucidate its role during the neurodevelopment and pathogenesis of BD. Dorsal forebrain organoids were generated from iPSCs from this family according to Sloan et al, 2018 protocol. Upon preliminary analysis of the growing cerebral organoids, neuroepithelial bud formation was examined across these lines. The NEBs were disorganized and reduced in number in patient organoids in comparison to the wildtype. At DIV 50, on immunostaining, Pax6 and Tuj1 positive cells were observed to be distributed radially around the NEB lumen in wildtype, whereas in patient-organoids the same was found to be disoriented. Hence our preliminary data suggests that there are early neurodevelopmental aberrations in the forebrain organoids generated from iPSCs from BD patients which can be further investigated for their pathogenic molecular mechanism.

Presenter: Shagufta Parveen **Poster Number: 37**

Modelling Folic acid Deficiency associated Neural Tube Defects using iPSC derived 3D Neural Cysts and Organoids

Shagufta Parveen, Tejashree Vanje, Althea Stella Anil Martis

Manipal Institute of Regenerative Medicine Manipal Academy of Higher Education

Neural tube defects [NTDs] are severe congenital malformations in humans. In India NTDs occur in ~2/1000 births with higher occurrences in North India.The etiology of NTDs is poorly understood. Studies reveal that they are manifestation of epi/genetic mechanisms and/or environmental factors influencing the architecture of neurulating cells. It is well established that maternal Folic Acid [FA] deficiency is a high- risk factor for NTDs. Peri-conceptional FA supplementation greatly reduces the risk of NTDs. FA metabolism is essential for nucleotide biosynthesis and Methyl donor generation through one carbon metabolism. Methyl donors are required for epigenetic regulation during embryonic and fetal development. FA is also essential for NSC proliferation and fate determination. Cellular and Molecular mechanisms that affect NT morphogenesis in maternal FA deficiency remain unclear.For this study we use iPSC derived 3D neural cysts and organoids. Neural organoids grown in absence of FA are smaller in size with poorly defined neural zones. Gene expression analysis reveals a lower expression of neural biomarkers DLX2, GFAP, PAX6 & βIII Tubulin and DNA methyl transferases. To demonstrate the correlation between NTDs and an epigenetic pathology we setup NTD models by growing neural cysts in presence of HDAC inhibitor valproate and DNMT inhibitor 5-azacytidine. These inhibitors are known teratogens causing neural malformations. We hypothesize a strong link between FA deficiency & differential epigenetic modification of genes associated with neurogenesis as one of the prime causes of NTDs and are employing the above models to dissect the cellular and molecular mechanisms of this developmental malformation.

Presenter: Poonam Yadav **Poster Number: 38**

Apoptotic Effect of Interferon (IFNϒ) and Tumor Necrosis Factor (TNFα) Induced Wharton's Jelly Mesenchymal Stem Cells (WJMSC) on Pancreatic Ductal Adenocarcinoma cells (PDAC) -A Cell based Model.

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Mesenchymal stem cells (MSCs) are promising tools in the cell therapies due to their anti-inflammatory, immunomodulatory, multipotent, self-renewal and tumor homing properties. The anticancer efficacy of MSCs have been shown in various cancer cell types in vitro. However, Pre-clinical & clinical studies showed limited efficacy with naïve MSC so cell priming is a new approach. My thesis objective is to determine the patho- mechanistic role of MSCs and its anti tumorogenic effect on PDAC cells when stimulated with Th1 type pro inflammatory cytokines TNF & IFN. Treating PDAC cells with MSC- conditioned media (CM)showed PI3/Akt pathway, Hedgehog pathway and EMT pathways were abrogated. Our earlier data showed treatment with WJMSC-CM is more potent towards inhibition of tumors migratory ability, down-regulation of the signal transducer-SMO and downstream target PTCH-2. A significant reduction in the downstream targets of PI3K/AKT (mTOR and HIF1) was also observed. These results suggest the role of MSCs and its products in treatment of cancer.This underlying mechanism need to be validates using robust model, either organoids or mice models to get in-sight into the pathophysiology and cellular interaction. Organoid model as an intermediate between mice-human experimentations, can delineate several aspects of cancer complexites. It provides the access to directly evaluates various features at cellular, structural and functional level. So, attending this lecture course will develop my understanding in this exciting area. Further, I want to utilize this opportunity and apply the knowledge gain in the area of cancer therapeutics using stem cells as an adjuvant agent.

Presenter: Pradip Paul **Poster Number: 39**

Three-Dimensional organoid model of the human forebrain to study neuropsychiatric disorders.

Pradip Paul, Vasavi Nallur Srinivasaraghavan, Salil Sukumaran, Mythri S. V., Meera Purushottam, Sanjeev Jain, ADBS Consortium, Reeteka Sud, Biju Viswanath

Molecular Genetics Laboratory, and ADBS lab, Department of Psychiatry, National Institute of Mental Health and Neurosciences, Bangalore, India.

Background

The organoid model is of great importance in understanding the development of disease, considering its promise to uncover hitherto unknown mechanisms of human brain development, assembly, and dysfunction. Our recent studies showed reduced cortical gray and white matter in bipolar disorder (BD) patients and abnormalities in migration of BD NPCs.

To explore further the defects in the corticogenesis of neuropsychiatric disorders, we generated human cortical organoids (hCOs) that resemble the in vivo cerebral cortex.

Methods

hCOs were generated using established protocols from the well-characterized healthy controliPSC line from the ADBS program. Briefly, the organoids were generated from iPSCs by neural induction, expansion, and differentiation for hCOs. These organoids were maintained for 125 days. To characterize the distribution of different neuronal subtypes, immunohistochemistry (IHC) was performed on 12 µm thick cryosections. Single cells from hCOs were also processed for flow cytometry.

Results:

Presence of neural stem cells (NESTIN) and neuronal cells (MAP2) along the ventricles and dendrites respectively were confirmed in the IHC slides from day45 hCOs. The presence of layer V cortical neurons (CTIP2) was confirmed by flow cytometry at day-105. This workshop would be a great opportunity for us to meet experts in the organoid field and enhance our technical know-how as we use this model in our lab to decipher cellular mechanisms associated with neuropsychiatric diseases.

Presenter: Pragyan Acharya **Poster Number: 40**

Upregulation of ELANE, MPO and CD177 genes in Acute-on-Chronic Liver Failure Derived Granulocytes

Pragyan Acharya1, Rohini Saha, MSc1, Sai Sanwid Pradhan, MSc2, Shalimar, MD3, Prasenjit Das, MD4, Priyanka Mishra, MSc1, Rohan Singh, MSc1, Venketesh Sivaramakrishnan, PhD2, Pragyan Acharya, PhD1#

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Abstract
Our laboratory works on complications of liver cirrhosis. Liver cirrhosis results from chronic injury to the liver and is an advanced stage of liver disease in which the liver increases in stiffness and, loses its functionality. Liver is the largest solid organ in the human body and is the central to its overall homeostatic functioning. Hence, liver cirrhosis is not only associated with disrupted liver function but also with disruptions in renal, brain and cardiac functions as well. Recent studies in our laboratory have focused on a complication of liver cirrhosis known as acute-on-chronic liver failure (ACLF), which is associated with innate immune dysfunction and high short-term mortality (~ 50% 28-day mortality). Neutrophil-to-Lymphocyte Ratio (NLR) is known to influence patient prognosis in ACLF. Recent studies from our lab demonstrate that ACLF patient derived neutrophils have distinct transcriptomic signatures and functionality. Significant upregulation of neutrophil specific genes were found in ACLF compared to diseased and healthy controls. The expression of inflammation associated genes ELANE, MPO and CD177 were highly upregulated in ACLF and their expression was higher in ACLF 28-day non-survivors. We further found elevated expression of CD177 protein on neutrophil surface in ACLF was confirmed by flow cytometry and confirmed that the genes ELANE, MPO and CD177 formed a pathogenic neutrophil gene signature in ACLF non-survivors. Future studies in our lab will focus on how different pathogenic neutrophil subsets identified in our laboratory to be part of various complications of chronic liver disease as well as cirrhosis, interact with the liver. One of our goals will be to study immune cell-liver interactions in liver organoid models and hence, I feel that the workshop will enable me to learn about the various considerations that I will need to

keep in mind to develop a liver- immune interaction model in our laboratory at Department of Biochemistry, AIIMS New Delhi.

Presenter: Preethika Nair **Poster Number: 41**

3D multicellular, patient-derived glioblastoma spheroids for personalized therapeutics.

