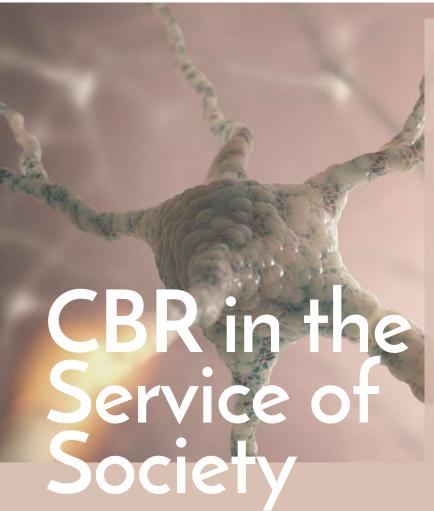
CBR Currents

Newsletter of the Centre for Brain Research, IISc



EDITORIAL



The Centre for Brain Research was established in 2015 as an autonomous, non-profit research organization in the Indian Institute of Science campus with a magnificent gift from the Pratiksha Trust founded by Dr. Kris Gopalakrishnan and Mrs. Sudha Gopalakrishnan. Its Governing Board is chaired by the Director of the Indian Institute of Science. Prof. Anurag Kumar (Director, IISc until July 2020) and Prof. Govindan Rangarajan (Director, IISc, since August 2020) have provided rock-solid support to CBR. Prof. Vijayalakshmi Ravindranath, India's leading neuroscientist, conceptualised the centre with a grand vision; CBR is where it is today largely because of her inspirational leadership.

The mandate of CBR is to carry out transformational research to understand the functioning of the aging brain in health and disease, and discover scientific methods for early diagnosis, prevention, postponement, and effective management of neurodegenerative diseases. With this focused and unique mandate, CBR is striving to work in a mission mode to achieve its objectives.

CBR has dedicated itself to offering its services to reduce the burden of neurodegenerative disorders for an important part of society, namely the elderly population. This noble pursuit has been possible because of the strong belief that Dr. Gopalakrishnan and Mrs. Sudha Gopalakrishnan have reposed on the creative potential and capabilities of Indian researchers. In this mission, CBR derives enormous strength through its relationship with the IISc: CBR works under the guidance and supervision of the Governing Council of IISc and the Director of IISc is the Chair of CBR's Governing Board. This unique partnership subsumes all aspects of research and innovation at CBR. As CBR surges ahead, it is clear that to accomplish the mission, CBR needs to be courageous, have the ability to take risks, make efforts to tackle difficult problems that have defied understanding for decades, and find scientific ways to reduce the socioeconomic burden of these disorders.

This newsletter, aptly named CBR Currents, will provide a quarterly update of research, innovation, service, and education activities at CBR. This inaugural issue, in commemoration of World Alzheimer's Day, highlights the two large-scale, comprehensive longitudinal studies of aging that define CBR: SANSCOG and TLSA. The uniqueness of the Indian population provides an ideal basis for carrying out such studies to identify potential protective factors and risk factors. SANSCOG covers approximately 10,000 people above the age of 45 years from the Taluka of Srinivasapura (about 100 km from Bangalore). These individuals are being assessed periodically, as they age, in several interdisciplinary dimensions, ranging from cognition to imaging to genetics. A parallel study funded by the Tata Trusts is being carried out wherein approximately 1000 subjects living in and around Bangalore are assessed in a similar manner. These two harmonized studies on rural and urban cohorts are generating precious data and our hope is that in the next few years, we will be able to discern the unique risk factors and protective factors of dementia in these two populations.

In this inaugural issue, we also have several other interesting features and hope you will like all of them. We look forward to your comments, suggestions, and ideas for improving and enhancing this newsletter; please write to director.cbr@iisc.ac.in

Y. Narahari, Director



CBR - An Extraordinary Vision



"The human brain is one of the world's biggest mysteries, which is yet to be fully understood. By funding and creating this Centre with IISc, we are working towards creating a globally recognized, world-class research facility that will be at the cutting-edge of research on the human brain." -

Mrs. Sudha and Dr. Kris Gopalakrishnan, CBR Donors;

Founder Trustees, Pratiksha Trust





"With India's elderly population rising rapidly towards an estimated staggering 32 crores by the year 2050, there is a concomitant increase in the burden of dementia and other aging-related neurodegenerative diseases. To address this impending health and socioeconomic crisis, research on the aging brain has emerged as the need of the hour. CBR is uniquely positioned not only to take on this challenge but also to enable

