RGCB

DISCOVERIES FOR A BETTER TOMORROW

Azadi Ka Amrit Mahotsav

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ANNUAL REPORT 2020-21

Rajiv Gandhi Centre For Biotechnology

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DIRECTOR'S PAGE 2021

The onset of 2021 ushered Rajiv Gandhi Centre for Biotechnology (RGCB) into the fourth decade of an eventful existence, which stands out for splendid achievements in its designated areas. It was in August 2020 that I took over as its Director after the superannuation of my illustrious predecessor Professor M. Radhakrishna Pillai. The excellent 15 years of his service transformed RGCB from a small state-funded research centre into a biotechnology research behemoth of international repute. I would like to place on record the sterling contribution and dexterous leadership of Prof. Pillai in making RGCB as one of the top research institutes in disease biology with a vibrant research atmosphere.

The year 2020 started with the world getting buffeted by once-in-a-century health crisis with spillover effects in the entire spectrum of life. The COVID-19 pandemic is truly a horrendous nightmare that is imagined only in wildest fantasies, and its unpredictable ramifications are still unfolding. When the nation responded with an active action plan to mitigate the overwhelming societal and economic devastations, RGCB, as a premier research and development organization in biotechnology, also chipped in with a quick and effective response.

In fact, RGCB has always played a major role whenever a public health crisis of great enormity has threatened to swamp the country. Our core CORONA RESEARCH group continues to work diligently and in a focused manner in various R&D activities for tackling and neutralizing the pandemic. We have an excellent research programme focusing on antiviral discovery, assay development against key viral and host targets, immunodiagnostics development, clinical studies to understand humoral and cell-mediated immunity with good extramural funding, and clinical collaboration. Our diagnostic facility, Laboratory Medicine and Molecular Diagnostics (LMMD), has been supporting the state by providing diagnostic services right from the beginning of the corona crisis.

So far, we have completed two lakh Real-Time PCR tests for COVID-19 diagnosis. In addition, our researchers closely worked with the industry for indigenous development of diagnostic kits and support reagents that led to the successful commercialization of diagnostics and kits in a record time. Our researchers developed both cell-based and cell-free kits for antiviral testing and the service is being used both by industry and academia. RGCB is one of the approved centers for the validation of all diagnostics and antivirals for COVID-19 application by ICMR.

Even though RGCB has shown its strength in studying the disease at the molecular and cellular levels, handling of live viruses for advanced research and product validation was not possible because of the lack of a BSL3 facility. It posed a problem in supporting vaccine development activities and advanced antiviral testing. Thanks to the Secretary, Department of Biotechnology, for the quick intervention and support to RGCB for establishing a dedicated BSL3 PLUS facility for the COVID-19 research. The new facility is nearing completion at our Akkulam campus. On its commissioning, RGCB will be in a position to support the nation for vaccine development research, vaccine efficacy testing, and antiviral testing.

We have also initiated a string of new programmes in the current year. A new lifetime imaging facility at Akkulam campus has been completed, and its mandate is to support workshops and training in lifetime imaging and resource development. RGCB has started a socially important research programme, known as 'Center for Excellence in Inclusive Technology Interventions for Tribal Heritage Resilience of Kerala', with support from Department of Science & Technology. We are documenting the traditional knowledge of livestock, ethno-veterinary practices, traditional paddy varieties, and cultivation practices, among other things, for their scientific validation using modern research techniques. A major goal of the project is product development based on tribal knowledge in ethno-veterinary medicine with a focus on value-added products from herbal extracts/essential oils from spices and aromatic plants.

Despite the COVID-19 pandemic and occasional institutional shutdowns, our publications have remain unaffected during this year. I take pride in announcing that the extramural funding significantly increased from the previous years. The exciting translational research leads from the labs include the discovery of Uttroside B as the candidate drug for the liver cancer that received recognition as an orphan drug status by the FDA, USA and signing of an MoU with Ximbio, the UK-based company for the commercial transfer of the cell-lined drug developed by RGCB. We have continued our Postgraduate teaching programme through online mode, and our first batch of Master's degree students graduated successfully in 2021. The Bioinformatics Group has also launched a well-structured training programme for researchers during this year.

The other exciting developments are the commissioning of a sprawling new hostel for students built over 40,000 square feet at the second campus that can accommodate 196 students. The 80,000 square feet second campus at Akkulam is getting ready and the recently recruited six new faculties will be moving to this campus by the end of this year.

WE LOOK FORWARD TO DEDICATING THE SECOND CAMPUS TO THE NATION BY THIS YEAR-END. THIS MARKS THE BEGINNING OF THE NEXT PHASE OF RGCB'S PLEDGE TO DELIVER RESEARCH AND DISCOVERIES TO THE PEOPLE AND THE COUNTRY.

We are very much grateful to the DBT Secretary for the sustained support both for the newer initiatives and also for the ongoing research programmes.

JAI HIND
Professor Chandrabhas Narayana
DIRECTOR, RGCB

OF AN UNTIRING JOURNEY: FIFTEEN YEARS OF RGCB LEADERSHIP

There are many who grow and prosper because of their association with flourishing institutions; there are only a few who create institutions that flourish. Professor M. Radhakrishna Pillai, who steered the course and destiny of Rajiv Gandhi Centre for Biotechnology (RGCB) for nearly 15 years and convert it into India's leading molecular biology and biotech R&D facility, surely belongs to the latter category.

Following a successful career as Professor of Molecular Medicine at the Regional Cancer Centre (RCC) in Thiruvananthapuram, Prof. Pillai joined RGCB as its Director on March 1, 2005 at the age of 44, making him then the youngest head of a national research institute. A scientist with over 31 years of postdoctoral research experience in disease biology and clinical biotechnology, he is an elected fellow of the Royal College of Pathologists (London), all three Indian Science Academies and the Indian Medical Academy – an enviable feat indeed!

When he took over the reins of RGCB, it was grappling with an ordinary performance index, limited infrastructure, skimpy funds and insufficient personnel. Undaunted by these formidable handicaps, he turned the adversity into opportunity and a blessed freedom of possibilities to explore, conceive and execute innovative ideas. It was because of his administrative acumen and persuasive skill that led to its takeover by Central Government's Department of Biotechnology as an autonomous institute in 2007. Since then, it has blossomed into a centre, best known for its distinct Disease Biology programmes with interdisciplinary sciences being effectively used to raise relevant questions in disease pathogenesis. Teaming up cell biologists with pathologists, polymer chemists and plant biologists to develop successful programmes in chronic and infectious diseases is a remarkable characteristic of RGCB. The quantity and quality of publications and patents have substantially increased over the past years to international standards.

Prof. Pillai, who demitted office on 31st August 2020 capping a career strewn with superlative feats, also successfully piloted RGCB's second-phase growth by creating a unique Bio- innovation Centre (BIC), marking a shift from investigator-driven to team-driven science for accelerated discovery and early translation. The Rs 100-crore BIC project has been conceptualized to interface with the present institute creating an excellent ecosystem for discovery science and translation. He also convinced the Kerala government to transfer 20 acres of land free of cost in the heart of the city for this project at Akkulam on the outskirts of the city, a remarkable achievement because even the Indian Air Force and Department of Space had to pay for land.

The RGCB Governing Council has also provisionally approved Rs 430-crore master plan for a national institute for viral disease biology and vaccine development, including high containment facilities.

Prof. Pillai leveraged RGCB's excellent expertise for nation-building through new startup industries and utilization of infrastructure for education, research and testing facilities by managing a technology development incubator, known as BioNest, at Kochi. Established in association with the state government, it serves to accelerate the commercialization of new technologies, nurture emerging ventures and assist new enterprises to forge appropriate links with other biotech companies, academia and government. BioNest, which has already incubated 26 companies, aims to provide a viable mechanism for licensing new technologies to upcoming biotech/pharma companies, to start new local ventures and to achieve early state value enhancement of the technology with minimum financial inputs.

It is not always ground-breaking accomplishments that make a scientist great but how he turns even the most trivial achievements into effective means to serve humanity. During 2006-2011, Kerala was swamped with serious outbreaks of chikungunya, dengue and the H1N1 flu pandemic. The state did not have a laboratory to do molecular viral diagnostics and turned to Prof. Pillai to provide RGCB's expertise in assisting its public health service. He established a Laboratory Medicine & Molecular Diagnostics (LMMD), which started off with three viral diagnostics and now performs over 40 viral and bacterial parameters. Arguably, it is currently the only facility in India performing these many parameters under one roof. Recognising these services, the Central Government's Department of Health Research designated it as a National Virology Network Grade 1 laboratory, which was also accredited by both NABL and NABH. With the advent of COVID-19 pandemic, it was only natural that RGCB became a leader for both the pandemic's diagnostics and an approved accredited validation centre for new diagnostic kits. A Rapid Antibody Card, a Viral Transport Media (VTM) kit and a viral RNA extraction kit are three key products developed by RGCB for curbing the pandemic, which have obtained manufacturing license from the Central Drugs Standard Control Organization (CDSO).

Under his stewardship, RGCB also supported the state government for DNA fingerprinting services, which were nationally lauded in the wake of the fireworks tragedy at Kollam and the Ockhi cyclone. The two massive tragedies required a large number of unidentified bodies to be distinguished and returned to the next of kin. The small DNA fingerprinting facility was upgraded to a full-fledged Molecular Forensics Laboratory, which worked overtime to identify the hundreds of bodies that were sent for DNA fingerprinting. This huge social service earned RGCB tremendous public goodwill. The laboratory, now accredited by both NABL and NABH, is self-sustaining and serves the country for human DNA fingerprinting, DNA barcoding for wildlife forensics and a research facility for biologists all over India. As a consequence of these achievements, RGCB is a senior partner in the India Human Genome Programme that aims to DNA fingerprint various sections of India's population.