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Glioblastoma Multiforme (GBM) is a cancer of the central nervous system (CNS), arising from glial cells. As of 2020, 54% of the global CNS tumour prevalence arise from Asian countries, with India being the second largest contributor (https://gco.iarc.fr/). GBM patients exhibit poor morbidity of less than 15 months even after chemotherapy, radiotherapy, and surgical resection. The mortality for India is 19.4%. Patient-to-patient heterogeneity and the lack of a disease model that can recapitulate human physiology in vitro pose obstacles to effective treatment. 3D models recapitulate the native tissue architecture, tumour microenvironment (TME), and cellular crosstalk.

The GBM tumour microenvironment has been reported to contain 30-35% of microglia and macrophages that aid in tumour growth. We have developed a 3D patient-derived spheroid GBM model with microglia to understand the role of innate immunity in GBM pathophysiology. Pattern recognition receptors such as the Nucleotide-binding oligomerization domain and leucine-rich repeat-containing proteins (NLRs) play an important role in immunosurveillance. The role of NLRs in GBM is poorly understood, with evidence for pro as well as antitumour effects in GBM. We want to understand the role of these NLRs in a cell-specific manner within the TME using our 3D GBM spheroid model. The data obtained from this study will be used along with the patient history to generate artificial intelligence-based models for better patient-specific prediction of tumour type, cellular crosstalk and personalized therapeutic strategies. The outcomes from this study shall enable us to address patient-to-patient heterogeneity, pre-clinical drug development, biomarker analysis, and basic cancer research.

Presenter: Pretty Garg **Poster Number: 42**

The secret to faster differentiation of serum-free, mature human astrocytes for disease modelling

Pretty Garg 1, 2, Katja Nieweg 2, Kurt Gottmann 2
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2 Heinrich Heine University, Duesseldorf, Germany

Differentiation of mature human astrocytes from induced pluripotent stem cells (iPSCs) takes 6 months to one year and is a major bottleneck for their application in disease modelling. Here, we established a small-molecule approach to directly generate mature human astrocytes from gliogenic neural stem cells. Compared to the conventional CNTF approach that yields immature astrocytes, MEK inhibition by PD0325901 ceases proliferation, upregulates the expression of recently established mature human astrocyte markers and induces mature functional properties such as calcium responses to glutamate. Differentiation of astrocytes by MEK inhibition involves a phospho-AKT1-dependent sustained activation of STAT1/3 and nuclear loss of astrocytic transcriptional repressor OLIG2. Our study thus uncovers a novel strategy for targeting astrocyte differentiation and maturation pathways.
With my background in stem cell biology to model neurodegenerative disorders, I believe this meeting will provide me with an excellent platform to further my research and career prospects.

Presenter: Raghavan Gurunath **Poster Number: 43**

Chitosan-based Nanocarriers for Non-coding RNA Delivery in Biomedical applications

Raghav Gurunathan
SRMIST

Chitosan is a well studied cationic polymer currently being explored as vectors for gene delivery. Chitosan is a unique polysaccharide copolymer of N-acetyl-D-glucosamine and D-glucosamine linked by a β-(1→4) glycosidic linkage, it is natural, biocompatible and biodegradable.Chitosan NPs have demonstrated potential as extremely efficient and secure vectors for in vivo delivery of non-coding RNAs. Regulatory non-coding RNAs(ncRNAs) are class of RNAs that does not encode a protein but nevertheless affects gene regulation. ncRNAs like siRNAs and miRNAs play crucial roles in regulating gene expression. Their application in the treatments of cancer, osteopathy, infections, and cardiovascular problems, has been the subject of extensive investigation. Although siRNAs and miRNAs share many characteristics, such as being short double-stranded RNA molecules that cause mRNA to be targeted and subsequently cleaved to silence genes at the post-transcriptional level, their precise mechanisms of action and potential therapeutic uses are still distinct. The primary distinction between them is that siRNA has a single target mRNA, while miRNA has many. Consequently, their therapeutic uses ultimately varies.Through the activation of the RNA-induced silencing complex(RISC), both the molecules regulate gene expression. In the case of siRNA, this results in enzymatic cleavage of the target mRNA due to siRNA's clear complementarity with its target. MiRNA can control the expression of numerous targets because, in contrast to siRNA, it only partially complements the mRNA of its target. MiRNAs are revolutionary for many therapeutic applications because it has been discovered that they are involved in major physiological and pathological mechanism in our bodies.

Presenter: Raghava Reddy **Poster Number : 44**

Modeling nephropathic cystinosis with human kidney organoids

Raghava Reddy and Benjamin S. Freedman
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Cystinosis is genetic disorder caused by loss of function mutations in a membrane transporter protein, cystinosin, leading to accumulation of cystine to excessive levels inside lysosomes which causes dysregulation of cellular metabolism. Kidneys are severely affected, amongst other organs. The effects of cystinosis on the kidneys are not well understood, and better treatments are needed. Human kidney organoids derived from induced pluripotent stem (iPS) cells offer many advantages including high-throughput assays for drug screening.
To model cystinosis, we edited iPS cells CRISPR-Cas9 to knockout the cystinosin gene. Cystine accumulation inside of cells and cell death were assayed to determine the disease phenotype in iPS cells and derived kidney organoids. With immunoflorescence staining, the effect of drugs on the architecture of organoids was determined.
The cystinotic iPS cells as well as organoids showed a dramatic increase in the accumulation of cystine in cells. Treatment with cystine significantly decreased viability of cystinotic cells, compared to isogenic controls, and drastically increased cystine accumulation in cystinotic cells and organoids. The number of organoids with cystinotic cell lines also decreased. Brightfield imaging showed cystinotic organoids were more vulnerable to cystine damage than controls. Immunofluorescence staining showed the architecture of organoids was perturbed. In conclusion, human iPS cell-derived kidney organoids recapitulate the pathophysiology of cystinosis in vitro and this disease model is useful for further therapeutic studies. I am a research scientist in the Freedman laboratory where this is a new project. Comments and suggestions on these findings from experts in the organoid field will help me plan my next experiments.

Presenter: Rahul Sharma **Poster Number: 45**

CARP2 regulates the Golgi dynamics upon EGF stimulation

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Cellular machinery upkeeping the protein and organelle quality control is fundamental and indispensable for survival. During the pathogenesis of neurological or non neurological disorders in humans, machinery components go awry. Cellular machinery comprises chaperones, ubiquitin ligases, lysosomes, proteasomes, etc. Ubiquitin ligases regulate virtually all aspects of cell survival, division, death, migration, etc. We demonstrate that CARP2 (Caspase-8 and -10 associated RING containing protein 2), an endosomal localized ubiquitin ligase, modulates the Golgi structure. Golgi bodies play a central role in vesicular trafficking and are vital for cell survival. Evolutionarily in eukaryotes, Golgi bodies exist in individual stacks composed of flattened disc-shaped cisternae. Moreover, mammalian cells have Golgi bodies in ribbon architecture. Golgi ribbons are individual stacks that are laterally linked to each other by tubular structures and Golgi matrix proteins. Golgi bodies perform various cellular functions like protein sorting, trafficking, secretion, glycosylation, etc. Its structural dynamics govern its functional aspects. Golgi adopts different structural morphology to meet the physiological needs associated with mitosis, stress, inflammation, DNA repair, autophagy, etc. Loss of Golgi integrity is associated with pathological conditions, notably cancer and neurodegeneration. Exogenous or EGF (Epidermal Growth Factor) upregulated CARP2 protein leads to the dispersal of Golgi bodies.In contrast, CARP2 knockout cells exhibit minimal dispersal of Golgi bodies even after EGF stimulation. Furthermore, we have identified the CARP2 targets and degraded the Golgin-45, a Golgi structural protein necessary for Golgi structural integrity. Hence, this evidence unravels the existence of complex signaling between endosome and Golgi bodies to regulate Golgi structural dynamics.

Presenter: Raja Sundari Meenakshi Sundaram **Poster Number:46**

Immunomodulatory profiling of Human Mesenchymal Stem Cells derived from various sources under in vitro inflammatory conditions

Raja Sundari Meenakshi Sundaram [1], Secunda Rupert[1], Jeswanth Sathyanesan[1], Rosy Vennila[2], Surendran Rajagopal[3]

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To determine the Immunomodulatory properties of Human MSCs derived from various sources by performing gene and protein expression studies in the co-cultured system under in vitro inflammatory conditions.

