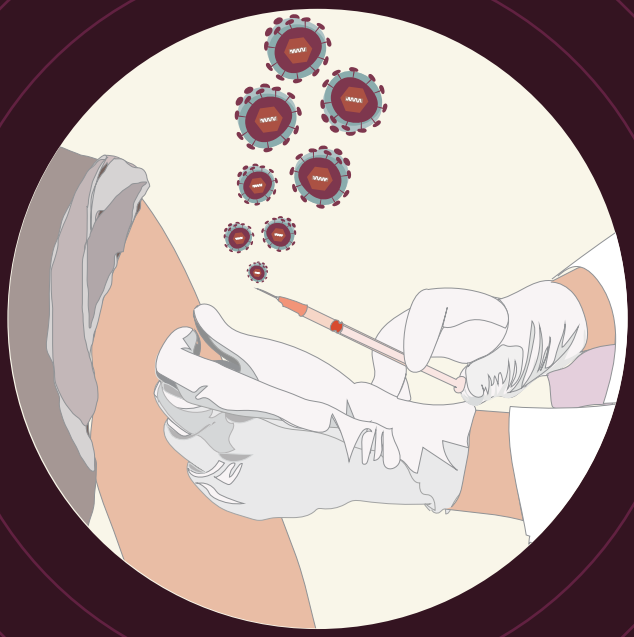
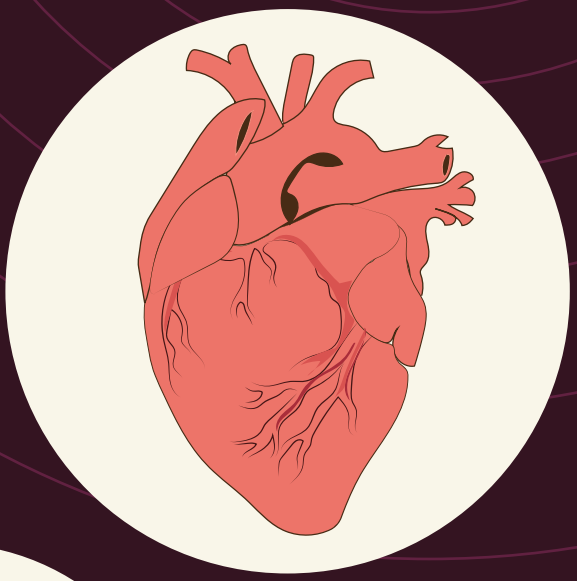
inStem

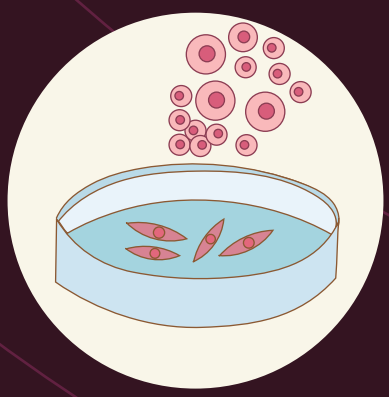
INSTITUTE FOR STEM CELL SCIENCE
AND REGENERATIVE MEDICINE

Annual Report

2019 - 2020







inStem

An Autonomous Institute of
the Dept. of Biotechnology, Govt. of India

YEAR AT A GLANCE
2019 -2020

Faculty strength: 12
PhD Students: 50
Publications: >55
Patents filed: 5
Technologies developed: 4

AWARDS & RECOGNITION

- Wellcome Trust- DBT India Alliance Intermediate Fellowship: Bhavana Muralidharan; Baskar Bakthavachalu
- Wellcome Trust- DBT India Alliance Early Career Fellowship: Anusree Mahanta
- DBT-Ramalingaswamy Fellowship: Sonia Sen
- iBiology International Young Scientist Seminar: Edries Hajam (one of four winners worldwide)
- BIRAC AMR Challenge: Tanay Bhatt (one of four winners)

ADVANCED SKILLING & TRAINING

iPSC training workshops:
- ADBS-3 week on-site: 23 participants
- ADBS-CiRA (Kyoto, Japan) 2 weeks: 8 participants
- CSCR: 10 participants
- ADBS-IBAB Bioinformatics Workshop : 20 Participants
- The Mouse Genome Engineering Facility: Microinjection / Crispr-Cas Workshop
- Interns from schools and colleges hosted in our laboratories from 3 months – 1 year: 30

COVID-19 RESPONSE

- inStem – NCBS COVID-19 testing laboratory has processed > 40000 samples since April, 2020
- Developing a compressed sensing (smart pool) protocol to test large number of samples by pooling in areas of high incidence of infection
- Participated in the PAN-India viral genome sequencing effort – 100 genomes sequenced at BLiSC
- Germicidal chemical that confers protection and can be coated on fabric to make masks and PPE
- Transgenic mouse resources that expresses the hACe2 transgene or deleted for the receptor
- Recognized as a DBT_AI kit (RT-PCR) validation centre
- COVID-19 biobank, a resource to facilitate efforts for academia and industry

SCIENCE OUTREACH & COMMUNICATION

- Science Exhibitions: Lab Culture_I – visited by more than 700 students over 2 months (July-August 2019)
- Two Open days: Visited by 1000 school children and 200 college Undergraduates
- India International Science Festival: Kolkata November 2019
- BLiSC Science Cafe: bringing scientists to the public in informal settings/ social venues – Five talks from inStem.
- Jigyasa Project, Mandram & BLiSC: communicating research in the vernacular (Tamil, Kannada initially): Two investigators from inStem
- National Science Day: Public talk and interactions with students from local schools & colleges – Alejandro S Alvarado, HHMI Investigator, Member NAS, USA
- @Brain Awareness Week: a global initiative to foster public awareness for brain science, highlighted work on ADBS and BDDM theme
- Covid Gyan website – an initiative of the TIFR Institutions, IISc, TMC, inStem, India Bioscience, Vigyan Prasar amongst others

PARTNERSHIPS

Annual Report
Contents

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Director's Note

April 2019-August 2020

At inStem, as in the rest of the world, the COVID-19 pandemic imposed an abrupt and unplanned pause to the humming research laboratories, meetings, seminars, classes, workshops and of course, the extended discussions, which are the life breadth of an active scientific community. As we grappled with the crisis, these months also brought to the fore the strong foundations of our training to deal with the new and unexpected, albeit in slightly more (lab) controlled ways! The campus worked with institutes in its neighborhood, in different parts of the country and the world, the state government, and our parent agencies to respond to a situation that left no one untouched. As its first response, inStem and NCBS set up a specialized COVID-19 testing laboratory that is safe and fully equipped to process samples referred to us by State Health Authorities that rapidly reached triple digits, within days of starting operations. The impressive speed and scale of this activity is owed to our own ***Corona Warriors***' – the dedicated and hugely motivated community of students, project staff, postdocs, laboratory, instrumentation and technical support staff, and members of administration, ably led by our faculty - who volunteered their time to ensure 24/7 operations from April 13, 2020. Apart from the testing effort, we have leveraged our facilities and expertise to contribute to the COVID-19 response in many other ways. Our scientists have focused on the development of new diagnostic tests, generated mice that can be used as a research and screening resource and identified a germicidal chemical formulation that can be coated on fabric to make an anti-viral mask, to highlight just a few. The many individual and community efforts are described in a section dedicated to this effort in the accompanying report. I take this opportunity to salute the spirit and ethos that defines our campus community! Our thanks to teams of volunteers who continue to operate the Peer-Connect helpline, a support network staffed by campus volunteers, to offer support where needed but also a source of verified information and guidance about campus norms and precautions. We remain deeply grateful to our donors – Azim Premji Foundation, Standard Chartered, Punjab National Bank (PNB) Housing, and The Nuclear Power Corporation of India Limited (NPCIL) – whose generous and timely support was and remains critical to the COVID-19 response from the campus. Most importantly, we owe a deep debt of gratitude to our personnel, facility and unit heads, contract staff and their supervisors, whose commitment and dedication ensured that live animal and plant resources, national facilities such as the Cryo-EM and basic services on the campus were maintained during the country-wide lockdown.

As we negotiate this enforced pause and gradually resume core research activities, this is also time to take stock of the achievements and milestones of the past year and look to the possibilities in the year ahead. I hope that the reports from the different themes and multi-institutional programmes hosted at inStem will give you a flavor of our efforts in this direction. Until as late as February, our rich calendar of meetings and outreach events was fully operational, with workshops and open days, through which we impart skilled training and engage in different formats with students in schools and undergraduate colleges in our vicinity. We look forward to resuming these activities as and when safely possible. In the interim, thanks to the efforts of our IT section, the use of electronic media to maintain connectivity in the form of campus seminars, student presentations, and thesis defenses has become the new normal, with some events clocking the highest audience numbers ever!

It is always a pleasure to write about the achievements of our young colleagues, the students, and early career researchers, who are the bedrock of our community. Edries Hajam, a doctoral student in Colin Jamora's laboratory was selected as one of four winners of the International 2020 Young Scientist Seminars (YSS), a competition sponsored by iBiology and their partners the Albert and Mary Lasker Foundation and the Alan Alda Center for Communicating Science. Tanay Bhatt, also in Colin Jamora's group, is one of four winners of AMR Quest 2020, launched by C-CAMP, Bengaluru with a focus on innovations in antimicrobial resistance (AMR). Drs. Anupam Dutta and Abrar Rizvi (postdoctoral fellows in Colin Jamora's group), received Biotechnology Ignition Grants (BIG) from BIRAC to help commercialize their research findings. Last, but not the least, Dr. Anusree Mahanta, was awarded the Wellcome Trust DBT India Alliance early career fellowship to investigate the physiological role of myeloid cells in regulating systemic metabolic homeostasis, under the mentorship of Tina Mukherjee. We congratulate our young colleagues for this well-deserved recognition and wish them the very best in their endeavors!

As part of our continuing efforts towards the translation of our research outcomes, Praveen Vemula and his group have recently successfully transferred the technology to irreversibly coat cellulose-based fabrics with a germicidal chemical that has the ability to rupture the membrane of bacteria and enveloped viruses. This timely effort is being directed to the immediate production of masks and other PPE coated for added protection and safety from the ongoing infection. This technology transfer, follows the start-up focused on protection from contact and inhalation induced pesticide toxicity, also from Praveen's group last year.

As in previous years, on behalf of all my colleagues at inStem, I express our sincerest appreciation and thanks to Dr. Kiran Mazumdar-Shaw (Chairperson & Managing Director, Biocon), Kris Gopalakrishnan (Co-founder, Pratiksha Trust) and TT Jagannathan (Chairman, TTK Prestige) for their generous support and the continuing engagement with our campus. Their support has been truly catalytic in many spheres of our activities, apart from making an enormous difference to the opportunities we offer our younger colleagues and we remain extremely grateful!

Finally, despite the challenges of the past months, we look forward to realizing the promise of new positions that will grow and undoubtedly enrich our community. Recruitments across the board have begun and we look forward to welcoming new colleagues to inStem and the campus. With the support of our community and the combined energies and efforts of our colleagues, taking important lessons from this year, inStem looks forward with renewed hope and confidence in its ability to initiate new directions in fulfilment of its charter.

Apurva Sarin
Director, inStem

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Administration Report

The Institute has completed eleven years in its pursuit for excellence in stem cell research and allied areas. Following the approval of the Revised Cost Estimate (RCE-II) in 2017 by the Department of Biotechnology, Government of India, the building was completed in October 2019. The Center for Stem Cell Research (CSCR) is a centre of the institute situated in Vellore.
The accounts of CSCR are integrated into the accounts of the institute.
The table below indicates the status of grants received and the manpower count at the end of March 31,2020.

Details	2019-20
Core grants received	Rs.67.20 Crore
EMG grants received	Rs.41.15 Crore
Number of Active grants (Nos)	70
Staff (including contractual and outsourced employees)	255

Important administrative events that occurred during 2019-2020 are as follows:
- The Bye-Laws of the institute duly approved by the competent authority were notified on November 07, 2019.
- The recruitment Rules for scientific, technical, and administrative cadre were notified in February 2020.
- The construction of the lab building was completed during 2019-2020
- The Hindi Week and Vigilance Awareness Week were observed in September 2019; and Swachh Bharat Abhiyan was also observed during 2019-20; oath to abide by the Constitution was taken during November 2019.

The following important meetings were conducted during 2019-20 in the normal course of its activities:

Sl. No.	Meeting	Date
1	23rd Finance Committee	03.04.2019
2	24th Finance Committee	24.09.2019
3	25th Finance Committee	17.03.2020
4	25th Governing Council	09.04.2019
5	26th Governing Council	25.09.2019
6	11th inStem Society	07.11.2019

The following audits were conducted during 2019-20:

Sl. No.	Type of Audit	Date
1	Statutory audit for financial year 2018-19	June-July 2019
2	Audit by CAG for the period 2017-19	23.10.2019 to 13.11.2019
3	Internal Audit for the period 2017-19 by IAW,MST	02.03.2020 to 06.03.2020

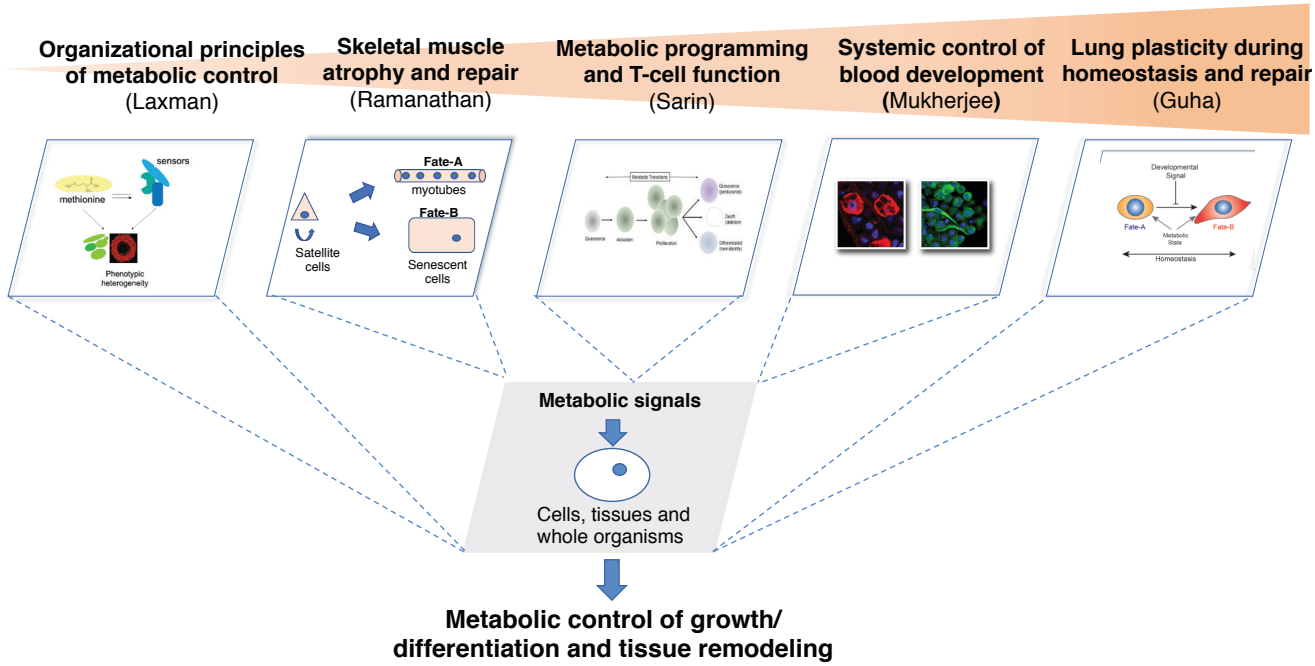
Shri. Srinivas Rao Palla has joined the institute as Senior Accounts Officer w.e.f. September 05, 2019. With the new joining at senior level, the processes and procedures have been streamlined during the year. M/s B.P.Rao & Co. Chartered Accountants were appointed as statutory auditors on November 15, 2019 for auditing books of accounts of inStem and CSCR for three financial years w.e.f. from 2019-20 till 2021-22.

Pawan Pahwa
Chief Administrative Officer, inStem

Image Credit: Arjun Guha, inStem

03 RCF

REGULATION OF CELL FATE



Mechanisms of metabolic control- from cells to systems

Apurva Sarin **Sunil Laxman** **Arvind Ramanathan** **Tina Mukherjee** **Arjun Guha**

The overarching goal of the Regulation of Cell Fate (RCF) theme at inStem is to build a comprehensive understanding of how metabolic reorganization or rewiring control cell fates to impact systemic physiology. The theme is building capacity to study models of complex systems and diseases; and address underlying metabolic organizations and mechanisms within, at a cellular level. The unifying hypothesis is that targeting metabolic mechanisms will enable us to understand how cells and tissues respond to nutritional, pharmacological, and environmental stimuli. Investigators in this theme work on biological systems to bridge our understanding of how critical metabolites or nodes of the metabolic network control the fates and functions of individual cells and tissues in complex systems.

03 Regulation of Cell Fate

The theme comprises five laboratories that work collaboratively on inter-related systems, and also develop associated enabling technologies. In particular, the theme has strengths in scaling from cells to tissue/animal physiology (and vice versa), using diverse systems with an underlying commonality. All these systems have inherent populations of cells that are non-dividing/quiescent, and which rapidly grow and/or proliferate upon changes in nutrient cues or environmental insult. These can all be considered systems where 'dormant' to 'active' transitions take place at a cellular level, leading to substantial physiological changes at the level of tissues and organs. The figure highlights these systems that span single cells, tissues, and whole organisms. Together, these help in elucidating the underlying metabolic signals that control processes of growth, differentiation, and tissue homeostasis. This understanding has led to the determination of small molecule and protein targets that can affect these processes. The physiologically relevant tissue-level systems under study are animal models of the lung/airway, muscle, the immune system, and hematopoiesis (blood cell development). At the cellular level, our investigators compliment these systems with suitable cellular models that can reveal conserved molecular/metabolic processes controlling dormant to activated/growth transitions. These cellular systems are also highly amenable to the precise dissection of metabolic and signaling mechanisms, using the range of biochemical, analytic, cell biological, genetic, and systems-level approaches that the investigators collectively bring. Two specific themes, directly relevant to metabolic control, are emerging from our studies. First, in a context dependent manner, these studies identify critical fate-determining metabolites that specifically control cell function and physiological outcomes. Second, specific developmental processes or transitions observed cannot be easily explained using simpler paradigms of transcriptional/signaling control, but require specific metabolic-control check points identified through our efforts. This ability to 'scale' discoveries, and contextualize findings from cellular to systemic is reflected in the published and ongoing studies emerging from the theme. We are now poised as a theme to collectively move towards understanding fundamental processes such as cellular plasticity during homeostasis and post-injury repair. Ongoing efforts are directed toward understanding how plasticity of epithelial cells in the respiratory system in fruit flies and in the airways of the lung is regulated. The research till date has shown that developmental signals like Wnt and Notch maintain the fates of differentiated yet plastic cells. The downregulation of these signals during remodeling, in their respective systems, is likely to facilitate changes in cell fate. In another example one of the investigators is elucidating the molecular events that underlie the regulation of mitochondrial and lipid metabolism during skeletal muscle atrophy using murine models. Parallel studies are also underway to elucidate the role of metabolic signals in muscle stem cell (satellite) activation and differentiation after injury. Tractable organoid models (for muscle and lung), which recapitulate whole-animal physiology are under development. These are amenable to study basic processes, and also for drug screening. Diseases including cancer, metabolic syndromes (such as cardiovascular dysfunction and diabetes despite a lack of obesity), all have underlying causes and vulnerabilities that stem from metabolic dysfunction. However, systemic studies of physiology (which suggest underlying metabolic causes) are often disconnected from studies identifying the molecular basis or metabolic organization within cells in such systems. The RCF theme at inStem aims to bridge this disconnect by developing and enabling technologies including mass spectrometry based approaches.

PUBLICATIONS

Apurva Sarin

• Saini N., Sarin A. (2020) **Nucleolar localization of the Notch4 intracellular domain underpins its regulation of the cellular response to genotoxic stressors.** *Cell Death Discov*.

Arjun Guha

• Kizhedathu A, Kunnappallil R.S., Bagul A. V., Verma P., Guha A. (2020) **Multiple Wnts act synergistically to induce Chk1/Grapes expression and mediate G2 arrest in *Drosophila* tracheoblasts.** *Elife*.

Arvind Ramanathan

• Sharma R., Ramanathan A. (2020) **The aging metabolome-biomarkers to Hub metabolites**. *Proteomics*.

• Wiley C.D. *et al.* (2019) **Secretion of leukotrienes by senescent lung fibroblasts promotes pulmonary fibrosis.** *JCI Insight*.

Sunil Laxman

• Bruhn C. *et al.* (2020) **The Rad53 (CHK1/CHK2)-Spt21 (NPAT) and Tel1 (ATM) axes couple glucose tolerance to histone dosage and subtelomeric silencing.** *Nat Commun*.

• Gupta R., Laxman S. (2020) **tRNA wobble-uridine modifications as amino acid sensors and regulators of cellular metabolic state.** *Curr Genet*.

• R. Gupta, Laxman S. (2020) **Steady-state and Flux-based trehalose estimation as an indicator of carbon flow from gluconeogenesis or glycolysis**. *Bio Protoc*.

• Gupta R. *et al.* (2019) **A tRNA modification balances carbon and nitrogen metabolism by regulating phosphate homeostasis.** *Elife*.

• Negi H. *et al.* (2020) **A novel polyubiquitin chain linkage formed by viral Ubiquitin is resistant to host deubiquitinating enzymes.** *Biochem J*.

• Shaw E. *et al.* (2020) **Anabolic SIRT4 exerts retrograde control over TORC1 signaling by glutamine sparing in the mitochondria.** *Mol Cell Biol*.

• Varahan S., Sinha V., Walvekar A., Krishna S., Laxman S. (2020) **Resource plasticity-driven carbon-nitrogen budgeting enables specialization and division of labor in a clonal community.** *Elife*.

• Varahan S., Walvekar A., Sinha V., Krishna S., Laxman S. (2019) **Metabolic constraints drive self-organization of specialized cell groups.** *Elife*.

• Vengayil V., Rashida Z., Laxman S. (2019) **The E3 ubiquitin ligase Pib1 regulates effective gluconeogenic shutdown upon glucose availability.** *J Biol Chem*.

• Walvekar A.S., Laxman S. (2019) **Methionine at the heart of anabolism and signaling: Perspectives from budding yeast.** *Front Microbiol*.

Tina Mukherjee

• Preethi P., Tomar A., Madhwal S., Mukherjee T. (2020) **Immune control of animal growth in homeostasis and nutritional stress in *Drosophila*.** *Front Immunol*.

• Cattenoz P.B. *et al.* (2020) **Temporal specificity and heterogeneity of *Drosophila* immune cells.** *EMBO J*.

RESEARCH TALKS

Apurva Sarin

• **Strategies promoting cell survival: Cross talk between the Notch pathway and metabolic signaling in T-cells.**
RePORT India Annual Meeting, Mumbai, February 2020

• **Cellular adaptations for survival in inflammatory contexts.**
Flowcytometry Workshop, JNCASR, Bangalore, June 2019

• **Metabolic signaling underpinning cell fate decisions in T-cells.**
(Invited seminar) CSIR-Central Drug Research Institute, Lucknow, June 2019

• **Cellular adaptations for survival: Metabolic control of cell fate decisions.**
Cell Biology and Microscopy Workshop, Institute of Life Sciences, Bhubaneshwar, December 2019

Arvind Ramanathan

• **Lipid metabolism mediated control of the senescent state.**
(Invited talk) NUS Singapore, ISLS-2020, March 2020

• **Role of lipid metabolism in cellular senescence.**
Lipid Center Meeting, MPI Dresden, December 2019

• **Role of arachidonic acid lipids in cellular senescence.**
Lipid Meeting, Amity University, Noida, December 2019

Sunil Laxman

• **Metabolic constraints determining specialization and division of labor within a cell community.**
La Vida Biology club seminar, IISER Behrampur, July 2020

• **Methionine as a growth signal and anabolism regulator.**
Lysosomes and autophagy 2020, IISc, Bangalore, January 2020

• **Methionine as a growth signal controlling anabolic programs.**
Genome Biology workshop, IISER-Trivandrum, Tiruvananthapuram, January 2020

• **Metabolic constraints determining specialized cell states in space, and over time.**
Phenotypic Heterogeneity and Cancer, IISc, Bangalore, January 2020

• **Methionine as an anabolic signal, and coupling to reductive biosynthesis.**
Lipid Center Meeting, MPI-CBG, Dresden, Germany, December 2019

• **Metabolic constraints determining specialized cell states in space, and over time.**
NISER, Bhubhaneshwar, October 2019

• **Methionine as a central growth signal.**
Institute of Life Sciences (ILS), Bhubhaneshwar, October 2019

• **Metabolic constraints determining specialized cell states in space, and over time.**
Dept. of Bioengineering, Northeastern University, USA, July 2019

Tina Mukherjee

• **Uncovering metabolic dependencies of myeloid development through *Drosophila***
(Invited talk) IGBMC-Strasbourg, Strasbourg, September 2019

• **Metabolic landscaping by blood cells: Insight into this novel function through *Drosophila* as the model**
Unistra-India Workshop, University of Strasbourg, Strasbourg, September 2019

• **Metabolic control of immune-competency by odors in *Drosophila***
National Institute of Oceanography, Goa, December 2019

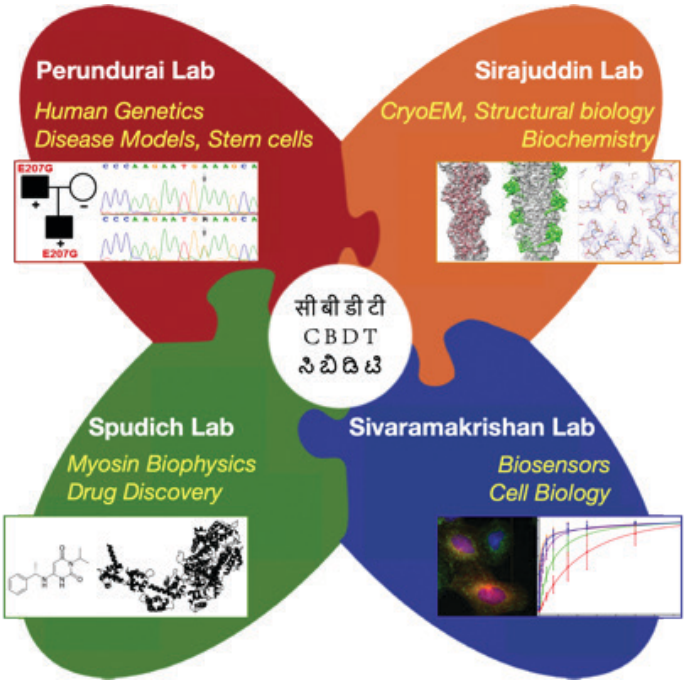
• **Metabolic landscaping by blood cells in *Drosophila***
Lipid center meeting, MPI Dresden, Dresden, December 2019

• **Uncovering metabolic roles of myeloid cells through *Drosophila***
(Invited talk) Gut meeting, NCCS, Pune, January 2020

• **Metabolic landscaping by immune cells of *Drosophila***
Signaling mechanisms in Immune and Glia Function satellite meeting, NCBS, Bangalore, January 2020

04 CBDT

CARDIOVASCULAR BIOLOGY AND DIESEASE THEME



Sivaraj Sivaramakrishnan **James Spudich** **Minhaj Sirajuddin** **Dhandapany Perundurai**

Hypertrophic cardiomyopathy (HCM) is a disease condition that afflicts 1 in 500 individuals worldwide. HCM manifests as the abnormal thickening of heart muscle, resulting in the constriction of ventricle size and consequent reduction in volume of blood pumped by the heart. HCM usually stems from genetic mutations in proteins in cardiac myocytes, the cells that drive heart contraction. While the molecular mechanisms underlying HCM in the North American and European patient populations are at advanced stages of scientific enquiry, the genetic basis of HCM in the Indian subcontinent remains vastly unexplored. Understanding the molecular basis of HCM in India holds the key to customize therapies for an estimated 26 lakh individuals afflicted by this disease. The team of scientists at Cardiovascular Biology and Diseases (CBDT) theme at inStem are focused on dissecting the molecular basis of HCM in the Indian subcontinent, with the goal of translating basic scientific research into the personalized targeting of cardiovascular disease.

04 Cardiovascular Biology and Diesease Theme

The CBDT theme has established an integrated workflow that leverages the groups' expertise to streamline dissection of the molecular basis of HCM in South Indian populations (Figure). This includes (1) the identification of genetic variations in HCM targets such as PKCα (Perundurai); (2) physiological studies using cardiac myocyte cell lines and model organisms (Perundurai); (3) biosensors in cells to map protein interactions (Sivaramakrishnan); (4) high-resolution structural biology and microscopy to study molecules and structures related to heart (Sirajuddin); (5) single-molecule biophysical techniques to probe enzymatic function (Spudich). The goal of the proposed research is to focus the efforts of this interdisciplinary investigator team on identifying and characterizing genetic mutations implicated in HCM in the South Indian patient population. The goal of the proposed research, as shown in the diagram, is to focus the efforts of this interdisciplinary investigator team on identifying and characterizing genetic mutations implicated in HCM in the South Indian patient population.