India's global excellence in this area." -

Prof. Govindan Rangarajan,
Director, Indian Institute of Science;
Chair, CBR Governing Board

CBR gets a New Home

The new building of Centre for Brain Research was formally inaugurated on 20th June 2022, by the Honourable Prime Minister of India, Shri Narendra Modi. The grand ceremony took place in the august presence of the Governor of Karnataka (Shri Thaawarchand Gehlot), the Chief Minister of Karnataka (Shri Basavaraj Bommai), Union Minister, Parliamentary Affairs; Coal; and Mines (Shri Pralhad Joshi), CBR Donors

(Dr. Kris Gopalakrishnan and Mrs. Sudha Gopalakrishnan), and other distinguished dignitaries. Prof. Govindan Rangarajan, Director - Indian Institute of Science, briefed the Prime Minister on CBR's vision and flagship research projects.

The inauguration coincided with the laying of the foundation for the upcoming Bagchi-Parthasarathy Multispeciality Hospital on the IISc campus. The day was also marked by the advent of CBR's presence in the Twitterverse through the handle @CBR_IISc.







Glad to inaugurate the Centre for Brain Research at @iiscbangalore. The joy is greater because I also had the honour of laying the foundation stone for this project. This Centre will be at the forefront of research on how to manage brain related disorders.



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The CBR building, generously funded by the Pratiksha Trust, has a built-up area of 1,10,000 sq.ft. with state-of-the-art laboratories (for genetics, informatics, cognitive science, and related research), faculty offices, a lounge for study participants, clinical assessment rooms, an auditorium, and provisions to house brain and DNA banks.



ಪ್ರಧಾನಮಂತ್ರಿ @narendramodi ಅವರು ಇಂದು ಭಾರತೀಯ ವಿಜ್ಞಾನ ಸಂಸ್ಥೆಯಲ್ಲಿ 280 ಕೋಟಿ ರೂ.ಗಳ ವಚ್ಚದಲ್ಲಿ ನಿರ್ಮಿಸಿರುವ ಮಿದುಳು ಸಂಶೋಧನಾ ಕೇಂದ್ರವನ್ನು ಲೋಕಾರ್ಪಣೆಗೊಳಿಸಿ, 425 ಕೋಟಿ ರೂ.ಗಳ ವೆಚ್ಚದಲ್ಲಿ ನಿರ್ಮಾಣ ವಾಗಲಿರುವ ಬಾಗ್ಚಿ- ಪಾರ್ಥಸಾರಥಿ ಆಸ್ಪತ್ರೆಗೆ ಶಂಕುಸ್ಥಾಪನೆ ನೆರವೇರಿಸಿದರು.

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The construction and furnishing were meticulously planned and overseen by a committee consisting of Prof. H.P. Khincha (Chair),

Mr. R. Mohan Das,

Prof. Y. Narahari,

Prof. B.K. Raghuprasad,

Prof. G. Rangarajan,

Prof. A. Sridharan,

Prof. B.R. Srinivasamurthy, and

Prof. Vijayalakshmi Ravindranath.

Research Highlights



SANSCOG and TLSA

As an endeavour toward its goal of reducing the population's dementia burden, CBR is spearheading large-scale, community-based, prospective, cohort studies among aging, rural Indians (projected n=10,000) and urban Indians (projected n=1,000). These flagship projects are primarily aimed at studying the trajectories of aging over a significant period of time and thereby, identifying the risk factors and protective factors for dementia and other aging-related brain disorders.

In the former study, namely Srinivaspura NeuroSenescence, and COGnition (SANSCOG) study, cognitively healthy subjects aged at least 45 years are recruited from a rural community in Srinivaspura, Karnataka. In the latter study, namely the Tata Longitudinal Study of Aging (TLSA), counterparts in an urban setting (i.e., in and around Bangalore) are recruited and monitored. Studies of such scale, vision, and deliverables are unprecedented in the Indian context.

The two studies are harmonised and proceed in parallel. Subjects of both studies undergo periodic,



detailed, and multimodal assessments that include clinical, cognitive, biochemical, genetic, and neuroimaging evaluations.

These assessments and analyses are carried out by a multi-disciplinary CBR team comprising of clinicians, psychologists, social workers, geneticists, and brain imaging experts.

In this section of **CBR Currents**, we aim to present highlights of findings that have emerged from the studies.