Methods

In this study, we established the in-vitro co-culture system under the mitogen-stimulated condition to comprehend the interaction between MSCs and MNCs. We used a Fluorescence-activated cell sorter (FACS) for studying the immunoregulatory properties. Gene expression profiling of major cytokines responsible for tissue repair and regeneration was studied by customized PCR array and the validation of major immunomodulatory molecules expressed in gene expression was confirmed by protein expression through ELISA.

Key findings

We observed the differential modulation of immune cells as well as the MSCs in the aspects of immunoregulatory markers and cytokine profile when co-culturing the MNCs from the same source with MSCs from various sources. We found some source-specific cytokine signatures under stimulated co-culture conditions. AT-MSCs showed significant up-regulation in VEGF, BM-MSCs showed up-regulation in PTGS-2 and WJ-MSCs showed increased expression of IDO. This remarkable increase in source-specific upregulation of cytokine gene expression was validated at the functional level by protein expression studies.

Conclusion

AT and BM-MSCs being the autologous source is extensively used for Stem Cell Therapy. WJ-MSCs, though an allogenic source, being a non-invasive source showed better immunomodulatory properties in terms of expansion of T-Regs and cytokine profile at gene level. This study results highlight that MSCs sourced from different tissues may exhibit unique cytokine signatures and thus may be suitable for specific regenerative applications.

Presenter: Rajiv Dixit **Poster Number: 47**

Modeling and Deciphering the Molecular Mechanism of Polyglutamine Neurodegenerative Diseases

Rajiv Dixit[1], Njoud N Al-Naama1, Alexandra Wong[1], Alokkumar Jha[1], M. Elizabeth Ross[1] [1]Centre for Neurogenetics Weill Cornell Medicine, New York City, New York, 10021

Neurodegenerative diseases affect millions of people with motor, psychiatric, emotional and cognitive manifestations, producing a major world-wide health care burden on society with no cure in sight. Age-related diseases like Huntingtin Disease (HD) and Dentatorubural Pallidoluysian Atrophy (DRPLA) are mainly characterized with the formation of protein aggregates within susceptible neurons resulting in their slow progressive death. DRPLA is a rare autosomal dominant neurodegenerative disease caused by the expansion of trinucleotide CAG repeats encoding poly-glutamine (PolyQ) tracts in the Atrophin1 gene. Our project seeks to better understand if the biology of PolyQ diseases are manifested much earlier during the development setting a stage for later disease advancement. We modeled to generate the pathogenic events by direct neuronal reprogramming method, using neurogenic miRNAs (miR-9/9* and miR-124) that drives the conversion of patient derived DRPLA and HD fibroblasts into medium spiny neurons (MSN), one of the major cell types effected by these diseases compared and contrasted with cells produced from iPSCs. To gain insight into mitochondrial dysfunction, live imaging of DRPLA and HD neurons showed significant higher levels of mitochondrial ROS using an indicator dye MitoSox Red, along with upregulation of cellular oxidative stress measured by Dihydroethidium and Nitroblue tetrazolium in DRPLA and HD patient cells compared to control MSNs with no significant change in mitochondrial pool (MitoTracker). RNA-seq analysis on multiple DPRLA lines confirms transcriptional dysregulation in mitochondrial and autophagy genes. Will continue examining over a range of developmental and maturation stages, to seek expression biomarkers of disease progression.

Presenter: Rambhadur Subedi **Poster Number: 48**

Recombinant fragment of human Surfactant Protein D (rfhSP-D) inhibits metastasis of PC3 and LNCaP prostate cancer cells: A potential immunotherapeutic mechanism

Rambhadur Subedi[1], Rupashree Salvi[1], Barnali Biswas[1], Uday Kishore[2], Taruna Madan[1]

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Previous studies from our group had reported induction of apoptosis by a recombinant fragment of human SP-D (rfhSP-D), a soluble pattern recognition receptor, in the prostate cancer cells and also in the tissue explants from patients of metastatic prostate cancer. In view of these findings, potential of rfhSP-D to inhibit prostate cancer metastasis was evaluated in vitro using the androgen-sensitive (LNCaP) and androgen resistant (PC3) cells.

Treatment of LNCaP and PC3 cells with rfhSP-D resulted in time dependent reduction in the cell migration capacity. Importantly, MMP9 levels were significantly downregulated in the treated cancer cells. The metastatic PC3 cells showed a significant reduction in the levels of N-Cadherin, Laminin and Vimentin, markers for Epithelial-Mesenchymal Transition (EMT). The androgen responsive LNCaP cells showed no significant change in the transcript levels of N-Cadherin and Laminin but exhibited a marked increase in E Cadherin, a marker of EMT inhibition. In view of the altered MMP expression, the in silico protein-protein docking analysis of rfhSP-D with Basigin, a regulator of MMP expression, was pursued. The suggested high probability of a direct interaction was confirmed using a pull down assay followed by Western blot.

These results infer that rfhSP-D significantly reduces the viability as well as the metastatic potential of the prostate cancer cells. Role of Basigin in rfhSP-D mediated inhibition of metastasis is being investigated in detail. The in vitro findings are being validated using TRAMP (Transgenic Adenocarcinoma of the Mouse Prostate) mice model, human prostate tumor organoids and organs-on-chips systems.

Presenter: Ritu Varshney **Poster Number: 49**

Development of isogenic stable tagged cell models using CRISPaint Technology for autophagy and neurodegenerative studies

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CRISPaint Technology, a CRISPR/Cas9 gene-editing tool, was used in this study to generate isogenic stable tagged cells. Using this technology, we could tag specific proteins at their C-terminus. Using this strategy, we labelled numerous genes at a time involved in autophagy (LC3B, SQSTM, ATGs, and LAMP1 etc.) and other linked pathways (AMPK, mTOR, and PI3K, etc.). We employed three plasmids carrying the Cas9 gene with donor gRNA, target gene gRNA, and donor (mCherry/ GFP). Cas9 is an endonuclease that cuts the target gene and donor molecule at a precise location recognised by the respective target gene gRNA and donor gRNA. The three plasmids were co-transfected in order to produce marked cells. Cells were drug-treated to select the labelled ones (e.g., puromycin). Only tagged cells were found to be viable upon drug selection, as the donor plasmid contained a selection marker (such as a puromycin resistance gene). Only these cells express the physiological level of the tagged proteins. To tag a large number of proteins, we employed gRNA from a variety of target genes. Additionally, single-cell cloning was carried out for each labelled cell line to produce monoclonal cell lines. "A single-cell clone is essentially formed from an original 'multiclonal' population but has been isolated to create a pure, clonal population that is genetically identical. We isolated clones of HEK293T labelled at multiple genes and allowed them to develop independently in order to generate monoclonal cell lines. These monoclonal cell lines will be beneficial in the high throughput screening of numerous sorts of molecules, drugs, phytochemicals etc.

Presenter: Sandhya Anand **Poster Number: 50**

Development of an in vitro model system reflecting early trophoblast development using human embryonic stem cells

Sandhya Anand, Dhanjit Kumar Das

ICMR-National Institute for Research in Reproductive and Child Health

Early life attachment determines your fate. Philosophical as it may sound, this stands to be the most crucial and least studied aspect of developmental biology. Following fertilization, the zygote develops into a blastocyst having an inner cell mass and an outer layer of trophoblast cells. Implantation and placentation are the key events post fertilization in determining the fate of an embryo. Trophoblast cells differentiate to cytotrophoblasts and syncytiotrophoblasts. The syncytiotrophoblasts invade the maternal uterine walls for attachment, allowing the implantation of the developing embryo. This establishes the feto-maternal connection finally developing into placenta. These early events in establishing a successful pregnancy continue to be an enigma. Unravelling them has remained largely impossible, owing to limited research due to unavailability of early stage blastocysts and ethical constraints.

In absence of a proper model, establishing an in vitro system using human embryonic stem cells offers to be a viable model system to recapitulate the early events. In the present study, BMP4 driven protocol was used to differentiate hESCs into trophectoderm lineage. The hESCs underwent typical morphological changes and expressed the early transcription factors CDX-2, TFAP2A, TFAP2C and GATA3 that dictate trophectodermal fate. Further differentiation with specific media increased expression of CGA, CGB with cells expressing HCG and ECAD indicating differentiation towards syncytiotrophoblast lineage. Characterisations and functional assays are underway.

This model would enable understanding the molecular mechanisms underlying initial trophoblast differentiation and to develop 3D organoids to study normal/abnormal development of human placenta in vitro.