Teaching has remained Prof. Pillai's primary passion. He successfully created RGCB's Ph.D programme as one of the best and most competitive in the country. Twenty-seven students took their Ph.D under his mentorship. Another notable event was his inception of

a Master's programme in Biotechnology at RGCB, with specialisations in disease biology, genetic engineering and molecular diagnostics. It has become one of the most sought after programmes in India.

He also led the way in taking science from laboratories to direct public benefit. An excellent example is his work on cervical cancer, the most frequent cancer in Indian women, caused by the human papillomavirus (HPV). Current estimates indicate around 132,000 new cases diagnosed and 74,000 deaths annually in India, accounting to nearly 1/3rd of the global cervical cancer deaths. Prof. Pillai deployed all his resources in molecular biology, genetics, biochemistry and epidemiology to redefine the empirical approach to HPV infection. Recognizing this, the WHO supported him to alleviate the huge economic and social burden of 3-dose vaccine against HPV in Indian women. He proved the efficacy of 2-dose vaccine, the first achievement of its kind in the world that led several countries to adopt the two-dose regimen, thus marking RGCB on the international map of achievements. He also proved that one dose of vaccine also had significant potential to prevent infections. Published in the prestigious Lancet Oncology, this study changed international paradigms for cervical cancer prevention.

Prof. Pillai always encouraged scientists in the institute to be self-sufficient in research funding. He set standards for this at RGCB by securing funds from the WHO and Bill & Melinda Gates Foundation; the National Institutes for Health, USA on measles vaccine failure; Centre for Excellence for Translational Breast Cancer Research from the Department of Biotechnology; a unique "glue grant" for translational cancer research with the RCC; and a national centre for translation of tribal technology from Department of Science & Technology. With more than 220 peer-reviewed publications and an H index of 42, he kept himself engaged in his pioneering research to understand the current research enterprise in the country. It was the prime reason for his success both as a scientific acolyte and institute commander, with the unique honour of heading a national research institute for 15 years on the trot.

Dr. Pillai's outstanding translational research on cervical cancer, the most frequent cancer in women in India caused by the human papillomavirus (HPV), was recognised by the Bill & Melinda Gates Foundation and the WHO, which supported him to alleviate the huge socio-economic burden of 3-dose vaccine against HPV. He proved the efficacy of 2-dose vaccine, the first achievement of its kind in the world that led several countries to adopt the two-dose regimen, thus marking RGCB on the international map of achievements.

Prof. Pillai also streamlined administrative and financial management and RGCB, turning it into an efficient institution with the best social welfare scheme in the country. It is the only institute of the Department of Biotechnology that has created a comprehensive pension scheme for its employees in service before 1st January 2004 on par with the old pension plan of Govt. of India. This was done by getting LIC to manage the institute's self- generated funds from clinical diagnostic, services & consultancies, and EPF contributions, with no additional burden on Govt. of India.

Prof. Pillai undoubtedly ranks among India's best-recognised researchers who leveraged his expertise and knowledge for the betterment of humanity.

RESEARCH REPORTS

METABOLIC ADAPTATIONS TOWARDS THE ONSET OF TYPE 2 DIABETES MELLITUS

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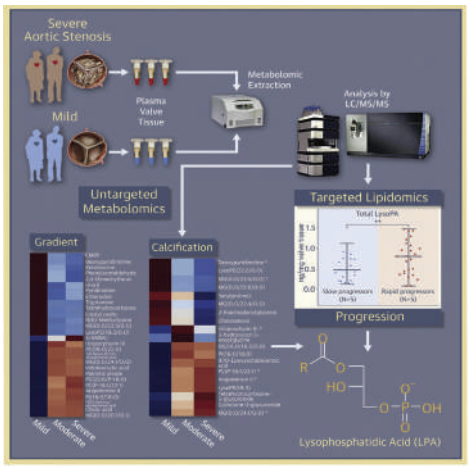
My laboratory focuses on studying the metabolic adaptations towards the onset of Type 2 Diabetes Mellitus. Leptin is an important adipose tissue–derived hormone that has been shown to be involved in pathophysiological mechanisms related to cardiovascular disease and diabetes. It is unknown whether leptin levels can predict early changes in alterations of energy and hormone metabolism and we conducted a study last year to investigate that. We performed an untargeted metabolomics analysis of fasting blood plasma from 110 healthy adults (Men: Women = 1:1; aged 18 - 40 years), using liquid chromatography-tandem mass spectrometry. Leptin level was positively associated with adiponectin and metabolites related to energy metabolisms (glycocholic acid and arachidic acid), progesterone metabolism (pregnanediol-3-glucuronide), and quercetin 3′-sulfate, a diet-derived metabolite. Leptin level was negatively with total calorie intake, levels of triglyceride, very -low-density lipoprotein, ponasteroside A and barringtogenol C levels. Our study indicates that leptin level reflects metabolome alterations and hence could be a useful marker to detect early changes in energy and hormone metabolisms (Aneesh Kumar et al., Metabolomics 2020).

From Left: Akhila Suresh S S, Kalaivani V, Gaddala Mohan Sravani, Gopika Satheesh



Surendran, A. et al. J Am Coll Cardiol Basic Trans Science. 2020;5(12):1163-77.

Despite being the most prevalent valvular disease, no medical therapies are available for Calcific Aortic Valve Stenosis (CAVS) other than valve replacement. Detailed knowledge of the mechanisms that lead to valvular calcification and stenosis is lacking. Identification of specific pathway or cellular mechanism directly involved in severity of disease and its progression is the key. We performed the largest and most comprehensive nontargeted and targeted metabolomics study in collaboration with St. Boniface Hospital, University of Manitoba, Winnipeg, Canada on stenotic human AVs at varying degrees of CAVS severity. Untargeted analysis identified 72 metabolites and lipids that were significantly altered ($p < 0.01$) across different stages of disease progression. Of these metabolites and lipids, the levels of lysophosphatidic acid were shown to correlate with faster hemodynamic progression and could select patients at risk for faster progression rate (Figure). This revealed that lipid molecules are the most perturbed molecules in CAVS progression (Surendran et al., JACC: Basic to Translational Science 2020).

Schematic of the study on metabolomic signatures of human aortic valve stenosis. This study is the first step towards the creation of a metabolomic map of calcified human aortic valves. The study highlights an independent association of LysoPA with Calcific Aortic Valve Stenosis CAVS severity. The study demonstrates that LysoPA levels are associated with faster CAVS progression rate.

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- **Kalaivani V, Jaleel A.** Apolipoprotein(a), an enigmatic anti-angiogenic glycoprotein in human plasma: A curse or cure? Pharmacol Res. 2020;158:104858.
- **Kumar A A, Satheesh G, Vijayakumar G, Chandran M, Prabhu P R, Simon L, Kutty V R, Kartha C C, Jaleel A.** Plasma leptin level mirrors metabolome alterations in young adults. Metabolomics. 2020;16(8):87.

NOVEL HOST-DIRECTED THERAPEUTIC STRATEGIES TO FIGHT TUBERCULOSIS

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Post-Doc: IISc, Bengaluru, SCTIMST, Thiruvananthapuram

Our previous studies showed that following infection with Mycobacterium tuberculosis (Mtb), levels of HDAC1 go up in macrophages, and is recruited to the promoter of IL-12B leading to the downregulation of its expression. Recently we found that host transcriptional repressor protein ZBTB25, Sin3a and Mtb protein Rv1899c associate with HDAC1 in the silencing complex. Pharmacological inhibition of ZBTB25 in infected macrophages resulted in the induction of autophagy and killing of intracellular Mtb (Madhavan et al., 2021). Currently we are studying the role of Rv1899c in macrophages during Mtb infection. We have proven that it is a poly ADP-ribose polymerase that ribosylates HDAC1, which we presume is a key step in the formation of the silencing complex during Mtb infection. Further studies in this direction are progressing.Also we showed that zerumbone, a natural sesquiterpene, activates sirtuin 1, and inhibits HDAC1and HDAC6 activity. Treatment of infected macrophages with zerumbone leads to an increase in the levels of LC3 protein and promotes the co-localization of LC3 and M. tuberculosis in autophagosomes (Fig 1). Enhancement of autophagy by zerumbone is dependent on sirtuin 1 activation and subsequent deacetylation of autophagy protein ATG5. While this process enhanced the release of IL-12 p40, a structural component of IL-12, it reduced the release of IL-10, leading to the inhibition of growth of intracellular Mtb.

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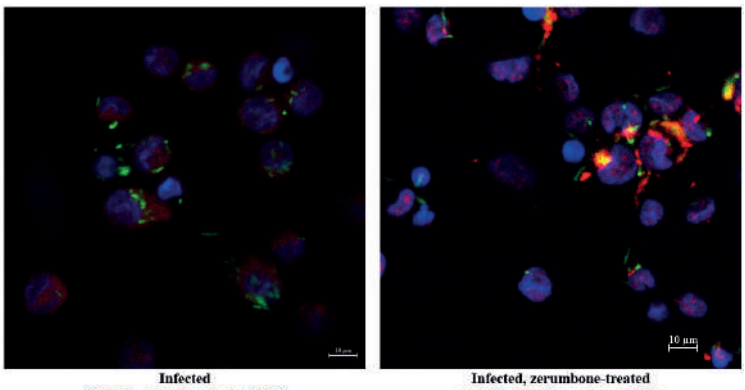
Front Row From Left: Sreejith G S, Aravind Madhavan, Arun K B



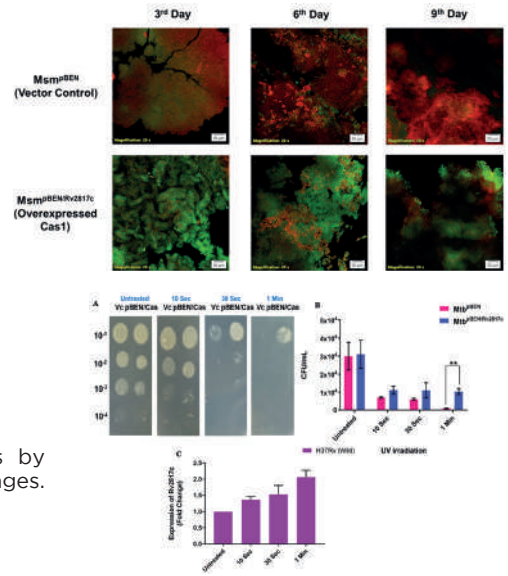


Fig 1: Zerumbone induces autophagic clearance of M. tuberculosis by enhancing the colocalization of M. tuberculosis-LC3 in human macrophages. M. tuberculosis (green) and LC3 (red) in macrophages at 24 hpi.