Therapeutic target for HCM

The classical PKCs (cPKC) are lipid and Ca^{2+}-dependent AGC kinases, which play critical roles in modulating diverse physiological and pathophysiological processes including cardiovascular performance and tumour generation. PKCα is the major classical isoform expressed in the adult human myocardium. It is up-regulated during heart failure, plays a significant role in stimulating downstream ERK1/2 to induce cardiac myocyte hypertrophy, and is associated with heart failure. As a result it has emerged as a potential therapeutic target in the treatment of heart disease. However, there are no known isoform-specific inhibitors for PKCα. To overcome these issues, we had developed a kinase toolbox termed '*systematic protein affinity strength modulation (SPASM)*' to map the protein-protein interaction landscape of PKCα. We broadly utilized this technology to probe GPCR conformation, GPCR-G protein interactions, and the activity state of downstream effectors including adenylyl cyclase and protein kinase C. The modular nature of SPASM sensors is ideally suited for high-throughput drug discovery applications.

Identifying Novel Indian HCM associated mutations

In an ongoing attempt to unravel new candidate genes, exome sequencing in 250 patients with HCM who are negative for known causes was undertaken. Systemic analysis for the presence of pathological variants in these unrelated patients and their family members resulted in the identification of two novel mutations in a gene encoding **PKCα (PRKCA)**, leading to the amino acid changes p.E207G and p.V566L, in two different patients.

Patient-specific induced pluripotent stem cells (iPSCs) model

We have generated iPSCs from patient fibroblasts bearing the E207G PRKCA mutation. iPSCs are differentiated into cardiomyocytes and subsequently purified by cell sorting using the cardiomyocyte-specific cell surface marker SIRPα. The cardiomyocytes differentiated from these patient-derived iPSCs exhibit multiple hallmarks of hypertrophy including cellular enlargement with fetal gene re-expression including ANP and BNP. Using a precision medicine approach, we are in the process of treating these cardiomyocytes with various drugs to rescue the hypertrophic phenotypes

High-resolution structural characterization

With the advent of cryogenic electron microscopy (CryoEM) technique, there is a renaissance in revisiting macromolecules that were previously not amenable for structural characterization using X-ray and NMR approaches. A comparative structural analysis of PKC isoforms with regulatory domains is also lacking in the field. Therefore, we aim to determine high-resolution structure of full-length PKCα and other isoforms using cryoEM single particle reconstruction methods.

In this regard we established methods to purify full-length PKCα from insect cells and baculovirus expression system. Currently we in the process of optimizing grid freezing conditions for cryoEM data collection. Previously we determined cryoEM structures of F-actin bound to small molecule toxins (phalloidin), peptides (lifeAct), proteins (Utrophin) and bundling proteins (nexilin) at near atomic resolution. Using this established structure elucidation pipeline, we will be able to determine high-resolution structures of full-length PKCα, which will enable us to understand the mechanisms of PKC function during HCM.

PUBLICATIONS

Dhandapany Perundurai

• Arif M., Nabavizadeh P., Song T., Desai D., Singh R., Bazrafshan S., Kumar M., Wang Y., Gilbert R.J., Dhandapany P.S., Becker R.C., Kranias E.G., Sadayappan S. (2020) **Genetic, clinical, molecular, and pathogenic aspects of the South Asian-specific polymorphic MYBPC3Δ25bp variant.** *Biophys Rev.*

• Thimmegowda G.G., Mullen S., Sottilare K., Sharma A., Mohanta S.S., Brockmann A., Dhandapany P.S., Olsson S.B. (2020) **A field-based quantitative analysis of sublethal effects of air pollution on pollinators.** *Proc Natl Acad Sci, USA.*

• Mittal A., Rana S., Sharma R., Kumar A., Prasad R., Raut S.K., Sarkar S., Saikia U.N., Bahl A., Dhandapany P.S. (2019) **Khullar myocardin ablation in a cardiac-renal rat model.** *M. Sci Rep.*

• Govindaraj P., Rani B., Sundaravadivel P., Vanniarajan A., Indumathi K.P., Khan N.A., Dhandapany P.S., Rani D.S., Tamang R., Bahl A., Narasimhan C., Rakshak D., Rathinavel A., Premkumar K., Khullar M., Thangaraj K. (2019) **Mitochondrial genome variations in idiopathic dilated cardiomyopathy.** *Mitochondrion.*

• Hauer N.N., Popp B., Taher L., Vogl C., Dhandapany P.S., Büttner C., Uebe S., Sticht H., Ferrazzi F., Ekici A.B., De Luca A., Klinger P., Kraus C., Zweier C., Wiesener A., Jamra R.A., Kunstmann E., Rauch A., Wieczorek D., Jung A.M., Rohrer T.R., Zenker M., Doerr H.G., Reis A., Thiel C.T. (2019) **Evolutionary conserved networks of human height identify multiple Mendelian causes of short stature.** *Eur J Hum Genet.*

Minhaj Sirajuddin

• Kumari A, Kesarwani S, Javoor M.G., Vinothkumar K.R., Sirajuddin M. (2020) **Structural insights into actin filament recognition by commonly used cellular actin markers.** *EMBO J.*

• Kesarwani S., Lama P., Chandra A., Reddy P. P., Jijumon A. S., Bodakuntla S., Rao B. M., Janke C., Das R., Sirajuddin M. (2020) **Genetically encoded live-cell sensor for tyrosinated microtubules.** *Journal of Cell Biology.*

RESEARCH TALKS

Dhandapany Perundurai

• **Functional genomics of children heart disease.**
Indo-US Workshop on Human Diversity and Health Disparities, CSIR-CCMB, Hyderabad, January 2020

Minhaj Sirajuddin

• **Genetically encoded live cell sensor for tyrosinated microtubules.**
(Invited Talk) Microscopy Workshop, ILS, Bhubaneshwar, December 2019

• **Genetically encoded live cell sensor for tyrosinated microtubules**.
(Invited Talk) Molecular Motors Transport & Trafficking Meeting, NBRC, New Delhi, October 2019

Sivaraj Sivaramakrishnan

• ***In cell* Biochemistry – Targeting synergies in dynamic protein ensembles.**
Department of Pharmacology, University of North Carolina, Chapel Hill, NC, Sept 2019

• **Dark side of GPCRs and protein kinases - allosteric regulation through intrinsically disordered regions.**
Department of Pharmacology, UT Southwestern Medical Center, Dallas, Texas, March 2020

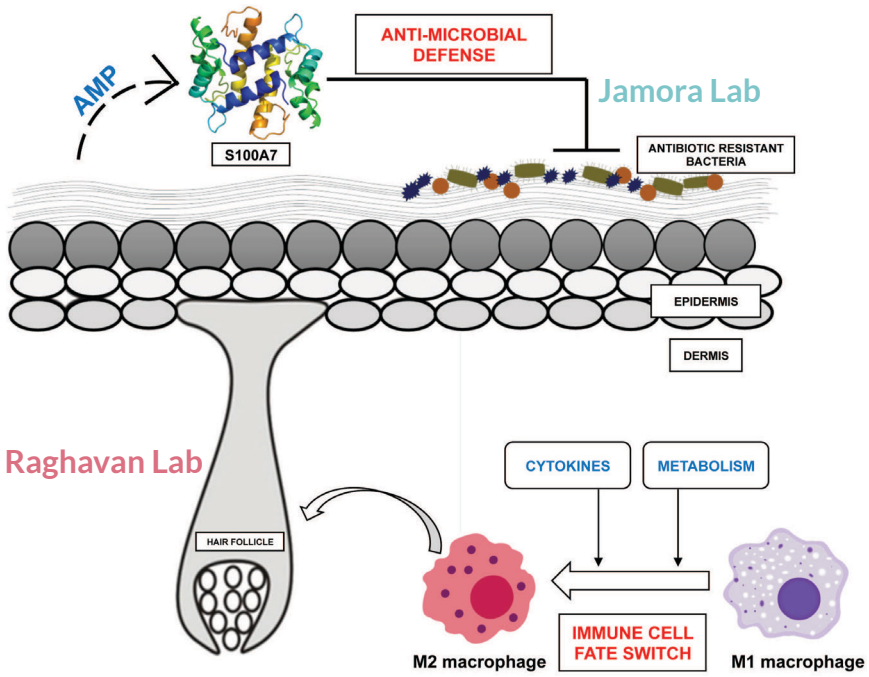
Outreach by Theme Investigators

Minhaj group have created a YouTube video describing how molecular motors are involved in color change in animals, with additional information for DIY style practicum instructions.

Video title: Color change with fish scale melanocytes and DIY instructions
Video link: https://www.youtube.com/watch?v=hyr2lCFF260

05 CITH

CENTRE FOR INFLAMMATION AND TISSUE HOMEOSTASIS



Colin Jamora **Srikala Raghavan**

The Centre for Inflammation and Tissue Homeostasis (CITH) has made significant advances in understanding both the canonical roles as well as emerging new functions of the immune system in tissue development, regeneration, and repair. CITH investigators have coalesced around the use of the mammalian skin as a powerful model system to understand tissue regeneration and repair with the ultimate goal of utilizing this knowledge for therapeutic applications. The skin and its appendages is one of the few organs that constantly regenerates throughout the lifetime of the animal; and owing to its vital role as the body's main barrier from the external environment, has evolved a remarkable capacity to rapidly heal itself when damaged. It is often under-appreciated that the skin is a major depot of cells and proteins associated with the immune system. Moreover, their presence in this organ, is often relegated simply to the need to have an immune defense persistently ready to quickly combat any infection that may enter through the skin, when injury comprises its barrier function. Despite this narrow view of the role of immune cells solely as defenders against pathogens, CITH laboratories are making significant contributions to the growing list of immune cell functions distinct from host-pathogen interaction and into the domain of tissue health and development.

05 Centre for Inflammation and Tissue Homeostasis

The mammalian immune system is classified into two distinct but interrelated systems. The innate immune system, which can be rapidly activated and are the first responders, but are relatively non-specific in what they destroy, and the adaptive immune system, comprising T-cells and B-cells, which are more precise in their targets but require more time to become activated. Recent works at CITH has elucidated how the innate immune response is regulated in the skin and identified its unconventional roles regulating tissue homeostasis and development.

Building upon their work on how inflammation regulates the compartmentalization of the skin into a separate epithelium (epidermis) and mesenchyme (dermis), the Raghavan laboratory has furthered expanded the functional repertoire of macrophages into the realm of regulating hair follicle development. Macrophages generally come in two flavors: 1. The M1 macrophage, which is well-known for its promotion of inflammation, and removal of cellular debris and microbes by 'eating' them (phagocytosis) and 2. The M2 macrophage, the less studied type of macrophages which have emerging roles in tissue repair.

The Raghavan laboratory is revealing not only how M2 macrophages are generated through the changes in cellular metabolism, but has also uncovered an unexpected role for these immune cells in promoting hair follicle growth. The lab is currently exploring the role of both anti-inflammatory drugs as well as metabolic modulators to regulate macrophage function and polarization in skin. The group is also working on delivery systems that administer these drugs to specific skin compartments. The long-term goal of this project is to identify therapeutic interventions for skin disorders such as atopic dermatitis and psoriasis.

Along similar lines of studying the innate immune response, the Jamora laboratory has been focusing on a class of molecules contained in the cells of the epidermis called Antimicrobial peptides (AMPs). These AMPs are stored in the epidermal cells and released upon injury or infection where they can effectively kill bacteria, viruses, and fungi. These peptides are becoming of particular interest because they are capable of eliminating bacteria that are otherwise resistant to antibiotics. The growing list of antibiotic resistant microorganisms is rapidly becoming a global health crisis and therapies to combat these so-called 'superbugs' are desperately needed. In addition to their classical role in killing microbes, AMPs are now also implicated in having important roles in cell proliferation, new blood vessel formation (angiogenesis), and wound healing.

The utilization of the body's own AMPs for controlling all these processes has been limited by the inability to control their release from the cells of the skin. This inability stems from the lack of our understanding on how AMP secretion is normally regulated. The Jamora laboratory teamed up with scientists from Unilever Ltd in Bangalore to uncover the process by which AMPs are released from the cell and use this knowledge to develop products that would be useful in fending off infection by antibiotic resistant bacteria. Their collaboration resulted in the discovery that the same cellular machinery that initiates the wound healing response in the skin is also responsible for the release of the stores of AMPs from the cell. Identification of these cellular proteins that determine when AMPs are secreted are now being developed as therapeutic targets to control this process.

PUBLICATIONS

Colin Jamora

• Bhatt T., Bhosale A., Bajantri B., Mathapathi M.S., Rizvi A., Scita G., Majumdar A., and Jamora C. (2019) **Sustained secretion of the Antimicrobial peptide S100A7 is dependent on the downregulation of caspase-8.** *Cell Reports.*

Srikala Raghavan

• Bhattacharjee O., Ayyangar U., Kurbet A.S., Ashok D., Raghavan S. (2019). **Unraveling the ECM-Immune Cell Crosstalk in Skin Diseases.** *Frontiers in Cell and Developmental Biology*.

• Krishna S. , Yim D.G., Lakshmanan V., Tirumalai V., Koh J.L., Park J.E., Cheong J.K., Low J.L., Lim M.J., Sze S.K., Shivaprasad P., Gulyani A., Raghavan S., Palakodeti D., DasGupta R. (2019). **Dynamic expression of tRNA-derived small RNAs define cellular states.** *EMBO Reports.*

RESEARCH TALKS

Colin Jamora

• Harnessing the Body's Innate Immune Defense to Combat Infection.
BMS College of Engineering for Women International Microbiology Webinar, Bangalore, 2020.

• Understanding the Wound Healing Program.
St. Joseph College, Department of Microbiology, Bangalore, India, 2020.

• Understanding the Wound Healing Program.
IDEA 2020 Conference. Bangalore, India.

• Antimicrobial peptides in the skin.
Skin Immunity Workshop, Jarkarta, Indonesia 2019.

• Mechanical and Epigenetic Regulation of Wound Healing.
Mechano-developmental Biology Meeting, Coorg, India 2019.

• Understanding the Wound Healing Program and Allied Diseases.
Indian Institute of Technology (IIT) – Hyderabad 2019.

Srikala Raghavan

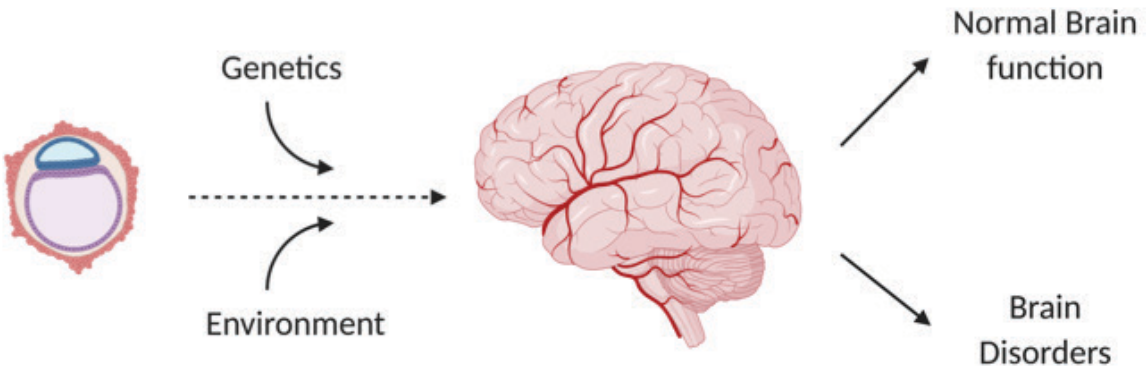
• Delineating the Immune-Epithelial Crosstalk in Embryonic Skin.
Japanese Society for Developmental Biology, May 2019.

• Junctional Instability can Override Intrisnsic Quiescence of Bulge Stem Cells.
Gordon Research Conference on Epithelial Differentiation and Keratinization, Newery Maine, July 2019.

• Getting Under our Skin.
Under the Raintree Women's Cultural Festival, November 2019.

06 BDDM

BRAIN DEVELOPMENT AND DIESEASE MECHANISMS



During development specific cells in the human embryo divide and differentiate to give rise to the adult human brain. These developmental events are influenced by both genetic and environmental factors (Image created with BioRender.com)

Raghu Padinjat **Sumantra Chattarji** **Bhavana Muralidharan**

Brain disorders are a global health challenge with the vast majority having no effective treatments. Despite obvious differences in their clinical presentation, many of these disorders appear to share molecular, cellular, and circuit mechanisms. Our vision is to accelerate the discovery of these mechanisms and thus facilitate the delivery of effective therapeutics for these disorders.The Brain Development and Disease Mechanisms theme at inStem seeks to understand the development of the mammalian brain at multiple scales of organization – from molecules to brain circuits and behaviour. In particular, we are interested in exploring cell-cell interactions and sub-cellular processes that underpin normal brain development and physiology that may result, when altered, in brain diseases. Such processes include but are not limited to membrane organization, translational control, chromatin regulation, RNA mediated mechanisms, and related processes. The work within this theme seeks to link basic biological mechanisms to aspects of human brain diseases to inform on the development of novel diagnostic and therapeutic options. The theme adopts a multi-disciplinary approach to understanding brain function through discovery, biology and disease modelling using modern stem cell technology including organoids, human genomics and gene editing technology, imaging and sophisticated physiological analysis. The scientific strategy of the theme links these technologies to clinical cohorts of relevant human brain diseases with associated biorepository resources as well as suitable animal models for in vivo analysis. A number of such resources have been attached including genomic data set, iPSC collections and clinical data sets (https://ncbs.res.in/adbs/home) and facilities for genetic and physiological analysis in rodent models (https://ncbs.res.in/research-facilities/acrc and https://www.instem.res.in/bddm/cns).

06 Brain Development and Diesease Mechanisms

The Centre for Neurodevelopmental Synaptopathies (CNS), led by Prof. Sumantra Chattarji (NCBS), is a DBT supported, international collaborative program between inStem, NCBS, and the University of Edinburgh. Its goal is to accelerate the discovery and delivery of effective therapeutics for neurodevelopmental disorders specifically Autism Spectrum Disorders (ASD)/ Intellectual Disability (ID). To this end, we combine a range of expertise in several fields of neurobiology including synaptic function and plasticity, human stem cells and cognition-behaviour. The program has established novel models and assay platforms for human ASDs 'in a dish' as well as protocols for the generation of functional cortical neurons, astrocytes, microglia, and oligodendrocytes. Our recent efforts have shown that glia play a pivotal role in the brain rather than being just supporting structures located around neurons. In diseased conditions, glia can be injurious or neuroprotective to neurons. How glia in ASD disease models affects overall brain function remains largely unexplored. Hence, a key focus of our current work is to examine cell autonomous versus non-autonomous effects of ASD/IDs on neurons and astrocytes. A cell culture system was established to derive mature functional astrocytes following cues from developmental biology and further co-cultured with neurons to study the non-cell autonomous effects. Using whole-cell patch clamp recordings, we found that human iPSC derived neurons fire bursts of action potentials. Control (healthy) neurons co-cultured with control astrocytes exhibited low burst frequency and higher burst duration. In contrast, Fragile X Syndrome (FXS) neurons co-cultured with FXS astrocytes displayed significantly higher frequency of bursts, but of lesser duration. Strikingly, when control neurons were co-cultured with FXS astrocytes the bursting profile of the control neurons resembled that of the FXS – with high burst frequency; and shorter burst duration. Consequently, when FXS neurons were co-cultured with control astrocytes the aberrant bursting activity was 'rescued' to resemble the healthy neurons with low burst frequency and longer burst duration. Thus, the genotype of astrocytes determines the electrophysiological phenotype of neurons. These experiments have identified a novel cellular target – astrocytes – that had not received attention in earlier research.

Accelerator Program for Discovery in Brain Disorders using Stem Cells (ADBS) Severe mental illness (SMI) are a major source of disability in young adults with about 2– 3% of the population at risk for developing these disorders both in India and across the world. These disorders are recognized as one of the major non-communicable diseases (NCD) and a significant contributor to morbidity as articulated by the World Health organization's New Delhi call for action on combating NCDs in India. Given this huge disease burden, the development of novel ways to diagnose and treat mental illness will have important positive social and economic benefits. To achieve this goal, there is a pressing need to understand the mechanistic basis of these disorders; such discovery could form the basis for the development of novel diagnostic and therapeutic approaches. The ADBS program, studies five major forms of SMI namely schizophrenia, bipolar disorder, obsessive compulsive disorder, substance dependence and dementia; that are thought to have a neurodevelopmental origin as well as an inherited basis. However, despite their high heritability, to date few genetic correlates that account for the high heritability have been identified. In order to study these disorders, in collaboration with Department of Psychiatry, National Institute for Mental Health and Neurosciences (NIMHANS), the National Centre for Biological Sciences (NCBS), and inStem, the program has assembled a prospective cohort of patients with a strong family history of SMI. The ADBS program is pursuing three distinct but complementary lines of analysis on these families: The families are being clinically characterized in depth to understand changes in structure and function at multiple levels of brain organization; they are being followed over a period of 20 years at three year intervals in order to define the temporal development of disease through regular and detailed

clinical phenotyping. We have established induced pluripotent stem cell lines (iPSC) and neural stem cell lines from affected individuals in these families and unaffected controls. These lines are being used to generate cellular models and mechanistic aspects of cellular neurobiology that lead to disease. Next Generation Sequencing and family-based bioinformatics analysis is being used to uncover the genetic basis of SMI. The multiple types of data generated by the ADBS program have been assembled into an integrated database to facilitate the application of sophisticated methods of data analysis to uncover new disease biology. The stem cell lines and other biomaterials are part of a biorepository that will allow the sharing and use of this resource to drive discovery biology in the area of SMI. The ADBS program has instituted mechanisms to facilitate the sharing of data and resources generated through its activities.

Control of cerebral cortex development in health and disease

The cerebral cortex is the seat for all higher-order functions in the brain namely learning, memory, language, and consciousness. For a functional cerebral cortex in adulthood, a diverse number of neurons and glia are to be produced adequately and wired up accurately during development. Chromatin level regulations play a very crucial role in building the neural network. Several neurodevelopmental disorders stem from mutations or perturbations to the process of chromatin regulation. Yet our molecular understanding of these mechanisms is very poor in the developing brain.

Bhavana Muralidharan's lab aims to understand chromatin-level control of brain development in health and in disease. At the fundamental level, we would like to explore the crosstalk between different chromatin complexes and tease out interactions at the molecular level to understand the fine-tuning of gene expression of downstream targets. These efforts will bring in-depth molecular insights into the dynamicity of the developing brain. To achieve this, a mouse model of cortical development is used to define detailed molecular mechanisms of individual genes of interest. The lab extends its work to understand cellular and molecular mechanisms of human neurodevelopmental disorders such as schizophrenia (SZ) and bipolar disorder (BPD). Mental illnesses are thought to be neurodevelopmental in origin but are poorly understood, in part due to the lack of appropriate models that adequately recapitulate the human disease. To overcome this problem, the lab utilises iPSC lines generated by the ADBS program from clinically dense families with SZ and BPD. Using 2D and 3D cerebral organoid cultures and CRISPR-Cas gene editing, the cellular and molecular origins of neuropsychiatric disorders is modelled in a dish.

PUBLICATIONS

CNS

• Chakraborty P., Datta S., McEwen B.S., Chattarji S. (2020) **Corticosterone after acute stress prevents the delayed effects on the amygdala.** *Neuropsychopharmacology.*

• Das Sharma S. *et al.* (2020) **Cortical neurons derived from human pluripotent stem cells lacking FMRP display altered spontaneous firing patterns.** *Mol Autism.*

• Ghosh Dastidar S., Das Sharma S., Chakraborty S., Chattarji S., Bhattacharya A., Muddashetty R.S. (2020) **Distinct regulation of bioenergetics and translation by group I mGluR and NMDAR.** *EMBO Rep.*

• Das R., Sengupta T, Roy S., Chattarji S., Ray J. (2020) ***Convolvulus pluricaulis* extract can modulate synaptic plasticity in rat brain hippocampus.** *Neuroreport*.

• Venkatasubramani J.P., Subramanyam P., Pal R., Reddy B.K., Srinivasan D.J., Chattarji S., Iossifov I., Klann E., Bhattacharya A. (2020) **N-terminal variant Asp14Asn of the human p70 S6 Kinase 1 enhances translational signaling causing different effects in developing and mature neuronal cells.** *Neurobiol Learn Mem.*

• Mastro T.L., Preza A., Basu S., Chattarji S., Till S.M., Kind P.C., Kennedy M.B., (2020) **A sex difference in the response of the rodent postsynaptic density to synGAP haploinsufficiency.** *Elife.*
• Yasmin F. *et al.* (2020) **Stress-induced modulation of endocannabinoid signaling leads to delayed strengthening of synaptic connectivity in the amygdala.** *Proc Natl Acad Sci U S A.*
• Dwivedi D. *et. al.* (2019) **Impaired reliability and precision of spiking in adults but not juveniles in a mouse model of Fragile X Syndrome**. *eNeuro.*
• Patel D. *et. al.* (2019) **Rodent models of social stress and neuronal plasticity: relevance to depressive-like disorders.** *Behav Brain Res.*
• Asiminas A. *et. al.* (2019) **Sustained correction of associative learning deficits following brief, early treatment in a rat model of Fragile X Syndrome.** *Science Translational Medicine*.
• Dongaonkar B. *et. al.* (2019) **Effects of Unipolar versus Bipolar Depression on Episodic Memory Updating.** *Neurobiology of Learning and Memory.*
• Chakraborty P., Chattarji S. (2019) **Interventions after acute stress prevent its delayed effects on the amygdala.** *Neurobiol Stress.*
• Bowling *et al.* (2019) **Altered steady state and activity-dependent *de novo* protein expression in fragile X syndrome: Implications for biomarker discovery.** *Nature Comms.*

ADBS

• Someshwar A. *et al*. (2020) **Adverse childhood experiences in families with multiple members diagnosed to have psychiatric illnesses.** *Aust N Z J Psychiatry.*
• Paul P., Iyer S., Nadella R.K., Nayak R., Chellappa A.S., Ambardar S., Sud R., Sukumaran S.K., Purushottam M., Jain S., Viswanath B. (2020) **Lithium response in bipolar disorder correlates with improved cell viability of patient derived cell lines.** *Sci Rep.*
• Sharma Y., Saha S., Joseph A., Krishnan H., Raghu P. (2020) ***In vitro* human stem cell derived cultures to monitor calcium signaling in neuronal development and function**. *Wellcome Open Res.*
• Mukherjee O. et. al. (2019) **Making NSC and Neurons from Patient-Derived Tissue Samples.** *Methods Mol Biol.*
• Raghu P., Joseph A., Krishnan H., Singh P., Saha S. (2019) **Phosphoinositides; regulators of nervous system function in health and disease.** *Fron. Mol. Neurosci*.
• More R.P., Rao M., Mukherjee O. (2019) **Genomic-QC: large-scale genomic data mining to assess the q, Banauality of HIPSC lines.** *Cell & Gene Therapy Insights*.

Bhavana Muralidharan

• Muralidharan B. (2020) **Understanding brain development – Indian researchers' past, present and growing contribution**. *The International Journal of Developmental Biology*.

RESEARCH TALKS

Bhavana Muralidharan

• Building the brain: Role of transcription factors and chromatin regulators.
(Invited talk) Heidelberg University, Germany, December, 2019.
• Building the brain: Role of transcription factors and chromatin regulators.
No Garland Neuroscience Meeting, IISER Pune, January, 2020.

Raghu Padinjat

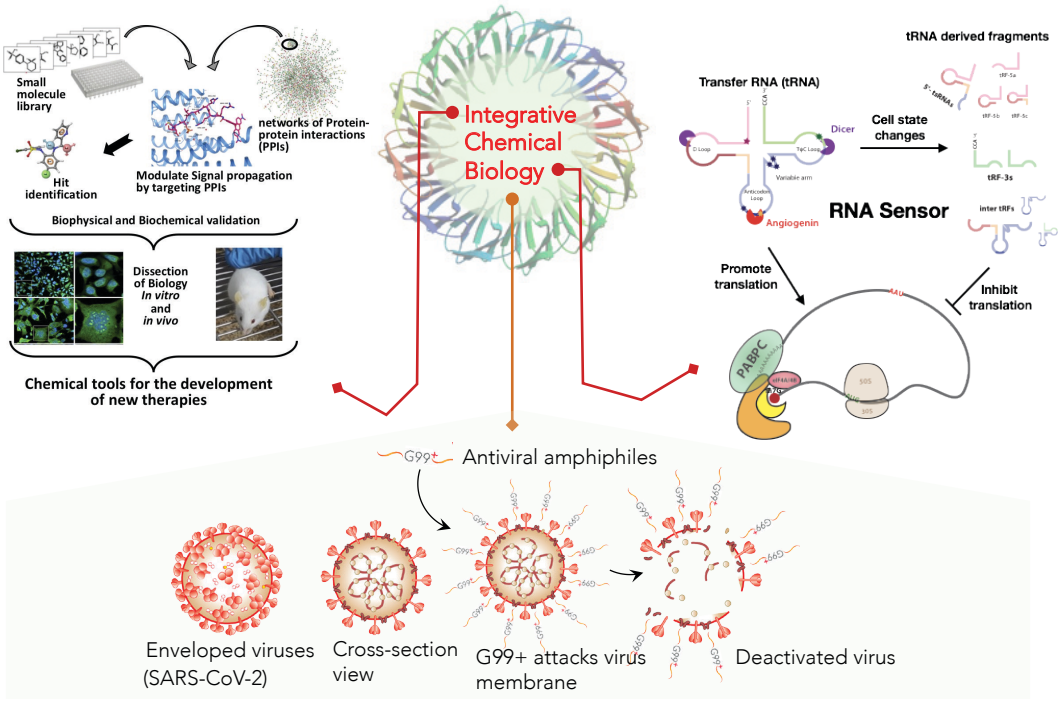
• Discovery biology of neuropsychiatric syndromes.
No Garland Neuroscience Meeting, IISER Pune, January, 2020.