Presenter: Saumya Sharma **Poster number: 51**

Development and characterization of cellular models for the study of megalencephalic leukoencephalopathy with subcortical cysts

Saumya Sharma[1, 2, 3], Debojyoti Chakraborty[1, 3]

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Megalencephalic leukoencephalopathy with subcortical cysts (MLC), is a pediatric leukodystrophy resulting in an enlargement in brain size and multiple neurological symptoms due to water and ion imbalance. Type I MLC results from autosomal recessive mutations within the MLC1 gene, a protein highly expressed in endothelial-contacting astrocytes. To study MLC pathogenesis, we have developed induced pluripotent stem cell (iPSC) models of MLC1 through CRISPR-Cas9 editing of the MLC1 locus. Targeting the cells with a Cas9 plasmid multiplexed with dual guide RNAs against MLC1 locus followed by single cell sorting based on a GFP reporter. Besides, somatic cell reprogramming of patient derived blood cells was also performed and multiple clones were isolated. A simple PCR based genotyping helped us in screening for the desired clone. Characterization of MLC deficient iPSCs demonstrated that these cells maintain their pluripotency and can be differentiated to all three germ layers. Ongoing astrocyte differentiations will help us better define MLC pathogenesis and astrocyte-mediated impacts while analyzing MLC regulation of vacuole formation and astrocyte function. Future analyses of transcriptomic and proteomic profile of iPSC-derived astrocyte models will enable identification of impacted pathways and development of targeted therapies for MLC patients.

Presenter: Secunda Rupert **Poster Number: 52**

Mesenchymal Stem Cell Derived Exosomes as Therapeutic Option for Liver Disease

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Liver diseases have become a major global health burden that comprises of broad spectrum of diseases with multiple causes. Their diagnosis and treatment have progressed greatly over the years however their clinical outcomes are still not satisfying. Most liver diseases progress to end-stage liver disease (ESLD), which is characterised by large amounts of matrix deposition that makes it difficult for the liver and its hepatocytes to regenerate. In this scenario, Liver transplantation was the only treatment for the end-stage liver disease. Moreover, the shortage of suitable organs, expensive treatment costs and surgical complications greatly reduced the patient's survival rates. So, need for an effective treatment modality has become imperative. Cell-free therapy has become the research hotspot in the field of regenerative medicine. Exosomes are membrane-derived nanovesicles released from variety of cells. They are known to be non-tumourigenic, with high biocompatibility. Exosomes from MSCs have been reported to play important roles in physiological or biological processes in acute or chronic liver disorders by horizontal transferring of genetic bio information from donor cells to neighbouring /distal target cells. They also promote hepatocyte proliferation and repair damaged liver tissue by participating in intercellular communication and regulating signal transduction serving as a new strategy for the treatment of liver diseases. In our study, we propose to isolate, characterize and understand the role of MSC derived exosomes in various liver disorders that includes virus-related liver diseases, alcoholic liver diseases (ALD), non-alcoholic fatty liver diseases (NAFLD), and liver cancers.

Presenter: Sharon Mariam Abraham **Poster Number: 53**

Explore glutamate receptor subunit dysfunction in cell and animal based model of schizophrenia (SCZ)

SHARON MARIAM ABRAHAM, MANJARI SKV, PRAGYA KOMAL

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Schizophrenia (SCZ) is a neurodegenerative, neurodevelopmental disorder which displays positive (hallucinations, delusions), negative (social withdrawal, speech poverty) & cognitive symptoms (working memory deficit). In India, 3 out of 1000 people suffer from SCZ as per a study by Gururaj et al. (2005). No effective drugs are available to cure/ reverse the pathogenesis of this neuropsychiatric disease.

In this regard, we explored whether Vitamin D3 (VD) pre-administration restores some negative symptoms of SCZ in MK-801 induced mouse model by restoring the N- methyl D- aspartate (NMDA) receptor subunit expression. Previously, we have confirmed the neuroprotective effects of VD in a 3-nitropropionic acid-induced mouse model of HD (Manjari et al., 2022).

MK- 801 (0.5 mg/kg) is a non- competitive NMDA receptor antagonist which is known to recapitulate some of the negative and cognitive symptoms of SCZ. In the present work, we explored the effect of VD on various behavior paradigms to assess locomotion, anxiety, working memory and attention in MK- 801 mice. Male C57BL/6J mice (3-4 months of age) were divided into four groups namely: (1) control (saline), (2) SCZ (MK 801, 0.5 mg/kg), (3) Only Vitamin D3 (VD; 500IU/kg) and (4) MK-801 (0.5 mg/kg) + VD (500IU/kg/day). A reverse transcription-polymerase chain reaction was also performed from the brain tissue sample of all groups of mice.

Our preliminary data show that VD pre-supplementation significantly normalizes the MK 801-induced alteration in the elevated plus maze, locomotor activity, memory and attention function of the SCZ mice reflecting some neuromodulatory effect in PFC circuitry. VD supplementation also restored the mRNA expression of NR2B, NR2A, NR1 subunit of N-Methyl-D-Aspartate (NMDA) receptor in PFC. Overall, we show a beneficial effect of VD in the restoration of negative and cognitive symptoms in SCZ via rescue of glutamatergic gene expression in the PFC.

Presenter: Bipin Raj Shekhar **Poster Number: 54**

Exome analysis in familial schizophrenia: identification of a shared pathway and modelling with induced pluripotent stem cells

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Schizophrenia is a highly heritable chronic neuropsychiatric condition. The symptoms include hallucination, asociality, delusion, lack of desire and cognitive impairment. There is no clear explanation for its onset, however, a variety of factors contribute to the pathogenesis. The pathophysiology of schizophrenia is still unknown, despite the fact that GWAS and NGS have identified several variations that increase the risk of the disease. Additionally, it is challenging to comprehend the involvement of several molecular pathways due to the lack of an appropriate model system. In this study, we looked at four familial cases of Schizophrenia who were subjected to whole exome sequencing. Prioritization revealed no genes shared by all the families, therefore we looked for a common pathway. Pathway analysis was done using all of the prioritised variants, and it showed that all 4 families share the glycosaminoglycan pathway. Therefore, in our sample, a potential changed glycosaminoglycan pathway may be a risk factor. In the affected sister of family 4, hemizygous deletion of the whole CNTNAP2 gene was discovered using microarray analysis. The CNTNAP2 gene is known to be connected to autism. Therefore, the hemizygous deletion in family 4 may be a risk factor for schizophrenia. Further, iPSCs have been developed as a cellular model in both the sisters of family 4 and successfully differentiated into cortical neurons. We identified variations in gene involved in glycosaminoglycan pathway thus we can conclude that these genes may be a risk factor for schizophrenia in our cohort along with CNTNAP2.

Presenter: Shiffali Khurana **Poster Number: 55**

Neuronal ExomiRNA-6988-5p regulates neurotransmission in Amyotrophic lateral sclerosis

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Amyotrophic lateral sclerosis (ALS) is a fatal, adult-onset neurodegenerative disorder characterized by loss of upper and lower motor neurons. It results in progressive muscle weakness leading to atrophy and finally death within 3-5 years of onset of symptoms. Mutations in SOD1 gene are commonly associated with ALS. Clinical pathology of ALS suggests the spread of interconnected neuronal cell death possibly mediated by exosomes, the small endocytic vesicles enclosing a substantial amount of misfolded pathogenic proteins and aberrantly expressed miRNAs. To examine the effect of mutant SOD1 on exosomal miRNAs, isolation of exosomes was done from conditioned media of wild type and mutant SOD1 expressing motor neuronal NSC-34 cells. Exosomal miRNome was carried out by Illumina 150bp paired-end sequencing. Mutant SOD1 downregulated expression of mmu-miR-6988-5p in NSC-34 cells. Target identification and pathway enrichment revealed that mmu-miR-6988-5p affected axon guidance, neurotransmission, muscle contraction. I intend to validate role of mmu-miR-6988-5p in patient-derived reprogrammed motor neurons and skeletal muscle cells. I believe this lecture course will help me in adding a new dimension to my research. I can create iPSC derived organoids to recapitulate 3D neuromuscular junction. Further, I want to pursue my research in neuroscience and brain organoids can serve as an important tool to get insight into neurodevelopmental and neurological disorders.

I have also analysed Exome of 100ALS patients and observed considerable genetic heterogeneity probably resulting in clinical heterogeneity. In this scenario, patient-specific organoids will aid in deciphering molecular mechanisms causing this heterogeneity and thereby be useful in personalised medicine.