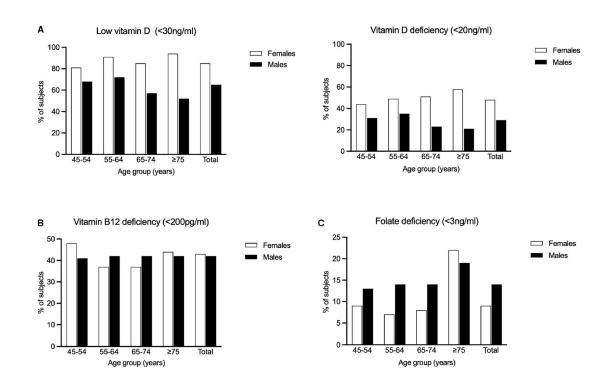
The burden of vitamin deficiency in an aging, rural community

Micronutrients, such as vitamins, are essential for several important physiological functions, and hence, for good health. Particularly, vitamin D, vitamin B12, and folic acid have been found to play a critical role in aging and late-life cognition. Early detection of these deficiencies and suitable public health interventions could go a long way in effectively tackling various health conditions, including aging-related disorders. An arm of the SANSCOG study attempted to estimate the burden of micronutrient deficiency in a fraction of the elderly enrolled in the study.

Detailed findings on vitamin deficiency:

- This rural community had an overall higher burden of vitamin D deficiency and vitamin B12 deficiency and a relatively low burden of folic acid deficiency.
- Over 3/4th of this population had low vitamin D. This goes against the

- popular belief that people from tropical countries, which receive sunshine throughout the year, are likely to have high or adequate levels of vitamin D.
- Minimal outdoor activity, increased modernization resulting in reduced manual labour in the open fields, and poor dietary sources of vitamin D are possible reasons for this deficiency.
- In the urban cohort (TLSA), the overall prevalence of vitamin D deficiency was found to be even higher. This is presumably because of lower engagement in outdoor activities compared to the rural subjects who are typically involved in agricultural work and hence receive more exposure to sunlight, which is protective against vitamin D deficiency.
- Women had higher prevalence of vitamin D deficiency than men. Elderly women aged 75 years and above seemed to be the most affected by this deficiency.
- This is concerning as these individuals are more vulnerable to cognitive decline. Other studies have shown that vitamin D deficiency is associated with risk of frailty, adverse mood changes, depression, and decline in immune function.
- The rural cohort had a high prevalence of vitamin B12 deficiency as well, probably owing to their dietary habits and the lack of use of supplements (unlike in the case of urban individuals). This is worrisome as cohort studies in other countries have shown that low levels of B12 are associated with poorer cognitive performance in specific cognitive domains.
- Individuals aged 75 years or above had a higher prevalence of folic acid deficiency compared to other age groups. This is a matter of concern given the association of folic acid deficiency with depression and dementia.



Percentages of the study population (prevalence) having (A) Low Vitamin D (<30 ng/ml) and Vitamin D deficiency (<20 ng/ml) (B) Vitamin B12 deficiency and (C) Folic acid deficiency

Why are these findings important?

- The findings reveal that micronutrient deficiencies are a major public health concern in rural India.
- The findings form the basis for further follow-up and periodic monitoring, which can give valuable insights to understand the causal association, if any, between micronutrient deficiencies and cognitive impairment (and other age-related disorders).
- Such insights can help inform public health policies and design suitable interventions to prevent or mitigate the adverse consequences of micronutrient deficiencies.
- The study underscores the need for wellstructured, community-level strategies, including vitamin supplementation or food fortification at the state or national level. India has several supplementation programs for children and pregnant women, but none for the elderly.
- There are no large studies available on the prevalence of these micronutrient deficiencies among the elderly from rural India.

References:

Sundarakumar JS, Shahul Hameed SK, SANSCOG Study Team and Ravindranath V, Burden of Vitamin D, Vitamin B12 and Folic Acid Deficiencies in an Aging, Rural Indian Community. *Frontiers in Public Health* (2021) 9:707036. doi: 10.3389/fpubh.2021.707036

Sundarakumar JS, Chauhan G, Rao GN, Sivakumar PT, Rao NP, Ravindranath V, SANSCOG and TLSA Investigators. Srinivaspura Aging, Neuro Senescence and COGnition (SANSCOG) study and Tata Longitudinal Study on Aging (TLSA): Study protocols. *Alzheimer's & Dementia* (2020) 16(Suppl. 4):e045681. doi: 10.1002/alz.045681







CBR welcomes new Principal Investigators

CBR is pleased to welcome and onboard four brilliant faculty members. These Principal Investigators bring to CBR their rich experience in neurodegeneration research and a repertoire of diverse skills. Summaries of their career trajectories and research interests follow.