Sumantra Chattarji

• Autism and 'Astrology': New insights from recordings in human brain cells.
(Invited talk) NATCONPH 2020, February 2020.
• Autism and 'Astrology': New insights from recordings in human cortical neurons.
IISER Mohali, December 2019.
• Autism and 'Astrology': New insights from recordings in human brain cells.
6th International Conference and 16th National Workshop 2019 Inauguration, November 2019.
• Fear and Fragile X Syndrome: 'Alternative facts' from the amygdala.
• EBPS Biennial Meeting, Braga, Portugal, August 2019.
• Plenary Lecture, Dutch Neuroscience Meeting, Lunteren, Netherlands (2019)
•Spring Hippocampal Research Conference, Taormina, Sicily, Italy (2019)
• Proteins and circuits in memory.
Copenhagen, Denmark (2019)

07 ICB

INTEGRATIVE CHEMICAL BIOLOGY



Ashok Venkitaraman **Praveen Kumar Vemula** **Dasaradhi Palakodeti**

Chemical Tools for Biological Applications

The systematic understanding of complex biological systems altered in human diseases remains a major challenge to the future development of new approaches for disease diagnosis or therapy. The Integrative Chemical Biology theme at inStem seeks to develop an integrated platform to address this challenge, by combining the understanding of fundamental processes that regulate cellular behaviour under altered cellular states, with the ability to modulate these processes using selective chemical probes. The Program on Chemical Biology and Therapeutics, a foundational program in this theme has been described in greater detail elsewhere in the report. The program has pioneered approaches for the systematic understanding of complex biological systems altered in human diseases in order to facilitate the future development of new approaches for disease diagnosis or therapy. The key outcomes of the other groups in this theme are highlighted below.

07 Integrative Chemical Biology

The Palakodeti lab is working on RNA sensors and has identified a novel class of small RNA molecules derived from transfer RNA (tRNAs) known as tRNA derived fragments (tRFs) or tRNA derived small RNAs (tsRNAs). The tRNAs are adaptor molecules that deliver amino acids to the growing peptide chain during protein synthesis and are also processed into small RNAs of varying sizes. These regulate proteins synthesis under altered cellular states and stress conditions. The group's work highlighted tRNAs as sensors of changing cellular metabolic states, leading to the fragmentation of the tRNA into tRFs, with consequences for regulation of protein synthesis. The group has shown that tRNAs were processed into tsRNA within 48hrs of treatment of mouse embryonic stem cell (mESC) with retinoic acid leading to differentiation of mESC to neural progenitors. Blocking the function of tsRNA using antisense oligos resulted in deficits in stem cell differentiation. The tsRNA upregulated during differentiation, bind to RNA binding proteins such as YBX1 and IGF2BP1 and inhibit translation initiation of specific transcripts critical for maintenance of stemness leading to differentiation (Krishna et al. 2019). The tsRNAs are also expressed in the regenerating model system, planaria. The stem cells and the regenerating tissue of the planarian showed expression of varying sizes of tRFs at different stages during regeneration, suggesting a potential role in the regeneration of specific tissues. Further, work in mESC and planaria show that the tRNAs could potentially be processed by endonucleases such as Angiogenin, Piwi and Dicer. However, not all tRNAs are processed into tRNA derived fragments and mechanism[s] that regulate the specificity in tRNA processing remain to be identified. The study showed that the depletion of methionine in mESC culture, lead to the generation of tsRNA derived from specific tRNA, which inhibit the translation of pluripotency genes leading to the differentiation of mESC. Thus, tRNAs could act as sensors of metabolic states, triggering the generation of tsRNA critical for cell state changes. The study raises the possibility of using tsRNAs as a means to achieve specific cell states. Since tsRNAs are upregulated in the primary tumours and their levels are significantly reduced during metastasis, the use of tsRNA as biomarkers for detection of cancers and for therapeutic intervention are avenues of future investigation.

The Vemula lab harnesses the power of chemical biology tools to solve unmet clinical needs. The laboratory has been developing low-molecular-weight amphiphilic molecules that can self-assemble to form a wide range of nanomaterials. The lab has focused on developing low-molecular-weight molecules as new chemical entities to treat alcoholic liver disease by repairing the gut barrier dysfunction by overexpressing the tight junction proteins and have demonstrated efficacy in preclinical animal models. Additionally, a substantial effort has been directed towards developing innovative polymeric-chemical-scaffolds to improve the shelf-life of stored blood. The charged-scaffolds developed can scavenge a wide range of damage-associated molecular patterns (DAMPs) such as extracellular DNA, histones, lipids, and iron produced by stored blood. The group has demonstrated that through the systematic scavenging of DAMPs, both the quality of transfused blood and critically, shelf-life/storage time show significant improvement. As a contribution to the COVID-19 pandemic, the lab has developed a germicidal-coated fabric that can be stitched into facemasks and other personal protective equipment (PPE). Upon contact, the chemical can deactivate viruses and bacteria. The chemical has been tailor-made based on Quaternary Ammonium Salt backbone and is designed to rupture the membrane of the bacteria and enveloped viruses. When coated on cellulose-based fabrics, the chemical is irreversibly linked to the cloth. This novel class of quaternary ammonium salts, when immobilized on the fabric, can efficiently kill bacteria and viruses. The germicidal fabric has shown a 99.99% kill rate (3 log reduction) against a wide range of enveloped viruses, such as lentivirus, Sendai virus, and human respiratory viruses, including COVID-19 causing coronavirus (SARS-CoV-2) and influenza virus (H1N1 flu) as well as gram-negative and gram-positive bacteria.

PUBLICATIONS

Dasarathi Palakodeti

• Ganesan S, Palani HK, Lakshmanan V, Balasundaram N, Alex AA, David S, Venkatraman A, Korula A, George B, Balasubramanian P, **Palakodeti D**, Vyas N, Mathews V. Stromal cells downregulate miR-23a-5p to activate protective autophagy in acute myeloid leukemia. ***Cell Death Dis.*** 2019 Sep 30;10(10):736.

• Sarkar A, Mukundan N, Sowndarya S, Dubey VK, Babu R, Lakshmanan V, Rangiah K, Panicker MM, **Palakodeti D**, Subramanian SP, Subramanian R. Serotonin is essential for eye regeneration in planaria Schmidtea mediterranea. ***FEBS Lett.*** 2019 Nov;593(22):3198-3209.

• Krishna S, Yim DG, Lakshmanan V, Tirumalai V, Koh JL, Park JE, Cheong JK, Low JL, Lim MJ, Sze SK, Shivaprasad P, Gulyani A, Raghavan S, **Palakodeti D**, DasGupta R. Dynamic expression of tRNA-derived small RNAs define cellular states. ***EMBO Rep.*** 2019 Jul;20(7):e47789.

Praveen Vemula

• Mukherjee D, Rakshit T, Singh P, Mondal S, Paul D, Ahir M, Adhikari A, Puthiyapurayi TP, **Vemula PK**, Senapati D, Das R, Pal SK. "Differential flexibility leading to crucial microelastic properties of asymmetric lipid vesicles for cellular transfection: A combined spectroscopic and atomic force microscopy studies" ***Colloids Surf B Biointerfaces*** 2020, *in press.*

• Singh R, Chandrashekharappa S, **Vemula PK**, Bodduluri H, Jala VR. "Microbial metabolite Urolithin B inhibits recombinant human monoamine oxidase A enzyme" ***Metabolites*** 2020, *10*, 258.

• Ghate V, Chaudhari P, Maxwell A, Lewis S, Pahal S, **Vemula PK.** "Rethinking Exosomes: From cell-to-cell courier services to individualized medicines" ***AAPS*** 2020, June. (Cover Feature) Invited Review in Magazine

• Badnikar K, Jayadevi SN, Pahal S, Sripada S, Nayak MM, **Vemula PK**, Subrahmanyam DM "Generic molding platform for simple, l ow-cost fabrication of microneedles" ***Macromol. Mater. Eng.*** 2020, 2000072. (Cover Feature)

• Sunnapu O, Ravipati P, Srinath P, Kalita S, Bhat PP, Harshitha SR, Sekar K, **Vemula PK,** Mahato M. "Design of cationic amphiphiles for generating self-assembled soft nanostructures, micelles, and hydrogels" ***Bull Mater. Sci.*** 2020, *43*, 172.

• Dhayani A, Kalita S, Mahato M, Srinath P, **Vemula PK.** "Biomaterials for topical and transdermal drug delivery in reconstructive transplantation" ***Nanomedicine*** 2019, *14*, 2713-2733.

• John G, Nagarajan S, Silverman J, **Vemula PK,** Pillai CKS. "Natural monomers: A mine for functional and sustainable materials – Occurrence, chemical modification and polymerization" ***Prog. Polym. Sci.*** 2019, *92*, 158-209.

RESEARCH TALKS

Dasaradhi Palakodeti

• Translation regulators in stem cell function and regeneration. At IISEWR Mohali, April 2019

• Dissect Translation regulatory mechanisms critical for stem cell function and regeneration. At IISc molecular biophysics department April, 2019.

• Regenerative and stem cell model to study ribosome biogenesis associated diseases". At the IBMF Symposia held at CMC Vellore, Feb 2020

Praveen Vemula

• Disease-responsive biomaterials for biomedical applications. Indo-US Conference, IIT (BHU), Varanasi, Feb 2020.

• Chemical technologies to prevent pesticide-induced occupational hazard. International Conclave on Occupational Health-2020, Mumbai, Jan 2020.

• Innovative biomaterials for protecting transplanted allografts. The 5th International Organ Protection Conference, Hangzhou, China, Nov 2019

PATENTS:

Badnikar KA, Nataraja Jayadevi S, Pahal S, Dhayani A, **Vemula PK**, Mathew J, Nayak MM, Narasimhaiah Subramanyam D. "Hollow microneedle device" India Provisional Application Number: 201941050005
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The Program on Chemical Biology and Therapeutics

Vadiraj Kurdekar, Saranya Giridharan, Jasti Subbarao, Mamatha B. Nijaguna, Jayaprakash Periasamy, Sanjana Boggarama, Amol V. Shivange*, Gayathri Sadasivam*, Muralidhara Padigaru*, Vijay Potluri*, Ashok R. Venkitaraman*, Kavitha Bharatham*. "Structure-guided synthesis and evaluation of small molecule inhibitors targeting protein-protein interactions of BRCA1 tBRCT domain" ***ChemMedChem*** (2019) *Senior authors

08 TIGS-CI

TATA INSTITUTE FOR GENETICS AND SOCIETY-CENTRE AT INSTEM

Suresh Subramani **Baskar Bakthavachalu** **Venkat Sresty Tavva** **Sonia Sen**
Farah Ishtiaq **Anirudha Lakshminarasimhan**

Recent advances in genetics have revolutionized our understanding of diseases and our ability to mitigate them. At TIGS-CI, we use these advances to understand and address the most pressing issues in healthcare and food security today.

08 Tata Institute for Genetics and Society-Centre at InStem

Understanding vector-borne diseases

India's burden of vector borne diseases is considerable. Yet, little is known about the distribution and seasonal occurrences of the vectors, their disease-carrying capacities across India or blood-feeding behaviour of female mosquitoes, which is central to disease transmission. At TIGS-CI we take a wholistic approach to addressing these lacunae in our understanding and towards building resources at inStem, as well as research capacity. We investigate the biology, neurobiology, behaviour and biogeographic distribution of the two major vectors of malaria and dengue, *Anopheles stephensi and Aedes aegypti*. We study the capacity to transmit disease while designing molecular effectors that prevent disease transmission. We anticipate that this integrative approach of studying mosquito population prevalence, diversity, niche overlap, insecticide resistance and behaviour will develop a deeper understanding of the vectors and more effective, informed and innovative strategies for reducing disease burden.

Developing rice varieties that can overcome biotic and abiotic stresses

India faces serious food shortages. The Global Hunger Index 2018 ranks India at 103 out of 119 countries. According to the Food and Agriculture Organisation of the UN, about 15% of the people in India do not have enough to eat, while an astounding 40% of our agricultural productivity is estimated to be lost to diseases and pests. This, coupled with a burgeoning population, shrinking land use due to urbanization, and a more lucrative export market, will pose severe food security issues for India in the coming decades. While genetic enhancement of rice through breeding is widely adopted, combining this with incorporating appropriate alleles with new genetic technologies can further accelerate crop improvement. At TIGS-CI, we seek to improve local rice varieties *(Oryza sativa L.)* by stacking desirable traits that can withstand different agroclimatic conditions. Successful development of such rice lines will help to greatly reduce crop losses, benefit agriculturists, and assuage food insecurity.

Understanding and mitigating antibiotic resistance in bacteria

Anti-microbial resistance (AMR), is a rising threat with over 700,000 lives lost each year. This, combined no discoveries of new antibiotics, has led the WHO to call AMR an urgent global priority. At TIGS-CI, we collaborate with Amrita University to investigate the causes of AMR and find ways to reverse it. Our approach involves mapping the genomic loci that confer multi-drug resistance in nosocomial bacterial strains, such as Pseudomonas aeruginosa. We then identify naturally-occurring bacteriophages from our environmental samples that can infect these resistant bacteria. These phages, if lysogenic, can then either be used to neutralize the bacteria or be used to deliver gene-editing machinery to convert the loci from resistant to sensitive.

Understanding and mitigating hematopoietic conditions.

Blood cell diseases, such as sickle cell disorders and thalassemias, disproportionately affect the poor and tribal populations in India. With over 40 million estimated carriers, a bulk of the non-communicable disease burden in India is attributed to blood disorders like hemoglobinopathy and thalassemia. At TIGS-CI we seek to develop stem cell therapies for genetic disorders of the blood. We use novel reporter embryonic stem (ES) cell lines and human pluripotent stem cells (PSCs) to establish hematopoietic progenitors for disease modelling and gene-editing in human blood stem cells. Using this approach, we will target disease causing loci, such as the beta-globin gene, for therapy.

In summary at TIGS-CI we address the most pressing needs of our society from the pivot of genetics. Ours is a unique experiment in Indian science – we are supported by philanthropic funding and are embedded in an intellectually vibrant campus. Our development in the short time of our existence demonstrates that this new model of research in India should be emulated widely.

PUBLICATIONS

• Nandakumar M. and Ishtiaq F. (2020). **Genetic drift and bottleneck do not influence diversity in toll-like receptor genes at a small spatial scale in a Himalayan passerine.** Ecology & Evolution (in Press).

• Ishtiaq F and Renner S. (2020) **Bird Migration and Vector-borne parasites transmission.** (Book Chapter) Diego Santiago-Alarcon and Alfonso Marzal (Eds): Avian malaria and related parasites in the tropics, 978-3-030-51632-1, 470677_1_En, (16). (in press)

• Guichard A, Haque T, Bobik M, Xu X-R S, Klanseck C, Kushwah RBS, Berni M, Kaduskar B, Gantz VM & Bier E. (2019). **Efficient allelic-drive in Drosophila**. Nature Communications, 1640.

RESEARCH TALKS

Baskar Bakthavachalu

• A juggling act by intrinsically disordered regions assisted mRNP assembly between memory and neurodegeneration
TIFR, Hyderabad, April 2019

Farah Ishtiaq

• Fine-scale ecology and population genetics of Culicoides tainanus in high elevation environment
Indian Society for Evolutionary Biologists, JNCASR, Bangalore, Oct 2019.

• Fine-scale population genetic structure of *Aedes aegypti* and its association with Dengue incidence
Symposium on flavivirus genomic exploratory surveys in vector populations either/and in India and Africa, NCBS, Bangalore Sept 2019.

• The Role of Bird Movement, Hypoxia, Immunity and Climate Change on Malaria Transmission
Plenary talk in Avian Biology Symposium, IISER Tirupati, Dec 2019

Sonia Sen

• Neural stem cell and their chromatin landscapes shape neural diversity in *Drosophila*.
Invited Talk, The Institute of Mathematical Sciences, Chennai, June 2019

• Generating neural diversity by integrating spatial and temporal cues within neural stem cells.
Asia Pacific *Drosophila* Research Conference, Jan 2020.

Venkata Sresty Tavva

• CRISPR/Cas: New genetic tools for crop improvement.
Emerging Trends in Plant Science Research 2020, Department of Botany and Biotechnology, Ravenshaw University, Cuttack, Mar 2020.

• Shift towards New Breeding Technologies: CRISPR/Cas-mediated Genome Editing.
Invited Talk. Institute of Forest Genetics and Tree Breeding (IFGTB), Coimbatore, Feb 2020

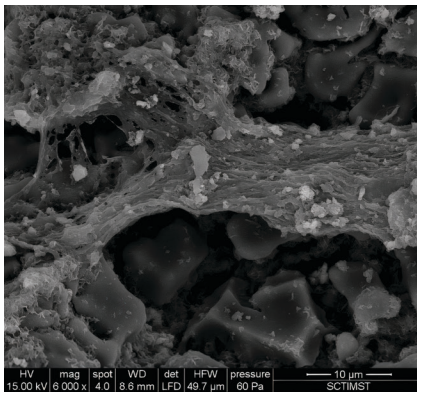
Suresh Subramani

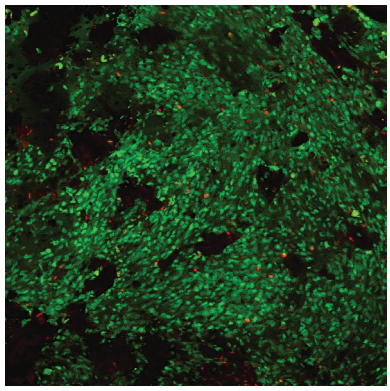
• Should we shoot the deadliest messenger on the planet or disarm them?
India Science Festival, IISER, Pune, Jan 2020.

• Harnessing new genetic technologies for vector control in healthcare.
ICGEB, New Delhi, Aug 2019.

09 CSCR

CENTRE FOR STEM CELL RESEARCH, CMC VELLORE

a. 

b. 

Tissue engineered bone at day 8 of culture: a. SEM image showing a band of clumped mesenchymal stem cells seeded on hydroxyapatite scaffold with good to excellent scaffold and cell to cell interaction; b. live dead assay showing more than 90% cell viability (green) on cell-seeded construct with few dead cells shown in red.

Alok Srivastava **Shaji R Velayudhan** **Mohankumar K Murugesan** **Srujan Marepally**
Sanjay Kumar **Vrisha Madhuri** **Sunil Martin** **Sarvanabhavan Thangavel**

The Centre for Stem Cell Research (www.cscr.in) continues to focus on translational research in cell and gene therapy towards regenerative medicine to bring stem cell science and other novel therapies to the management of patients with unmet needs. The concept of teams working on specific themes through multidisciplinary collaborations is being further enhanced to move closer to this goal. Described on the next page are very brief outlines of the major thrust thematic areas of research at CSCR. Three thematic research programs in multi-individual, multi-disciplinary, and multi-institutional programs are described on the next page.

09 Centre for Stem Cell Research, CMC Vellore

Musculoskeletal Regeneration

This program is coordinated by Vrisha Madhuri with a large team of clinical and basic scientists including several external collaborators. This group aims to develop novel therapies to address unmet needs of patients with bone, cartilage and muscle disorders. The major focus is on clinical translation related to physis, articular cartilage, and bone regeneration. For articular cartilage regeneration, small and large animal studies have been completed with differentiated Mesenchymal stem cells (MSCs) with either growth factors or miRNA on indigenous scaffolds with successful outcome (DST). There is a new focus on using biomolecules on scaffold for regeneration with in vitro studies completed and ongoing large animal studies for segmental bone defect and osteochondral defects (Indo-Danish, DBT). The continued follow up for pilot human physeal regeneration with culture expanded autologous chondrocytes has shown success at 6 years and patient recruitment for phase 1 clinical trial is under progress (DHR). This group has also achieved success in physeal regeneration using hydrogel scaffolds in large animal model. A first of its kind pilot study on human bone defect regeneration study with tissue engineered bone has been completed with a follow up of 2.5 to 4.5 years and further preclinical work is ongoing in the area of bone regeneration using biomolecules. A phase I/II clinical trial, Boost to Brittle Bones, has been initiated in collaboration with Karolinska Institutet, Sweden for the treatment of osteogenesis imperfecta (OI) using fetal liver mesenchymal stem cells (Indo-Swedish, DBT); a parallel study is being conducted for screening genetic heterogeneity in children with OI (ICMR). A new pilot study for the treatment of urinary incontinence using autologous muscle derived cells has been approved (ICMR). Under international collaboration, the work on non-invasive manipulation of physeal cartilage and muscle derived stem cell for anal sphincter repair continues.

Gene Therapy

A major focus of research at CSCR is on gene therapy. Our goal is to capitalize on the recent advances in the world towards gene therapy of monogenic haematological disorders and make them possible for patients in India. Several scientists and physicians are involved with this work which is coordinated by Alok Srivastava (AS) and includes R V Shaji (RVS), Saravanabhavan Thangavel (ST), Mohankumar Murugesan (MM) and Srujan Marepally (SrM) at CSCR and several other faculty from CMC, Vellore as well as many external collaborators.

Haemophilia: Two clinical trials for haemophilia A and B are being initiated at CSCR / CMC, Vellore using two different technologies. More details on these are provided in the NAHD section of the report. To explore other options for gene transfer technologies for haemophilia, work is ongoing for developing a novel ex-vivo gene therapy by targeted integration of FVIII transgene in hematopoietic stem cells through CRISPR-Cas9 technology (MM). Given the expertise for lipid-based gene transfer at CSCR, work is also ongoing on applying this approach to haemophilia through liver-targeted liposomal formulations (SrM). Both cellular and transgenic haemophilia animal models will be used to test these approaches. An industry collaboration has been established with Intas Pharmaceuticals for the development of rAAV8-hFIX-Padua based gene therapy for Hemophilia B. This work is coordinated at CSCR by Sanjay Kumar. In-vivo efficiency of expression in being evaluated in the transgenic haemophilia mouse models at CSCR.

To improve the current approaches of gene therapy for Hemophilia A, Mohankumar Murugesan is working on a novel ex-vivo gene therapy approach for targeted integration of FVIII in hematopoietic stem cells for the treatment Hemophilia A. A protocol has been developed for effective transfection of Cas9-RNP complex for the targeted integration of transgene in to lineage specific promoter. towards developing a novel lipid mediated gene therapy strategy for hemophilia, galactosylated

lipid nanocarriers have been developed that can specifically deliver nucleic acids including pDNA, siRNA, mRNA effectively into the liver. Further, safety profiles and therapeutic efficacy are being assessed in Hemophilia B mouse model.

Haemoglobin disorders: Another major thrust of the gene therapy is on the major haemoglobin disorders such as thalassemia and sickle cell disease which are major public health problems in India. Two approaches are currently under development – lentiviral vector-based gene transfer approach which is already being evaluated in animal models (RVS/AS - details under the NAHD section) and a novel gene-editing approach using the CRISPR-Cas9 technology for correction of the phenotype of β-thalassemia major and sickle cell disease by altering the expression γ-globin chains through transcriptional modifications (ST/MM) in collaboration with two groups at the University of California, USA.

COVID-19: Srujan Marepally's lab has developed a novel Shikimoylated Mannose Receptor Targeting (SMART) nanoparticle system for delivering mRNAs into dendritic cells for vaccine development, synthesized chemically modified mRNA and validated functionally. The group has also developed tools for COVID-19 research as pseudovirion and human ACE-2 receptor stably expressing HEK-293 cells for in vitro neutralization efficiency of the vaccine. The animal studies are under progress.

Other diseases: Using CRISPR/Cas9 gene editing tools, preclinical studies are also ongoing to develop gene correction in Wiskott-Aldrich syndrome (WAS). Gene editing tools and strategies are being tested for the targeted integration of the WAS transgene in the hematopoietic stem cells. Newer areas of research are being established to assess antitumor functions of NK cells, γδ T cells and αβ T cells with the specificity and robustness of Chimeric Antigen Receptors (CARs). The area of immune cell therapy is being coordinated by Sunil Martin.

Cellular Reprogramming and its Application - Disease Modeling and Haplobanking

The area of cellular reprogramming technology is coordinated by R. V. Shaji at CSCR. This technology is now being applied to two areas of translational research, disease modeling, and haplobanking. Generation of iPSCs for disease modelling of haematological diseases: RVS lab has been working on establishing iPSC-based disease models for haematological diseases. His group successfully generated iPSCs from patients with Fanconi anaemia and haematopoietic cells generated from these iPSCs mimic Fanconi anaemia disease in culture. Currently, this cellular system is being used for understanding the molecular basis of Fanconi anaemia. Recently, this group generated iPSCs from a patient with Diamond Blackfan anaemia, a genetic disease that cause ineffective erythropoiesis. A major translational effort has also been initiated towards establishing a 'haplobank' for generating iPSCs from individuals homozygous for HLA haplotypes. This area is coordinated by Dolly Daniel from Department of Transfusion Medicine and Immunohaematology, CMC, Vellore and R. V. Shaji from CSCR. More details on the haplobanking project are provided in the NAHD section.

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Alok Srivastava

• Brown H., Doering C., Herzog R., Ling C, Markusic D., Spencer T., Srivastava A, Srivastava A. (2020) **development of a clinical candidate AAV3 Vector for gene therapy of Hemophilia B**. *Human Gene Therapy.*

Elizabeth Vinod

• Vinod E., Parameswaran R., Amirtham S., Livingston A., Ramasamy B., Kachroo U. (2020) **Comparison of the efficiency of laminin versus fibronectin as a differential adhesion assay for isolation of human articular cartilage derived chondroprogenitors.** *Connective Tissue Research.*

• Kachroo U., Zachariah S., Thambaiah A., Tabasum A., Livingston A., Rebekah G., Srivastava A., Vinod E. (2020) **Comparison of human platelet lysate versus fetal bovine serum for expansion of human articular cartilage derived chondroprogenitors.** *Cartilage.*

• Kachroo U., Ramasamy B., Vinod E. (2020). **Evaluation of CD49e as a distinguishing marker for human articular cartilage derived chondroprogenitors.** *Knee.*
• Vinod E., Jefferson T., Amirtham S., Prince N., Geevar T., Rebekah G., Ramasamy B., Kachroo U. (2020) **Correlation between synovial fluid calcium containing crystal estimation and varying grades of osteoarthritis using a rabbit model: Potential diagnostic tool.** *J Clin Orthop Trauma.*
• Vinod E., Ramasamy B., Kachroo U. (2020) **Comparison of immunogenic markers of human chondrocytes and chondroprogenitors derived from non-diseased and osteoarthritic articular cartilage.** *Journal of Orthopaedics, Trauma and Rehabilitation.*
• Amirtham S., Ozbey O., Kachroo U., Ramasamy B., Vinod E. (2020) **Optimization of immunohistochemical detection of collagen Type II in osteochondral sections by comparing decalcification and antigen retrieval agent combinations.** *Clinical Anatomy.*
• Vinod E., Kachroo U., Amirtham S., Ramasamy B., Sathishkumar S. (2020) **Comparative analysis of fresh chondrocytes, cultured chondrocytes and chondroprogenitors derived from human articular cartilage.** *Acta Histochemica.*
• Vinod E., Ozbey O., Sabareeswaran A., Kachroo U., Sathishkumar S., Ramasamy B. (2019) **Comparison of monosodium iodoacetate model of osteoarthritis between in-vivo and ex-vivo osteochondral unit in rabbits.** *J Clin Orthop Trauma.*
• Vinod E., Francis D., Jacob T., Amirtham S., Sathishkumar S., Kanthakumar P., Oommen V. (2019) **Autologous platelet rich fibrin as a scaffold for chondrocyte culture and transplantation: An in vitro bovine study.** *J Clin Orthop Trauma.*
• Vinod E., James J., Kachroo U., Sathishkumar S., Livingston A., Ramasamy B. (2019) **Comparison of incremental concentrations of micron-sized superparamagnetic iron oxide for labelling articular cartilage derived chondroprogenitors.** *Acta Histochem.*

Jeyanth Rose

• Rose J., Lalgudi S., Joshua A., Paul J., Thambaiah A., Wankhar S., Chacko G., Kuriakose T., Korah S. (2019) **An experimental study to test the efficacy of mesenchymal stem cells in reducing corneal scarring in an *ex-vivo* organ culture model.** *Experimental Eye Research.*
• Richard A., Rose J., Korah S., Keziah M., Arambhan S., Arthi A., Jaisakthi S., Vijayarajan V. (2019) **Quantification of corneal transparency in post-mortem human corneas using laser scatter image analysis.** *Clin Exp Optom.*

Sarvanabhavan Thangavel

• Ramalingam S., Thangavel S. (2019) **CRISPR-Cas9 probing of infectious diseases and genetic disorders.** *Indian J Pediatr.*

Srujan Marepally

• Sharma N., Dhyani A., Marepally S., Devadoss A. (2019) **Nanoscale lipid vesicles functionalized with nitro-aniline derivative for photoinduced nitric oxide (NO) delivery.** *Nanoscale Advances.*

Vrisha Madhuri

•Madhuri V., Selina A., Loganathan L., Kumar A., Kumar V., Raymond R., Ramesh S., Vincy N., Joel G., James D., Kandagaddala M., Antonisamy B. (2020) **Osteogenesis imperfecta: Novel genetic variants and clinical observations from a clinical exome study of 54 Indian patients.** *Ann Hum Genet.*
• Ramesh S., Sävendahl L., Madhuri V., Zaman F. (2020) **Radial shock waves prevent growth retardation caused by the clinically used drug vismodegib in *ex-vivo* cultured bones.** *Sci Rep.*
• Rajagopal K., Ramesh S., Madhuri V. (2020) **Early addition of parathyroid hormone-related peptide regulates the hypertrophic differentiation of mesenchymal stem cells.** *Cartilage.*
• Madhuri V., Ramesh S., Varma H., Sivadasan S., Sahoo B., John A., Fernandez F., Rajagopal K., Mathews V., Balakumar B., Dinesh V., Chilbule S., Gibikote S., Srivastava A. (2020) **First report of a tissue-engineered graft for proximal humerus gap non-union after chronic pyogenic osteomyelitis in a child.** *The Journal of Bone and Joint Surgery.*
•Ramesh S., Zaman F., Madhuri V., Sävendahl L. (2019) **Radial extracorporeal shock wave treatment promotes bone growth and chondrogenesis in cultured fetal rat metatarsal bones.** *Clin Orthop Relat Res.*

PATENTS:

Compact liposomal vehicle for delivery of large molecules. March 2020.
Application No. 202041010160
Compositions and methods for reactivating developmentally silent genes. May 2020.
Application No. 202041020165

TRAINING AND OUTREACH:

Annual Cell and Gene Therapy Symposium: CSCR has been organizing an annual symposium on Cell and Gene Therapy for the last 4 years. The aim of this meeting is to provide a platform for scientists and physicians working in this field of research to come together and discuss the advances in the field. The 5th Annual Cell and Gene Therapy Symposium was held on September 03-04, 2020.