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- **Madhavan A, Arun K B, Pushparajan A R, Balaji M, Kumar R A.** Transcription Repressor Protein ZBTB25 Associates with HDAC1-Sin3a Complex in Mycobacterium tuberculosis-Infected Macrophages, and Its Inhibition Clears Pathogen by Autophagy. mSphere. 2021;6(1):e00036-21.
- **Arun K B, Madhavan A, Abraham B, Balaji M, Sivakumar K C, Nisha P, Kumar R A.** Acetylation of Isoniazid Is a Novel Mechanism of Isoniazid Resistance in Mycobacterium tuberculosis. Antimicrob Agents Chemother. 2020;65(1):e00456-20.

CHARACTERIZATION OF UNSCHEDULED DNA SYNTHESIS ASSAY IN AN ENDOMETRIAL CANCER CELL LINE, AN3CA.

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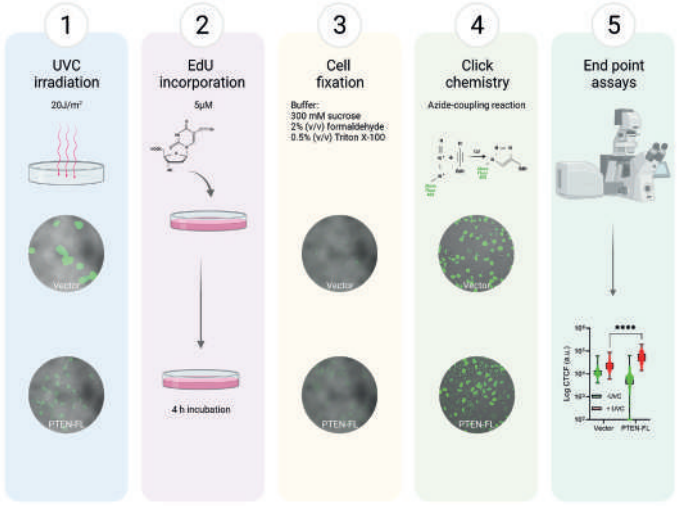
The research theme of our laboratory is understanding how genomic instabilities and DNA repair defects contribute to tumor initiation, development, and therapy. We are interested in endometrial cancer primarily for two reasons: first, unlike most other cancers, endometrial cancer is rising worldwide in both incidence and associated mortality. And second, it has the highest mutational burdens in the DNA damage response genes. Through The Cancer Genome Atlas analyses, we have found that the expression of DNA damage binding protein 2 (DDB2), a gene of nucleotide excision repair (NER) pathway, is negatively correlated with PTEN-negative endometrial cancers. PTEN is a major tumor suppressor, and its loss-of-function drives the disease. Unscheduled DNA synthesis (UDS) occurs outside the S-phase of the cell cycle in response to helix-distorted DNA damage by NER. UDS assay is implicated in determining the NER activity quantitatively in keratinocytes and fibroblast cells and has been instrumental in discovering many NER genes. But it remains challenging for highly proliferative tumorigenic epithelial cells. Here, we used EdU incorporation followed by a click-chemistry reaction to label the newly synthesized DNA of PTEN-defective AN3CA endometrial tumor cells before and after UVC irradiation. We reconstituted a full-length PTEN in AN3CA cells. By employing laser scanning confocal microscopy and flow cytometry analyses, we successfully optimized and characterized the UDS assay in the absence and presence of the tumor suppressor gene PTEN.

Fathima Hameed J S



Step 2, Cells were incubated with a fresh medium containing Click-chemistry compatible alkyne-EdU to incorporate newly synthesized DNA. Step 3, Cell were fixed in a formaldehyde-based buffer that quenched the green signal of GFP reporter of Vector and PTEN-FL. Step 4, Cellular DNA containing alkyne-EdU was coupled with azide conjugated Alexa Fluor 488 by Click-chemistry. This cycloaddition reaction was catalyzed by copper and formed a five-membered hetero atom ring, which produced a robust green signal of Alexa Flour 488. Step 5, The incorporated EdU coupled Alexa Fluor 488 signal was detected under a laser scanning confocal microscope. We carefully analyzed and calculated the cell total corrected fluorescence (CTCF) by measuring the distinct low signal of repair synthesis proficient cells compared to S-phase cells with relatively higher signal.

The figure depicts the key steps in an unscheduled DNA synthesis (UDS) assay. Step 1, Reconstructed full-length PTEN (PTEN-FL) and PTEN-null (Vector) AN3CA cells were irradiated with 254 nm ultraviolet wavelength to activate the repair synthesis by NER.

SELECTED PUBLICATIONS

- **Varghese P C, Rajam S M, Nandy D, Jory A, Mukherjee A, Dutta D.** Histone chaperone APLF level dictates the implantation of mouse embryos. J Cell Sci. 2021;134(1):jcs246900.

REGULATION OF MITOCHONDRIAL QUALITY IN CARDIOMYOCYTES

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Mitochondrial dysfunction is associated with the development and progression of heart failure, cardiomyopathy and other vascular abnormalities like diabetic microvascular disease and atherosclerosis. Recent evidence suggests that increasing mitochondrial quality can improve cardiac function and prevent further deterioration of cardiovascular diseases. Using H9C2 cardiomyocytes, primary endothelial cells, and rat hearts, we study the role of two quality control pathways, mitochondria-derived vesicle (MDV) formation and actin cages (Figure A) around damaged mitochondria. Mitochondria-derived vesicles act as a first line of defense transporting damaged and unfolded mitochondrial proteins to lysosomes for degradation. Actin cages are also formed around damaged mitochondria to prevent its refusion with the network. We purified mitochondria-derived vesicles by in vitro budding and subjected them to mass spectrometry to analyze vesicular contents. We hope to further characterize this pathway to understand cargo selectivity, vesicle generation, trafficking routes and destinations of MDVs. We hope to utilise cutting edge reversible proximity labelling techniques to analyse the trafficking route map of MDVs.

Nidhi Y Nair

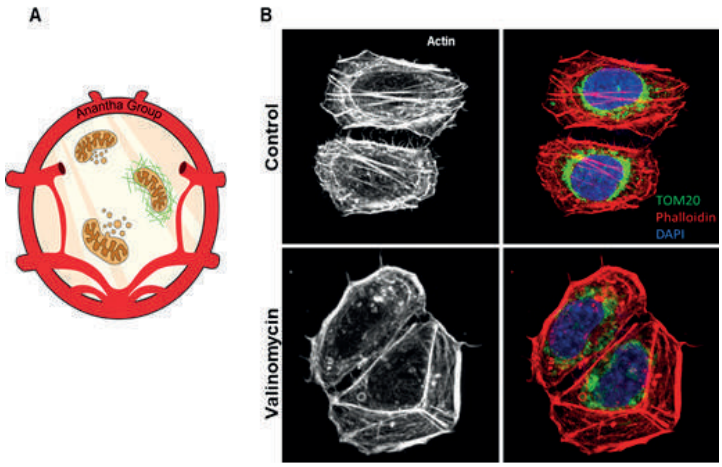

Figure 1: A) Schematic representation of Mitochondria-derived vesicles and B) Actin cage formation around mitochondria. C) Valinomycin induces mitochondrial swelling and actin cage formation D) Cardiomyocytes treated with Valinomycin show increased actin ring formation that is RhoJ dependent. E) Mitochondria derived vesicles, isolated biochemically from rat hearts, show isoform specific incorporation of inner membrane protein Opa1. MDVs containing Opa1 and Tom20 increase with Antimycin A, a complex III inhibitor treatment and reduce with N-ethyl Maleimide treatment. F) Rat heart-derived MDVs are highly enriched for inner membrane and matrix proteins.

Actin cage formation is best elicited using the K+ ionophore valinomycin (Figure B). We will further characterize the role of actin regulators of the RhoGTPase family in modulating actin cage formation around mitochondria. Our study will highlight novel ways to modulate mitochondrial health in cardiomyocytes and endothelial cells.

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- **Sundararaman A, Mellor H.** A functional antagonism between RhoJ and Cdc42 regulates fibronectin remodelling during angiogenesis. Small GTPases. 2021;12(4):241-245.
- **Wei H, Sundararaman A, Truelsen S L B, Gurevich D, Thastrup J, Mellor H.** In Vitro Coculture Assays of Angiogenesis. Methods Mol Biol. 2021;2206:39-46.