Dr Jonas Sundarakumar Assistant Professor

Joined on 24 May 2022

Jonas is a National Board-certified Psychiatrist who, after his MBBS and Post-graduate Diploma in Psychiatry from Christian Medical College, Vellore, obtained MRCPsych from the Royal College of Psychiatrists, UK, and DNB (Psych) from the National Board of Examinations, New Delhi. His understanding, as a clinician, of the devastating impact of dementia on patients and caregivers bolsters his research endeavours. He leads the efforts for the large-scale populationbased, prospective, aging, cohort study in rural India (SANSCOG study) and is involved in the Tata Longitudinal Study of Aging (TLSA) on a Bengaluru-based urban cohort. He is also interested in investigating the neuropsychological impact of COVID-19

including the effect on modifiable risk factors of dementia. He contributes to international collaborations such as the CNS-SARS-CoV2 consortium, Worldwide FINGERS network, and Alzheimer's Disease Data Initiative (ADDI).

Recent publications:

Sundarakumar JS, Stezin A, Menesgere AL, Ravindranath V. Rural-urban and gender differences in metabolic syndrome in the aging population from southern India: Two parallel, prospective cohort studies. eClinicalMedicine. 2022;47:101395.

Sundarakumar JS, Raviteja KV, Muniz-Terrera G, Ravindranath V. Normative data for three physical frailty parameters in an aging, rural Indian population. Health Science Reports. 2022;5(e567).

For more information, visit https://www.cbr.iisc.ac.in/people/jonas-sundarakumar/



Dr Chinnakkaruppan Adaikkan

Assistant Professor Joined on 17 June 2022

Chinna carried out his Ph.D. thesis research at the University of Haifa, Israel, and at the RIKEN Center for Brain Science, Japan. He uncovered the principles of associative taste aversion learning and memory. During his time at the Picower Institute for Learning and Memory at the Massachusetts Institute of Technology, USA, first as a postdoc and later as a research scientist, he demonstrated the neural circuit basis of cognitive dysfunctions in mouse models of Alzheimer's disease. The research in Chinna's laboratory aims to understand the neurophysiological and molecular mechanisms of brain responses to brain stimulation. This will be accomplished through a multidisciplinary approach including

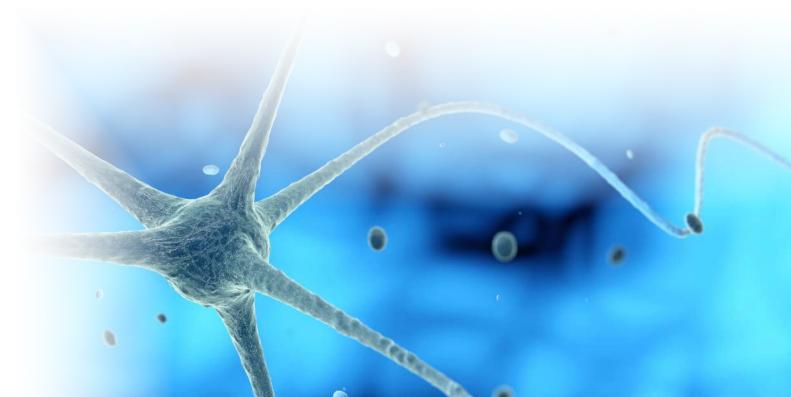
genetics in mice, high-density linear probe electrophysiology, and biochemical analysis.

Recent publications:

Adaikkan C, Wang J, Abdelaal K, Middleton SJ, Bozzelli PL, Wickersham IR, McHugh TJ, Tsai LH. Alterations in a cross-hemispheric circuit associates with novelty discrimination deficits in mouse models of neurodegeneration. Neuron. 2022 Aug 17:S0896-6273(22)00668-7.

Adaikkan C, Middleton SJ, Marco A, Pao PC, Mathys H, Kim DN, Gao F, Young JZ, Suk HJ, Boyden ES, McHugh TJ, Tsai LH. Gamma Entrainment Binds Higher-Order Brain Regions and Offers Neuroprotection. Neuron. 2019 Jun 5;102(5):929-943.e8.