10 MULTI-INSTITUTIONAL PROGRAMS

inStem's collaborative, interdisciplinary structures are reflected in and strengthened by our multi-institutional programmes described in the sections that follow. Given the complexity of the basic research and clinical problems addressed at inStem and leveraging the environment of excellence on the campus, we have nurtured international partnerships to combine resources and expertise that cannot be found in a single institution.

ADBS : Accelerator Program for Discovery in Brain Disorders Using Stem Cells

The Accelerator program for Discovery in Brain disorders using Stem cells (ADBS) is a venture to understand the genetic and cellular basis of severe mental illness by harnessing the power of modern human genetics and stem cell technology. This is a collaboration between three institutions from Bengaluru, India – the Institute for Stem Cell Science and Regenerative Medicine (inStem), the National Centre for Biological Sciences (NCBS) and the National Institute for Mental Health and Neurosciences (NIMHANS). The overall goal is to uncover the genetic, cellular and molecular basis of mental illness and relate these to clinical findings. Severe mental illnesses are a major source of disability in young adults with about 2– 3% of the population at risk for developing these disorders both in India and across the world. These disorders are recognized as one of the major non-communicable diseases (NCD) and a significant contributor to morbidity as articulated by the World Health organization's New Delhi call for action on combating NCDs in India. Given this huge disease burden, the development of novel ways to diagnose and treat mental illness will have important positive social and economic benefits. To achieve this goal, there is a pressing need to understand the mechanistic basis of these disorders; such discovery could form the basis for the development of novel diagnostic and therapeutic approaches. The ADBS

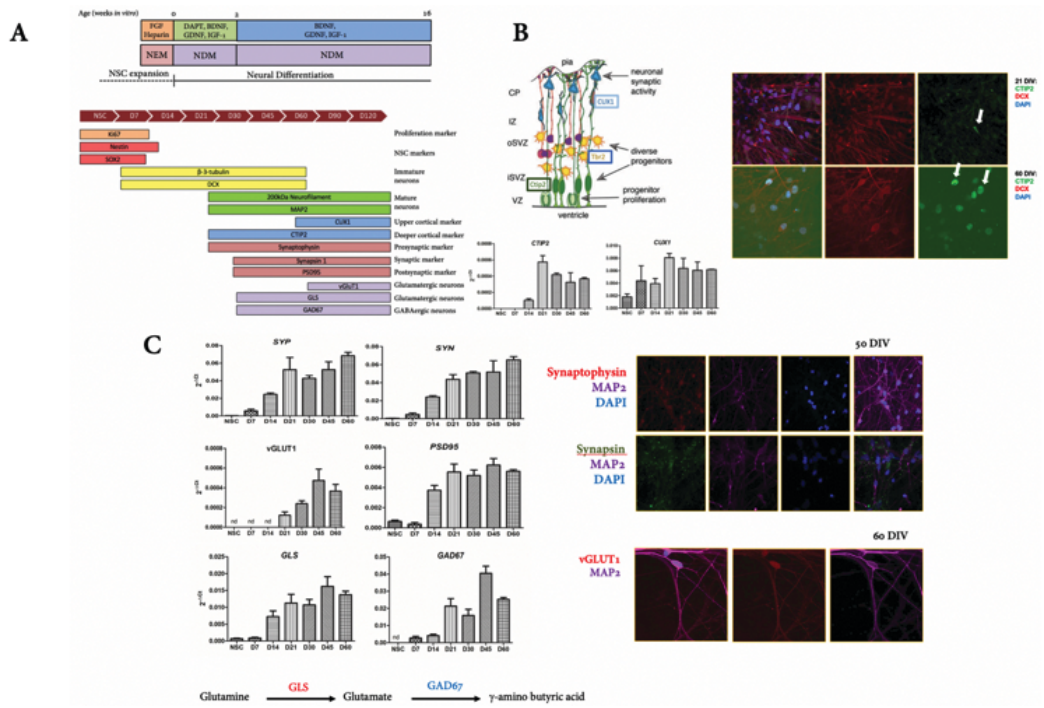

Figure 1: Protocol for the differentiation of NSC into a cortical neuron 'disease in a dish' model. (A) The protocol used for this is depicted (B) The markers seen in the various layers of the human cerebral cortex are depicted in the cartoon. Immunofluorescence images from the differentiated cultures showing expression of some of these is shown. qRT-PCR analysis showing expression of cortical markers is shown. (D) Expression of synaptic markers at the RNA and protein level are shown as a function of the age of the culture.

program studies five major forms of severe mental illness (SMI) namely schizophrenia, bipolar disorder, obsessive compulsive disorder, substance dependence and dementia. All of these disorders are known to have an inherited basis. Despite their high heritability, to date few genetic correlates that account for this high heritability have been identified. In order to study these
disorders, the program has assembled a prospective cohort of families with a strong family history of SMI. The ADBS program is pursuing three distinct but interactive lines of analysis on these families:

(i) The families have been clinically studied in depth to understand changes in structure and function at multiple levels of brain organization; they will now be followed over a period of twenty years at 3 year intervals in order to define the temporal development of disease through regular and detailed clinical phenotyping.

(ii) We have established induced pluripotent stem cell lines from affected individuals in these families and unaffected controls. These lines are being used to generate cellular models and mechanistic aspects of cellular neurobiology that lead to disease.

(iii) Next Generation Sequencing and family-based bioinformatics analysis is being used to uncover the genetic basis of SMI. The multiple types of data generated by the ADBS program are being assembled into an integrated database to facilitate the application of sophisticated methods of data analysis to uncover new disease biology. The stem cell lines and other biomaterials have been assembled into a biorepository that will allow the sharing and use of this resource to drive discovery biology in the area of SMI. The ADBS program has instituted mechanisms to facilitate the sharing of data and resources generated through its activities.

Outreach Activities

A key objective of the ADBS program is to expand and facilitate the application of modern stem cell technology and genomics for discovery in human disease biology in India. To this end, ADBS has undertaken a series of initiatives: A training program is organized annually by the Accelerating the Application of Stem cell technology in Human Diseases (ASHD) program and the Centre for iPS Cell Research and Application (CiRA), Kyoto University, Japan. As part of this effort, every year CiRA hosts Indian researchers at its laboratories in Kyoto, Japan for a training program that features instruction on methods for working with human iPS cells. 8 early career researchers from across India attended this training program in November 2019. In collaboration with the Institute of Bioinformatics and Applied Biotechnology, Bengaluru, ADBS conducted a 3-day workshop on Genome/Transcriptome Sequence Analysis (November 13-15, 2019) at NCBS. 18 researchers from various institutes attended the workshop. A hIPSC workshop was conducted from 15th to 24th January 2020. 9 participants attended this workshop, which focused on techniques involved in the generation and maintenance of high-quality hIPSCs from human somatic cells.

Dedicated website (www.ncbs.res.in/adbs). This page contains information on the scientific elements of the ADBS program, participating institutes and scientists and is also the portal through which the scientific community can access the biorepository contents and request items from it. Access to the biorepository contents is following registration and verification of credentials. Social media platforms: The ADBS program has dedicated social media platforms to spread information about the work of the program. Facebook page: https://tinyurl.com/y2cjerye and the Twitter handle of ADBS is @BrainStem_ADBS and a Linkedin profile: https://www.linkedin.com/company/adbs-brainstem

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• Raghu P., Joseph A., Krishnan H., Singh P., Saha S. (2019) **Phosphoinositides; regulators of nervous system function in health and disease.** *Fron. Mol. Neurosci.*

•Mukherjee O. *et al.* (2019) **Making NSC and Neurons from Patient-Derived Tissue Samples**. *Methods Mol Biol.*

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•Paul P., Iyer S., Nadella K.R., Nayak R., Chellappa A.S., Ambardar S., Sud R., Sukumaran S.K., Purushottam M., Jain S., Viswanath B. (2020) **Lithium response in bipolar disorder correlates with improved cell viability of patient derived cell lines.** *Sci Rep.*

CNS: Centre for Neurodevelopmental Synaptopathies

Neurodevelopmental and neurodegenerative brain disorders represent a major and growing public health challenge in the developed and developing worlds. The goal of the CNS program has been to accelerate the discovery and delivery of effective therapeutics for neurodevelopmental disorders specifically Autism Spectrum Disorders and Intellectual Disabilities (ASD/IDs). The centre combines a range of expertise in several fields of neurobiology including synaptic function and plasticity, human stem cells and cognition-behaviour.

Stem Cell Biology – 'Understanding Autism in a Dish'

Mounting evidence from recent pathological, radiological, and genetic studies have shown that glia play a pivotal role in the brain rather than being just supporting structures located around neurons. In diseased conditions, glia can be injurious or neuroprotective to neurons. How glia in ASD/ID models affect overall brain function remains largely unexplored. Hence, a key focus of this program is to examine cell autonomous versus non-autonomous effects of Fragile X Syndrome (FXS) on neurons and astrocytes.

An in vitro cell culture system was established to derive mature functional astrocytes following cues from developmental biology; and further co-cultured with neurons to study the non-cell autonomous effects. Using whole-cell patch clamp recordings, we found that human iPSC derived neurons fire bursts of action potentials. Control (healthy) neurons co-cultured with control astrocytes exhibited low burst frequency and higher burst duration. In contrast, FXS neurons co-cultured with FXS astrocytes displayed significantly higher frequency of bursts, but of lesser duration. Strikingly, when control neurons were co-cultured with FXS astrocytes, the bursting profile of the control neurons resembled that of the FXS – with high burst frequency and shorter burst duration. Consequently, when FXS neurons were co-cultured with control astrocytes the aberrant bursting activity was 'rescued' to resemble the healthy neurons with low burst frequency and longer burst duration. Thus, the genotype of astrocytes determines the electrophysiological phenotype of neurons.

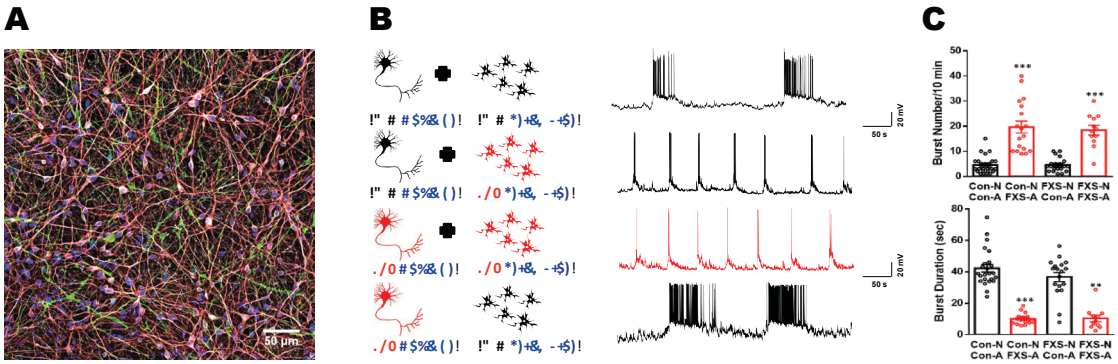


Figure: Human iPSC derived neurons were co-cultured with the human iPSC derived astrocytes (β-III tubulin/Map2ab/GFAP/DAPI- 20X) for 8 weeks in vitro to form a dense network of neurons and glia. B) Glial modulation of the network activity of neurons and C) quantification of burst firing parameters – burst frequency calculated as number of bursts/10 min and burst duration.

Novel Models for Studying Autistic Function: Rat Behavioural Models

By directly testing genetically diverse causal mutations associated with ASD/IDs in a variety of parallel verticals of behavioural, electrophysiological, and biochemical analyses, we have generated nine new rat models of ASD/IDs using novel Crispr-Cas9 editing techniques. Further, we have successfully completed multi-level analysis of neural dysfunction in seven of these rat models of ASD/IDs, the only and largest collection of such models in the world. In carrying out these studies, the following significant results have been achieved: (i) The cellular physiology of each mutation converge in a brain region-specific manner and are highly conserved across species (ii) The divergence in behavioural phenotypes between models of ASD/ID across rodent species contrasts with the clear convergence at the biochemical and cellular levels (iii) Sustained correction of associative learning deficits can be achieved if given earlier in life. This was demonstrated using brief, early reatment with lovastatin, in a rat model of FXS (iv) A novel framework, across biological scales from behaviour to synapses, for understanding the neural basis of abnormal amygdala function, and its implications for the emotional symptoms in ASD/IDs

Collaboration with Accelerator program for Discovery in Brain disorders using Stem cells (ADBS)

We anticipate that high value familial major mental illness pedigrees with defined genetic mutations will be identified through the inStem/NCBS/NIMHANS partnership. We have provided technical knowhow on rig set up, supply logistics etc. and working with ADBS investigators. We will prioritise patient lines to undergo systematic study for identification of potential neuronal and / or glial phenotypes

NAHD: Novel Approaches to Hematological Disorders

The program at CSCR / CMC - Novel Approaches to Hematological Disorders (NAHD) aims to enhance current methods / technologies including gene therapy for hereditary blood disorders such as haemophilia, thalassemia and sickle cell disease, all of which are causes of significant morbidity and mortality in India. To ensure maximum impact on hereditary hemoglobin diseases in the population at risk in India, this collaborative initiative blends these efforts with a community outreach program for the control of major haemoglobin disorders.

The NAHD has three components – Gene Therapy, Applications of iPSC Technology (Haplobanking) and Control of Thalassemia and Sickle Cell Disease. A brief summary of the different components are given below:

Gene Therapy

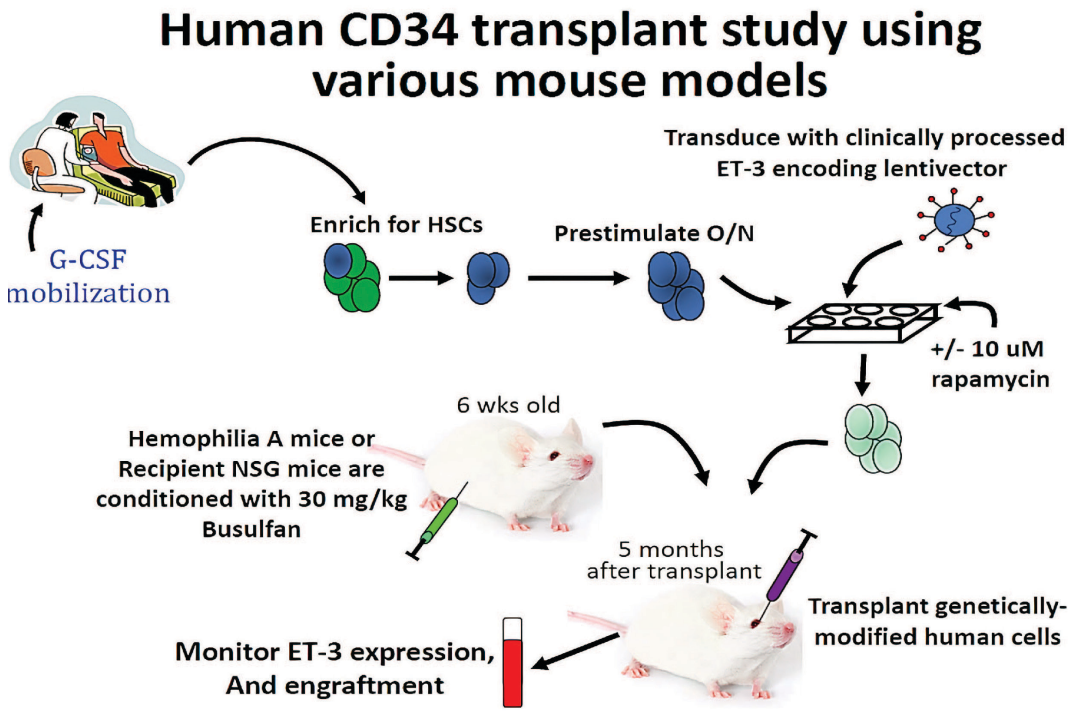
I. Clinical trials for gene therapy of Hemophilia A & B

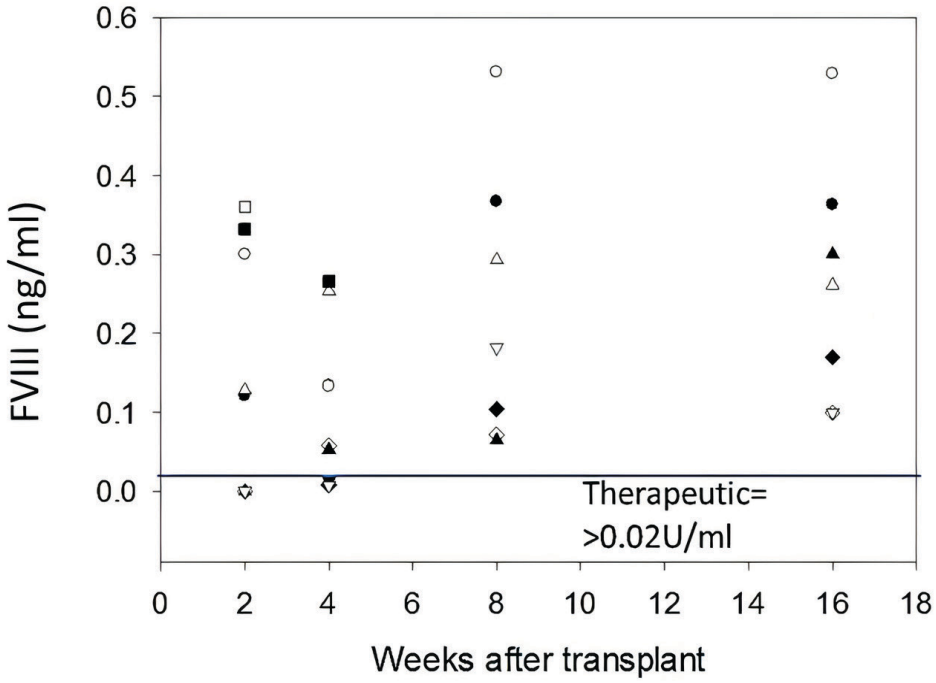
Hemophilia B: As mentioned in the previous year's report, a unique transgene was designed for this clinical trial. This data was recently published (Brown *et al* Human Gene Therapy August 2020). This data established the in-vivo functionality of this transgene and allowed us to proceed towards further development of a clinical product. As also reported last year, there was a setback in the plans for this clinical trial as the collaborating vector manufacturing facility in USA was unable to produce the vector at the right titers to allow for cost-effective production of the required quantity of the vector for the proposed clinical trial. We now have a very exciting new possibility. Our collaborators at Emory University have established a new GMP facility through their company - Expression Therapeutics (ET). They have acquired a team of senior GMP scientists from another facility and have agreed to do the engineering'/standardization runs in their facility with the highest priority and then transfer the know-how/technology to us at CSCR/CMC.

Hemophilia A: Apart from this, a novel lentiviral vector-based gene therapy for haemophilia A has also been developed over the last two years in collaboration with the scientists at the Emory University, Atlanta, USA (AS). This collaboration has led to the development of an alternative gene therapy product - a haematopoietic stem cell based lentiviral vector mediated gene therapy product for the treatment of haemophilia A. This is novel approach - first in human proposed clinical trial of gene therapy for haemophilia A (factor VIII deficiency) where the FVIII transgene is packaged in a lentiviral vector to transduce the haematopoietic stem cell (HSC) for stable integration and lifelong expression is similar to the principles being applied in the gene therapy for the major haemoglobin disorders. The product has been tested in pre-clinical mouse models and shown to be safe and effective (Doering et al Human Gene Therapy 2018; 29:1183). The clinical vector is also ready for use in a clinical trial, jointly applied for conduct in USA and India.

II. Standardization of anti-AAV Antibody assays

The goal is to standardize assessment of anti-AAV antibody through different assays to allow appropriate selection of patients for gene therapy. This work is coordinated by Asha M Abraham along with Hubert Daniel, and Rajesh Kannangai from Department of Clinical Virology, CMC, Vellore and Sanjay Kumar and Alok Srivastava from CSCR. It is being done in collaboration with the University of Florida, USA. Both binding and neutralizing antibodies are being assessed through the whole capsid and serotype-specific peptide ELISAs and transduction inhibitions assays (TIA) respectively. The whole capsid and peptide ELISAs have been standardized for AAV 3, 5 and 8. TIA by mCherry based flow-cytometry had been standardized





for AAV 3 and 5.

III. Late pre-clinical research - Lentiviral & Genome editing approach for Thalassemia and Sickle Cell Disease:

This project aims to evaluate lentiviral vectors for developing gene therapy for the major haemoglobin disorders. This is coordinated by R. V. Shaji and Alok Srivastava. In collaboration with Emory University, lentiviral vectors have been generated for gene therapy of haemoglobinopathies. These vectors have been evaluated and those which high efficiency for the expression of beta globin gene have been identified for testing in mouse models. Recently, a

lentiviral vector has been developed that can down regulate the expression of BCL11A only in erythroid cells, and this vector is found to increase the expression of gamma globin gene significantly. Further experiments are being carried out in mouse models and in the cultured erythroid cells from patients with haemoglobinopathies.

Another important component of this program is the gene editing approach to reactivation of fetal haemoglobin production. This work is being carried out by Saravanabhavan Thangavel and Mohankumar Murugesan using the CRISPR-Cas9 technology in collaboration with the University of California. For beta hemoglobinopathies, two different strategies of disease reversal are being developed. One strategy involves the correction of disease-causing mutation, the second strategy is to mimic the naturally existing beneficial mutations for reactivation of fetal gamma-globin activation. Towards these, reagents have been developed and conditions have been optimized for genetic manipulation in primary hematopoietic stem cells. Currently both labs are testing haemoglobin expression pattern in the erythroid cells differentiated from manipulated HSPCs.

IV. Early pre-clinical research for Hemoglobin / Erythroid disorders

The aim is to create disease models for two monogenic erythroid disorders, Diamond Blackfan Anemia (DBA) and Congenital Dyserythropoietic Anemia (CDA), by creating mutations in the associated genes by CRISPR/Cas9. The target genes have been successfully disrupted by CRISPR/Cas9. Currently, a novel approach to introduce biallelic mutations along with selection markers to screen colonies for target mutations is being established. Methods to differentiate iPSCs to haematopoietic progenitor to erythroid cells have also been developed. An iPSC line that expresses Cas 9 from AAVS1 site in doxycycline individual manner has been developed.

B. Haplobanking - Bank of iPS Cells from Individuals with Homozygous HLA Haplotypes

This project is aimed at creating a bank of iPSCs derived from individuals homozygous for the most common HLA haplotypes in the Indian population. PBMNCs were isolated from two hundred and thirty-five homozygous HLA haplotype donors and cryopreserved in GMP facility. A xenofree protocol has been established for GMP production of iPSCs from ex-vivo cultured erythroid cells, generated 18 clones from six donors (three clones per donor), and subsequently, generated iPSCs from 15 donors (five clones per donor) with the top 20 haplotypes in GMP facility. Out of these 30 clones, 10 clones were further expanded by extended passaging under GMP conditions. These established iPSCs lines from top 10 homozygous haplotypes showed pluripotent stem cell morphology, proliferation, and pluripotent marker expression. Further detailed molecular characterization for identity, sterility, differentiation, and genomic stability is under progress.

Control of Thalassemia and Sickle Cell Disease: Creating a Model for India

This program is led by Kuryan George, Shantidani Minz and Alok Srivastava along with several other senior colleagues from the departments of Community Health, Haematology, Transfusion Medicine and Immunohaematology, and Obstetrics and Gynecology at CMC, Vellore in collaboration with the National Health Mission of the Government of Odisha. This is a unique program in terms of scale and complexity in this field in the world. Six districts have been identified to implement the first phase of this program. Towards increasing capacity and capability for treatment of major haemoglobin disorders in Odisha, training workshops were conducted at different levels (State / Regional / District levels) for doctors and healthcare workers of Odisha to train them in management of these disorders and effective implementation of the field program.

PUBLICATIONS

• Brown H.C., Doering B.C., Herzog R.W., Ling C., Markusic D.M., Spencer H.T., Srivastava A., Srivastava A (2020). **Development of a Clinical Candidate AAV3 Vector for Gene Therapy of Hemophilia B.** *Hum Gene Ther.*

PATENT

Compositions and methods for reactivating developmentally silent genes. (May 2020).
Application No. 202041020165

CCBT: Centre for Chemical Biology and Therapeutics

The Centre for Chemical Biology and Therapeutics (CCBT) was established to explore innovative approaches to modulate intracellular signalling pathways disrupted in disease through a unique, integrated and multidisciplinary program. Our first goal is to target the molecular recognition of phosphorylated proteins - a key class of protein modification vital for signalling - by specific domains. We have made strong progress towards our first focus, BRCT domains, which represent an important class of domains that recognize pSer or pThr motifs using structurally distinct mechanisms and participate in many different signalling pathways that control genome duplication and repair. We have reported (Periasamy *et al*., Cell Chemical Biology, 2018; Vadiraj *et al*., ChemMedChem, 2019) the development of Bractoppin, a first drug-like inhibitor of phosphopeptide recognition by the human BRCA1 tBRCT domain, which selectively inhibits substrate binding *in vitro*, and in cells, selectively blocks BRCA1-dependent signals triggered by DNA damage. Chemical matter surrounding the discovery and SAR of Bractoppin, as well as its potential uses, has been protected in a patent filing (United States Patent Application Publication No.: US2018/0346461A1).