REGULATION OF MULTIDRUG RESISTANCE GENES BY STEMNESS-ASSOCIATED FACTORS IN EMBRYONIC CARCINOMA (EC) CELLS

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Ph.D: CUSAT, Kochi
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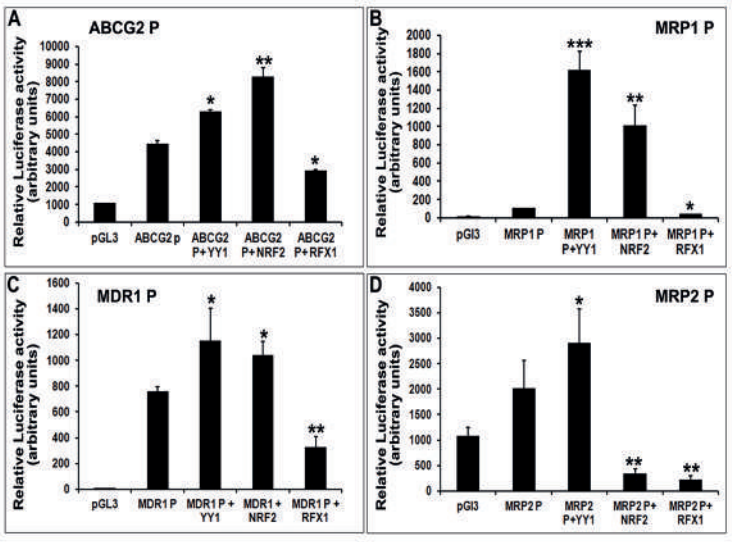
In GCTs, the malignant tumors arise from primordial germ cells, tumors appear to be re-grown from the resistant stem cells (EC cells). The embryonic carcinoma (EC) cells are actually the malignant caricature of ES cells. Like ES cells, EC cells when differentiated lose their pluripotency and become drugs-sensitive due to the down-regulation of MDR genes. The fact that MDR proteins are down-regulated when these cells lose their pluripotency and eventually switched off once they are terminally differentiated, suggests the presence of an in vivo mechanism that regulates the MDRs in EC cells. Understanding the mechanism behind the regulation of MDR genes in EC cells will shed light on formulating better strategies for targeting cancer stem cells. Our initial in silico analysis of MDR promoters suggested binding of a few stemness-associated factors. The selected regulators included possible negative regulators (For example: RFX1,) and positive regulators (such as YY1, NRF2). Since YY1, RFX1 and NRF1 were picked up by all the programs we thought to investigate their role in regulation of MDRs.

From Left: Midhuna Raj K, Joby Issac, Jayasree R, Pooja S R



We found that all MDR genes were down-regulated in differentiated EC cells. Both YY1 and NRF2 showed a similar pattern whereas, RFX1 showed an increased expression during differentiation. Immunocytochemical analyses revealed that these stemness-associated factors, co-expressed with MDRs in EC cells, but the percentage of co-expression was different with each other. Luciferase assays suggested that YY1 and NRF2 positively regulate, and RFX1 negatively regulate MDR genes (Figure). Further, ChIP analysis proved the in vivo interaction of these factors with MDR promoters in EC cells. Our results suggest that MDR genes are differentially regulated in EC cells by the stemness-associated factors. YY1 and NRF2 were found to be positive regulators, and on the other hand RFX1 was found strictly to be a negative regulator of MDR genes.

MDR promoters are differentially regulated by YY1, NRF2 and RFX1 in EC cells. Luciferase analysis revealed that YY1, NRF2 and RFX1 could directly bind and regulate major MDR promoters, ABCG2, MDR1, MRP1 and MRP2. While YY1 and NRF2 showed a positive effect on ABCG2, MRP1 and MDR1 promoters, RFX1 acted as a negative regulator. MRP2 was positively regulated by YY1, while it was negatively by both NRF2 and RFX1 in EC cells.

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- **Issac J, Raveendran P S, Das A V.** RFX1: a promising therapeutic arsenal against cancer. Cancer Cell Int. 2021;

HISTONE MODIFIERS REGULATES THE CHROMATIN DYNAMICS IN PLASMODIUM FALCIPARUM

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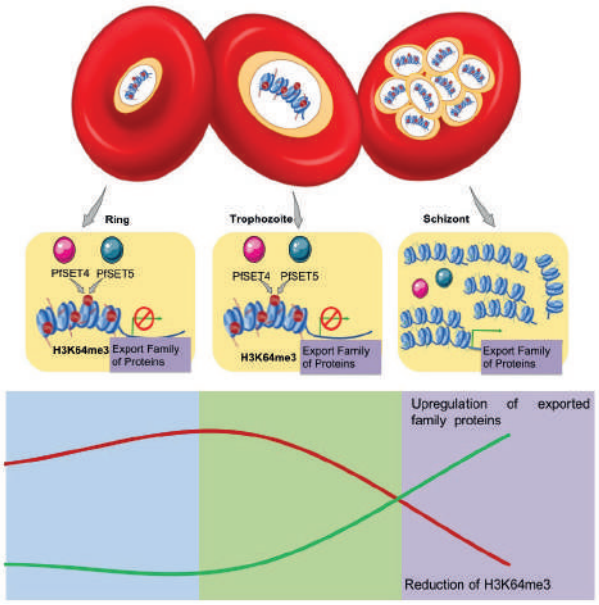
Ph.D: Jacobs University, Breman, Germany
Post-Doc: Stuttgart University, Stuttgart, Germany

Plasmodium spp. have lost many transcription factors and the stage-specific gene expression is strongly depends on the nature of chromatin structure in the parasite. The dynamic nature of chromatin structure regulates the stage specific gene expression, particularly exportome family proteins that are essentially involved to remodel the RBC and assist for successful growth of parasite. The molecular regulators of chromatin organization in various developmental stages of human malaria parasite remain elusive. We hypothesized that histone modifications at unconventional position on histone core region may regulate nucleosome organization, chromatin plasticity and further may regulate the exportome gene expression in Plasmodium spp.

We have identified epigenetic methyl marks at unconventional site such as H3K64 position on core histones of P. falciparum. Interestingly, the methylation site is located at the core histone on lateral surface of the nucleosome and reside very proximal to DNA contact point on histones. We characterized H3K64me3 mark and found it highly dynamic on the chromatin, enriched in ring, trophozoite stages and reduced in multinucleated schizont stage. This is first evidence show the dynamic deposition of the histone methylation marks in various developmental stages of P. falciparum. We have done a detailed characterization of H3K64me3 mark and have identified that the PfSET4 and PfSET5 enzymes of P. falciparum specifically methylate at H3K64. The global ChIP sequencing analysis has revealed that stage-specific dynamic distribution of H3K64me3 regulates the exportome family proteins in Plasmodium spp. This is first molecular evidence that shows the direct role of epigenetic players in stage specific gene expressions and this study is published in J Biol Chem, 2021 (Figure 1).



Schematic representation of Epigenetic control on expression of exportome in Plasmodium spp. The exported proteins are essential to remodel the RBCs for successful growth. A novel epigenetic modification H3K64me3 mark exhibits a dynamic association to the various developmental stages of parasite. The H3K64me3 mark is present in ring and trophozoite stages and reduced in schizont stage of parasite during its development in RBC. Such dynamic association of H3K64me3 mark controls the stage expression of exported proteins and explains the unique mode of exportome gene regulation in the malaria parasite.

From Left: Aparna S, Gayathri G, Dhakshmi S, Jabeena C A, Devadathan VS

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STIL-A NOVEL LINK IN SHH AND WNT SIGNALING, ENDOWING ONCOGENIC AND STEM LIKE ATTRIBUTES TO COLORECTAL CANCER

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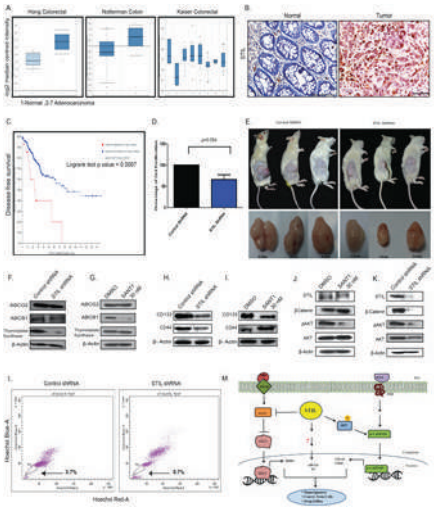
Colorectal cancer (CRC), ranking third in incidence and second in cancer associated mortality worldwide, is one of the most deadly cancers in late stage of diagnosis. Currently, the prime challenges concomitant with CRC management are therapy resistance and disease relapse owing to residual tumor cells. Discovery of a potent gene regulating tumorigenesis and drug resistance is of critical clinical importance. STIL, an oncogene which happened to be significantly altered in the mRNA sequencing of a young CRC patient (36 yr old male) in our lab, intrigued us to study its molecular insights and possible role in colorectal oncogenesis. Oncomine dataset mining revealed significant enrichment of STIL gene in cancer tissues in three different studies, as well as in our clinical cohort of CRC samples procured from RCC Thiruvananthapuram. High expression of STIL was associated with a very low disease-free survival rate among CRC patients as seen from Kaplan Meier plots of studies from c-Bioportal cancer database. STIL silencing reduced proliferation and tumor growth in CRC. Further, STIL was found to regulate stemness markers CD133 & CD44 and drug resistant markers Thymidylate synthase (TS), ABCB1 & ABCG2, both in in-vitro and in-vivo CRC models. STIL has been considered as an integral part of Sonic hedgehog (Shh) signalling as evidenced by numerous studies till date, where interaction of STIL with SUFU inhibits the repressor function of SUFU towards GLI1 resulting in activation of Shh-Gli1 cascades. Interestingly, we perceived STIL mediated regulation of stemness and drug resistant genes, CD133, ABCG2 and TS to be independent of the Shh signalling. Remarkably, we found STIL to regulate β-catenin levels through p-AKT, independent of Shh pathway. This partially answers Shh independent regulatory mechanism of CSC markers by STIL. Our study therefore suggests a dynamic role of STIL in molecular manifestation of CRC as evidenced by our invitro and in vivo analysis.

From Left: Rajshree R Nair, Shilpa R, Meera R Nair, Vijayalekshmi SK, Samu John, Ketakee Mahajan, Evangeline Surya Hermon, Krishna R, Anjana Soman



(A) STIL m-RNA expression in normal colon and tumor obtained from Oncomine datasets. (B) Differential expression of STIL protein in our clinical cohort CRC samples. (C) Kaplan-Meier plot showing association of high mRNA expression with patients' survival and disease free survival in CRC cases (c-Bioportal). (D) Bar graph showing cell proliferation of HT-29 cells upon STIL silencing. (E) Representative images of Control and STIL-silenced tumor xenograft in mice. (F & G) Immunoblot showing expression of ABCG2, ABCB1 and thymidylate synthase protein expression, upon STIL silencing, and SANT1 treatment (to inhibit Shh signalling) respectively. (H & I) Immunoblot showing expression of CSC markers upon STIL silencing and SANT1 treatment respectively. (J & K) Immunoblot showing effect of SANT1 treatment and STIL silencing on β-catenin, AKT and p-AKT protein expression. (L) Dot plot showing side population cells in control and STIL-silenced cells. (M) Schematic representation showing possible mechanistic regulation of multifaceted role by STIL in CRC. Unpaired t-test results showing p value ≤0.05, Scale bar is 20Qm.