For more information, visit https://www.cbr.iisc.ac.in/people/chinnakkaruppan-adaikkan/





Dr Sivaprakasam Ramamoorthy

Assistant Professor Joined on 23 June 2022

Siva's doctoral research at the Medical University of Vienna, Austria, was devoted to studying dopaminergic systems and their role in memory formation. As a postdoc at the Duke University Medical Center, North Carolina, USA, his work was focused on determining which astrocyte subtype represents adult neural stem cells and the mechanisms underlying post-stroke recovery. During his stint as a senior postdoc at the Mount Sinai Icahn School of Medicine, New York, USA, his work centered on the role of the apolipoprotein E4 (APOE4) in tau pathology. At CBR, his group will elucidate the systemic regulation of proteostasis

in order to understand the molecular underpinnings of the normal aging process and neurodegenerative diseases.

Recent publications:

Saroja SR, Gorbachev K, Julia T, Goate AM, Pereira AC. Astrocyte-secreted glypican-4 drives APOE4-dependent tau hyperphosphorylation. Proceedings of the National Academy of Sciences of the United States of America. 2022 Aug 23;119(34):e2108870119.

Saroja SR, Sharma A, Hof PR, Pereira AC. Differential expression of tau species and the association with cognitive decline and synaptic loss in Alzheimer's disease. Alzheimer's & Dementia. 2021 Dec 7:10.1002/alz.12518.

For more information, visit https://www.cbr.iisc.ac.in/people/sivaprakasam-ramamoorthy/





Prof. Thomas Gregor Issac

Associate Professor

Joined on O1 July 2022

After his MBBS from M.O.S.C Medical College, Kerala, Thomas pursued PhD in Clinical Neurosciences under the ICMR MD-PhD Talent Search programme. His research focused on the role of renin-angiotensinaldosterone system in cognitive deterioration in patients with cerebral small vessel disease. He completed MD and DNB in Psychiatry. Subsequently, during his DM (Geriatric psychiatry) at NIMHANS, his dissertation was a naturalistic follow-up study on older adults with unipolar major depression after in-patient care in a tertiary centre. At CBR, he leads the efforts for TLSA towards understanding the role of modifiable risk factors that could increase the incidence of

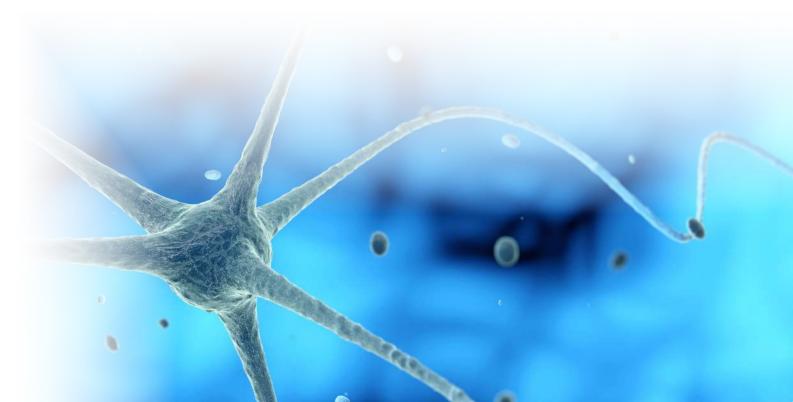
dementia in our elderly. His research also gives importance to the ethical and sociological aspects of aging and is expected to provide input to policy considerations.

Recent publications:

Vasanthra CR, Ammapattian T, Antony S, Rao GN, Prasad KM, Anu KN, **Issac TG**, Sivakumar PT. Homebased care of persons with dementia during COVID-19 pandemic: Caregivers' experiences. Journal of Geriatric Mental Health 2022;9:9-12.

Suhas S, Malo PK, Kumar V, **Issac TG**, Chithra NK, Bhaskarapillai B, Reddy YCJ, Rao NP. Treatment strategies for serotonin reuptake inhibitor-resistant obsessive-compulsive disorder: A network meta-analysis of randomised controlled trials. The World Journal of Biological Psychiatry. 2022 Jun 14:1-16.