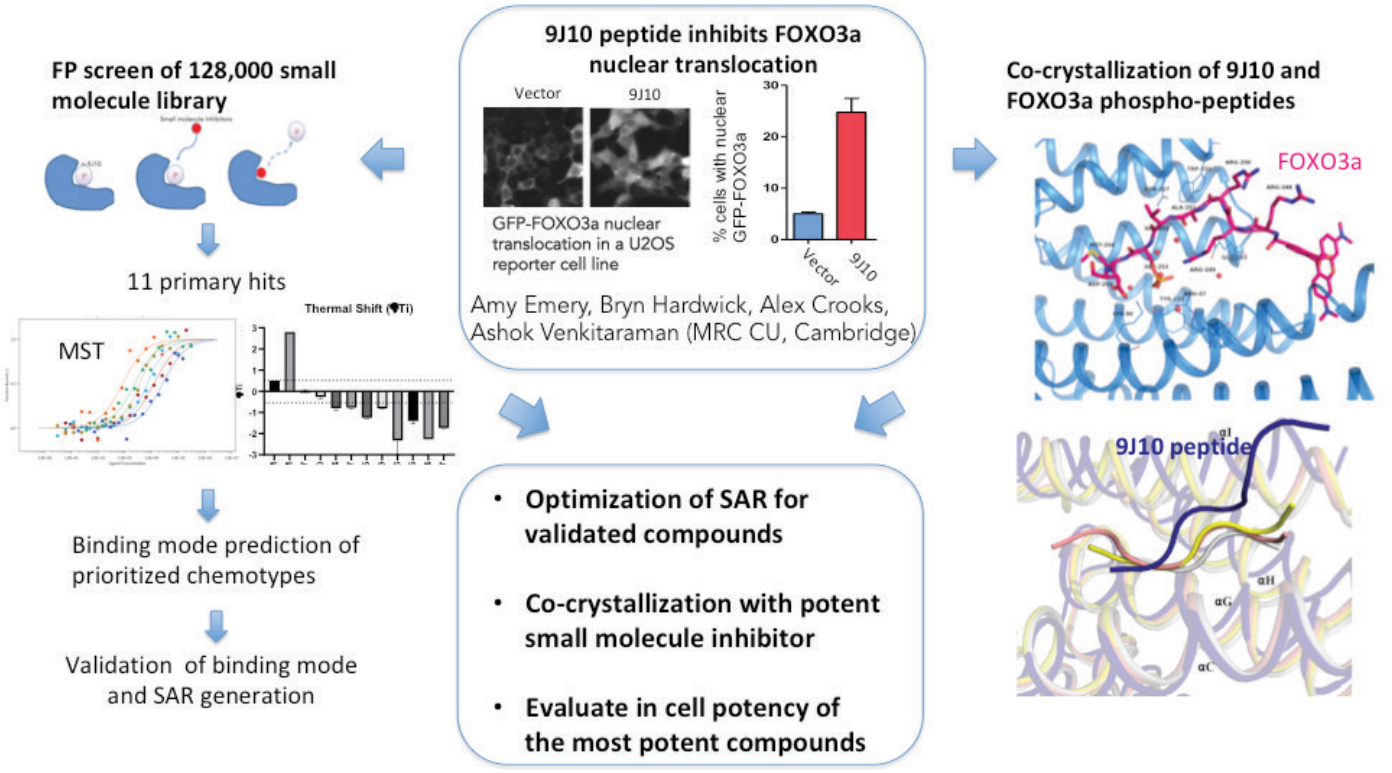
Thus, our success has now opened new opportunities for interrupting intracellular signalling by other members of the human tBRCT domain family, as well as other phosphopeptide-recognizing domains, previously considered "undruggable", against which we expect to create a palette of selective small-molecule leads, exemplifying an attractive new approach for enlarging the druggable proteome. We have thus embarked upon targeting 14-3-3ε recognition of phosphorylated FOXO3a, in collaboration with the Venkitaraman lab at the MRC Cancer Unit, Cambridge. FOXO3a is a tumour suppressor that is typically inactivated in a subset of cancers by post-translational modification, rather than by mutation of the gene. FOXO3a is retained in the cytoplasm through the activation of the PI3K/Akt pathway and is unable to translocate to the nucleus where it can carry out transcription of genes involved in cell cycle arrest and apoptosis. Our collaborators have identified a bioactive peptide, 9J10, using novel PROTEINi technology, that binds to 14-3-3ε and inhibits its interaction with FOXO3a, thereby allowing the possibility of reactivating FOXO3a as a strategy for the treatment of cancer. To identify small molecule inhibitors of the 14-3-3ε / FOXO3a interaction, in collaboration with the Cambridge team, two parallel strategies were strategized:
i) High-throughput screening with a small molecule library and
ii) Structural elucidation of 14-3-3ε complexed with 9J10 or FOXO3a phosphopeptides.

The identified minimal 14-3-3 binding motif of 9J10 was used to screen a diversity library of 128,000 drug-like molecules using a FP (Fluorescence Polarization) assay. Eleven hits identified in the primary screen were re-ordered, reconfirmed in FP and were further validated in orthogonal assay, Micro Scale Thermophoresis (MST). Six compounds showed effective dose dependent inhibition and engaged the target as evidenced by the thermal stability of the compound-bound to 14-3-3ε. The predicted binding modes are being experimentally validated to optimize the potency of the compounds, and develop structure activity relationships. Together, these results provide scope for developing novel 14-3-3ε small molecule inhibitors that could reactivate FOXO3a in the cell-based assays developed in Cambridge.

We determined the first crystal structures of 14-3-3ε complexed with FOXO3a or 9J10 phosphopeptides at a resolution of 1.85 Å and 3.16 Å respectively. For a 14-3-3ε dimer, a 9J10 or FOXO3a peptide binds at the substrate-binding groove of each monomer where the pSer makes interaction with conserved residues of 14-3-3ε in a canonical way. The FOXO3a bound similar to that of other canonical

phospshopetides. Interestingly, 9J10 bound 14-3-3ε revealed a number of structural differences compared to other phosphopeptide-bound 14-3-3ε structures; (i) The binding of 9J10 to 14-3-3ε was accompanied by the movement of the C-terminal helices closer to the 9J10 peptide binding groove, causing 14-3-3ε to adopt a relatively 'closed' conformation. (ii) Whilst canonical phosphopeptides bind in an extended conformation, 9J10 adopted a distinct, bent conformation and (iii) The binding of 9J10 is facilitated by unique interactions of the three consecutive arginines in the 9J10 peptide. These differences speak to the ability of biodiverse peptides from ancient genomes to engage novel, functionally relevant binding sites within human proteins, with potential implications for inhibitor discovery.

Thus, our success with these strategies in interrupting intracellular signalling by not only tBRCT domain family, but as well as other phosphopeptide-recognizing domains like 14-3-3 that were previously considered 'undruggable', against which we expect to create a palette of selective small-molecule leads, exemplifies an attractive new approach for enlarging the druggable proteome.



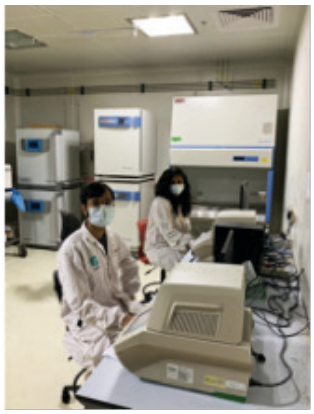
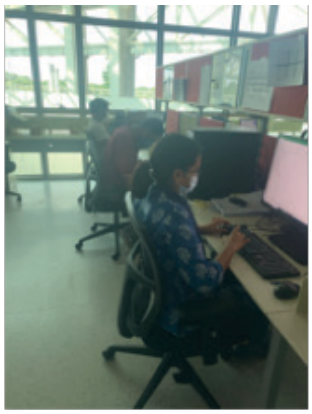
PUBLICATIONS

• Kurdekar V., Giridharan S., Subbarao J., Nijaguna M.B., Jayaprakash Periasamy, Boggarama S., Shivange A.V., Sadasivam G., Padigaru M., Potluri V., Venkitaraman A.R., Bharatham K. (2019) **Structure-guided synthesis and evaluation of small molecule inhibitors targeting protein-protein interactions of BRCA1 tBRCT domain.** *ChemMedChem*

11 COVID-19

COVID - 19 RESPONSE



COVID-19 RESPONSE

The COVID-19 pandemic has had devastating impact on global public health with crippling socioeconomic consequences. The goal of containing the spread of SARS-CoV-2, the virus causing COVID-19, relies on a comprehensive strategy of rapid testing of the virus in the population, effective treatments, and the development of therapeutics to prevent viral infection. As the pandemic was taking hold in India, the Institute for Stem Cell Science and Regenerative Medicine (inStem) and its partnering institutes in the Bangalore Life Science Cluster – the National Centre for Biological Science, (NCBS, TIFR) and the Centre for Cellular and Molecular Platforms (C-CAMP) - recognized the need to rapidly contribute on all these fronts. The swift deployment of the campus's world class research infrastructure and highly skilled personnel has resulted in a broad spectrum of efforts ranging from testing and diagnostics, generating enabling resources to facilitate the understanding of viral infection and progression, and interdisciplinary research programs to find new anti-viral treatments. Altogether, the large breadth of programs contribute significantly in the national efforts to combat SARS-CoV-2 and reduce its detrimental impact on society.

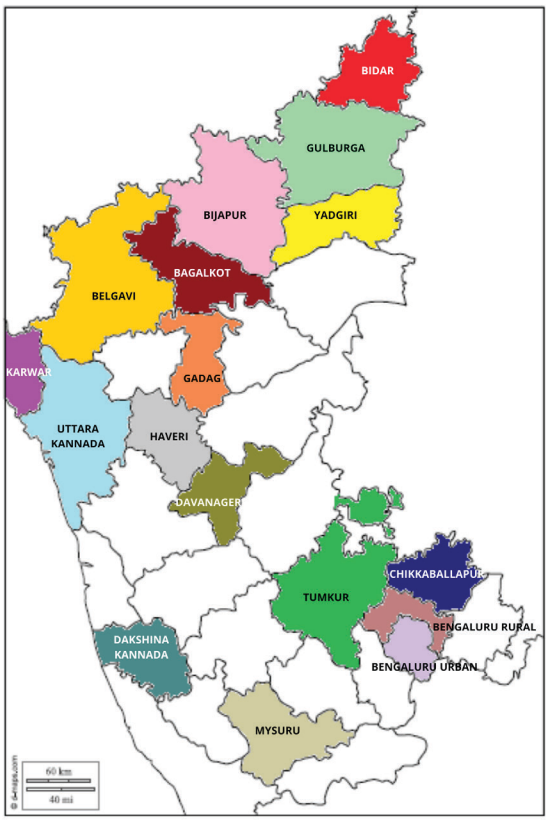
11 COVID - 19 Response

Testing & Diagnostics

COVID-19 Testing laboratory

Recognizing the need for aggressive testing in India's battle against COVID-19 during early April, inStem and NCBS brought their resources, community and facilities together to set up a testing laboratory. This was bolstered by the support of the Secretaries of the Department of Biotechnology (DBT), the Department of Atomic Energy (DAE) and the Indian Council of Medical Research (ICMR), and the guidance of the biosafety and human ethics regulatory committees. Within less than a week of receiving approvals, the laboratory began its operations in a dedicated space with teams of volunteers comprised of postdoctoral fellows, graduate students, interns and administration working closely with members of our staff including Colin Jamora, Dasaradhi Palakodeti, Bhavana Muralidharan, Tina Mukherjee, Arjun Guha, Praveen Vemula, and Ravi Muddashetty from inStem and Raghu Padinjat, Uma Ramakrishnan, Varadharajan Sundaramurthy, PV Shivaprasad and Vinothkumar K. Raghunath from NCBS. The testing laboratory not only meets the highest standards for safety and ethical management of information, but also emphasizes the overall well-being of the volunteer team who undergo routine medical checkups and have access to support programs for their mental health. Over 50 volunteers from across inStem and NCBS enabled the facility to run every day of the week for 12 hours per day. The testing facility has since tested more than 40,000 samples from Karnataka. These efforts have been buoyed by generous philanthropic support from the Azim Premji Foundation, to enable free-of-cost testing for COVID-19 to a large number of people from disadvantaged and marginalised communities from the city of Bangalore and across several districts of Karnataka.

COVID-19 samples from various districts in Karnataka



Developing a rapid diagnostic technique for COVID-19 Testing

The COVID-19 pandemic has strained testing capabilities worldwide, illustrating the urgent need to find economical and scalable ways to test more people. Not only is inStem involved in performing the tests and validating kits, but the institute is actively involved in discovering new ways to scale up the testing process. In partnership with theorists at NCBS and IIT Bombay, Dasaradhi Palakodeti of inStem has contributed to the development of a new way to increase testing capacity. The method called Tapestry, is a novel quantitative nonadaptive pooling scheme to test up to 1000 samples at once using the same amount of reagents that are normally employed for running only 100 samples. The underlying molecular diagnostic test is any real-time RT-PCR diagnostic panel approved for the detection of the SARS-CoV-2 virus. In cases where most samples are negative for the virus, Tapestry accurately identifies the status of

each individual sample with a single round of testing in fewer tests than simple two-round pooling. This testing method was developed as an Android application called BYOM Smart Testing, which guides users through the pipetting steps required to perform the combinatorial pooling. The results of the pooled tests can be fed into the application to recover the status and estimated viral load for each individual sample. More information of this technique can be found at: https://doi.org/10.1101/2020.04.23.20077727

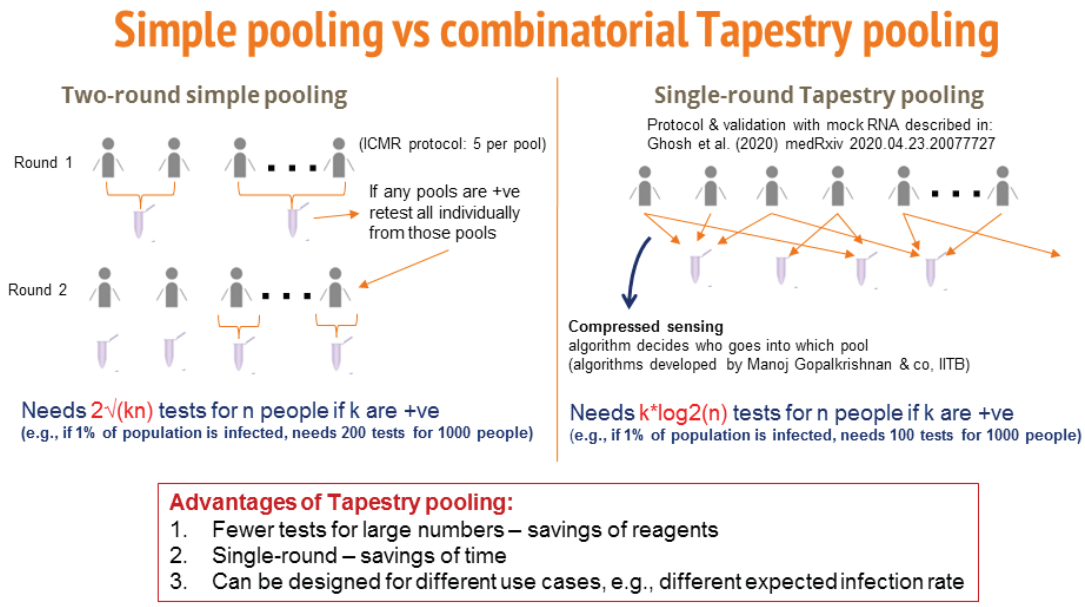


Image from https://covid-gyan.in/te/node/1047

Validation Centre

As a natural extension of the infrastructure and trained personnel to handle patient samples and to conduct COVID-19 testing efficiently, inStem and NCBS have received designation from the ICMR-NIV to serve as a validation centre for new testing kits developed by academic and biotechnology laboratories. The inStem validation centre will use patient samples received through the testing facility to gauge their performance in providing results with the same sensitivity and accuracy as the currently approved testing kits.

Research Resources

In addition to the activities to address the immediate public health need to test individuals and control the spread of the virus causing COVID-19, ultimately the cure for the disease will lie in scientific advances to understand how SARS-CoV-2 infects humans and affects different organs of the body.

Generating mouse models to study COVID-19

There are no cell culture systems that can reproduce the complex interactions that take place during the pathogenesis of the SARS-CoV-2 virus . These processes affect multiple tissues and has a systemic effect, and inflammation has been shown to be a major contributor to tissue damage. To date there is no in vitro system capable of reproducing these interactions that recapitulate what happens in the human disease. In addition, the DBT has issued a call to generate models for this disease to increase our understanding of the viral life cycle and pathogenesis. Mice are the predominant model to study in vivo processes in laboratories across the world, but they lack the receptor on their cells (called ACE2) that SARS-CoV-2

uses to enter human cells. With major support from the National Mouse Resource grant from the DBT, the campus Mouse Genome Engineering Facility and Animal Care and Resource Centre were able to use the state-of-the-art infrastructure and highly skilled personnel to rapidly deploy these resources to generate mouse models of COVID-19 infection. In general, we have generated three so-called "humanized" mice wherein the mice express the human version of ACE2, thereby rendering the animal susceptible to infection by the SARS-CoV-2 virus. The plasmid for the transgenic mouse was kindly gifted by Paul McCray, University of Iowa. The animals will be shared with academic and biotech researchers nationwide to facilitate their projects to identify new modes of treating infected patients (or blocking infection in the first place). In addition the facility staff is lending their expertise to industry by serving as co-principal investigators on a DBT funded to develop other strains of mice that would be useful to study the efficacy of different vaccines or treatments.

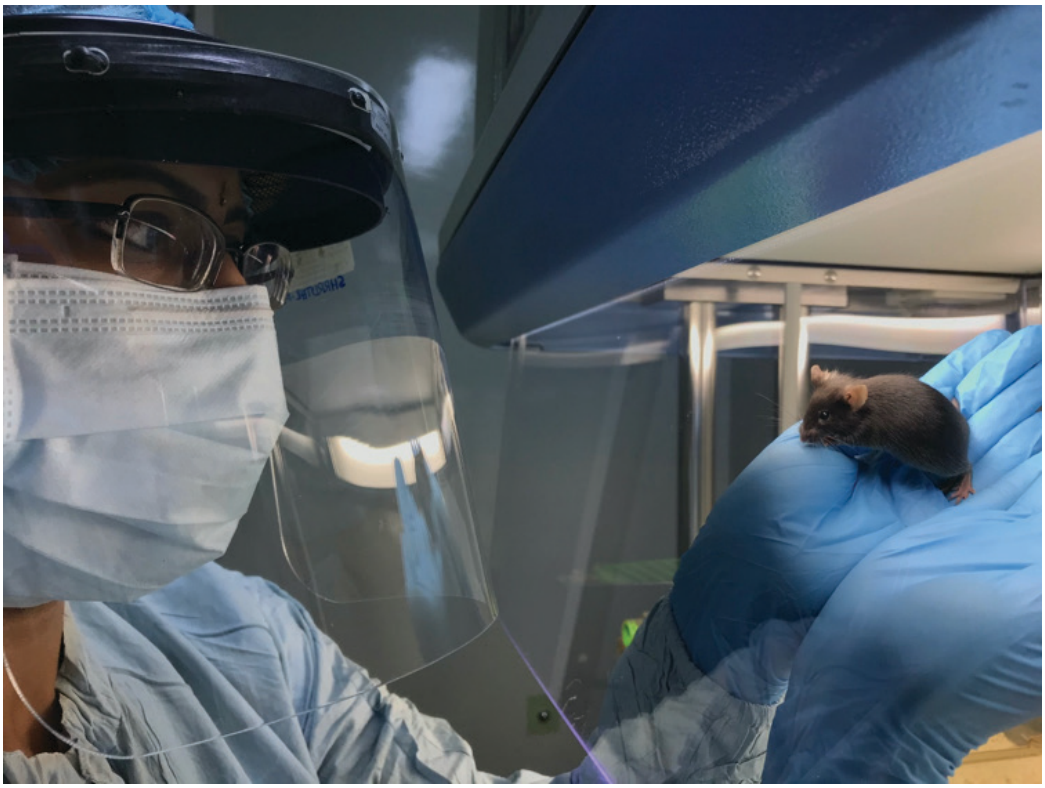


Image credit: Aurelie Jory, In-charge Campus Mouse Genome Engineering Facility

COVID-19 Biorepository

inStem is one of the five dedicated biorepositories established by the Department of Biotechnology for clinical and viral samples linked to the coronavirus disease (Covid-19). The purpose of this biorepository is to share biological materials from infected patients with clinicians and researchers from the academia and industry to speed up innovations to combat the pandemic. Starting off with the storage of nasopharyngeal and oropharyngeal swab samples, the biorepository is teaming up with Hospitals in Bangalore to grow the collection to include serum (blood), sputum, bronchoalveolar lavage and stool samples. This endeavor aims to collect samples that are ethically obtained, well-documented, and tested from approximately 500 adult patients in its first year. These samples will be shared with researchers in academia and industry to increase our understanding of the virus, the variability in the severity of symptoms caused by this infection in different individuals, and potential new routes of therapeutic intervention.

Research

COVID-19 disease amelioration

There are team-based projects currently underway aimed at blocking the infection of humans by SARS-CoV-2:

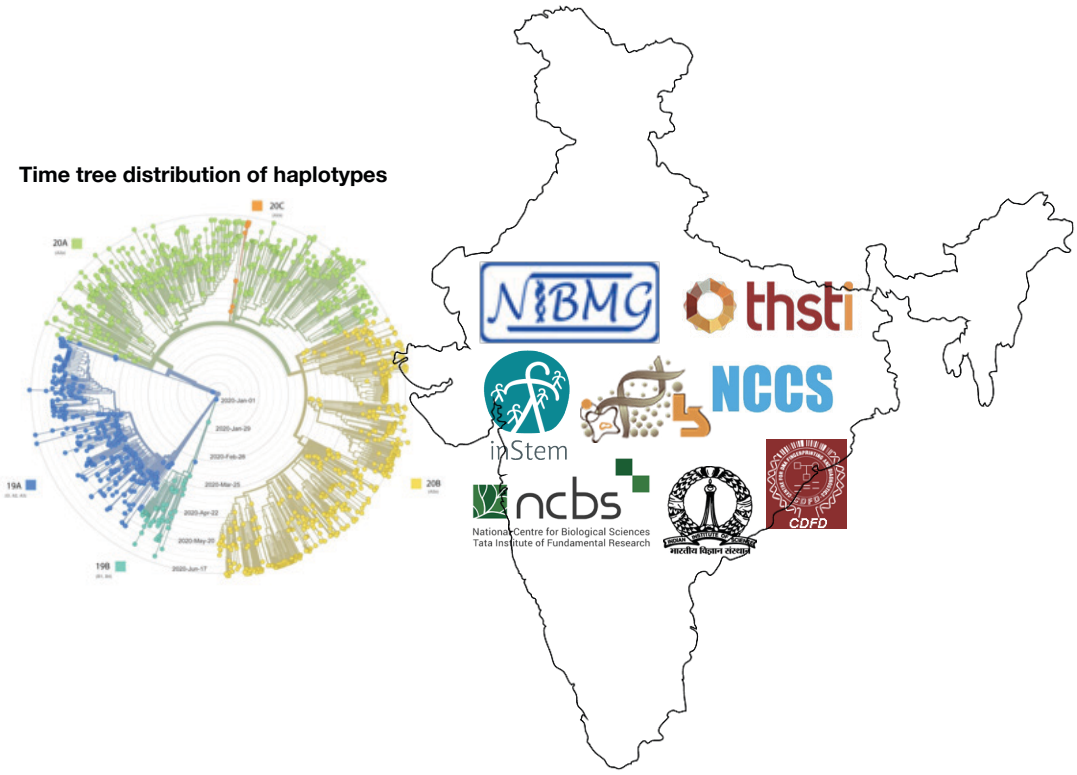
1. Scientists from inStem (Arjun Guha and Praveen Vemula) and NCBS (Satyajit Mayor, Vardharrajan Sundaramurthy, Vinothkumar K Raghunath) are working to repurpose FDA-approved drugs for the inhibition of SARS-CoV-2 entry into cells. The central hypothesis is that drugs that inhibit endolysosomal acidification in cells will prevent viral entry into cells by preventing fusion of the viral envelope with the endolysosomal membrane. This hypothesis is predicated on the observations that drugs like Bafilomycin or Hydroxychloroquine that inhibit endolysosomal acidification also inhibit viral entry into cells. The primary screen for drugs that inhibit endolysosomal acidification has identified 38 compounds from the 1280-compound LOPAC (explain this) library. Of these, 15 compounds have been shortlisted for further analysis based on a series of secondary screens. Validation of these 15 compounds as antivirals using an S protein-expressing lentivirus infection assay is currently underway. The establishment of lung organoids, which can be extended to test SARS-CoV-2 infection assays will further expand the repertoire and scope of pre-clinical assays. These studies will then be extended to the mouse models of COVID-19 pathogenesis being developed with support of the DBT National Mouse Resource grant on the campus (see above).

2. An academic-industry collaboration between the laboratory of Colin Jamora and the Research & Development unit of Hindustan Unilever in Bangalore is studying the regulation and function of the rich source of antimicrobial peptides (AMPs) in the skin. Over the past few decades AMPs have garnered attention for their ability to kill a whole spectrum of microorganisms including viruses and antibiotic resistant bacteria. With the exploding worldwide public health problem of antimicrobial resistance, coupled with the dearth of new classes of antibiotics, AMPs are emerging as an attractive alternative to combat these so-called "superbugs". Though naturally produced AMPs avoid all the limitations found with synthetic forms of these peptides, an outstanding question in the field was how they can be released on demand. Building earlier work (https://www.cell.com/cell-reports/pdfExtended/S2211-1247(19)31412-3), the collaborative team is studying whether the AMPs secreted from the skin are capable of targeting the SARS-CoV-2 virus.

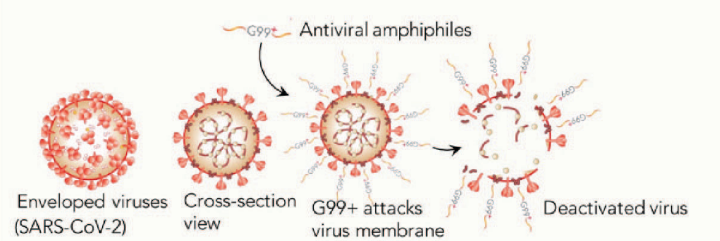
A partner in the PAN-INDIA 1000 SARS-CoV-2 RNA Genome Sequencing Consortium

inStem is a partner in the PAN-INDIA 1000 SARS-CoV-2 RNA Genome Sequencing Consortium, which has achieved its initial goal of completing the sequencing of 1000 SARS-CoV-2 genomes from nasopharyngeal and oropharyngeal swabs collected from individuals testing positive for COVID-19 by Real Time PCR. The samples were collected across 10 states covering different zones within India. Given the importance of this information for public health response initiatives investigating transmission of COVID-19, the sequence data is being released in GISAID database. This information will improve our understanding on how the virus is spreading, ultimately helping to interrupt the transmission chains, prevent new cases of infection, and provide impetus to research on intervention measures. This will also provide us with information on evolution of the virus, genetic predisposition (if any) and adaptation to human hosts. One thousand and fifty two sequences were used for phylodynamic, temporal and geographic mutation patterns and haplotype network analyses. Initial results indicate that multiple lineages of SARS-CoV-2 are circulating in India. Detailed mutational analysis across India to understand the gradual emergence of mutants at different regions of the country and its possible

implication will help in better disease management. The campus engagement with this national consortium was spearheaded by Dr. Dasaradhi Palakodeti at inStem and Dr. Aswin Seshasayee of NCBS. Together, their laboratories sequenced the genomes of 100 viral samples received through the campus COVID 19 testing laboratory using the Shotgun Method and Direct Targeted Method and analyzed the data to study the phylodynamics of SARS-CoV-2. These results are posted online at https://doi.org/10.1101/2020.08.03.233718(biorxiv).



Engineering of a germicidal-fabric capable of killing respiratory viruses, including SARS-CoV-2.
Praveen Vemula's group has developed a germicidal-coated fabric that can be stitched into a facemask and other personal protective equipment (PPE). The germicidal fabric termed G-fab is expected to kill viruses and bacteria upon contact. G-fab technology has shown a 99.99% kill rate against a wide range of viruses, including COVID-19 causing coronavirus (SARS-CoV-2) and influenza virus (H1N1 flu) and against various harmful bacteria, including gram-negative and gram-positive bacteria. A non exclusive licence to a company called Color Threads, from Tirupur, India will commercialise the G-fab technology. The launch of the antiviral face masks (G99+ antiviral) is anticipated as the first outcome of this technology.



12 Science Communication and Outreach

. Outreach is a critical part of our role as scientists at inStem. The guiding principle of our outreach program is to instill excitement in young minds via emphasizing real-world problems through collaboration, hands-on interaction with lab scientists and easy to understand illustrative and 3D models. This is an important part of our mandate as an institute as it plays a key role for inspiring the next generation of scientists. We have conducted a successful repertoire of outreach events that we expect will excite and promote curiosity in the minds of school and college students, and the lay public.

ENGAGEMENT WITH SCHOOLS AND UNDERGRADUATE COLLEGES

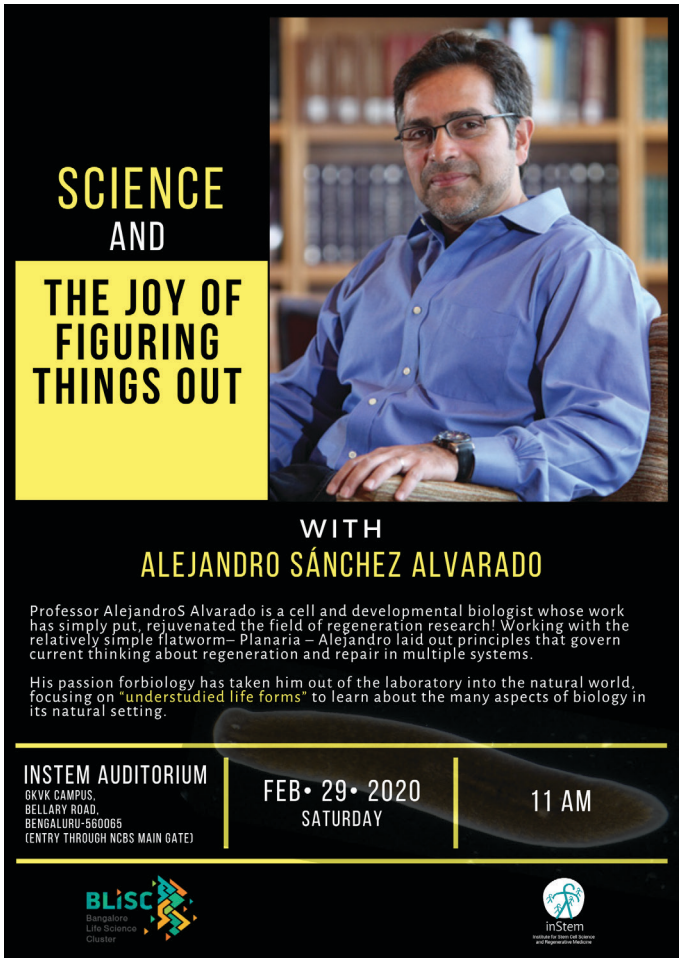
Stimulating discussions at the Lab Culture exhibit.