Presenter: Shreya Kandpal **Poster Number: 56**

Role of nutrients in shaping epithelial architecture

Shreya Kandpal

TIFR

Nutrients affect all aspects of cellular behaviour ranging from cell growth and proliferation to even fate specification. They are also known to affect the morphology of various tissues. One such tissue system is the epithelia. Epithelial tissues form the outermost protective barrier of organs and also organisms. They help in maintaining the internal milieu and also perform specialised functions such as absorption, secretion etc.

During development, the availability of nutrients can affect the morphogenesis of these epithelial tissues which may have a functional consequence later in life. Preliminarily we have found that the supplementation of certain amino acids affects the morphology of the embryonic zebrafish bilayered epidermis and intestinal epithelium. It will be interesting to see what molecular players mediate this effect and how metabolism is rewired in these tissues.

To determine the effect of nutrients on human intestinal epithelium, we will be using enteroids, and elucidating their response when subjected to various nutrient perturbations. This will be done by looking at changes in their architecture and polarity in response to various environmental stresses. It will help provide an understanding as to how nutritional perturbations can affect the intestinal epithelium leading to various disorders. As there are increasing cases of intestinal disorders due to adoption of western diet, this work will help provide a mechanistic understanding in their emergence.
This conference will help in understanding how organoids are used to answer questions related to development and emergence of disorders and the various techniques used for such analyses.

Presenter: Ashitha SNM **Poster number: 57**

Investigating Immune Functions of neuronal genes burdening Autism Spectrum Disorder: An integrated gene expression and mutation analysis

Ashitha SNM [1, 2], Snijesh V.P.[4], Meghana K.R.[3], Ramachandra Nallur B.[3], Meera Purushottam [1, 2], Biju Viswanath[1, 2], Sanjeev Jain[1, 2]

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Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by social-communication deficits, restricted-repetitive behaviours and interests. Neuroinflammation is often implicated in ASD pathogenesis. Recent studies in rats indicate immune activation deregulates the expression of genes associated with synaptogenesis, axonal guidance, synaptic contact and neurogenesis. Thereby, we explored the overlapping immune functions of neuronal genes through systematic in silico functional analysis of ASD-associated genes from databases (db) like SFARI-db, Denovo-db and Genes4denovo-db. Enrichment analysis was performed with EnrichR to identify genes with prominent neuro-immune functions that were further subjected to protein-protein interaction (PPI) and tissue-specific functional network analysis on STRING and HumanBase, respectively. Prioritised neuro-immune genes were investigated for ASD brain-tissue specific gene expression, biological functional similarity with high-risk ASD genes using tool GOSemSim and were checked for mutations within 15 in-house WES data from Indian ASD children obtained on Illumina HiSeq 2500. From three databases ten thousand ASD-associated genes were collated; 1518 genes had neuroimmune functions, including 950 genes with statistically significant PPIs. Of these, 618 and 590 genes displayed neuronal and immune cell specific functional networks, respectively with 193 common genes holding prominent neuro-immune functions. Their involvement in ASD pathogenesis were validated using ASD brain post-mortem tissues and 15 in-house ASD WES data. Genes BDNF, ANK3, PLCB1, SET, SYT1, LAMB1, PRKAR1, BRCA2, NTRK1 were found differentially expressed in brain tissues and carried deleterious variation in our WES data. Thus, our study provides the first genetic evidence for neuroinflammation commonly observed in ASD subjects.

Presenter: Soumita Goswami **Poster Number: 58**

Microglia Secreted ICAM-1 reduces Amyloid Beta (Aβ) mediated neuroinflammation by targeting ERK pathway and improves synaptic health in 5xFAD mice

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Neuroinflammation is one of the major hallmarks of Alzheimer's Disease (AD). Microglia, being the major representative of CNS immune system, innately respond to Amyloid beta (Aβ) and get contrastingly reactivated at different stages of the disease. However, molecular targets to manipulate this transformation towards the enrichment of anti-inflammatory subtype are yet to be uncovered. Here, we interrogated the kinetics of Soluble Intra Cellular Adhesion Molecule (sICAM-1) secreted from Aβ-treated microglia as well as astrocytes and its role in amelioration of different aspects of AD. We have found that sICAM-1 is one of the major secretory cytokines to be upregulated in glial condition medium in response to Aβ1-42 oligomer. When we treated primary glial cells with rat recombinant ICAM-1 it reversed the Aβ1-42 mediated microglial as well as astrocytic reactivation, improved neuronal health and reverted microglia towards anti-inflammatory subtype as observed by immunostaining and western blot analysis. Moreover, ICAM-1 was found to inhibit Aβ mediated ERK activation in microglia to reduce subsequent inflammation. Lastly, ICAM-1when injected interperitoneally in 5xFAD transgenic mice it refurbished synaptic protein expressions and restored synaptic health and reduced Aβ plaque load. Therefore, ICAM-1 plays a pivotal role in regulation of neuroinflammatory meshwork of AD and targeting ICAM-1 or its receptor Lymphocyte Function Associated Antigen 1 (LFA1) could be a good therapeutic strategy.

Presenter: Subashchandrabose Chinnathambi **Poster Number: 59**

Purinergic receptor P2Y12 involves in Tau oligomers-induced microglial phagocytosis and endocytic trafficking via filopodia associated actin remodelling

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Tau is a microtubule-associated protein, which mainly functions in the stabilization of neuronal axons, cargo trafficking and axonal outgrowth under physiological conditions. Tau oligomers are escaped from damaged neurons, spread through synapses and enters extracellular space via various mechanisms such as- exosomes, neurotransmitters, membrane leakage and cell-to-cell connections, etc. Microglia is the brain-resident immune cells in brain, which function in constant surveillance of synapses and maintenance of tissue homeostasis. Microglia senses the accumulated amyloids by various receptors such as- Toll-like receptors (TLRs), G-protein coupled receptors (GPCRs), scavenging receptors, purinergic receptors and complement receptors etc. Upon activation, microglia secretes a variety of cytokines and chemokines, which induce the infiltration of peripheral monocytes and T-cells into the brain. The disease-associated microglia (DAMs) become ignorant to phagocytosis, called ‘primed’ state, which causes improper synaptic elimination, amyloid propagation, oxidative damage and neuronal death. Actin remodelling consists of various microstructures such as- lamellipodia, filopodia, podosome, invadopodia, focal adhesion-stress fiber, and cortical actin layerHere, we found that Tau oligomers directly interacted with purinergic receptor P2Y12 that lead to microglial migration, activation and phagocytosis of Tau via remodelling membrane-associated actin structures such as- filopodia, lamellipodia and podosome. Moreover, P2Y12 signalling has impacted on Tau deposits degradation by forming actin microstructures. Lastly, we evidenced P2Y12-mediated endocytosis of Tau oligomers and its cellular trafficking, cytosolic accumulation and lysosomal degradation. These functions of P2Y12 in microglial chemotaxis, actin remodelling and Tau clearance can be intervened as therapeutic strategies in AD.

Presenter: Subhashika Govindan **Poster Number: 60**

Neuro-toxicogenomic mapping of TMT induced neurotoxicity using human minibrain reveals associated adverse molecular events

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Genome-wide transcriptomic interrogation of organoids and 3D tissue models are increasingly used for characterizing drug, toxicity responses and neurodevelopmental disorders. We established here a neuro- toxicogenomic assay by utilizing “minibrain”, a human in vitro 3D brain model system and a low-cost, highly multiplexable RNA-seq methodology (BRB-seq) for screening the effect of trimethyltin chloride (TMT) induced neurotoxicity. We demonstrate that transcriptomic profiling is insightful to the cellular composition and regional identity of the minibrain. Further, we characterize the transcriptomic changes associated with the dose-time neurotoxic response of minibrain upon exposure to TMT. The distinct gene expression changes and molecular candidates identified with our pipeline provides insight to map the key events involved in the adverse outcome pathway of TMT associated neurotoxicity. We identify processes such as endoplasmic reticulum stress, dysregulation of synaptic genes and downregulation of neuron-morphology associated genes upon exposure to TMT. In response to TMT, we identify activation of an early response homeostatic mechanism in minibrain and an interplay of STAT pathways correlating with the dose severity. In this study, we present a neuro- toxicogenomic assay that demonstrates the power of a low-cost transcriptomic screening to study chemical induced neurotoxicity.

Presenter: Sudip Sen **Poster Number: 61**

Using human fetal neural stem cells to develop a disease model for cerebral palsy

Sudip Sen
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How will attending the meeting be useful to you?