For more information, visit https://www.cbr.iisc.ac.in/people/thomas-gregor-issac/





In quest of PhD @ CBR

Ph.D. students form an integral part of any academic research ecosystem and CBR is no exception. Doctoral students are admitted through either the CBR-MAHE program (wherein the degree is conferred by the Manipal Academy of Higher Education) or the CBR-IISc program (wherein the students are admitted by IISc under the supervision of IISc faculty and the co-supervision of a CBR faculty member). With the recently concluded admissions in July 2022, the CBR Ph.D. student strength has risen to 19. Equipped with training in diverse areas such as neurobiology, life sciences,

biochemistry, and informatics, and palpable passion to contribute to knowledge generation, these students are all set to help steer CBR's research projects along the mission of the Centre.

Starting this year, the Ph.D. courses offered at CBR are being opened up to colleagues from departments and centres of IISc who wish to audit them. Semester 1, which commenced earlier this month, entails intensive lectures and practical sessions in neuroscience, human genetics, genomics, bioinformatics, and research and publication ethics.

"This deep and thorough experience will be immensely important in shaping our future research," believes

Mr Anant Gupta, a student who has recently initiated his Ph.D. research under the guidance of Dr Reddy P Kommaddi.

According to Ms Rupsa Roy Choudhury of Dr Smitha Karunakaran's group, one of the major perks of the program is the opportunity to be a part of interdisciplinary journal clubs. "We get to know about new developments in neuroscience and exciting techniques that we can employ in our own work!," she acknowledges.

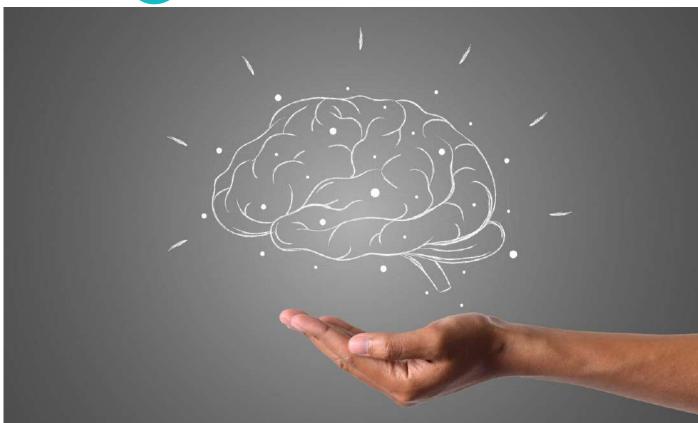
"Since childhood, it has been a dream for me to be of service to the elderly people of our society," declares Ms Shruti Pandey (Ph.D. student in the group of Prof. Ravi Muddashetty), "and I feel privileged to have joined an institute that focuses on studying aging and developing solutions to problems like dementia that the elderly around us are dealing with."

Ms Jani Siddhi, who has joined Prof. Bratati Kahali's group, shares similar excitement. "After my master's degree, I was seeking a Ph.D. program where I could grow and be a part of cutting-edge research. CBR was the ideal fit for my aspirations to become a good researcher and do translational work. I am certain that the next few years would be like *safar khoobsurat hai manzil se bhi*."

CBR Currents is proud of its student community and looks forward to its stupendous research accomplishments. Watch this space for success stories from the labs and fields and other updates on the CBR Ph.D. program.







Rendezvous with TLSA participants

On 15 July 2022, CBR hosted an informal gathering (online) of current and prospective participants of the Tata Longitudinal Study of Aging (TLSA). During this 90-minute meeting, the TLSA team provided an overview of the progress of the study and updates on recent developments. The multiple dimensions of brain aging and aging-related brain disorders were explained in simple terms and the indispensability of longitudinal studies on aging for effective healthcare was reiterated. The team also used the platform to seek participants' feedback and to strengthen community engagement. The session, attended by more than 175 participants from across

Bangalore, was very well-received. The participants unequivocally lauded the team's efforts to coordinate their involvement in the study and manage the assessment sessions smoothly. The TLSA team answered general questions related to the diagnosis, prevention, and management of dementia, and specific questions pertaining to the study's progress and future plans. Among various suggestions for further enhancing their experience, the participants requested for such awareness meetings and get-together sessions to be held more frequently. The participants were thanked for their enthusiastic participation; they were assured of continued cordial engagement by the CBR team and of the project's commitment to contribute to holistic brain healthcare for the elderly.