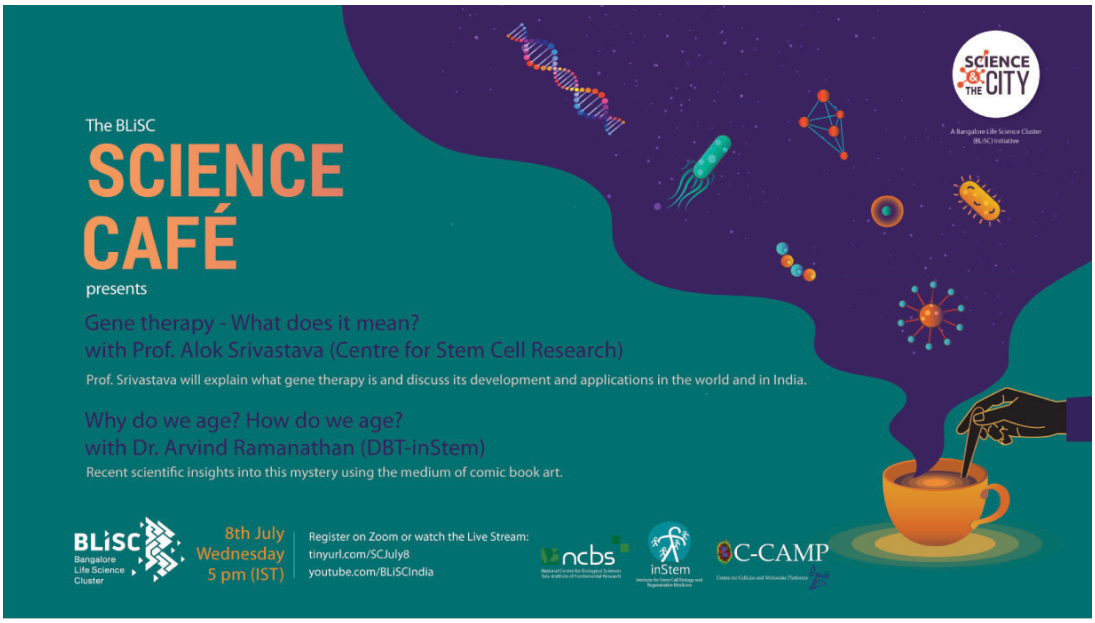
Curious young minds at work

School students touring the Lab Culture at InStem gallery. Image

A successful example of outreach were the Lab culture events (organized in conjunction with the Museums and Field Stations Facility) that were designed to invite school children within and outside of Bengaluru to showcase and inspire new scientific ideas and projects being pursued by researchers at inStem. In the first part of this event between 4th of July and 14th of August 2019, we hosted 817 students from 20 schools. These students had a hands-on and personal interactions with the young. researchers at inStem who were proud and excited to speak about their work. In the second part of this event (from the 3rd of October 2019 to 9th of January 2020) over 2500 students from around 75 schools and colleges had the opportunity to visit the institute. Extensive interactions in Kannada, Hindi and English were enabled to familiarize students with what the pursuit of fundamental and applied questions in biology entails in a laboratory setting. The students had numerous questions regarding career choices and laboratory techniques that were answered by scientists from the Institute.

inStem held an event geared toward college students on 23rd October 2019. Through this event we generated great interest in the India International Science Festival (IISF), 2019. The National Science Day on February 29, 2020 was celebrated by conducting an outreach event with inStem SAB member, Prof. Alejandro Sanchez (Scientific Director, Stowers Institute for Medical Research, USA, Member, National Academy of Sciences USA, HHMI investigator) where he gave a talk titled 'Science and the joy of figuring things out'. This was followed by an interactive session with many of the visiting students. A central theme of the National Science Day was women in science where scientists from inStem had an opportunity to speak about their perspectives. The Fly Facility on campus had a successful school outreach session with students at Sarkari Prauda shale (Hebbal, Bengaluru) in Kannada language with the Akshaya Patra Foundation on 17 Feb 2020. The Jigyasa Project is a Bangalore Life Science Cluster (BLiSC) initiative that in partnership with Mandram to communicate science to non-English speaking students. inStem scientists Ravi Mudashetty and S. Ramaswamy engaged with this project. The Undergraduate Lecture Series is organised by the post-doctoral fellows association at NCBS with postdocs at inStem. The 7th iteration of this annual Lecture Series took place on Sunday mornings between February 2nd and March 22nd. 2020.



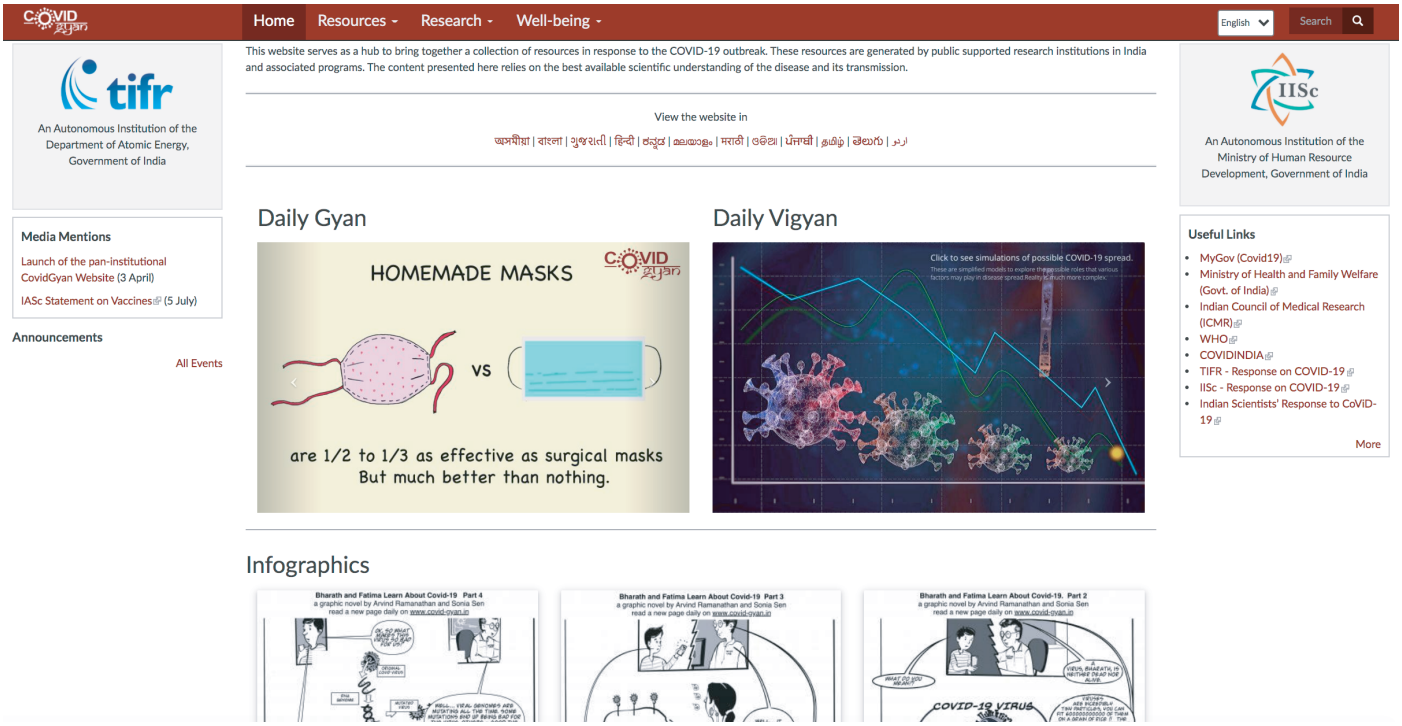


SCIENTIFIC OUTREACH TO THE PUBLIC VIA EXHIBITS AND SOCIAL MEDIA EVENTS

The traveling exhibition titled '*Energiewende*' (with the relevant theme of energy sustainability) was hosted in inStem Atrium from the 18th - 23rd of November, 2019. The opening event was held on 18th November that included a panel discussion with Amir Bazaz (IIHS), Martin Rohlmann (German Consulate General), Palak Aggarwal (Batti Ghar), Tejal Kanitkar (NIAS). The BLiSc Science Café series are interactions with the lay public about various scientific areas of importance and ongoing research in our laboratories. Five speakers from inStem, Aditi Bhattacharya (October '19), Srikala Raghavan (November '19), Deepti Trivedi (March '20), Alok Srivastava and Arvind Ramanathan (July '20) have presented at this forum. In an interesting twist the medium of comics was used to educate and excite the lay audience in one of the sessions. The inStem social media engagement programs have been particularly effective in communicating the impact of your scientific research to the public. Srikala Raghavan a faculty at inStem conducted a 'ask me anything' session over twitter on Skin Health (17th March 2020). inStem in conjunction with centres and facilities hosted within the campus as the Brain Awareness Week held from 18th - 25th March 2020. Two faculty that lead Brain research Prof. Raghu Padinjat and Dr. Bhavana Muralidharan discussed their collaborative work. Numerous researchers including Drs. Deepti Trivedi, Geetha, Rakhi and Anupam Hazra discussed their work over social media outlets. Faculty and students of inStem participated in the Global Bio India conference, coordinated by the DBT, BIRAC, Confederation of Indian Industry (CII), Association of biotechnology led enterprises (ABLE) and Invest India, held in New Delhi from Nov 21-25, 2019 where technological capabilities of inStem were showcased in a dedicated booth and a presentation at a session dedicated to the autonomous institutes of DBT. Our faculty and researchers participated in the 5th India International Science Festival held in September 2019 at Kolkata. IISF an annual event targeting young and dynamic minds from across India to share in the vision of building interdisciplinary science in biology, physics, chemistry, and engineering.

NATIONAL INITIATIVES

The Institute stands in support of numerous national initiatives including the Swachh Bharat Mission. On 27th September a panel discussion was conducted on Water & Clean Energy (Jagdish Krishnaswamy, Sanjiv Sambandan, and Seema Mundoli, moderated by Vishwanath S) in the context of Swachh Bharat Mission completing 5 years in October 2019. InStem has contributed to the national COVID-19 response by establishing a testing centre that has reported more than 40000 samples, from multiple districts in Karnataka, free of cost, supported by philanthropy and the departments of BT and DAE. This and other activities are described in a separate section in the report.The COVID-gyan website serves as a national hub to bring together a collection of resources in response to the COVID-19 outbreak. Our faculty support the website which is an inter-institutional website with TIFR Institutions, IISc, TMC, inStem, India Bioscience, Vigyan Prasar amongst others.



Photographs courtesy: Arjun Guha, inStem;

LIST OF STUDENTS AWARDED PHD DEGREES 2019-2020

Neha Pincha
Guide: Prof. Colin Jamora
Thesis Title: Understanding the role of PAI-1 in the development of fibrosis
Degree awarded from Manipal University, April 2019

Jyoti Dubey
Guide: Prof. S Ramaswamy
Co-Guide: Prof. Sandhya Koushika
Thesis Title: Characterization and mapping of mutants with mitochondrial distribution defects in TRNs and long-term imaging of ***C.elegans***
Degree awarded from Manipal University, May 2019

Ambika S Kurbet
Guide: Dr. Srikala Raghavan
Thesis Title: Understanding the role of sterile inflammation in embryonic skin
Degree awarded from SASTRA University, August 2019

Thanuja Gangisetty
Guide: Prof. S Ramaswamy
Thesis Title: Structural and functional characterization of sialic acid uptake and metabolism in pathogenic bacteria
Degree Awarded from Trans-Disciplinary University, January 2020

Sreenath R
Guide: Dr. Ravi S. Muddashetty
Thesis Title: Understanding the role of BDNF-mediated translational regulation of actin modulators during dendrite development.
Degree awarded from Manipal University, July 2020

Srikar Krishna G
Guide: Dr. Dasaradhi Palakodeti
Co-Guide: Dr. Yashoda Ghanekar
Thesis Title: tRNA derived small RNAs (tsRNAs): Novel regulators of cell state transitions
Degree awarded from SASTRA University, July 2020

Nishan B.S.
Guide: Dr. Akash Gulyani
Thesis Title: Complex light sensing in simple eyed flatworms reveals new sensory paradigms
Degree awarded from SASTRA University, July 2020

Vairavan Lakshmanan
Guide: Dr. Dasaradhi Palakodeti
Thesis Title: Ending the message right: Polyadenylation centred gene regulation in planarian stem cells
Degree awarded from SASTRA University, July 2020

Preeti Madhav Kute
Guide: Dr. Ravi S. Muddashetty
Thesis Title: NMDAR mediated translation at the synapse is regulated by MOV10 and FMRP
Degree awarded from SASTRA University, Sept 2020

RESEARCH DEVELOPMENT OFFICE

Research at the Bangalore Life Science Cluster which includes NCBS, inStem and C-CAMP, spans a diverse range of questions and approaches in the broad area of life sciences. The Research Development Office (RDO) was created to facilitate research and training at the Cluster, via research funding and research collaborations.

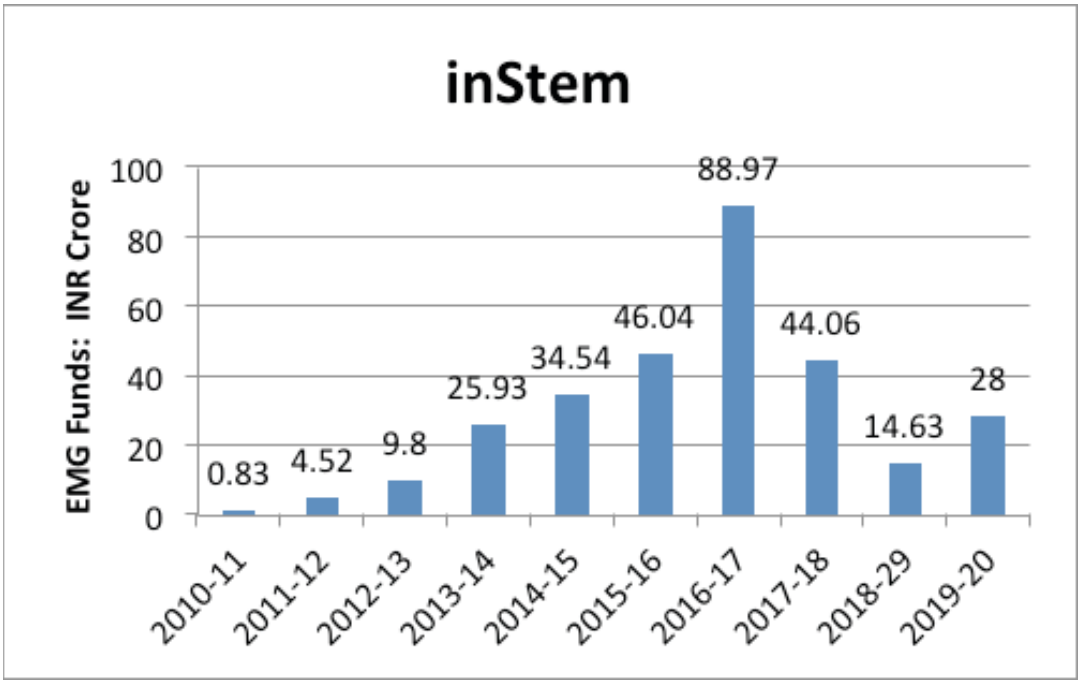
In 2020, the RDO completed a decade of operations at BLiSC, supporting the diverse needs of the campus in fundraising, grants management and contract negotiation for research funding from national and international funding agencies, corporate sources and charitable organizations. The RDO has also supported the establishment of national and international collaborations via grants, agreements and facilitating interactions with potential collaborators.

Generous funding from the Government has been invaluable in establishing large institutional programs on campus such as the Program on Chemical Biology and Therapeutics (PCBT), BLiSC for Multiscale Basic and Applied Research in the Biological Sciences (B-LIFE), Program on Chemical Ecology, Centre for Neurodevelopmental Synaptopathies (CNS), the National Mouse Research Resource (NaMoR) and the Macromolecular Crystallography and Scattering Facility. The RDO manages all these large programs.

Work at the RDO is made possible by a dynamic and professional team who are committed to offering several key services to the campus at the boundaries of science, management and outreach. We look forward to a rewarding journey further ahead for the RDO, supporting campus research funding, the Endowment Fund and research collaborations.

Vineetha Raghavan

Extramural grant (EMG) funds at inStem (in INR Crore)



INSTEM LEADERSHIP COMMITTEES 2019-2020

DIRECTOR
Prof. Apurva Sarin

SOCIETY

Dr. Renu Swarup, *Secretary to the Government of India, DBT, New Delhi - President*
Prof. Apurva Sarin, *Director, inStem, Bengaluru*
Dr. Alka Sharma, *Advisor & Scientist G, DBT, New Delhi*
Mr. B. Anand, *Addl Secretary & FA, DBT, New Delhi*
Mr. Chandra Prakash Goyal, *Joint Secretary (Admin), DBT, New Delhi*
Prof. K. VijayRaghavan, *Principal Scientific Adviser to the Govt. (Signatory to MoA)*
Dr. Kiran Mazumdar Shaw, *CMD, Biocon India Ltd., Bengaluru (Signatory to MoA)*
Prof. H. Sharat Chandra, *Hon. Director, Centre for Human Genetics (Signatory to MoA)*
Prof. Jyotsna Dhawan, *Chief Scientist, CCMB, Hyderabad (Signatory to MoA)*
Prof. Satyajit Mayor, *Centre Director, NCBS-TIFR, Bengaluru (Signatory to MoA)*
Dr. J. V. Peter, *Director, CMC, Vellore*
Prof. P. Balaram, *Molecular Biophysics Unit, IISc, Bengaluru (Signatory to MoA)*
Prof. S. Ramaswamy, *Visiting Professor, inStem, Bengaluru (Signatory to MoA)*
Prof. Goverdhan Mehta, *Former Director, IISc & CSIR Bhatnagar Fellow, Bengaluru (Signatory to MoA)*
Mr. Pawan Kumar Pahwa, *Head-Admin & Finance, inStem, Bengaluru (Non-member Secretary)*

GOVERNING COUNCIL

Dr. Renu Swarup, *Secretary to the Government of India, DBT, New Delhi - Chairperson*
Prof. Apurva Sarin, *Director, inStem, Bengaluru*
Mr. B. Anand, *Additional Secretary & Financial Advisor, DBT, New Delhi*
Mr. Chandra Prakash Goyal, *Joint Secretary (Admin), DBT, New Delhi*
Dr. Alka Sharma, *Advisor & Scientist G, DBT, New Delhi*
Dr. Niloo Srivastava, *Scientist 'E', DBT, New Delhi*
Prof. Satyajit Mayor, *Centre Director, NCBS-TIFR, Bengaluru*
Prof. Upinder S Bhalla, *Dean, NCBS, Bengaluru*
Dr. J. V. Peter, *Director, CMC, Vellore*
Prof. Alok Srivastava, *Head- CSCR, CMC Vellore*
Dr. Sandeep Trivedi, *Director, TIFR, Mumbai*
Dr. Gagandeep Kang, *Executive Director, THSTI, Faridabad*
Dr. Soniya Nityanand, *Professor and Head, Dept. of Hematology, SGPGI, Lucknow*
Prof. Jyotsna Dhawan, *Chief Scientist, CCMB, Hyderabad*
Dr. Dinakar Salunke, *Director, ICGEB, New Delhi*
Dr. B. S. Ramakrishna, *Director, SIMS Institute of Gastroenterology, Chennai*
Dr. Mammen Chandy, *Director, Tata Medical Centre, Kolkata*
Prof. S. Ramaswamy, *Visiting Professor inStem, Bengaluru*
Prof. Colin Jamora, *inStem, Bengaluru*
Mr. Pawan Kumar Pahwa, *Head-Admin & Finance, inStem, Bengaluru (Non-member Secretary)*

SCIENTIFIC ADVISORY COMMITTEE

Prof. Azim Surani, *Wellcome Trust / Cancer Research UK Gurdon Institute, University of Cambridge, UK*
Prof. Alejandro Sánchez Alvarado, *Howard Hughes Medical Institute, USA*
Dr. Marco Foiani , *IFOM (FIRC Institute of Molecular Oncology, Milan), Italy*
Dr. Satyajit Rath, *IISER Pune, India.*
Prof. Mriganka Sur, Picower *Institute for Learning and Memory, Massachusetts Institute of Technology, USA*
Prof. Helen Skaer, *Emeritus Professor, University of Cambridge*
Dr. Mahendra Rao, *NIH CRM (NIH Center for Regenerative Medicine), USA*
Prof. Satyajit Mayor, *Director, NCBS, TIFR Bangalore*
Prof. Upinder S. Bhalla, *Dean, NCBS*
Prof. Apurva Sarin, *Director, inStem*

FINANCE COMMITTEE

Mr. B. Anand, *Addl Secretary & Financial Adviser, DBT, New Delhi - Chairperson*
Prof. Apurva Sarin, *Director, inStem, Bengaluru*
Dr. Alka Sharma, *Adviser & Scientist G, DBT, New Delhi*
Prof. Satyajit Mayor, *Centre Director, NCBS-TIFR, Bengaluru*
Prof. Upinder S. Bhalla, *Dean, NCBS, Bengaluru*
Prof. Alok Srivastava, *Head-CSCR, CMC, Vellore*
Mr. Pawan Kumar Pahwa, *Head-Admin & Finance, inStem, Bengaluru – Member Secretary*

STAFF

ACADEMIC

Apurva Sarin, *Director*
Colin Jamora, *Professor, IFOM-inStem JRL*
Srikala Raghavan, *Associate Investigator*
Dasaradhi Palakodeti, *Associate Investigator*
Praveen Vemula, *Associate Investigator*
Arvind Ramanathan, *Associate Investigator*
Arjun Guha, *Associate Research Investigator*
Tina Mukherjee, *Assistant Investigator*
Sunil Laxman, *Assistant Investigator*
Minhaj Sirajuddin, *Assistant Investigator*
Dhandapany Perundurai, *Assistant Investigator*
Bhavana Muralidharan, *Assistant Investigator*

Sivaraj Sivaramakrishnan, *Visiting Professor*
S. Ramaswamy, *Visiting Professor*

ADMINISTRATION

Pawan Kumar Pahwa, *Chief Administrative Officer*
Sreenath B. A., *Admin Officer (Purchase)*
Nagaraja B. S., *Officer on Special Duty*
Shrikant Bhat, *Junior Management Assistant*
Raju B. Verma, *Junior Management Assistant*
Valsala Neyyan, *Administrative Assistant*
Shobha R., *Assistant Administrative Officer*
Sunitha R., *Project Assistant (Admin)*
Shobha B. N., *Project Secretary*
Supriya N., *Project Secretary*

SCIENTIFIC & TECHNICAL

Rajesh R., *Engineer D (System Administrator)*
Anand Kumar V., *Engineer D (Electrical)*
Chakrapani, *Junior System Administrator*

B.P.RAO & CO.
CHARTERED ACCOUNTANTS

No.5, POORNA PRASAD ROAD,
HIGH GROUNDS, BANGALORE –560 001.
PH : 22200200, 22200201.
FAX : 22205030.
E-MAIL: bpraoco@gmail.com

INDEPENDENT AUDITOR'S REPORT

To,
The Members
Governing Council of
M/s. Institute for Stem Cell Science and Regenerative Medicine
G K V K Post, Bellary Road
Bangalore-560065

Opinion

We have audited the financial statements of **Institute for stem Cell Science and Regenerative Medicine** (hereinafter referred to as 'Institute'), which comprises the Balance Sheet as at March 31, 2020, and the Income and Expenditure Account for the year then ended, and notes to the financial statements, including a summary of significant accounting policies

In our opinion, the accompanying financial statements give a true and fair view of the financial position of the Institute as at 31st March 2020, and of its financial performance for the year ended in accordance with the Accounting Standards issued by the Institute of Chartered Accountants of India (ICAI).

Basis for Opinion

We conducted our audit in accordance with the Standards on Auditing (SAs) issued by ICAI. Our responsibilities under those Standards are further described in the Auditor's Responsibilities for the Audit of the Financial Statements section of our report. We are independent of the entity in accordance with the Code of Ethics issued by ICAI and we have fulfilled our other ethical responsibilities in accordance with the Code of Ethics. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Emphasis of Matter

We draw attention to Note 8 of Schedule 25 to the Financials statements, which states that Rs.4.31Cr of previous year expenditure has been accounted during the year.

Our opinion is not modified with respect to the matters stated under 'Emphasis of Matter'.

B.P.RAO & CO. Bangalore 560 001. Chartered Accountants

Also At:
No.45, Medavakkam Tank Road, Kalpak, Chennai – 600 010. Ph. 26413112, 26421872.
No.14/C, 5th Main, Yadavgiri, Mysore – 570 020. Ph. 2515929, 2514880.
"Shanthi", No.12/62, 1st Floor, Reservoir Street Cross, Basavanagudi, Bangalore - 560 004. Ph: 80 2662 2101 / 2662 2201

Responsibilities of Management and Those Charged with Governance for the Financial Statements

Management is responsible for the preparation of the financial statements in accordance with generally accepted accounting principles in India. This responsibility includes the design, implementation and maintenance of internal control relevant to the preparation and presentation of the financial statements that give a true and fair view and are free from material misstatement, whether due to fraud or error.

In preparing the financial statements, management is responsible for assessing the entity's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless management either intends to liquidate the entity or to cease operations, or has no realistic alternative but to do so.

Those charged with governance are responsible for overseeing the entity's financial reporting process.

Auditor's Responsibilities for the Audit of the Financial Statements

Our objectives are to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinion. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with SAs will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these financial statements.

As part of an audit in accordance with SAs, we exercise professional judgment and maintain professional skepticism throughout the audit. We also:

• Identify and assess the risks of material misstatement of the financial statements, whether due to fraud or error, design and perform audit procedures responsive to those risks, and obtain audit evidence that is sufficient and appropriate to provide a basis for our opinion. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control.

• Obtain an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the entity's internal control.

• Evaluate the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made by management.

• Conclude on the appropriateness of management's use of the going concern basis of accounting and, based on the audit evidence obtained, whether a material uncertainty exists related to events or conditions that may cast significant doubt on

the entity's ability to continue as a going concern. If we conclude that a material uncertainty exists, we are required to draw attention in our auditor's report to the related disclosures in the financial statements or, if such disclosures are inadequate, to modify our opinion. Our conclusions are based on the audit evidence obtained up to the date of our auditor's report. However, future events or conditions may cause the entity to cease to continue as a going concern.

We communicate with those charged with governance regarding, among other matters, the planned scope and timing of the audit and significant audit findings, including any significant deficiencies in internal control that we identify during our audit.

We also provide those charged with governance with a statement that we have complied with relevant ethical requirements regarding independence, and to communicate with them all relationships and other matters that may reasonably be thought to bear on our independence, and where applicable, related safeguards.

Other Matter

a. The Previous year Financial Statements was audited by another auditor viz., M/s. B.R.V.Goud & Co., who have expressed an unmodified opinion on those statements as on 31-03-2019 vide their audit report dated 19.08.2019.

b. We have not audited the financial statements of the Vellore branch (CSCR), whose financial statements reflect total assets of Rs.13,52,14,707, total revenue of Rs.7,61,06,942 and excess of expenditure over income of Rs.3,06,94,111 for the year ended as on 31-03-2020, as considered in the financial statement of the Institute. These financial statements have been audited by other auditor whose report have been furnished to us by the Management.