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PHYTOCHEMICAL IDENTIFICATION OF BIOACTIVE COMPOUNDS FROM CUSCUTA REFLEXA BY GCMS

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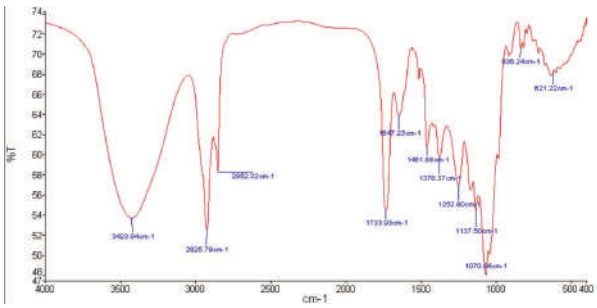
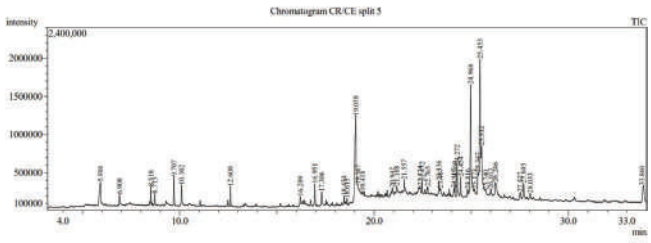
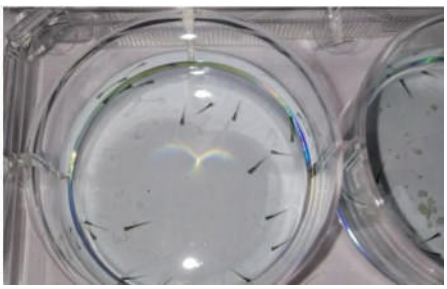
Scientist F, Plant Biotechnology & Disease Biology Program
Ph.D and Post-Doc: JNTBGRI, Palode

Cuscuta reflexa Roxb., is a herbaceous medicinal parasitic stem climber which belongs to the family Convolvulaceae. Many traditional systems of medicine use the whole plant as a cure for jaundice and for the treatment of tumours. Our earlier studies revealed the anti-inflammatory potential and anti-Hepatocellular carcinoma effect of water extract of C.reflexa. Further studies revealed that Chloroform extract of this plant reduced the proliferation of Hep 3B cells in a dose and time dependent manner through the intrinsic mitochondrial apoptotic pathway. In vivo study using the liver carcinoma xenograft tumour model, (on 4-6 weeks old NOD-SCID male mice) revealed the preventive tumorigenic effect of extract. Evaluation of the effect of extract on angiogenesis, wound healing, teratogenicity and general behaviour in Zebrafish (Danio rerio) are ongoing at RGCB zebrafish facility. (Fig3) Qualitative phytochemical screening of this extract confirmed the presence of alkaloids, steroids and cardiac glycosides.In the present investigation, to identify the important functional groups and phytochemical constituents, the chloroform extract of Cuscuta reflexa, was analyzed by Fourier transform infrared spectrometer (FTIR) and Gas chromatography –mass spectrometry(GC-MS). The results of the FTIR spectra confirmed the presence of functional groups with peaks at 3423.22 cm_1(OH-stretching), 2925.61 cm_1(CH-stretching), 1630.91cm_1 (C=C- stretching), 1546.54 cm_1(skeletal vibrations of aromatic and heteroaromatic rings),1309.39 cm_1 (OH bend), 1045.30cm-1 (cyclohexane ring vibrations)(Fig.1)GC-MS analysis confirmed the presence of about 40 compounds in the chloroform extract. Many of the compounds were reported to have anticancer activity including n-hexadecanoic acid and its derivatives which are among the major components present in the extract (Fig2).

From Left: Sreeja R G, Gayathri L T







Scanning electron micrograph of HA-GEL cottony matrix with redox sensitive PLGA nanoparticle (arrows) dispersed (Mag: 8000X).

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RAMAN SPECTROSCOPY FOR DRUG-PROTEIN INTERACTION, DIAGNOSIS AND STRUCTURE-FUNCTION STUDIES OF PROTEINS

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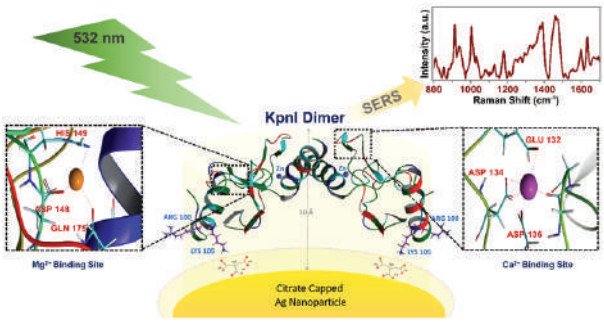
Transdisciplinary Biology Program
Ph.D: IISc, Bangalore
Post-Doc: Cornell University, Ithaca, NY, USA

We have been using Raman spectroscopy and surface-enhanced Raman spectroscopy (SERS) to study drug-protein interactions, diagnostic applications, protein structure-function studies, and using SERS as a screening tool for pre-screening drugs. In the past year, the group has been looking at Extracellular Vesicles (EV) under autophagic conditions as disease markers. EVs are considered a precursor to the onset of the diseases and there is a great interest in unequivocally distinguishing the EVs originating from various cells in simple, easy, and fast methods. Raman spectroscopy can be used as fingerprinting technique to identify closely related systems, we started to develop the technique of Raman spectroscopy to detect EVs and develop a protocol to distinguish EVs under autophagic conditions as a prelude to disease markers (J. Phys. Chem. B 124, 10952 (2020)). As part of the structure-function relationship of proteins studied using SERS, we have looked at the DNA cleavage KpnI endonuclease restriction enzyme. The metal ions make the KpnI's DNA cleavage activity high fidelity like in the case of Ca2+/low concentration of Mg2+ or promiscuous as in the case of high concentration of Mg2+. A combined SERS and molecular dynamics (MD) approach showed that Ca2+ ion activates an enzymatic switch in the active site, which is responsible for the high fidelity activity of the enzyme. Thus, SERS in combination with MD simulations provides a powerful tool for probing the link between the structure and activity of enzyme molecules that play vital roles in DNA transactions. (J. Phys. Chem. B 125, 2241 (2021)). Inhibition of protein misfolding and aggregation is imperative in controlling amyloid diseases. Small molecules which bind to the protein to retain them in the monomer form have drawn a lot of attention. In this direction, we have been looking at the hen egg-white lysosome (HEWL) aggregation driven by pH change. It is observed that HEWL at high pH of 12 shows the formation of aggregates and is seen as breaking and formation of disulfide bonds in the system. But there is no clear evidence for the same. We have used Raman spectroscopy and MD simulations to study the correlation of the breaking and forming of disulfide bonds and the conversion of alpha-helix to beta-sheets responsible for the aggregation of the HEWL. Now it is possible to study the protein dynamics using a much simpler technique like Raman spectroscopy. The group is now setting up a Raman imaging facility for looking at bio-films, tissues, etc in RGCB for various applications.

From Left: Shobha, Sushmitha, Priyanka Jain, Niloyendu Roy, Janaky Sunil, Divya Chalapathi, Anjana Joseph, Samyabrata Sen



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HISTONE CHAPERONE IN DEVELOPMENT

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Post-Doc: University of Kansas Medical Centre, Kansas City,KS, USA

Our recent findings from the lab demonstrated that histone chaperone and DNA repair factor Aprataxin PNK like factor (APLF) could regulate Epithelial to mesenchymal transition (EMT), during reprogramming of murine fibroblast and in breast cancer metastasis. EMT constitutes the first cellular transition during development that lead to the distinct specification of inner cell mass vs trophectiderm. So, we investigated the function of APLF in murine development. We showed that APLF is predominantly restricted to trophectoderm and lineages derived from trophectoderm in pre and post implantation embryos. shRNA mediated downregulation of APLF induced hatching of embryos in vitro with significant increase in E cadherin (Cdh1) and caudal domain 2 (Cdx2) expression. Aplf shRNA microinjected embryos failed to implant in vivo. Rescue experiments neutralized the -knockdown effects of APLF both in vitro and in vivo. Significant reduction in Snai2, Tead4, Gcm1 while gain in Cdh1, Cdx2 and soluble Flt1 level marked inhibition of EMT in differentiating APLF knocked down Trophoblast Stem Cells, derived in the laboratory. We predict that elevated level of Cdh1/Cdx2/sFlt1 upon APLF-downregulation might contribute towards the impaired implantation of embryos. Hence, our findings suggest a novel role of APLF in implantation and in the post-implantation development of mouse embryo. Interestingly, terminal human placenta also showed the presence of APLF being mostly confined to the syncyotrophoblasts. We anticipate that APLF might contribute in the establishment of maternal-fetal connection, as its fine balance is required to achieve implantation and thereby contribute to the normal mammalian development.