Applause from the NSF Director

Dr Sethuraman Panchanathan, Director of the National Science Foundation (NSF), USA, and winner of IISc's prestigious Distinguished Alumnus Award, spent 10 August 2022 on the IISc campus. Besides accepting the Distinguished Alumnus award, delivering the first MA Govinda Rau Founder Memorial Lecture, and participating in discussions with the IISc Leadership, he kindly found time to visit CBR. This visit, facilitated by Donor Dr Kris Gopalakrishnan, provided an opportunity for the CBR team to give him an overview of the Centre's longitudinal studies on aging, highlights

of the outcomes thus far, and the expected impact in the long run. Appreciating the scale of the efforts invested in the studies, Dr Panchanathan remarked that these would generate a wealth of data that would be immensely useful not only to India but to the entire world. He expressed confidence that CBR has the requisite expertise, infrastructure, and other resources to emerge as an international leader in the field of dementia research. His commendation and valuable suggestions are sure to go a long way in invigorating CBR's ongoing research endeavours and future initiatives.



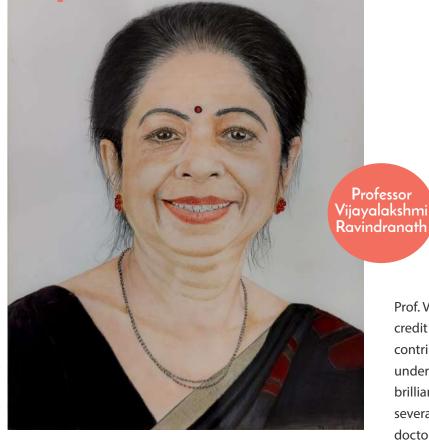
Sowing the seeds of interdepartmental collaboration

Globally, interdisciplinary collaboration has not only accelerated the pace of research but also intensified its impact by breaking or blurring boundaries and enabling innovative strategies and processes in increasingly complex areas. It is being felt, stronger than ever before, that significant advancements in research and development cannot be achieved by work done in silos. With the aim of identifying precise themes for collaboration with various IISc departments, CBR organized an expository session on 12 August 2022. This meeting saw participation from at least 10 IISc departments/centres represented by 18 faculty members with expertise and research interests



complementary to ongoing studies, and hence, to the mandate of CBR. The Director and Faculty of CBR made brief presentations on the mission of the Centre and its flagship and faculty research projects. Ideas for collaboration and research synergy have been invited. The session has set the stage for the exploration and pursuit of focused and longstanding theme-based partnerships, perfectly aligned with the CBR mandate.

Saluting the Inspirational Leader



CBR owes in infinite measure to Professor Vijayalakshmi Ravindranath, the founding Director of CBR. It was she who transformed the magnificent dream of the CBR Donors Dr Kris Gopalakrishnan and Mrs Sudha Gopalakrishnan into a practical reality, working assiduously since 2014. Her visionary leadership and strategic planning have created a platform for CBR to enable India's excellence at the world level in the fundamental area of studying the aging brain to reduce the burden of neurodegenerative diseases of the elderly population. CBR is the third institution that Prof. Vijayalakshmi Ravindranath has given shape to, the other two being the National Brain Research Centre (NBRC) at Manesar, where she was the founding Director from 1999 to 2009 and the Centre for Neuroscience at the Indian Institute of Science where she was the founding Chair during 2009 to 2016. She was the Director of CBR until May 31, 2022.

Prof. Vijayalakshmi Ravindranath has to her credit several decades of influential research contributions in the pathogenic mechanisms underlying neurodegeneration. During her brilliant career, she has rigorously trained several generations of doctoral and postdoctoral researchers. Her contributions have been deservedly recognised by several scientific bodies: she is an elected Fellow of all the 3 science academies in India: Indian National Science Academy (INSA), Indian Academy of Sciences (IASc), and National Academy of Sciences, India (NASI). She is a Fellow of the National Academy of Medical Sciences, India, the Indian Academy of Neurosciences, The World Academy of Sciences (TWAS), and the American Academy of Advancement of Science, USA (AAAS). She is a recipient of the prestigious S.S. Bhatnagar Prize (1996), Omprakash Bhasin Award (2001), the J.C. Bose National Fellowship (2006), S.S. Bhatnagar Medal, INSA (2016) and the coveted civilian honour, Padma Shri (2010).

CBR Currents, in its inaugural issue, salutes the creative contributions of Prof. Vijayalakshmi Ravindranath in shaping CBR into a unique centre that has the potential to do path-breaking discoveries and deliver precious, enduring services to an important part of the society, namely the elderly population.

Art by Mr.G.Rajesh, CBR







Editor: Madhankumar Anandhakrishnan

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