CP arises in neonates due to (perinatal) hypoxic brain injury. To understand the etiopathogenesis of CP, we have developed an in vitro model for CP. Human fetal neural stem cells (FNSCs) were isolated from aborted fetal brains (after ethical clearances and informed consent) and differentiated into different neural cell types including neurons, astrocytes and oligodendrocytes. By exposing these different cell types to hypoxia, we want to understand the changes in these cell types when they are exposed to hypoxic injury. Our primary research question is: “why are premature babies more vulnerable to hypoxic brain injury?”

We have some interesting findings suggesting that hypoxia may influence neural development and plasticity; that astrocytes are relatively resistant to hypoxic brain injury; the mechanism why premature oligodendrocytes are more vulnerable to hypoxic brain injury, etc. We also have evidence to believe that there might be ongoing intercellular interactions between the different cell types that may play a role in the etiopathogenesis of CP.

The fact that the human brain is more complex than the rodent brain, and the lack of tissue samples (or tissue biobanks for CP), make it extremely challenging to study this complex disease. Understanding cell interactions between different cell types with the help of organoids will help us understand this complex disease in a more comprehensive manner. It will help decipher the intercellular interactions and mechanisms elucidating the etiopathogenesis of cerebral palsy.

Presenter: Swati Sharma **Poster Number: 62**

Investigating retinal cellular dynamics in eye disorders using Zebrafish embryos and retinal organoids

Swati Sharma, Van Annika Zean Rick Lenze,Cerys Manning, et al.

School of Medical Sciences, Division of Developmental Biology and Medicine, Faculty of Biology Medicine and Health, University of Manchester, UK

The visual function of the eye is dependent on early eye morphogenesis to acquire the necessary three-dimensional shape and size of a mature eye. Alterations in morphogenesis lead to the developmental eye disorders namely Microphthalmia (reduced eye size), Anophthalmia (no eye) and Coloboma (optic fissure closure defects) (MAC conditions) which occur 1 in 10000 births and account for up to 25% of childhood blindness. We analyse the MAC patients' gene dataset which show enriched cell adhesion and cytoskeletal gene mutations. This is medically relevant because translation of patient genes into tractable cellular morphogenesis mechanisms during early development is lagging. We hypothesise that MAC conditions, involving morphogenetic defects initiates during early development, could result from cytoskeletal and adhesion mutations affecting eye morphogenesis. In MAC condition, defects might initiate from local dynamic cell shape changes regulated by intrinsic cytoskeletal generated forces and transmitted to neighbouring cells through extrinsic cell-cell adhesions. We will address how local retinal cell shape changes and dynamics can affect global optic cup architecture and how changes in these dynamics can influence local-global coupling leading to MAC conditions. We plan to address this by perturbing cell adhesion and cytoskeletal genes found in MAC patients using CRISPR knockout in Zebrafish embryos. We will analyse the local changes in retinal cellular dynamics, shape, size, motility, tension and global changes in optic cup architecture during early eye development. After performing the MAC patients' gene screening in Zebrafish embryos, the selected gene will further mechanistically dissect in mouse and human retinal organoids.

Presenter: Trinath Jamma **Poster Number: 63**

Host gut microbial metabolites regulate activated immune cell-driven EMT in intestinal epithelial cells

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Incidences of intestinal malignancies are on the rise in the recent past across age groups in both developed as well as developing countries. Identified underlying causes include chronic inflammation in the intestine in addition to the loss of APC tumor suppressor gene function. At the cellular level dialogue among intestinal epithelial cells, lamina proposal immune cells and gut microbial dysbiosis has been considered to be determining factors towards gut health. However, the molecular cues that mediate finely tuned dialogue among these three entities remain unexplored to a larger extent. Advancements in the allied areas led to the precise identification of small molecule metabolites of gut microbial origin and host gut microbiota-derived secondary metabolites with several immunomodulatory functions. In this context, we observed that one such metabolite namely bile acids regulated activated immune cell gene expression. Further, we identified a soluble mediator with immuno-oncogenic potential whose reduced expression in presence of bile acid prevented activated immune cell-driven EMT. Additionally, the receptor utilized by the bile acid to mediate its function in immune cells has also been identified in vitro. Overall, we observed that gut microbiota-derived bile acids fine-tune the activated immune cell effect on intestinal epithelial cells which could be one of the underlying mechanisms associated with inflammation-driven intestinal malignancies in vivo.

Presenter: Trupti Agrawal **Poster Number: 64**

Retinal commitment of RB1 null induced pluripotent stem cells is independent of pRB expression

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Purpose: This study aims to generate RB1 null models of human induced pluripotent stem cells (hiPSCs) to understand the effects of loss-of-function on retinal development and maturation in vitro.

Methods: Adipose-derived mesenchymal cells from familial retinoblastoma patient was reprogrammed into iPSCs using episomal reprogramming (RB1+/- hiPSCs). Isogenic mutant lines were also generated by CRISPR- Cas9 mediated editing (RB1-/- hiPSCs). Mutant iPSC lines were characterized by RT-PCR, immunofluorescence, western blotting and karyotyping. Healthy control and mutant iPSCs were differentiated into retinal lineage using established protocols.

Results: The patient specific heterozygous RB1+/- and CRISPR-edited homozygous RB1-/- iPSC lines maintained their stemness, pluripotency, genomic integrity and formed embryoid bodies comprising of cell types of all three germ layers. Upon differentiation into retinal lineages, two of the mutant hiPCS lines formed normal eye-fields in 2D cultures at 4 weeks, comparable to that of the healthy control hiPSC line. The eye-field cells of all mutant lines expressed the early neuro-retinal precursor markers PAX6, RX, CHX10, MITF, SOX10 and also formed retinal pigmented epithelial patches, suggesting normal retinal lineage commitment. When the EFPs were excised and grown in suspension cultures, the retinal progenitors underwent self-organization and formed well laminated neuro-retinal cups in control and RB1+/- hiPSCs. The molecular changes in the mature retinal organoid needs to be further evaluated.

Conclusion: The iPSC models confirm that either a partial or total loss of RB1 does not affect their stemness, pluripotency or retinal lineage commitment. This model can be used for research as well as chemotherapeutic drug screening applications.

Presenter: Tungadri Bose **Poster Number: 65**

One Size Doesn't Fit All - Towards Personalized Probiotics

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Background: A link between the gut-microbiome, digestive health, and overall wellbeing is now well established. While imbalance in the gut-microbiome has been associated with multiple diseases, probiotics have proven benefits in restoring a healthy gut-microbiome.

Objective: Evaluating whether the efficacy of probiotics vary among individuals with different gut-microbiome composition or dietary preferences.

Methods: Representative gut-microbiomes from individuals harbouring three distant 'enterotypes' and following different diets, viz. Indians consuming vegetarian-diet, Spanish following Mediterranean-diet and French following European-diet were used for the study. Bacterial species comprising the three microbiome communities were cocultured (in-silico) with commonly consumed probiotics under simulated dietary conditions following a Flux Balance Analysis approach.

Results: Outcomes were evaluated based on the extent the probiotics promoted the growth of beneficial microbes constituting the microbiota, and how well did the probiotics grow in the given dietary context. In both these aspects, Streptococcus thermophilus was found to be most compatible with vegetarian diet. In contrast, the benefits of Bacillus cereus were more apparent among European and Mediterranean diets. Lactobacillus species were seen to promote the growth of beneficial microbes among all diet/ gut-microbiome types but grew best in vegetarian-diet. Alternatively, irrespective of diet type, the gut-microbiome composition was seen to drive the growth of Bifidobacterium breve.

Conclusion: Health benefits of probiotic supplementation can vary among individuals. Efficacy of probiotic supplementation is dependent on both the gut-microbiome composition as well as the individual's dietary preferences. Due diligence of the dietary preferences and microbiome composition while choosing a suitable probiotic candidate/ dosage is solicited.