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Mayur Balkrishna Shirude, Pallavi Chinnu Varghese
Front Row From Left: Bindhu M S, Debparna Nandy, Ishita Baral, Sruthy M R

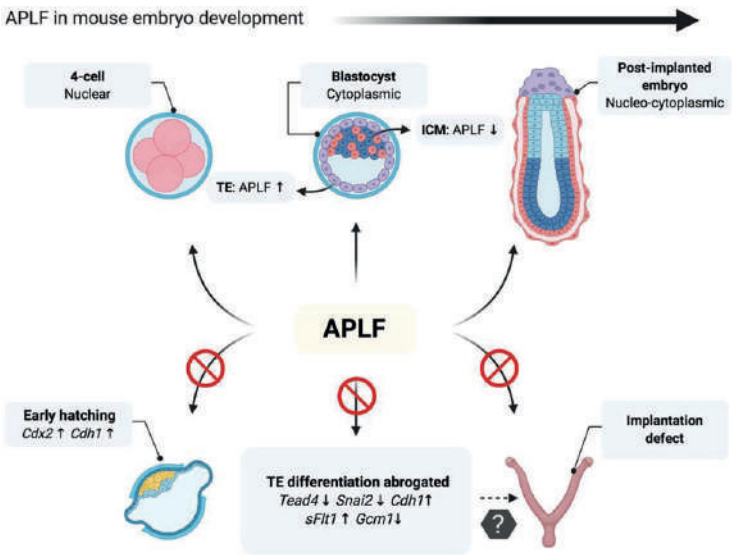

Figure . Schematic representation of the probable role of APLF in mouse embryonic development. Dynamic expression of APLF in the pre-implantation embryo is followed by increased expression at the post-implantation stage. Downregulation of APLF results in induced hatching of pre-implantation embryos, defects in implantation and abrogation of differentiation of trophoblast stem cells derived from TE of the blastocyst.

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HUMAN PAPILLOMAVIRUS (HPV)- RELATED OROPHARYNGEAL CANCER BURDEN AND THE NATURAL HISTORY OF ORAL HPV INFECTIONS: AN INDIAN PERSPECTIVE

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Ph.D: ACTREC, Navi Mumbai
Post-Doc: International Agency for Research on Cancer (IARC-WHO), Lyon, France

It is noteworthy that systematic population-level evidence for the proportion of HPV-positive OPC is still lacking for India. Cancer registry data were collected from Chennai metropolitanregion and Dindugal district were assessed. The oropharyngeal cancer incidence change in men from 2.2 in 1987 to 3.1 in 2011 reflects a near doubling of the number of diagnosecases. Similar changes were not observed in women. Moving forward, this approach is being extended to other centres and data are being collated in the same format. A total of 94samples have been successfully genotyped. Based on these data, HPV DNA positivity of~25% is noted at the oropharynx, irrespective of the center. These are consistent with theresults from the western world. The manual CINtec Histology p16 INK4a Kit (9511, mtmlabs) kitwas applied to 98 cases, a score of 4 or greater was considered positive for p16 INK4a expression. The HPV specific primers were designed to amplify 65-75bp sequences across E6*I splice site. Cellular ubiquitin C gene (ubC) gene amplification, yielding a 81bp was chosen as the internal control. Based on these results we expect a HPV positivity rate at theoropharynx of ~30% consistently across centers, consistent with western data.

Back Row From Left: Kannan T R, Jinu Austin
Central Row From Left: Purnima Kartha N, Devika V A, Aiswarya Ajith, Soumya V, Swetha Jeevan, Sinumol George
Front Row From Left: Shreya Sara Ittycheria, Subha Sankaran, Lekshmi S R, Divya Jayalekshmy

Biomarkers of oral cancer risk prediction:

Oral cancer (OC) is the most common malignancy in India for which oral premalignant lesions (OPML) serve as early indicators of damage. Although it has been recognized for decades that not all OPMLs progress to frank malignancies, no biomarkers exist that can identify OPML patients with a high risk of progression. At present, OC treatment and prognosis is heavily dependent on stage. Yet, the ability of staging to predict prognosis is limited. The project aims to focus biomarker discovery based on mutation patterns (by targeted gene sequencing using custom-prepared primers from QiagenGeneRead kit) andmicro RNA (miRNA) profiles. Focused analysis of the mutations and miRNAs identified were planned in a series of 200 new OPML (for validation of pre-diagnostic biomarker) and 500OC cases. We have successfully identified 24 oral leukoplakia that transformed to oralcancer

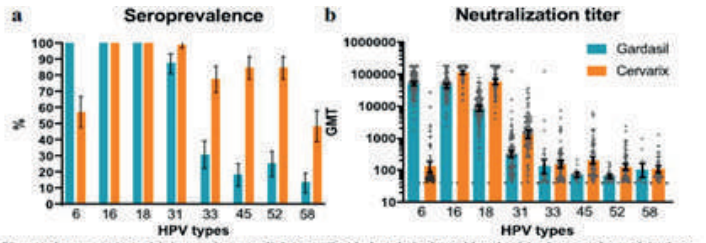

Figure shows seropositivity and neutralizing antibody levels induced by the bivalent and quadrivalent vaccines. (a) Percentage of vaccine recipients with neutralizing antibody titers of >40 to vaccine HPV type. Bars indicate boundaries of 95% confidence interval (b) Geometric mean titer of Month 7 neutralizing antibody levels. Dots represent the EC50 values of one serum. Serum concentrations inhibiting 50% of the PsV infection (EC50 values) were calculated from median of triplicates.

and similar control group of 27 age, sex and tobacco habit matched oral leukoplakiascreen positive subjects who did not progress to frank malignancy. For aim 2, we hadplanned the inclusion of 240 individuals; so far we have identified 300 oral cancer cases bystage.

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MOLECULAR CHARACTERIZATION OF ZINGIBER-PYTHIUM PATHOSYSTEMS

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Ph.D: University of Hyderabad, Hyderabad

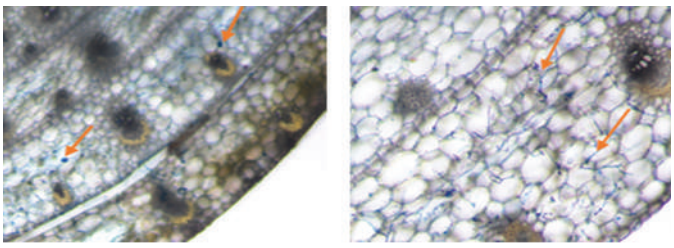
This year we continued the characterization of the molecular basis of Pythium pathogenesis in compatible and incompatible Zingiber hosts. The species of the soil-borne necrotrophic oomycete genus Pythium cause the economically important soft rot disease in the spice crop ginger (Zingiber officinale). Previously, we identified soft rot resistance in certain accessions of the wild congener Z. zerumbet. We have a dual interest in the study of Pythium pathogenesis in Zingiber host: to develop a method for controlling ginger soft rot and understand the molecular events that decide the resistance or susceptibility in the host. The most potent elicitor chosen following screening was found re-programming ginger biology at different levels when the elicitor treated plants were inoculated with soft-rot pathogen Pythium myriotylum. The genome of Pythium myriotylum was sequenced and assembled. Using in-silico methods we predicted the repertoire of effector genes in P. myriotylum genome. The dual RNA-seq of P. myriotylum inoculated soft-rot susceptible ginger and resistant Z. zerumbet at different time periods following pathogen inoculation detected intensive expression re-programming of P. myriotylum genes in both the pathosystems. However, as compared to resistant Z. zerumbet, the number of P. myriotylum genes that showed modulation in the

From Left: Lini Varghese, Sheela G, Gayathri R Satheesh, Vinitha M R, Swathi P S

expression was at least two-fold higher in the susceptible ginger. Earlier we identified a set of genes putatively controlling soft rot resistance in Z. zerumbet. Silencing some of such genes in Pythium resistant Arabidopsis thaliana by virus-induced gene silencing (VIGS) method induced disease infection, providing a functional validation of the involvement of such genes in producing soft rot resistance in the host.

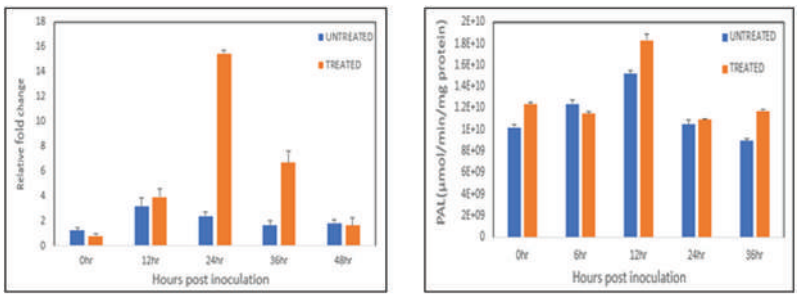
A B C

Elicitor treated ginger plants showing 30% tolerance upon *P. myriotylum* inoculation (**C**) as compared to untreated inoculated plants (**B**).



A B

Trypan blue staining provides the evidence for the suppression of pathogen ingress following elicitor treatment in ginger. Pathogen reached second leaf whorl in untreated plants at 12 hours post inoculation (**A**) while hyphae is contained at the first whorl in treated plants (**B**).



A B

Significant induction in the expression of HSR gene (**A**) and the activity of phenyl Phenylalanine ammonia lyase enzyme (**B**) in the elicitor treated and pathogen inoculated ginger plant.

Symptomatic, phytopathological, molecular and physiological consequences of elicitor treated spice crop ginger following the inoculation with soft rot pathogen Pythium myriotylum.

PRODUCTION OF BACTERIAL POLY (3-HYDROXYBUTYRATE-CO-3-HYDROXYVALERATE) AND EVALUATION OF POLYMER INDUCED CYTOTOXICITY.