Our opinion is not modified with respect to the matters stated under 'Other Matter'

For B.P.Rao and Co.
Chartered Accountants
FRN: 003116S

Prashanth. C
Partner
M No:214431
UDIN **20214431AAAADA4204**

Place: Bangalore
Date: 15.09.2020

INSTITUTE FOR STEM CELL SCIENCE & REGENERATIVE MEDICINE, BANGALORE

(Registered under the Karnataka Societies' Registration Act)

GKVK, BELLARY ROAD, BANGALORE - 560 065

RECEIPTS AND PAYMENTS STATEMENT FOR THE YEAR ENDED MARCH 31, 2020

(Amount -Rs)

RECEIPTS	CURRENT YEAR	PREVIOUS YEAR	PAYMENTS	CURRENT YEAR	PREVIOUS YEAR
I. **Opening Balances**			**I. Expenses**		
a) Cash in hand	-	-	a) Establishment Expenses	108,694,603	86,140,537
b) Bank Balances			b) Administrative Expenses	350,323,002	202,184,112
i) in current accounts	83,953,501	98,433,823		**459,017,605**	**288,324,649**
ii) in deposit accounts	362,167,415	749,027,856	**II. Payments made against projects**	**258,000,963**	**390,839,886**
iii) in savings accounts	59,739,232	59,234,479	**III. Investments made**		
	505,860,148	**906,696,158**	a) Out of Earmarked/End. Funds	-	-
II. Grants Received			b) Out of own funds		
a) From Govt. of India	672,000,000	820,700,000	**IV. Increase in Current Assets**	**9,527,687**	**-**
b) From State Govt.	-	-	**V. Capital Expenditure**		
	672,000,000	**820,700,000**	a) Purchase of fixed assets-Projects	60,215,533	183,017,820
III. Project Receipts-Projects	**284,264,231**	**150,822,611**	b) Exp. On Building	65,781,543	452,557,224
IV. Increase in Current Liab	**85,969,337**		c) Exp on Equipments & Furnitures	168,455,690	81,128,070
V. Decrease in Current Assets		**11,360,721**		**294,452,766**	**716,703,114**
VI. Interest Received			**VI. Refund of surplus money/Loans**	-	-
a) On Bank deposits	25,153,906	27,373,010	a) To the Govt. of India	-	-
b) on Loans, Advances etc.		-	b) To the State Govt.		-
	25,153,906	**27,373,010**	**VII. Finance Charges (Interest)**	-	-
VII. Other Income (Specify)	**19,854,002**	**7,708,874**	**VIII. Decrease in Current Liabilities**	**-**	**22,933,576**
VIII. Amount Borrowed	-	-	**IX. Closing Balances:**		
IX. Any other receipts	-	-	a) Cash in hand	21,943	-
			b) Bank Balances		
			i) in current accounts	40,752,806	83,953,501
			ii) in deposit accounts	393,815,116	362,167,415
			iii) in savings accounts	137,512,740	59,739,232
				572,102,605	**505,860,148**
TOTAL	**1,593,101,626**	**1,924,661,374**	**TOTAL**	**1,593,101,626**	**1,924,661,374**

Vide our report of even date

For B. P. RAO & CO.

Chartered Accountants

FRN 003116S

For B. P. RAO & CO.
Chartered Accountants
Partner

(Prashanth. C)

Partner (M.No.214431)

(Srinivasa Rao Palla)

Senior Accounts Officer

(Pawan Kumar Pahwa)

Head Administration

(Prof. Apurva Sarin)

Director

INSTITUTE FOR STEM CELL SCIENCE AND REGENERATIVE MEDICINE BANGALORE

(Registered under the Karnataka Societies' Registration Act.)

GKVK, BELLARY ROAD, BANGALORE - 560 065

INCOME AND EXPENDITURE ACCOUNT FOR THE YEAR ENDED MARCH 31, 2020

(Amount- Rs.)

Paticulars	Schedule	Current Year	Previous Year
INCOME			
Income from Projects - to the extent of expenditure included	**3**	258,000,963	390,839,886
Income from Sales and Services	**12**	9,411,509	1,840,898
Grants/Subsidies	**13**	412,000,000	322,500,000
Fees/Subscriptions	**14**	-	-
Income from Investments	**15**	-	-
Income from Royalty, Publications etc.	**16**	-	-
Interest earned	**17**	12,465,062	7,958,076
Other Income	**18**	10,442,493	5,867,976
Increase/(decrease)in stock of Finished goods and works-in-progress	**19**	-	-
TOTAL (A)		**702,320,027**	**729,006,836**
EXPENDITURE			
Establishment Expenses	**20**	108,694,603	92,171,599
Other Administrative Expenses	**21**	350,323,002	215,840,228
Expenditure on Grants/Subsidies etc.	**3**	258,000,963	390,839,886
Interest	**22**	-	-
Depreciation (Net Total at the year -end -corresponding to Sch.8)		379,791,972	254,048,955
TOTAL (B)		**1,096,810,540**	**952,900,668**
Balance being excess of Expenditure over Income (A-B)		**-394,490,513**	**-223,893,832**
Less- Transfer to Capital Reserve - equivalent to depreciation charges	**2(1)**	379,791,972	254,048,955
Less- Transfer to/from General Reserve - Recurring Grant Account	**1(B)**	-14,698,541	30,155,123
Balance being surplus/deficit carried to Corpus/Capital Fund			-
SIGNIFICANT ACCOUNTING POLICIES	**24**		
CONTINGENT LIABILITIES AND NOTES ON ACCOUNTS	**25**		

Vide our report of even date

For B. P. RAO & CO.

Chartered Accountants

FRN 003116S

For B. P. RAO & CO.
Chartered Accountants

(Prashanth. C)

Partner (M.No.214431)

(Srinivasa Rao Palla)

Senior Accounts Officer

श्रीनिवासराव पल्ला / Srinivasa Rao Palla
वरिष्ठ लेखा अधिकारी / Senior Accounts Officer
स्टेम कोशिका विज्ञान और पुनर्योजि औषधि संस्थान
Institute for Stem Cell Science and Regenerative Medicine (inStem)
जैव प्रौद्योगिकी विभाग, भारत सरकार के अधीन स्वायत्त संस्थान
(An under Department of Biotechnology, Govt. of India)
जीकेवीके पोस्ट, बेल्लारी रोड / GKVK Post, Bellary Road.
बेंगलुरु – ५६००६५ / Bengaluru - 560065

(Pawan Kumar Pahwa)

Head Administration

पवन कुमार पाहवा / Pawan Kumar Pahwa
मुख्य प्रशासनिक अधिकारी / Head Administration
स्टेम कोशिका विज्ञान और पुनर्योजि औषधि संस्थान
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(An under Department of Biotechnology, Govt. of India)
जीकेवीके पोस्ट, बेल्लारी रोड / GKVK Post, Bellary Road.
बेंगलुरु – ५६००६५ / Bengaluru - 560065

(Prof. Apurva Sarin)

Director

प्रो.अपूर्वा सरीन / Prof. Apurva Sarin
निदेशक / Director
स्टेम कोशिका विज्ञान और पुनर्योजी औषधि संस्थान
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बेंगलुरु – ५६० ०६५ / Bengaluru-560 065

INSTITUTE FOR STEM CELL SCIENCE AND REGENERATIVE MEDICINE BANGALORE

(Registered under the Karnataka Societies' Registration Act.)

GKVK, BELLARY ROAD, BANGALORE - 560 065

BALANCE SHEET AS AT MARCH 31, 2020

(Amount- Rs.)

Paticulars	Schedule	As at 31.03.2020	As at 31.03.2019
CORPUS/CAPITAL FUND AND LIABILITIES			
CORPUS/CAPITAL FUND	**1**	245,415,651	187,085,297
RESERVES AND SURPLUS	**2**	2,955,954,355	3,088,559,687
EARMARKED/ ENDOWMENT FUNDS	**3**	267,103,358	288,366,779
SECURED LOANS AND BORROWINGS	**4**		-
UNSECURED LOANS AND BORROWINGS	**5**		-
DEFERRED CREDIT LIABILITIES	**6**		-
CURRENT LIABILITIES AND PROVISIONS	**7**	137,399,339	51,430,002
TOTAL		**3,605,872,703**	**3,615,441,765**
ASSETS			
FIXED ASSETS	**8**	3,003,220,481	3,088,559,687
INVESTMENTS - FROM EARMARKED /ENDOWMENT FUNDS	**9**		-
INVESTMENTS - OTHERS	**10**	600	600
CURRENT ASSETS, LOANS, ADVANCES ETC.	**11**	602,651,622	526,881,478
MISCELLANEOUS EXPENDITURE (TO THE EXTENT NOT WRITTEN OFF OR ADJUSTED)			-
TOTAL		**3,605,872,703**	**3,615,441,765**
SIGNIFICANT ACCOUNTING POLICIES	**24**		
CONTINGENT LIABILITIES AND NOTES ON ACCOUNTS	**25**		

Vide our report of even date

For B. P. RAO & CO.

Chartered Accountants

FRN 003116S

For B. P. RAO & CO.
Chartered Accountants
Partner

(Prashanth. C)

Partner (M.No.214431)

UDIN: 20214431AAAAC2...

11/07/2020

(Srinivasa Rao Palla)

Senior Accounts Officer

श्रीनिवासराव पल्ला / Srinivasa Rao Palla
वरिष्ठ लेखा अधिकारी / Senior Accounts Officer
स्टेम कोशिका विज्ञान और पुनर्योजि औषधि संस्थान
Institute for Stem Cell Science and Regenerative Medicine (inStem)
जैव प्रौद्योगिकी विभाग, भारत सरकार के अधीन स्वायत्त संस्थान
(AI under Department of Biotechnology, Govt. of India)
जीकेवीके पोस्ट, बेल्लारी रोड / GKVK Post, Bellary Road.
बेंगलुरु – ५६००६५ / Bengaluru - 560065

(Pawan Kumar Pahwa)

Head Administration

पवन कुमार पाहवा / Pawan Kumar Pahwa
मुख्य प्रशासनिक अधिकारी / Head Administration
स्टेम कोशिका विज्ञान और पुनर्योजि औषधि संस्थान
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बेंगलुरु – ५६००६५ / Bengaluru - 560065

(Prof. Apurva Sarin)

Director

प्रो.अपूर्वा सरीन / Prof. Apurva Sarin
निदेशक / Director
स्टेम कोशिका विज्ञान और पुनर्योजी औषधि संस्थान
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INSTITUTE FOR STEM CELL SCIENCE AND REGENERATIVE MEDICINE BANGALORE
(Registered under the Karnataka Societies' Registration Act.)
GKVK, BELLARY ROAD, BANGALORE - 560 065
SCHEDULES FORMING PART OF BALANCE SHEET AS AT MARCH 31, 2020

(Amount- Rs.)

SCHEDULE-1 - CORPUS/CAPITAL FUND:	Current Year	Previous Year
(A) NON-RECURRING GRANT		
Balance at the beginning of the year	99,961,894	135,447,188
Add: Contributions during the year	260,000,000	498,200,000
Less: Expenditure incurred during the year	186,971,106	533,685,294
Adjustments, if any	-	-
BALANCE AS AT THE YEAR END (A)	**172,990,788**	**99,961,894**
(B)RECURRING GRANT		
Balance as at the beginning of the year	87,123,404	56,968,280
Adjustment pertaining to previous years	-	-
Transferred from Income & Expenditure	-14,698,541	30,155,123
BALANCE AS AT THE YEAR END (B)	72,424,863	**87,123,403**
TOTAL (A) + (B)	**245,415,651**	**187,085,297**

(Amount- Rs.)

SCHEDULE -2 - RESERVES AND SURPLUS:	Current Year	Previous Year
1: CAPITAL RESERVE		
As per last account	3,088,559,688	2,744,009,746
Less: Adjustments of previous years	-	-
Addition during the year (See Note -1 below)	247,186,639	716,703,114
Less: Deduction during the year(See Note -2 below)	379,791,972	372,153,173
TOTAL	2,955,954,355	**3,088,559,687**
2: REVALUATION RESERVE:	-	-
3: SPECIAL RESERVES:	-	**-**
4: GENERAL RESERVE:	-	-
Total Reserves & Surplus	**2,955,954,355**	**3,088,559,687**

Note 1 : This represents Total additions made to the Fixed Assets during the year, consisting of Rs.18,69,71,106/- acquired out of Core Funds and Rs.6,02,15,533/- acquired out of Project Funds.
Note 2 : This represents the Depreciation on Fixed Assets for the year, consisting of Rs.25,14,55,811/-on Fixed Assets acquired out of Core Funds & Rs.12,83,36,555/- on Fixed Assets acquired out of Project

INSTITUTE FOR STEM CELL SCIENCE & REGENERATIVE MEDICINE, BANGALORE

(Registered under the Karnataka Societies' Registration Act)

GKVK, BELLARY ROAD, BANGALORE - 560 065

SCHEDULE -3-EARMARKED / ENDOWMENT FUNDS **SCHEDULE FORMING PART OF BALANCE SHEET AS AT MARCH 31, 2020**

(Amount -Rs.)

Sl No.	Project Title (Name of PI if applicable)	Opening Balance	Received during the year	Interest received	Refund	Expenditure		Total Expenditure	Balance as on 31-03-2020
						Capital	Revenue		
A	***From Government***								
1	DBT/JRF (8125-Zirmire)	55,852					113,051	113,051	-57,199
2	CSIR Fellowship (8131-Nitya Nandkishore)	10,027					10,027	10,027	-
3	DBT JRF (8138-Oindrilla Banerjee)	77,262	74,400				185,000	185,000	-33,338
4	DBTRA Fellowship (8139 Randhir Singh)	203,008	559,260				762,268	762,268	-
5	Mahendra Rao (8146)	722,445	320,525					-	1,042,970
6	DBTRA Fellowship (8149-Bhakti J Vyas)	25,000	468,000				463,000	463,000	30,000
7	DBTRA Fellowship (8152-Sarayu R)	42,500	579,600				622,100	622,100	-
8	DBTRA Fellowship (8153-Mohd M)	126,156	581,739				577,009	577,009	130,886
9	ICMR Fellowship(8155-Radhika Rao)	48,015	455,400				466,207	466,207	37,208
10	ICMR Fellowship (8158-Edries Y H)	415,665	273,065				481,465	481,465	207,265
11	ICMR Fellowship (8159-Isha Rana)	-	500,787				523,187	523,187	-22,400
12	CSIR Fellowship (8162-Abhinava Yadav)	15,068	-					-	15,068
13	CSIR Fellowship (8163-Drisya Dileep)	18,301	-				18,301	18,301	-
14	CSIR Fellowship (8164-Lakshmi Kripa)	20,000	-				-	-	20,000
15	Lady Tata Fellowship (8165-Subhasini Pandey)	-31,250	480,000				448,750	448,750	-
16	CSIR Fellowship (8166-Imtiyaz Gulami)	9,998	581,860				571,860	571,860	19,998
17	DBT RA Fellowship (8167-Anupam Dutta)	13,048						-	13,048
18	DBT RA Fellowship (8168-Anusree Mahanta)	544,000	349,700				827,133	827,133	66,567
19	DBT RA Fellowship (8169-Archana Kumari)	594,000	349,700				881,800	881,800	61,900
20	DBT RA Fellowship (8170-Sanjeeb K)	190,400	653,220				781,785	781,785	61,835
21	DBT RA Fellowship(8171-Rakesh Dey)	377,600	653,220				800,998	800,998	229,822
22	DBT Inspire Fellowship (8172-Vineeth V)	324,000	996,040				716,000	716,000	604,040
23	DBT JRF Fellowship (8173-Harshadri)	9,166						-	9,166
24	DBT JRF Fellowship (8178-Uttkarsh I)	23,583	509,100				484,800	484,800	47,883
25	DBT JRF Fellowship (8179-Sonal Joshi)	-	327,520				307,520	307,520	20,000
26	DBT JRF Fellowship (8180-Vishwaja Javeri)	-	573,100				538,100	538,100	35,000
27	DST Inspire fellowship (8181- Manisha Goyal)	-	451,520				307,520	307,520	144,000
28	DBT SRF Fellowship (8182-Pratul Jain)	-	373,694				373,694	373,694	-
29	DBT RA Fellowship(8183-Shruti Balachandra)	-	562,020				524,520	524,520	37,500
30	DST Inspire fellowship (8184- Michelle Dsouzal)	-	451,520				481,873	481,873	-30,353
31	CSIR Contingency received to Sreenath R. (8127)	-	70,000				68,824	68,824	1,176
32	Sumana Ghosh (8186)	-	116,603				-	-	116,603
32	*Other Miscelleaneous Grant*		42,000				*0*	-	42,000
33	Molecular Mechanisms of Sialic Acid Uptake by gram-negative bacteria (8203-Prof. Ramaswamy S.)	3,074	-			-	3,074	3,074	-
34	Gene Circuits regulating Stem Cell fate and organogenesis - Ramalingamswamy Fellowship (8211 - Dr. R. Sambasivan)	-405,445	1,041,953		889	-	635,619	635,619	-
35	Novel Cell Surface Markers for endodermal stem and progenitor cells in health and disease (8214) & (8270) & CSIR	2,049,435					1,679,317	1,679,317	370,118
36	Therapeutic approaches to augmentation of Adult cardiac stem cells (8217- Prof. Jyotsna Dhawan)	754,889	-					-	754,889
38	DBT Twinning Programme for the North East - Molecular Mechanism of target recognition and clevage by the CRISPR-CAS bacterial immune system (8220-Prof. Ramaswamy)	388,853	-					-	388,853
39	Centre for Brain Development and Repair - CBDR (8221-Prof. Sumantra Chattarji)	23,255,615	104,476,807	1,745,434	3,054,906	164,396	65,043,979	65,208,375	61,214,575
40	Muscle SC self renewal: A stressful matter (8225- CEFIPRA Grant - Prof. Jyostns Dhawan)	187,054	-					-	187,054

41	Molecular mechanisms that regulate cyto skeletal modelling in cardiac hypertrophy by developing an in-vitro human cariomyocyte culture microfluidic system (8229 - Prof. Jyotsna Dhawan)	451,756	-					-	451,756
42	Imaging signalling dynamics with fluroscent biosensors : towards a quantitative understanding o cell migration and adhesion (8230 - Dr. Akash Gulyani)	162,356		-	162,356			-	-
43	Jawaharlal Nehru Science Fellowship - Prof. Azim Surani (8233 - Prof. Azim Surani)	4,827,123			290,486		4,536,637	4,536,637	-
44	B-LIFE: Bangalore Lifesciences Cluster for Multiscale basic and applied research in biological Sciences (8234- Prof. Ramaswamy)	104,718,827	-	4,067,418		54,700,157	12,490,181	67,190,338	41,595,907
46	Imaging synaptic plasticity an control: Novel protein carbon nanotube fluorscent sensors for regulation of protein translation-(8239 Dr. Akash Gulyani)	536,842	-					-	536,842
47	Indo Swiss Grant-DST-SNSF-(8240-Dr. Akash Gulyani)	397,564			359,327		38,237	38,237	-
48	Ramalingaswami Fellowship-(8241 Arjun Guha)	610	472,000	2,158			474,768	474,768	-
49	Agreement with Uniliver(8245-Dr. Colin Jamora)	1,325,495	1,076,726	67,693			942,961	942,961	1,526,953
50	Elucidting the role of PAI-1 mediate signaling in cutaneous fibrosis-(8246 Dr. Colin Jamora)	324,546			324,546			-	-
51	Structure-Function studies on nucleotide sugar transporters Indo Argentina program-(8249-Prof.Ramaswamy)	-43,335	-					-	-43,335
52	Programme support on metabolic control of cell fate-(8250-Prof. Apurva sarin)	6,964,633	-	237,664	368,088		6,095,152	6,095,152	739,057
53	Accelerating the application of stemcell technology in human disease (ASHD)-8251 (Prof. Apurva, Dr. Raghu Padinjat)	32,925,323	15,314,182	1,585,197	2,136,021		19,742,003	19,742,003	27,946,678
54	Role of Euchromatic histone mythyl transferase in human neural development-8253 (Prof. Shravanthi Ramapalli)	1,004,500			132,593		871,907	871,907	-
55	Genetic program governing Vertbrate head Mesoderm Specification(8256-Ramkumar Sambasivan)	1,856,558		-	1,309,743		546,815	546,815	-
56	Mining the Genome and Metagenome of Marine Microbiome for PKS-NRPS Biosynthetic Gene Cluster and Bioactive Small Molecules : A Cordinated R & D Initiative in marine Genomics (8257-Dr. Praveen Kumar Vemula)	299,222	-	12,491			130,740	130,740	180,973
57	Ramalinga Swamy Grant (8258-Tina Mukharjee)	-123,892	500,197	4,117	17,197		381,103	381,103	-17,878
58	Understanding the Regulatory Function of the TAD domain in Notch Family proteins : A Comparision of Notch 1 & Notch 4 signaling in Mammalian cells.(8259 -Apurva Sarin)	49,260	-				57,729	57,729	-8,469
59	NeuroStem : Stem cell Models for Discovery of RNA-Mediated regulation in Neurodeneration(8260-Dr.Ravi Muddshetty)	1,512,428	4,587,269	48,229	386,800		5,809,374	5,809,374	-48,248
60	Genetic Program governing Vertebrate development & Evolution :Role of Twist in Dual germ layer potential of Head Neural Crest(8262-Ramkumar Sambasivan)	251,874	-	-			251,874	251,874	-
61	Investigate the Role of Ubiquitination and autophagy pathways in Hematopoietic cell Development and maintenance in Drosophila(8263-Dr.Tina Mukharjee)	-50,046	400,000	2,145			352,099	352,099	-
62	Proceedings of the Rajiv Gandhi University of Health Sciences,Bangalore for collaborative Research with INSTEM(8268-Dr Colin Jamora)	57,941	-				57,941	57,941	-
63	Genetic Program Controlling Mesoderm Differentiation(8272-Ramkumar Sambasivan)	-160,789	1,496,035	4,478	47,208		1,103,369	1,103,369	189,147
64	Accelerating the application of stemcell technology in human disease (ASHD)-8273 (Prof. Apurva, Dr. Raghu Padinjat)	1,517,915	1,725,485	60,429	138,934		2,471,190	2,471,190	693,705
65	Implementation of Phase-II for Centre for Chemical Biology and Therapeutics (CCBT)(8274-Prof. Ashok Venkitaraman)	18,782,244	35,344,748	762,394		1,741,873	43,624,154	45,366,027	9,523,359

66	Financial approval of the Swarna Jayanti Fellowship to Dr.Dasaradhi Palakodeti(8276-Dasaradhi Palakodeti)	174,948	-	12,650	98,676		2,449,757	2,449,757	-2,360,835
67	Role of Mechanical Signaling in Maintaining Stem Cell Quiescence in Mouse Skin(8277-Srikala Raghavan)	36,317	1,600,000	9,870			2,453,781	2,453,781	-807,594
68	Indo French Centre for Promotion of Advances Research-IFCPAR (8279-Dr Minhaj S)	728,459	507,689	40,631	49,183		176,830	176,830	1,050,766
69	Understanding the role of miRNAs in governing regeneration polarity in Schmidtea mediterranea. (8281 Nishta Nayyer)	7,961		-7,961				-	-
70	Scientists without boundaries at the Bangalore life science cluster (8283)	4,180,669	5,000,000	233,874			3,332,199	3,332,199	6,082,344
71	Financial Sanction under National Post-Doctoral Fellowship to Dr.Anupam Mittal under the Mentorship of Dr.Dhandapany Perundurai, inStem (8285)	136,322					136,322	136,322	-
72	Financial Sanction under National Post-Doctoral Fellowship to Dr.Kanaga Vijayan under the Mentorship of Dr.S Ramaswamy, inStem (8289)	180,939	-				180,939	180,939	-
73	Prophylactic catalytic dermal cream to prevent pesticide exposure during farming practices (8290 Sandeep C)	-12,200	1,000,000	1,119	12,548	-	882,892	882,892	93,479
74	Structure-Function Studies on Nucleotide Sugar Transporters (8291-S Ramaswamy)	105,123					774,217	774,217	-669,094
75	Sialic Acid Scavening,Catabolic & Sialyation Pathways : Putative Targets for New Antimicrobial Agents (8294 S Ramaswamy)	4,466,137	4,522,782	214,828	222,782		4,652,339	4,652,339	4,328,626
76	Ribosome Heterogeneity based on rRNA methylation during neuronal differentiation and its impact on translation (8297 Ravi Muddashetty)	-196,574	2,000,000	12,653		-	2,054,373	2,054,373	-238,294
77	WOSA (8298 Ritusree Biswas)	-27,633	-	1,260	23,754	-	442,400	442,400	-492,527
78	Virtual National Oral Cancer Institute (8299 S Ramaswamy)	696,258			277,758		418,500	418,500	-
79	Tata Education & Development Trust (8292)	30,875,847	6,056,556	882,432	38,167,170	2,125,373	-2,368,153	-242,780	-109,555
80	Identification of regulators of myeloid-cell homeostasis predisposing animals to metabolic disorders and insulin resistance (8451 Tina Mukharjee)	1,063,957	-	30,472		772,266	569,379	1,341,645	-247,216
81	Financial Sanction under National Post-Doctoral Fellowship to Dr.Avinanda Benerjee under the Mentorship of Dr.Srikala Raghavan (8453)	6,501	849,471	3,160		-	859,132	859,132	-
82	N PDF Fellowship to Dr. Venkatramanan G. Rao(8454)	28,065				-	548,231	548,231	-520,166
83	Elucidating the function of the euchromatic histone lysine methyltransferase 1(EHMT 1) in obesity and diabetes (8455 Mahua Chakraborty)	465,146		5,243	20,972	-	1,056,118	1,056,118	-606,701
84	8456 Tina Mukharjee	428,699	-	4,123		-	859,547	859,547	-426,725
85	Bugwork Ltd 8457 Ramaswamy	215,279	4,470,000	42,876		-	2,512,464	2,512,464	2,215,691
86	Regulationof damage-induced cellular plasticity in the lung(8458 Arjun Guha)	431,299	885,000	14,908		-	1,273,676	1,273,676	57,531
87	Characterization of novel variant human embryonic stem cells with features of neoplastic progression 8460 Shravanti Rampalli	443,233	-	16,211		-	608,926	608,926	-149,482
88	Dissecting the Role of chromatin remodeling factor TIP60 in regulation of regeneration in Planaria (8461 Bharti Jaswal)	475,154	-	10,868	11,174	-	754,378	754,378	-279,530
89	Financial Sanction under National Post-Doctoral Fellowship to Dr.Kavyasree Manjunath under the Mentorship of Dr.Ramaswamy S. inStem 8462	12,710	1,066,524	1,042		-	1,041,363	1,041,363	38,913
90	Molecular, structural and functional mapping of eye regeneration using novel light sensing assays (8463 Akash Gulyani)	415,403	1,380,000	15,501		-	1,679,609	1,679,609	131,295
91	Fabrication of stainless steel microneedles and evaluating their biocompatible during repeated injections, in vivo. (8464 Praveen Kumar Vemula)	2,194,962	-			-	2,194,962	2,194,962	-
92	Pro Adjuvant polymer based Dissovable Microneedlies for Transdermal Sustained Delivery of vaccines(S8465 Suman Pahal)	804,213	-	3,051		-	1,060,078	1,060,078	-252,814

93	Fabrication of Catalytic nano-Fibre based facemask and clothing to prevent pesticide-induced neuronal dysfunction and mortality(8468-Prof. Praveen Kumar Vemula)	-	4,053,520	37,543		-	1,773,933	1,773,933	2,317,130
94	National post doctoral fellowship to Dr. Naveen Kumar(8469-Dr. Naveen Kumar)	-	1,117,974	1,342		92,882	943,619	1,036,501	82,815
95	DST post Doctoral fellowship in Nano Science & Technology TO Dr. Utkarsh Bhutani(8470-Dr. Naveen Kumar)	-	1,002,153			-	830,500	830,500	171,653
96	Profiling of bromodomain specific interacting partners using unnatural amino acid mutagenesis (Ramalingaswami Fellowship)-(8473-Dr. Sonia Sen)	-	1,050,000	16,469		-	50,000	50,000	1,016,469
97	National post doctoral fellowship to Dr. Siddhartha Datta(8476-Dr.Siddhartha Datta/Sumantra Chatterjee)	-	1,118,400	13,584		-	293,600	293,600	838,384
98	Analysis of deficient fear learning and memory in a novel rat model of fragile X syndrome FXS(8477-Dr.Pradeep kumar Mishra)	-	1,120,240	10,937		198,135	258,040	456,175	675,002
99	Leveraging stem cell technology to facilitate discovery for human disease biology in India(8479-Prof.Apurva Sarin/ Prof.Raghu Padinjat)	-	24,688,280	406,601		-	-	-	25,094,881
100	Regulation of metabolic homeostasis by Trna modifications(8483-Dr.Sunil Laxman)	-	1,771,900	24,639		-	275,863	275,863	1,520,676
101	Delineating the Immune-Epithelial Crosstalk in Embryonic Skin(8484-Dr.Srikala Raghavan/Dr.Dasaradhi Palakodeti)	-	3,054,080	48,583		-	104,160	104,160	2,998,503
102	Architecture of axonemal doublet microtubule inner junction(8485-Dr.Minhaj Sirajuddin)	-	2,334,500	38,448		-	-	-	2,372,948
103	Understanding selective drug mechanisms using hypertrophic patient-specific induced pluripotent stem cell (Ipsc)-derived cardiomyocytes (8487- Dr. Dhandapany)	-	2,088,119	34,390				-	2,122,509
104	**Total : (A)**	**255,993,468**	**250,526,183**	**10,781,194**	**47,613,111**	**59,795,082**	**214,810,989**	**274,606,071**	**195,081,663**
105	**From other than Government**								-
106	Workshop on X-Ray Crystallography (8223-Dr. Vinod Nayak)	114,591	-				-	-	114,591
107	Regulation of epithelial stem cell homing in cutaneous wound healing (8226- Dr. Subhasri Ghosh)	2,679,182	-	44,711			1,914,726	1,914,726	809,167
108	Research Project awarded by L'Oreal (8232- Dr. Colin Jamora)	1,379,668	2,988,704	75,025			2,563,642	2,563,642	1,879,755
109	Structure and function studies of Sarcomere Proteins implicated in cardiomyopatheis (8235- Dr. Minhaj)	3,557,706	-	134,372			2,414,237	2,414,237	1,277,841
110	Nutrient sensing and regulation of cell fate (8236- Dr. Sunil Laxman)	1,003,887	2,466,771	12,535	152,875	306,001	4,248,371	4,554,372	-1,224,054
111	Innovative multi-model approach to identify novel candidate genes and small chemical molecules for cardiomyopathies"(8278-Dr.P Dhandapani)	10,464,174	-	417,068			6,044,194	6,044,194	4,837,048
112	Metabolic Regulation of Fungal Morphogenesis(8286-Dr Sriram V)	1,571,704	1,781,913	36,353		-	1,638,067	1,638,067	1,751,903
113	Structural and functional insights into bacterial sialic acid transport (8293-Dr Parveen Goyal)	1,925,651	2,433,459	20,734			2,853,292	2,853,292	1,526,552
114	Support world class research in Neurobiology(8467-Prof. Apurva Sarin)	-	10,000,000	104,611			2,968,698	2,968,698	7,135,913
115	Donation from Kiran Mazumdar Shah(8474-Prof. Apurva Sarin)	-	20,000,000	329,388		-	-	-	20,329,388
116	Regulation of cerebral cortical development by chromatin modifiers in health and disease(8475-Dr.Bhavana Muralidharan)	-	3,007,943	45,702		-	232,967	232,967	2,820,678