Presenter : Vadde Sudhakar Reddy **Poster number: 66**

Neuroprotective role of vitamin B12 in Streptozotocin-induced diabetic rat brain

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Diabetes is associated with increased risk for neuropathological features such as neuronal cell death, altered neurotrophic support, astrogliosis, synaptic dysfunction, ER stress were found in both diabetes and neurodegenerative diseases. Vitamin B12 is an essential micronutrient, whose deficiency has been linked to neurodegenerative diseases, cognitive impairment, and neuropathy. However, the neuroprotective role of vitamin B12 and its molecular basis in diabetic rat brain remains elusive. Diabetes was induced in SD rats using Streptozotocin (STZ) and animals were divided into 3 groups i) control (CN), ii) diabetes (D), and (iii) diabetes with B12 supplementation (DBS). At the end of four months, the cerebral cortex (CC) was collected. The histopathology was performed using H&E and nissil body staining, cell death by TUNEL assay. Neurotrophic support, synaptogenesis, astrogliosis, and ER stress markers were analyzed using immunoblotting, and immunofluorescence. Vitamin B12 supplementation showed a reduction in cellular degeneracy, increased neuronal cell density, and decreased chromatolysis in diabetic rat CC. Additionally, B12 supplementation restored the neurotrophic factors (BDNF, NGF, and GDNF), improved synaptic density-related markers (SYP & PSD95), and attenuated astrogliosis (GFAP). Furthermore, B12 supplementation reduced the ER stress (GRP78, pPERK, pATF4, CHOP) and alpha synuclein expression. In the same line, B12 supplementation decreased neuronal cell death by reducing the TUNEL positive cells and cleaved caspase-3 levels. Our present study demonstrates a neuroprotective role of B12 in STZ-induced rat brain. In future, we aim to study impact of B12 deficiency on neurodevelopment specificlly cell types such as neurons, astrocytes, and glial cells using cerebral organoids.

Presenter: Vaishali Saini **Poster Number: 67**

Understanding EBV-induced Alzheimer's disease using cerebral organoid models

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Cerebral organoids are three-dimensional tissues derived from induced pluripotent stem cells and can mimic the functionality of the human brain pertaining to their stable architecture. The Epstein-Barr virus is a potent neurotropic virus known to infect the neurons of the central nervous system to induce demyelination and neuroinflammation. This ubiquitous human herpesvirus is potentially the major contributor to Alzheimer's disease leading to cognitive decline and immune dysregulation. In our lab, we have demonstrated the role of EBV infection and its possible role in the cells of the neural milieu that might lead to Alzheimer's disease. Viral infections are difficult to modulate in two-dimensional cultures and in-vivo models. The 2D cultures lack the ability to mimic the spatial organization while studies in in-vivo models pose a challenge due to the host range restrictions of the viruses leading to differential observations in the animals and humans. Our aim is to use the cerebral organoids as the in-vitro model for studying the underlying mechanism of Epstein-Barr virus-mediated infection in Alzheimer's disease. We hereby propose a methodology to characterize the neurotropic infectivity of the EBV in Alzheimer's disease by combining the brain organoids with immune-staining, single-cell sequencing by utilizing RNA-Seq and Ribo-Seq, and physiological assays that are better studied through cerebral organoids. Our approach would elucidate and support a positive relationship between EBV infection and Alzheimer's disease in the cerebral organoids to further identify plausible interventions in the prevention of the disease.

Presenter: Vinithra Ponnusamy **Poster Number: 68**

Obesity and tongue papillae density-What organoids could do?

Vinithra Ponnusamy, Gowtham Subramanian, Selvakumar Subramaniam

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Obesity is a complex nutritional disorder influenced by calorie intake and eating behaviors. Reduced taste sensitivity, particularly to fat and sweetness, is a major factor in the susceptibility to obesity caused by overeating, even though other factors are linked to weight gain. Taste bud cells within papillae, such as circumvallate, foliate, and fungiform papillae across the tongue epithelium, express the taste receptors that are responsible for taste perception. Hence, the papillae density could be an important phenotypic marker for taste sensitivity and obesity development. Our recent study among Indian population revealed that total papillae density and BMI had a direct negative correlation (r= -0.43), with papillae density decreasing as BMI increased. Additionally, taste sensitivity was increased in people with higher papillae density. With these findings, it is imperative to have a thorough understanding of taste cell proliferation and differentiation pathways, particularly the Wnt, hedgehog (Hh)signaling, to determine the impact of papillae on obesity. Although various research groups have attempted to create 3D invitro cell culture system for taste cell organoids, an invitro taste bud with complete functionality is still absent. Therefore, the lecture series may provide a better setting for learning the concept and steps for framing an organoid work that could be applied to taste cell biology. A regenerative treatment for taste loss brought on by cancer or any other disease that results in taste cell degeneration might be made possible with further research. Thus, this model might more accurately replicate the taste buds for the benefit of humans.

Presenter: Vorapin Chinchalongporn **Poster Number: 69**

MR spectroscopy reveals a maturing neurochemical profile of human cerebral organoids imaged at different developmental stages

Vorapin Chinchalongporn 1, Fermisk Saleh 1, 5, Wendy Oakden 1, Ryan Oglesby 1, 2, Rajshree Biswas 3, Andrea
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When derived from patients with neurological disorders, human pluripotent stem cell-derived cerebral organoids (COs) exhibit many features of a donor's pathology, highlighting their potential for disease modelling and personalized medicine. Animal model and human imaging studies have identified neurochemical abnormalities in several neurodegenerative diseases. Here we applied magnetic resonance spectroscopy (MRS) as a novel discovery platform to identify the neurochemical signature of COs. For quality control, human embryonic stem cell-derived COs were shown to expressed markers of neural progenitor cells (PAX6, SOX2), cortical neurons (TBR1, SATB2) and glia (GFAP). Moreover, extracellular recordings performed using a multi-electrode array (Neuroprobe) identified spontaneous electrical activity in aged COs. Finally, high-resolution, non-invasive nuclear magnetic resonance (NMR) spectroscopy was used to assess these hESC-derived COs, employing a 500 MHz Bruker NMR spectrometer with a magic angle spinning (MAS) probe. Eight hESC-derived COs were scanned at different levels of maturity ranging from 103 to 133 days. Representative spectra from 103- and 104- day old organoids show remarkable reproducibility. Excellent spectral quality was observed with high signal-to- noise ratio, very narrow linewidths (<2 Hz), and a large number (>17) of observable metabolites, including our primary target metabolites N-acetylaspartate (NAA), myo-inositol, and cholines. The relatively low amplitude NAA peak was indicative of an early developmental phenotype, similar to that of the embryonic human brain. These preliminary NMR results support the feasibility of detecting CO neurochemistry using NMR. This platform will now be applied to models of disease and aging with the goal of identifying novel biomarkers of neurodegenerative disease.

Presenter: Yogesh Sardana **Poster Number: 70**

Comparing Protective Effects of Melatonin and Quercetin in Swiss Mice on Modulation of Mitochondrial Dysfunction during Lead Induced Neurotoxicity.

YOGESH SARDANA
Central University of Punjab

Lead is a known neurotoxin, which upon exposure, hampers the neurodevelopmental process in growing children and leads to chronic neurodegenerative disorders like Parkinson's disease in adults. Overuse of fertilizers and improper disposal of industrial waste has rendered Punjab's Malwa region's groundwater heavily contaminated with toxic metals like Uranium, Arsenic, Cadmium and Lead. According to a 2017 report, Bhatinda groundwater had a Lead concentration of 28.04mg/l, which is exceedingly higher than the permissible levels (0.001mg/l), set by Bureau of Indian Standards (BIS). In this study we proposed mitochondria as the primary organelle targeted by Lead in mediating neuro-toxicity. To substantiate the idea, we administered Swiss mice with acute doses of Lead Acetate for about a month and evaluated its effect on the neuro-behaviour, metabolic activity, in house-anti-oxidant defence and the mitochondrial quality control system. Molecular expression analysis of genes regulating mitochondrial fission, fusion and biogenesis was performed to assess the early MQC response, induced by Pb stress. Results from biochemical assays like Reduced Glutathione Test (GSH) and Lipid Peroxidation Assay (LPO), indicated a compromised anti-oxidant defence and elevated oxidative stress in the brain tissue. Aberrant neuro-behaviour and altered mitochondrial dynamics suggested the deteriorating effect of Lead on mice brain. Oral supplementation with Melatonin and Quercetin were compared for their potential anti-oxidant activity and protective action against Lead induced stress by restoring MQC balance, and reducing oxidative stress levels in brain tissue.

Presenter: Zandile Nxumalo **Poster No.: 71**

Using various 2 DimensionalZandile Nxumalo (2D) cancer cell lines to screen for anti-cancer drugs for applications in the development of a predictive high throughput (HTS) drug screening platform.