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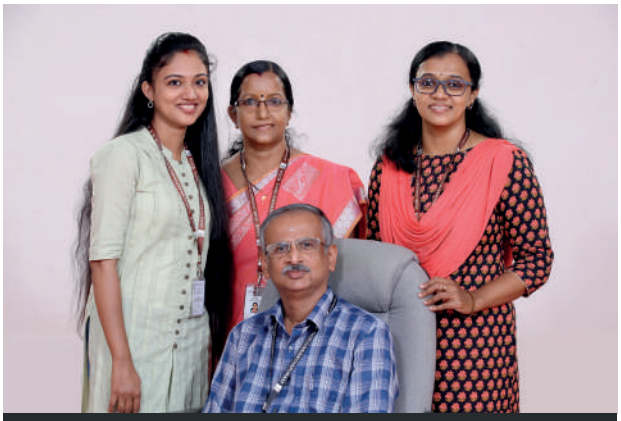
Bacterial polyhydroxyalkanoates (PHA) are considered as a green substitute for synthetic plastics. However, several disadvantages like poor mechanical properties and inadequate functionalities limit their application potential. To evade these hurdles, PHAs need to be modified to fortify enhanced potential in specific applications. The study described production of poly(3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV), copolymer of 3-hydroxybutyrate (3-HB) and 3-hydroxyvalerate (3-HV) in the bacterial strain Bacillus aryabhattaiPHB10 for the first time and evaluated the polymer induced cytotoxicity in-vitro with PHBV/poly(ethylene glycol) (PEG) blends. The B. aryabhattaistrain produced 2.8 g/L PHBV, equivalent to 71.15% of cell dry mass in a medium supplemented with propionic acid, after 48 h incubation. The optimum temperature and pH for the copolymer accumulation was 31 °C and 7, respectively. The gas chromatography–mass spectrometry and nuclear magnetic resonance analyses confirmed the polymer obtained as PHBV. The differential scanning calorimetry analysis revealed that the melting point of the material as 90 °C and its thermal stability up to 220 °C. The average molecular weight (Mn) and polydispersity index of the sample was estimated by gel permeation chromatography analysis and observed as 128.508 kDa and 2.82, respectively. The PHBV showed tensile strength of 10.3 MPa and elongation at break of 13.3%. The superior properties of PHBV such as better thermal behaviour, plasticity, toughness and biodegradability make them a more attractive bioplastic. The PHBV and their blends with PEG were tested for cytotoxicity on human keratinocytes (HaCaT cells) and the cells incubated with PHBV/PEG2kDa blends were 99% viable, whereas with the PHBV alone showed comparatively higher cytotoxicity (Fig 1). The significant improvement in the cell viability of PHBV/ PEG2kDa blends indicates its potential as a candidate for skin graft applications.



From Left: Athira S S, Geetha S L, Priya P

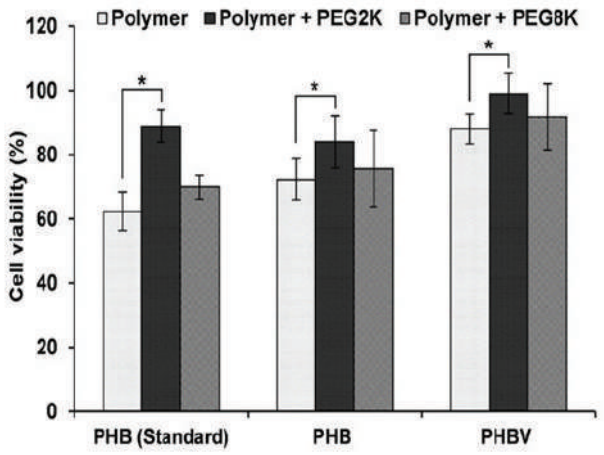


Fig 1: Cytotoxicity of the polymers obtained from B. aryabhattai PHB10 and the polymer/PEG blends. (PEG2K = PEG with Mw 2000 Da; PEG8K = PEG with Mw 8000 Da) (*p < 0.05)

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CARDAMONIN ATTENUATES EXPERIMENTAL COLITIS AND ASSOCIATED COLORECTAL CANCER

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Scientist E-I, Cancer Research Program
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Post-Doc: UT M.D Anderson Cancer Center, Houston, TX, USA,
Virginia Commonwealth University, Richmond, VA, USA

The main focus of the laboratory is to understand the role of inflammation in physiology (innate immune response) and pathophysiology (cancer). Colorectal cancer (CRC) is currently one of the most commonly diagnosed cancersworldwide. However, in several countries, CRC incidence rates in young adults (aged 40-50 years) are increasing, and the opposite trend is observed in older adults.Many epidemiological studies clearly demonstrated a direct link between the usage of nutraceuticals and health benefits. Nutraceuticals are dietary products with a cocktail of chemical components, including flavonoids,chalcones etc., and showed a therapeutic benefit on human health beyond their nutritional aspect and in most cases without any apparent side effects. Cardamonin is a naturally occurring chalcone majorly from Zingiberaceae family, which includes wide spices in India. Herein we investigated the anti-inflammatory property of cardamonin using different in vitro and in vivo systems.In a mouse model of dextran sodium sulfate (DSS) inducedcolitis cardamonin treatment protected the mice from colitis. Subsequently, we evaluatedthe therapeutic potential of this chalcone in a colitis-associated colon cancer model. Weperformed a microRNA profiling in the different groups and observed that cardamoninmodulates miRNA expression, thereby inhibiting tumor formation. Based on different studies published from our laboratory we conclude that cardamonin (a) is a potent anti-inflammatory agent and has the ability to suppress NF-kB and iNOSsignaling; (b) Protected the mice from inflammation associated colitis (c) modulate the expression of microRNAs (d) inhibited the proliferation of colorectal cancer cell lines in vitro (e) increased the levels of reactive oxygen species and induced apoptosis. Cardamonin is a promising spice derived nutraceutical with the potential to be developed as a future chemotherapeutic agent against colitis and colorectal cancer.

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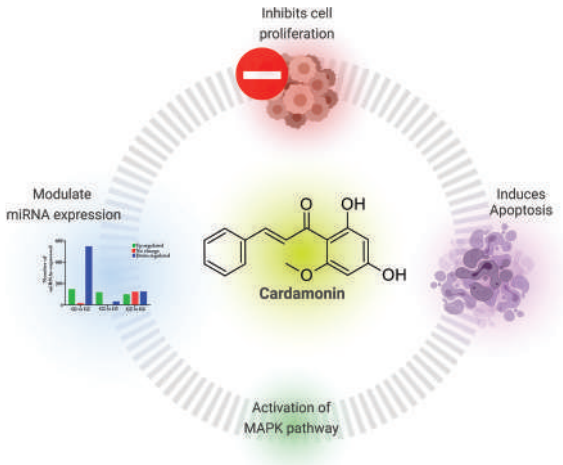
Front Row From Left: Rajeev J Thampi, Yadu Vijayan, Arun V



Legend for figure: Graphic illustration showing the various effects of cardamonin and major pathways regulated in colorectal cancer

SELECTED PUBLICATIONS

- **James S, Aparna J S, Babu A, Paul A M, Lankadasari M B, Athira S R, Kumar S S, Vijayan Y, Namitha N N, Mohammed S, Reshmi G, Harikumar K B.** Cardamonin attenuates experimental colitis and associated colorectal cancer. Biomolecules. 2021;11(5):661.
- **Mohammed S, Vineetha N S, James S, Aparna J S, BabuLankadasari M B, Maeda T, Ghosh A, Saha S, Li Q Z, Spiegel S, Harikumar K B.** Regulatory role of SphK1 in TLR7/9-dependent type I interferon response and autoimmunity. FASEB J. 2020;34(3):4329-4347

MEASLES PROJECT: FIELD ACTIVITIES WERE LIMITED DUE TO COVID PANDEMIC SITUATION

IYPE JOSEPH, MBBS, MPH
Program Scientist, Pathogen Biology Program
MBBS: Government Medical College, Thiruvananthapuram.
MPH: SCTIMST, Thiruvananthapuram

Leptospirosis Project: Collaborative efforts with Holy Cross Hospital, Kottiyam, Kollam are progressing. Sample collection from patients with clinically suspected Leptospirosis is being done. No isolate in this year.

Nutritional Anemia control project: New project under preparation in collaboration with Dr. Sajeena Manjima, Integrated Farming System Research Station (IFSRS), Karamana, Thiruvananthapuram, Kerala Agricultural University (KAU). The project involves anemia detection, anemia correction with home grown iron-rich foods followed by evaluation of response.

COVID-19: During the period before test facilities became commonly available in Kerala State, a surveillance system was implemented for five major private hospitals in Thiruvananthapuram, Kerala. Samples were tested at LMMD and reported back. This was done as part of social responsibility of RGCB, using internal funds.

Epidemiological support is given to other scientists in their study on immune responses following infection and vaccination against COVID-19.

Selected as Member in the "Surveillance Cross-cutting Sub-group of the World Health Organization (WHO) Diagnostic Technical Advisory Group (DTAG) for Neglected Tropical Diseases". The appointment is for three years.

Administrative duties: Designated as COVID-19 Nodal Officer in RGCB. Activities undertaken include Patient management within RGCB, Home management for about 150 patients and Vaccination for 300 persons.