117	An ex-vivo method metabolic capacity to determine protein as an early diagnostic marker(8478-Dr.Aditi Bhattcharya)	-	4,500,000	62,216		114,450	607,887	722,337	3,839,879
118	Inducible gene drive based approach to control infectious insect vectors(8480-Dr. Baskar Bakthavachalu)	-	4,500,000	60,289		-	839,329	839,329	3,720,960
119	Best of Indian Science Series-I(8481-Dr.Minhaj Sirajuddin)	-	982,000	10,293		-	357,000	357,000	635,293
120	Joint Agreement between Instem and Eyestem(8482-Dr.Arjun Guha)	-	750,000	12,352		-	-	-	762,352
121	Interest received on Grants	-						-	-
122	Wadhwani Foundation	4,806	-				11,772	11,772	-6,966
123	Gates Foundation Grant-8242	572,402	1,210					-	573,612
124	Fraxa-8247	885,852	-	39,449			262,283	262,283	663,018
125	Results of EMBO Young Investigator Programme Selections-2016(8275-Minhajuddin Sirajuddin)	1,920,718	768,500	104,157			206,358	206,358	2,587,017
126	Simons Autism Research Project (8282-Sumnatra Chatterji)	2,223,878	2,509,282	73,252			4,733,160	4,733,160	73,252
127	Develop an Insect (Mosquito) repellent formulation based on the natural insecticide nootkatone -8288 Praveen Vemula)	505,337	849,502	34,125			293,473	293,473	1,095,491
128	Directors Descreationory Fund (8296)	502,633	2,092,441	-			4,389,575	4,389,575	-1,794,501
129	Cryo-EM Meeting (8234-S Ramaswamy)	165,090					165,090	165,090	-0
130	Terumo Inc (8466) Mahendra Rao	2,896,032	2,918,000	135,519			3,377,555	3,377,555	2,571,996
131	Collaborative Agreement between Phoremost & Instem(8471-Dr.Kavitha Bharatham/Dr.Anandi Karumbat)	-	4,159,059	48,199			1,232,506	1,232,506	2,974,752
132	Collaborative Agreement between Artus & Instem(8472-Dr.Praveen Kumar Vemula)	-	8,067,250	107,300			1,552,157	1,552,157	6,622,393
133	CSIR & Project Cost Contingency	-	728,000	-		-	283,635	283,635	444,365
134	Covid funds (8042)	-	6,000,000	-		-	-	-	6,000,000
		-						-	-
	Sub Total : (C)	**32,373,311**	**81,504,034**	**1,907,650**	**152,875**	**420,451**	**43,189,974**	**43,610,425**	**72,021,695**
D. CSCR - CMC- VELLORE								-	-
	Interest received on Grants	-						-	-
	Grand Total: (A+B+C+D)	**288,366,779**	**332,030,217**	**12,688,844**	**47,765,986**	**60,215,533**	**258,000,963**	**318,216,496**	**267,103,358**

SCHEDULE - 4 - SECURED LOANS AND BORROWINGS:	Current Year	Previous Year
NIL		

SCHEDULE -5 - UNSECURED LOANS AND BORROWINGS:	Current Year	Previous Year
NIL		

SCHEDULE-6 - DEFERRED CREDIT LIABILITIES	Current Year	Previous Year
NIL		

(Amount- Rs.)

SCHEDULE -7 CURRENT LIABILITIES AND PROVISIONS	Current year	Previous Year
A. CURRENT LIABILITIES	-	-
1. Acceptances	-	-
2. Sundry Creditors	-	-
(a) For Goods	55,012,667	2,122,964
(b) Others	4,627,234	1,175,415
3. Advance Received		-
4. Interest accrued but not due on:		-
(a) Secured Loans/Borrowings		-
(b) Unsecured Loans /borrowings		-
5. Statutory Liabilities :		-
(a) Overdue		-
(b) Others	1,212,397	-
6. Other Current Liabilities	53,791,312	29,142,376
TOTAL (A)	**114,643,610**	**32,440,755**
B. PROVISIONS	-	-
1. For Taxation	-	-
2. Gratuity	3,346,694	-
3. Superannuation/Pension	-	-
4. Accumulated Leave Encashment	3,558,697	-
5. Trade Warranties/Claims	-	-
6. Others	15,850,338	18,989,247
TOTAL (B)	**22,755,729**	**18,989,247**
Grand TOTAL (A+B)	**137,399,339**	**51,430,002**

INSTITUTE FOR STEM CELL SCIENCE AND REGENERATIVE MEDICINE, BANGALORE

(Registered under the Karnataka Societies' Registration Act)

GKVK, BELLARY ROAD, BANGALORE - 560 065

SCHEDULE FORMING PART OF BALANCE SHEET FOR THE PERIOD ENDED MARCH 31, 2020

SCHEDULE - 8 (Amount -Rs.)

DESCRIPTION	GROSS BLOCK				Rate	DEPRECIATION				NET BLOCK	
	As on 1-4-2019	Additions	Deductions	Up to 31-03-2020		As on 1-4-2019	Additions	Deductions	Up to 31-03-2020	As on 31-03-2020	As on 31-03-2019
(A) Own Funds											
Land Development Works	1,701,110		-	1,701,110	10%	696,622	100,449	-	797,071	904,039	1,004,488
Land (Nominal Value)	1			1	0%	-	-	-	-	1	1
Other Misc. facilities	2,526,642		-	2,526,642	10%	1,034,685	149,196	-	1,183,881	1,342,761	1,491,957
Buildings (Residential)*	193,049,174	-		193,049,174	5%	43,062,372	7,499,340	-	50,561,712	142,487,462	149,986,802
Buildings(Non-Residential)	118,538,228	-	-	118,538,228	10%	48,240,372	7,029,786	-	55,270,158	63,268,070	70,297,856
Laboratory Equipment	369,062,690	90,486,988	-	459,549,678	15%	204,518,019	38,254,749	-	242,772,768	216,776,910	164,544,671
Laboratory Equipment(Goods-in -Transit)	-	47,266,127	-	47,266,127	15%	-	-		-	47,266,127	-
Computer Equipment	5,469,557	361,772	-	5,831,329	40%	5,439,498	156,732	-	5,596,230	235,099	30,059
Office Equipment	4,492,995	1,715,513	-	6,208,508	15%	3,205,463	450,457	-	3,655,920	2,552,588	1,287,532
Furniture & Fixture	9,723,190	7,534,691	-	17,257,881	10%	3,071,382	1,418,650	-	4,490,032	12,767,849	6,651,808
Capital / Building	1,966,464,209	65,781,543	-	2,032,245,752	10%	196,646,421	183,559,933	-	380,206,354	1,652,039,398	1,769,817,788
Sub Total (A)	**2,671,027,796**	**213,146,634**	**-**	**2,884,174,430**		**505,914,834**	**238,619,292**	**-**	**744,534,126**	**2,139,640,304**	**2,165,112,962**
(B) Project Funds											
Furniture & Fixture	315,984	-	-	315,984	10%	182,268	13,372	-	195,640	120,344	133,716
Laboratory Equipment	972,004,321	60,215,533	-	1,032,219,854	15%	303,245,583	109,346,141	-	412,591,724	619,628,130	668,758,738
Capital / Building	189,180,635	-	-	189,180,635	10%	-	18,918,064	-	18,918,064	170,262,571	189,180,635
Sub Total (B)	**1,161,500,940**	**60,215,533**	**-**	**1,221,716,473**		**303,427,851**	**128,277,577**	**-**	**431,705,428**	**790,011,045**	**858,073,089**
(C) CSCR -Vellore											
Buildings	3,000,000	-	-	3,000,000	10%	1,485,394	151,461	-	1,636,855	1,363,145	1,514,606
Laboratory Equipment	212,272,232	21,090,599	-	233,362,831	15%	148,806,299	12,683,480	-	161,489,779	71,873,052	63,465,933
Computer Equipment	35,746,731	-	-	35,746,731	40%	35,744,765	786	-	35,745,551	1,180	1,966
Furniture & Fixture	7,875	-	-	7,875	10%	3,899	398	-	4,297	3,578	3,976
Sub Total (C)	**251,026,838**	**21,090,599**	**-**	**272,117,437**		**186,040,357**	**12,836,125**	**-**	**198,876,482**	**73,240,955**	**64,986,481**
(D) Wadhwani Foundation											
Laboratory Equipment	684,372		-	684,372	15%	300,838	57,530	-	358,368	326,004	383,534
Computer Equipment	848,633	-	-	848,633	40%	845,012	1,448	-	846,460	2,173	3,621
Sub Total (D)	**1,533,005**	**-**	**-**	**1,533,005**		**1,145,850**	**58,978**	**-**	**1,204,828**	**328,177**	**387,155**
Grand Total (A+B+C+D)	**4,085,088,579**	**294,452,766**	**-**	**4,379,541,345**		**996,528,892**	**379,791,972**	**-**	**1,376,320,864**	**3,003,220,481**	**3,088,559,687**

*The residential building (50 Nos. Flats) at CB Site Yelahanka is constructed jointly by NCBS and inStem and the land on which it is constructed belong to NCBS. The cost is shared between both the Institutes and there is an MoU signed between both the Institutes to this effect.

(Amount- Rs.)

SCHEDULE -9 - INVESTMENTS FROM EARMARKED /ENDOWMENT FUNDS	Current Year	Previous Year
NIL		

(Amount- Rs.)

SCHEDULE -10 - INVESTMENT OTHERS	Current Year	Previous Year
1. In Government Securities	-	-
2. Other approved securities	-	-
3. Shares	-	-
4. Debentures and Bonds	-	-
5. Subsidiaries and Joint Ventures - Shares of C-CAMP- (Company registered under Section 8 Company Act)	600	600
6. Others (to be specified	-	-
TOTAL	**600**	**600**

(Amount- Rs.)

SCHEDULE -11 - CURRENT ASSETS, LOANS, ADVANCES ETC.	Current year	Previous Year
A. CURRENT ASSETS:	-	-
1. Inventories:	-	-
a) Stores and Spares	-	-
b) Loose Tools	-	-
c) Stock-in-trade	-	-
Finished Goods	-	-
Work -in-progress	-	-
Raw Materials	-	-
2. Sundry Debtors:	-	-
a) Debts outstanding for above six months		-
b) Others	80,830	2,364,156
3. Cash balances in hand (including cheques/drafts)	21,943	-
4. Bank Balances:		-
a) With Scheduled Banks:		-
- On current Accounts	40,752,806	83,953,501
- On Deposits Accounts(includes margin money	393,815,116	362,167,415
- On Savings Accounts	137,512,740	59,739,232
b) With Non-Scheduled Banks:		-
- On current Accounts		
- On Deposits Accounts(includes margin money	-	-
- On Savings Accounts	-	-
5. Post Office Savings Accounts	-	-
TOTAL (A)	**572,183,435**	**508,224,304**

B. LOANS, ADVANCES AND OTHER ASSETS	-	-
1. Loans:	-	-
a) Staff	-	-
b) Other Entities engaged in activities /	-	-
Objectives similar to that of the Entity	-	-
c) Others (specify)	-	-
2. Advances and other amounts recoverable in		-
cash or in kind or for value to be received:		-
a) On Capital Account	3,740,923	5,653,330
b) Prepayments	753,590	8,206,901
c) Others	24,597,031	1,909,076
3. Income Accrued:		-
a)On investments from earmarked/endow. Funds		-
b) On investments - others	-	-
c) On Loans & Advances		-
d) Others - On Fixed Deposits	1,376,643	2,887,867
(includes income due unrealized Rs……..)		-
		-
4. Claims Receivable:	-	-
TOTAL (B)	**30,468,187**	**18,657,174**
GRAND TOTAL (A+B)	**602,651,622**	**526,881,478**

(Amount- Rs.)

SCHEDULE -12 : INCOME FROM SALES AND SERVICES	Current Year	Previous Year
1) Income from Sales	-	-
a) Sale of Finished Goods	-	-
b) Sale of Raw Material	-	-
c) Sale of Scraps	-	-
2) Income from Services:	-	-
a) Labor and Processing Charges	-	-
b) Professional /Consultancy Services	-	-
c) Agency Commission and Brokerage	-	-
d) Maintenance Services (Equipment/ Property)	-	-
e) Others (Facility User charges)	**9,411,509**	**1,840,898**
TOTAL	**9,411,509**	**1,840,898**

(Amount- Rs.)

SCHEDULE -13: GRANTS/SUBSIDIES (Irrevocable Grants and Subsidies received)	Current Year	Previous Year
1) Central Government	412,000,000	322,500,000
2) State Government(s)	-	-
3) Government Agencies	-	-
4) Institutions/Welfare Bodies	-	-
5) International Organizations	-	-
6) Others (specify)-PNB	-	-
TOTAL	**412,000,000**	**322,500,000**

(Amount- Rs.)

SCHEDULE-14: FEES/SUBSCRIPTIONS	Current Year	Previous Year
NIL		

(Amount- Rs.)

SCHEDULE-15: INCOME FROM INVESTMENTS	Current Year	Previous Year
NIL		

(Amount- Rs.)

SCHEDULE - 16: INCOME FROM ROYALTY, PUBLICATIONS ETC.	Current Year	Previous Year
NIL		

(Amount- Rs.)

SCHEDULE - 17 : INTEREST EARNED	Current Year	Previous Year
1) On Term Deposits:		
a) With Scheduled Banks	10,152,499	6,682,676
b) With Non-Scheduled Banks		-
c) Interest of CSCR Vellore	-	-
d) Others		-
2) On Savings Accounts:		-
a) With Scheduled Banks	2,312,563	1,275,400
b) With Non-Scheduled Banks		-
c) With Institutions		-
d) Others		-
3) On Loans:		
a) Employees /Staff		-
b) Others		-
4) Interest on Debtors and Other Recoverable		-
TOTAL	12,465,062	**7,958,076**

(Amount- Rs.)

SCHEDULE - 18: OTHER INCOME	Current Year	Previous Year
1) Profit on Sale /disposal of Assets:	-	-
a) Owned assets	-	-
b) Assets acquired out of grants, or received free of cost	-	-
2) Export Incentives realized	-	-
3) Fees for Miscellaneous Services	-	-
4) Miscellaneous Income *	10,442,493	5,867,976
TOTAL	**10,442,493**	**5,867,976**

(Amount- Rs.)

SCHEDULE - 19: INCREASE/DECREASE IN STOCK OF FINISHED GOODS & W.I.P	Current Year	Previous Year
NIL		

(Amount- Rs.)

SCHEDULE - 20: ESTABLISHMENT EXPENSES	Current Year	Previous Year
a) Salaries and Wages	85,610,426	74,618,780
b) Bonus and Allowances		-
c) Contribution to Provident Fund	3,810,623	3,408,841
d) Contribution to other Fund (specify) - LS &Pension Contributions	1,030,887	1,113,104
e) Staff Welfare /expenses	2,827,818	1,735,893
f) Expenses on Employees' Retirement and Terminal Benefits		-
g) Others (specify)- Honorarium	353,250	149,589
h) Fellowships (JRF/SRF)	15,061,599	11,145,392
TOTAL	**108,694,603**	**92,171,599**

(Amount- Rs.)

SCHEDULE - 21: OTHER ADMINISTRATIVE EXPENSES ETC.	Current Year	Previous Year
a) Purchases - Laboratory & Computer Consumables	130,217,381	102,714,352
b) other Laboratory expenses	7,437,637	-
c) Membership Fees	-	-
d) Electricity and power	84,855,124	42,070,663
e) Water charges	4,828,785	2,494,951
f) Contract for Services-CSIR	3,060,380	20,602,684
g) Repairs & Maintenance	54,966,962	10,831,282
h) Training	-	-
i) Rent, Rates, Taxes and fees	3,086,598	381,891
j) Vehicles running and maintenance		-
k) Potage, Telephone and Communication charges	2,067,930	2,962,102
l) Printing and Stationery	1,306,113	1,326,000
m) Travelling & Conveyance Expenses	6,583,747	4,889,316
n) Expenses on Seminars/Workshops	2,564,479	2,427,339
o) Subscription Expenses	599,616	1,227,184
p) Expenses on Fees - Consultancy Fee/Honorarium	420,000	315,120
q) Auditors Remuneration	76,700	154,580
r) Hospitality Expenses	1,149,276	5,522,643
s) Security Charges	16,845,947	7,582,700
t) Bank Charges	137,888	13,900
u) Other Contingent Expenditure	645,414	5,023,260
v) Advertisement & Publicity	1,934,756	1,235,963
w) Sports facility management	436,360	-
x) Campus maintenance	17,027,553	4,064,298
y) Canteen Expenses	7,844,763	-
z) Other office Expenses	2,229,593	-
TOTAL	**350,323,002**	**215,840,228**

(Amount- Rs.)

SCHEDULE - 22: EXPENDITURE ON GRANTS, SUBSDIES ETC.	Current Year	Previous Year
a) Grants given to Institutions/Organizations		-
b) Subsidies given to Institutions/Organizations		-
c) Expenditure incurred out of Grants (As per Schedule -3)	258,000,963	390,839,886
TOTAL	**258,000,963**	**390,839,886**
Note: Name of the Entities, their activities along with the amount of Grants/Subsidies are to be disclosed		

(Amount- Rs.)

SCHEDULE - 23: INTEREST	Current Year	Previous Year
NIL		

INSTITUTE FOR STEM CELL SCIENCE AND REGENERATIVE MEDICINE, BANGALORE

(Registered under the Karnataka Societies' Registration Act)
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SCHEDULE FORMING PART OF ANNUAL ACCOUNTS FOR THE PERIOD ENDED MARCH, 31, 2020

SCHEDULE 24 - SIGNIFICANT ACCOUNTING POLICIES

1. ACCOUNTING CONVENTION

The Financial statements are prepared on the basis of historical cost convention.

2. INVESTMENTS

Investment are carried at cost. The decline in their value, which is other than temporary is provided for.

3. PROPERTY, PLANT & EQUIPMENT (PPE)

3.1 PPE are capitalized at cost of acquisition inclusive of inward freight, duties and taxes and incidental and direct expenses related to acquisition and it is carried in the balance sheet net of accumulated depreciation.

3.2 Cost of PPE acquired out of project funds are also taken as Assets of the Institute by crediting corresponding amount to Capital Reserve. In the event of the asset being returned to the agency sanctioning the grant, the written down value will be adjusted by reversing the entries.

4. DEPRECIATION

4.1 Depreciation is provided on written down value method as per rates specified in the Income-tax Act, 1961.

4.2 In respect of additions to /deduction from fixed assets during the year, depreciation is considered at full rates irrespective of the date of acquisition.

4.3 The total amount of depreciation on assets acquired out of Core funds for the year is transferred from Capital Reserve to Income and Expenditure Account. However, depreciation on assets acquired out of Project funds are adjusted directly from the Capital Reserve without routing through Income & Expenditure Account.

5. GOVERNMENT GRANTS / SUBSIDIES

5.1 Grants received from the Government are of two types: (a) Non-Recurring Grants - which are for the purpose of acquiring Capital Assets. The amount of grants received is initially credited to Corpus / Capital fund account and expenditure incurred for acquisition of capital assets is debited thereto. The balance in this account represents the unspent amount of non-recurring grant. The amount equivalent to capital assets added during the year is added to capital reserve account. (b) Recurring Grants - which are for the purpose of recurring expenditure and are taken directly to Income & Expenditure Account. Unspent balance/excess of expenditure over income is shown in Reserves & Surplus Account distinctly under General Reserve. The combined balance in this account is the total unspent balance of grants.

5.2 Government grants / subsidy are accounted on receipt basis.

6. EARMARKED/ENDOWMENT FUNDS

6.1 Project Funding by both Government and non-government agencies to whom a statement of account of the expenditure incurred together with a utilization Certificate of the amount released has to be furnished are accounted under this heading. Fellowships/Scholarships sanctioned by UGC/CSIR and other agencies are also accounted under this head in order to watch the balance available/recoverable on each such awards. Based on the conditions and limits stipulated in the sanction order, expenditure is incurred.

6.2 Such Earmarked/Endowment Funds towards specific projects, to the extent unspent is carried in the Balance Sheet as a liability under the head "Earmarked/Endowment Funds". Project-wise details of funds received and corresponding expenditure during the year is furnished along with opening and closing unspent balances of specific funds under Schedule 3. When tangible Fixed Assets are acquired out of the projects funds, the appropriate head of Fixed Assets is debited with corresponding credit to Capital Reserve. Every year Capital reserve is reversed to the extent of depreciation, calculated under the WDV method at the rates of depreciation prescribed under the Income Tax Rules, 1962. Upon Completion of the project in its entirety, the same is removed from the list in Schedule 3.

7. FOREIGN CURRENCY TRANSACTIONS

7.1 Transactions denominated in foreign currency are accounted at the exchange rate prevailing at the date of the transaction.

7.2 Current assets, foreign currency loans and current liabilities are converted at the exchange rate prevailing as at the year end and the resultant gain / loss is adjusted to cost of fixed assets, if the foreign currency liability relates to fixed assets, and in other cases is considered to revenue.

8. LEASE

Lease rentals are expensed with reference to lease terms.

9. RETIREMENT BENEFITS

9.1 The provision for leave encashment is provided based on the actuarial valuation. The Institute has a plan with Life Insurance Corporation of India who provides the actuarial valuation.

9.2 The provision for gratuity is provided based on the actuarial valuation. The Institute has a group gratuity plan with Life Insurance Corporation of India who provides the actuarial valuation.

SCHEDULE 25 - CONTINGENT LIABILITIES AND NOTES ON ACCOUNTS

1. CONTINGENT LIABILITIES

1.1 Claims against the Entity not acknowledged as debts - Rs.NIL/- (Previous year Rs.146722/-) being demand from I.T. department on account of TDS mismatch in TRACES. Action is being taken to rectify the mismatch.

1.2 In respect of:

- Bank guarantees given by / on behalf of the Entity - Rs. NIL /- (Previous year Rs. NIL/-)
- Letters of Credit opened by Bank on behalf of the Entity - Rs. NIL/- (Previous year Rs. NIL/-)
- Bills discounted with banks Rs. NIL/- (Previous year Rs. NIL/-)

1.3 Disputed demands in respect of:
- Income-tax Rs.NIL/- (Previous year Rs. NIL/-)
- Sales-tax Rs. NIL/- (Previous year Rs. NIL/-)
- Municipal Taxes Rs. NIL/-(Previous year Rs. NIL/-)

1.4 In respect of claims from parties for non-execution of orders, but contested by the Entity - Rs. NIL/- (Previous year Rs. NIL/-)

2. CAPITAL COMMITMENTS

Estimated value of contracts remaining to be executed on capital account and not provided for Rs. NIL/- (Previous year Rs.9,18,49,000/)

3. LEASE OBLIGATIONS

Future obligations for rentals under finance lease agreements for plant and machinery amount to Rs. NIL/- (Previous year Rs. NIL/-)

4. CURRENT ASSETS, LOANS AND ADVANCES

In the opinion of the Management, the current assets, loans and advances have a value on realization in the ordinary course of business, equal at least to the aggregate amount shown in the Balance Sheet.

5. TAXATION

The Society is registered under section 12A of the Income Tax Act, 1961 under the category Charitable Trust. The Society is filing the income tax return by claiming exemption under section 11 of the Income Tax Act, 1961.

6. FOREING CURRENCY TRANSACTIONS (Amount in Rs.)

6.1 Value of Imports Calculated on C.I.F. Basis:

Particulars	**Current Year**	**Previous Year**
Purchase of Finished Goods	NIL/-	NIL/-
Raw Material & Components (including in transit)	NIL/-	NIL/-
Capital Goods	4,33,64,107/-	22,07,18,604/-
Stores, Spares & Consumables	2,14,89,354/-	8,47,61,423/-

6.2 Expenditure in foreign currency:

Particulars	**Current Year**	**Previous Year**
Travel	17,52,216/-	20,32,934/-
Interest payment	NIL/-	NIL/-
Collaboration Expense	2,90,19,460/-	4,93,63,434/-
Remuneration	29,23,780/-	37,36,836/-
Professional Charges		
Publication charges & Training	12,56,976/-	NIL/-

6.3 Earnings:

Particulars	**Current Year**	**Previous Year**
Value of Exports		

7. Remuneration to auditors

Particulars	**Amount**
As Statutory Auditors	76,700/-
For Taxation Matters	NIL/-
For Certification	NIL

8. During the year the following expenditure pertaining to previous years has been accounted

Particulars	**Amount (Rs.)**
Water Charges	16,36,408
Electricity Maintenance	1,71,63,934
Electricity Maintenance (Provision)	1,19,00,000
Canteen Servies	12,56,142
Electricity	86,88,851
Travel	7,74,555
Campus Maintenance	1,71,740
Repairs & Maintenance	5,96,210
Sports Facility Management	1,74,931
Security Charges	7,60,972
TOTAL	4,31,23,743

The above mentioned expenditures have been booked on accounts of debit notes raised by NCBS.

9. In respect of few Earmarked /Endowment Funds, the amount spent exceeds the grant amount received. However the expenditure is within the sanctioned amount for the respective funds and the Institute will recover the excess amount spent from the balance of the grant amount to be received.

10. The Institute, National Centre for Biological Sciences (NCBS) and C-Camp are located in a common campus. As per the MOU entered into between the three entities, common expenditure incurred by NCBS is shared by all the three entities. The Institute accounts these expenditures on the basis of the Debit Note raised by NCBS.

11. The Institute's Building and Infrastructure are located on Lease Hold Land. The lease deed is between The University of Agricultural Sciences (UAS) and Department of Bio-Technology, Ministry of Science and Technology (DBT) have entered into a Lease Deed on 04-11-2009 whereby the UAS has granted 20 acres of land on 49 years of lease to DBT for establishment of the Institute.

12. Corresponding figures for the previous year have ben regrouped / rearranged, wherever necessary.

13. Schedules 1 to 25 are annexed to and from an integral part of the Balance Sheet as at March 31, 2020 and the Income and Expenditure Account for the year ended on that date.

Our Corona Warriors


Abrar Rizvi


Afroze Chimthanawal


Ansil B.R


Akshay Hegde


Umer Farooq


Uma Ramakrishnan


Vairavan Lakshmanan


Vanessa Paynter


A. Padmavathi


Edries Yousaf


Bilal Akhtar


Aishwarya Venugopal


Aditi


Ajay Tomar


Ankita Kapoor


Ankush Bhardwaj


Sarayu R


Vikas


Shah-e-Jahan Gulzar


Anurag Singh


Anusha Jahagirdar


Anandi Karumbati


Asha Channakkar


Vivek Hari


Bhavana


Binita Dam


Sujanthi

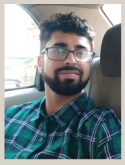

Sujaya T


Bishal Bashak


Isha Rana


Dhananjay Chaturvedi


Deepa Kale


Sunny Kataria


Supriya N


Chandan Mithra


Dyuti Saha


Deepanshu


Srikar Krishna G


Shreyas Niphadkar


Sriram Varahan

Steffi Raju

Bilal Akhtar

Charuhansini

Gaurav Kansagara

Jagdish

Johan Ajnabi

Kavya Menon

Kriti Biligiri

Masood Ahmad

Krithika Badarinath

Mayooreshwar

Mayur Thorat

Megan Aylward

Neenu Joy

Neetu Saini.

Michelle D'Sousa

Nehal Gurung

Patricia Panikulam

Pilot Dovih

Praveen Vemula

Preethi P

Ravi Muddashetty

Rimple Dalmeida

Sankhanil Saha

Preethi P.

Shakuntala M

Shreyas Arvindekar

Arjun G.

Abhik Dutta

Aditi Mishra

Aditya Iyer

Radhika

Akshay Hegde

Amruta Naik

Kiran

Ritusree

Rishav

Sabarinath

Sahanawaz Molla

Sahanawaz Molla

Sonia Sen

Sricharan

Suraj RC

Leora D'Souza

Vishwaja Jhaveri

Swati Prasad

Tanay Bhatt

Vignesh. K.

Vinaya S.

Vineeth V

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Ravi S.

Ravindra Z.

Manaswi P.

Manish P.

Nitish

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