Zandile Nxumalo, Deepak balaji thimiri Govindaraj, et al.
CSIR

The efficacy of widely available cancer therapy options is mainly based on the molecular and biochemical profile from patient cohort from high income countries. Thus, there is a critical need to study on low-middle income countries cancer patient such as African cohort. In addition, gynecological cancer is under-studied and hence is an unmet medical need due to high chemo-resistance and recurrence rates in African patients. The project goals are to develop a high-throughput in-vitro drug screening platform that will use patient-derived samples to predict how adjuvant therapy would affect African ovarian cancer patients. By employing our proposed approach, we hope to find drug or drug combinations that can combat chemotherapy resistance and ultimately offer tailored-specific therapeutic alternatives for African cancer patients within clinically appropriate timeframes to the prescribing oncologist. We have demonstrated the cytotoxicity of clinically approved drugs on various 2D cancer cell lines. We believe drug sensitivity screening would be a gold standard to evaluate the drug dosage response. Thus, we aim to implement this method with automated drug screening pipeline in
cancer cell lines and patient derived samples due to the controlled conditions and repeatable procedures. Based on our findings we are certain that by choosing the correct tumor model at the stage of ex-vivo testing we will establish an automated technology platform for drug sensitivity screening on patient samples, thereby allowing immediate benefit to the patient who donates the sample for analysis and thus contributing towards efforts for individualized treatment as a part of personalized medicine.

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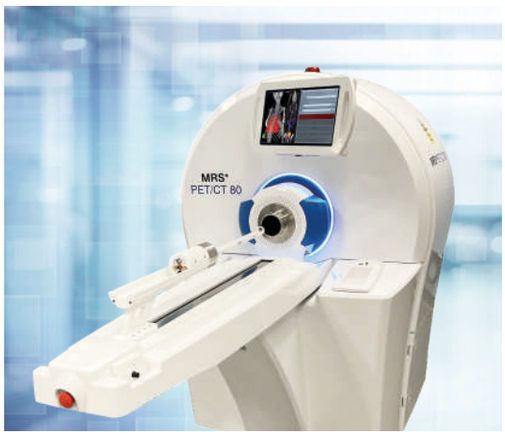

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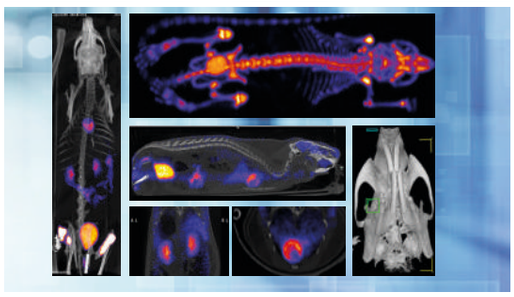

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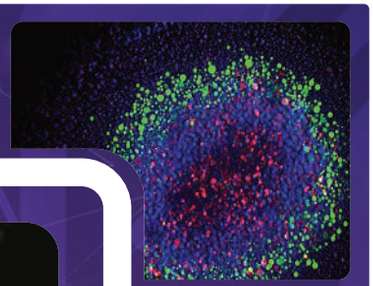

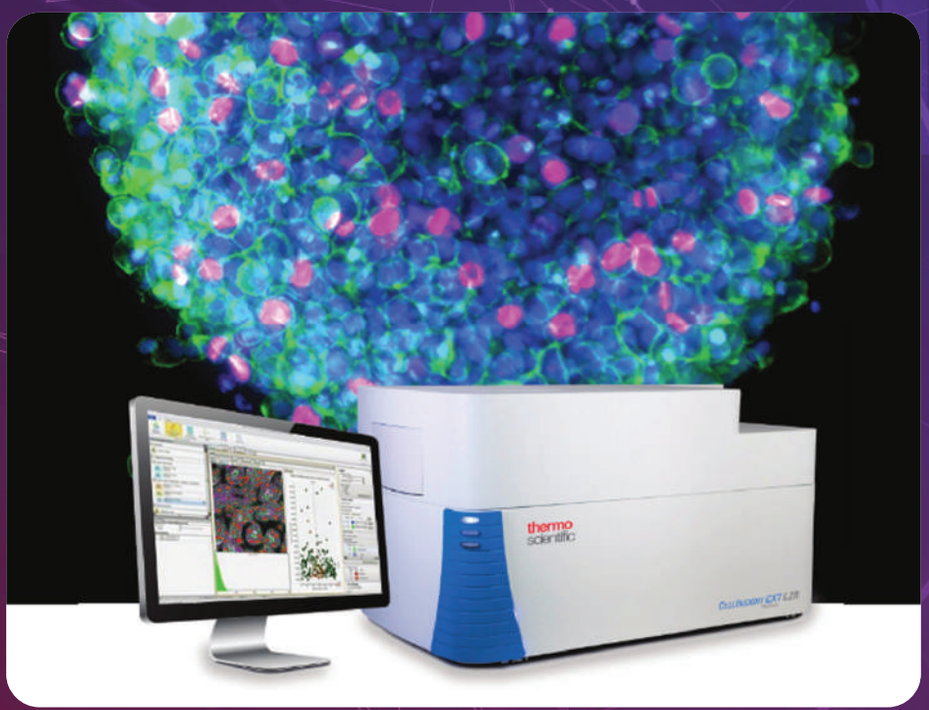

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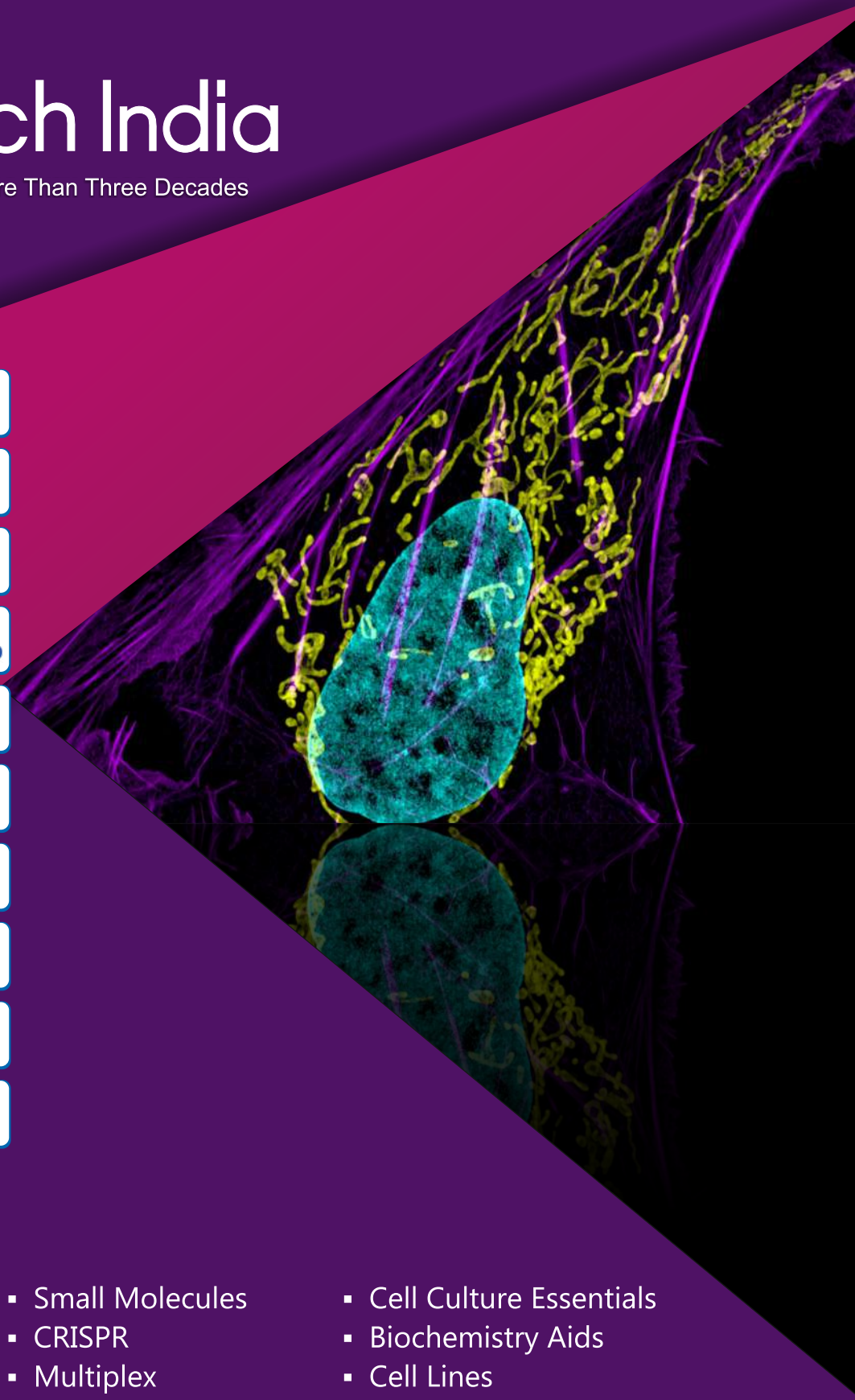

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