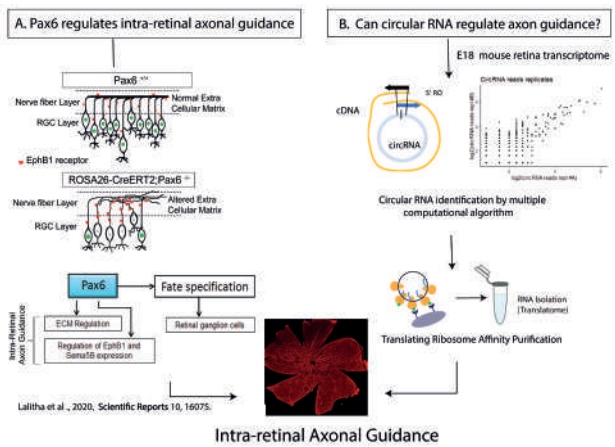
IDENTIFYING MOLECULES INVOLVED IN RETINAL GANGLION CELL AXON GUIDANCE

JACKSON JAMES, Ph.D

Scientist F, Neurobiology Program
Ph.D: CUSAT, Kochi
Post-Doc: SCTIMST, Thiruvananthapuram,
University of Nebraska Medical Center, Omaha, NE, USA

We have previously showed that retinal ganglion cells (RGCs) could be generated from ES cells and transplanted into the retina to replenish the degenerated RGCs in Glaucoma (Jagatha et al., 2009, Biochemical and Biophysical Research Communications 380, 230–235). Although the transplanted cells were found to have incorporated into the retina, there are no evidences for successful recovery of vision. We have also transplanted Embryonic Stem Cell derived neural progenitors into NMDA induced RGC ablated animal models and observed a partial recovery in the vision through behavioral experiments (Divya et al., 2017, Front. Cell. Neurosci. 11). Even though we could observe a partial recovery, there was no evidence that the transplanted cells were able to guide their axons and make synaptic connections with the brain visual centers. Therefore, it is prudent to first understand how axon guidance happens during early retinal development and then mimic those conditions in the adult retina to properly guide the axons of the transplanted RGCs to the optic disc. We have shown from RNA-Seq data that Pax6 in addition to RGC fate specification also controls intraretinal axon guidance and fasciculation by maintaining a proper extra cellular matrix and regulating EphB1 and Sema5b during early retinogenesis (Lalitha et al., 2020, Scientific Reports 10, 16075.). From the same transcriptome data, we have found several circular RNAs (circRNAs) unanimously identified by three different algorithms (CIRI, CIRCexplorer2 and find-circ). From total RNA sample of embryonic retina, a simple PCR with the divergent primers showed the presence of back-splicing events. We functionally classified the host genes of the circRNAs by gene ontology (GO) enrichment analysis and found that functional groups related to microtubule organization and axon guidance are overrepresented amongst the enriched GO terms. Given the crucial developmental timepoint when growth cone (GC) guidance of young neurons is very important, biogenesis of circRNA induced us to find the regulatory role of circRNA in GC guidance.

Back Row From Left: Akhila G N, Parvathy Surendran, Surya Suresh, Jyothi P Nair
Front Row From Left: Sreedevi L R, Biju S Nair, Budhaditya Basu, Meera V



Intra-retinal Axonal Guidance

A. Pax6 in addition to RGC fate specification controls intraretinal axon guidance and fasciculation by maintaining a proper extra cellular matrix and regulating EphB1 and Sema5b during early retinogenesis.

B. Several circular RNAs (circRNAs) unanimously identified by three different algorithms i.e., CIRI, CIRCexplorer2 and find-circ. The potential of circular RNA being translated is currently being studied. The focus of this program is to understand the role circular RNA in retinal ganglion cell axon guidance

SELECTED PUBLICATIONS

- **Lalitha S, Basu B, Surya S, Meera V, Riya P A, Parvathy S, Das A V, Sivakumar K C, Nelson-Sathi S, James J.** Pax6 modulates intra-retinal axon guidance and fasciculation of retinal ganglion cells during retinogenesis. Sci Rep. 10(1):16075.

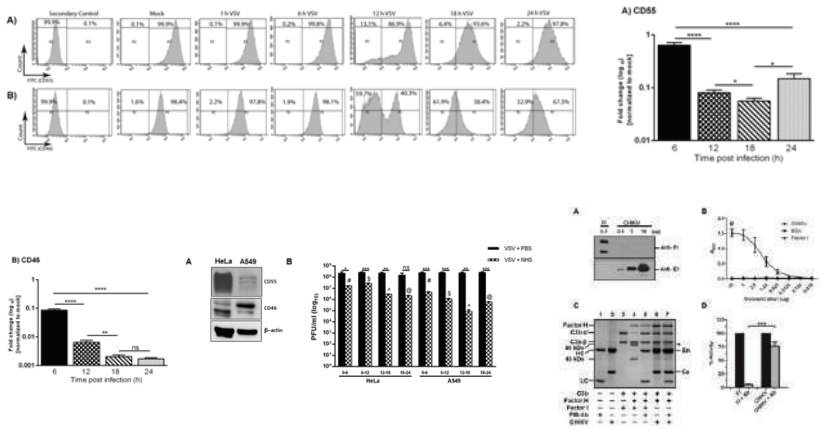
EXPLOITING HOST COMPLEMENT REGULATORS – ARSENALS IN RNA VIRUS ARMORY TO EVADE COMPLEMENT

JOHN BERNET JOHNSON, Ph.D
Scientist E-I, Pathogen Biology Program
Ph.D: NCCS, Pune
Post-Doc: Wake Forest University Health Science, Winston-Salem, NC, USA

Viruses with RNA genome have proved to be potent pathogens of both humans (SARS CoV2, Nipah virus, ebola virus) and animals (Newcastle disease virus, blue tongue virus). Using model or human pathogens like vesicular stomatitis virus (VSV), Chandipura virus (CHPV) both rhabdoviruses and chikungunya virus an alphavirus, we have focused on understanding the complex mechanism of interaction of these viruses with the human complement system. While VSV and CHPV could activate complement readily resulting in virus neutralization via the classical pathway of complement, CHIKV was a weak activator of complement and resisted neutralization. A major question that arose was, how these viruses go on to productively infect the host also resulting in significant mortality (CHPV) and morbidity (CHIKV). In depth analysis revealed that VSV recruited at least two host membrane bound complement regulatory proteins (CD46 and CD55). Interestingly, CD55 was found to have a more dominant role than CD46, which could be correlated to the reduction in CD46 protein levels and early shutting down of CD46 transcription by VSV. This is quite significant because VSV generated from a cell line known to naturally express more CD46 (A549 cells) was highly sensitive to complement compared to those generated in HeLa cells, known to express CD55 to a greater concentration. Unlike the rhabdoviruses, CHIKV was found to resist complement and our investigations revealed that the virus had a unique factor I like activity that could specifically inactivate C3b and not C4b. Using a

From Left: Umerali K, Nisha Asok Kumar, Reshma K M

factor I function-blocking monoclonal antibody and protease inhibitor cocktail we could also demonstrate that the factor I like activity associated with CHIKV is of viral origin. Thus our investigations have started unravelling the complexities in RNA virus-complement interactions and the smart evasive strategies adopted by these viruses. These findings are critical for developing potent therapeutics and novel viral vectors.



Evasion strategies adopted by viruses are tailored to protect them from complement dependent neutralization. Selective maintenance of a host regulator, CD55 over CD46 both at the protein (1) and transcript level (2) was observed in VSV infected cells which offered greater protection to the virus from complement (3). Chikungunya virus on the other hand was found to possess the host regulatory enzyme, factor I like activity which is not a common phenomenon. Interestingly this factor I like activity based on immunoblotting (4A), ELISA (4B) and a specific inhibitor with a monoclonal antibody against human factor I (4C & D) demonstrates that this activity is of viral and not host origin

SELECTED PUBLICATIONS

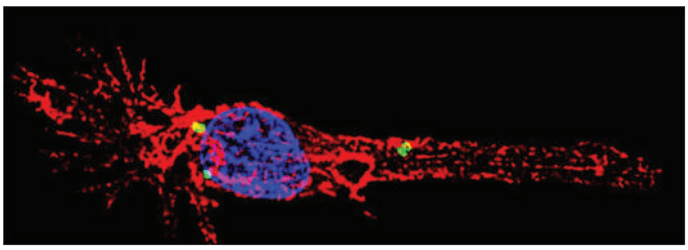
- **Nag J, Mukesh R K, Suma S M, Kunnakkadan U, Kumar N A, Johnson J B.** A Factor I-Like Activity Associated with Chikungunya Virus Contributes to Its Resistance to the Human Complement System. J Virol. 2020;94(7):e02062-19.
- **Asok Kumar N, Muraleedharan Suma S, Kunnakkadan U, Nag J, Koolaparambil Mukesh R, Lyles D S, Johnson J B.** Functional dissection of the dominant role of cd55 in protecting vesicular stomatitis virus against complement-mediated neutralization. Viruses. 2021;13(3):373.

HOST-PATHOGEN INTERACTIONS IN PNEUMOCOCCAL INFECTIONS

KARTHIK SUBRAMANIAN, Ph.D
Scientist C, Pathogen Biology Program
Ph.D: National University of Singapore, Singapore
Post-Doc: Karolinska Institutet, Stockholm, Sweden

The global respiratory gram-positive bacteria, Streptococcus pneumoniae (the pneumococcus) is a respiratory tract bacteria and the major causative of fatal diseases such as pneumonia, septicemia and meningitis. Pneumonia is the leading cause of death due to lower respiratory tract infections worldwide in young children below 5 years age accounting for 600000-800000 deaths every year. Therefore S. pneumoniae is classified by the WHO as a priority pathogen that needs urgent research into pathogenesis and development of new and effective antibiotics. The major focus of my laboratory is to study the molecular pathogenesis of pneumococcal infections and investigate the mechanisms underlying pneumococcal interaction with the host immune cells and immunoevasion. Pneumococci express several virulence factors such as polysaccharide capsule, surface proteins (such as adhesins, factor H binding proteins, neuraminidases etc.) and pore-forming toxin, pneumolysin to evade the host immune response. We discovered that, the toxin, pneumolysin binds to the human mannose receptor on human dendritic cells and lung macrophages at sublytic doses, enabling bacterial invasion and intracellular survival by promoting anti-inflammatory response (Nature microbiology 2019). In a translational approach, we designed peptides from the toxin binding region of MRC-1 to competitively inhibit toxin mediated binding to MRC-1 on host cells and pneumococcal disease severity (EMBO Mol. Med 2020). Further, we also developed biocompatible calcium phosphate nanoparticles conjugated to peptides for enhanced bioactivity and intranasal delivery of peptides to lungs. In the upcoming years at RGCB, my lab will investigate how the intracellular pneumococci reprogram host immune cells at the phenotypic and functional using a combination of FACS sorting, RNA sequencing and mass-spectrometry. We will also investigate the molecular composition and immunomodulatory role of extracellular vesicles secreted from pneumococci- infected macrophages and explore their potential for immunotherapies

Saba Parveen



Pneumococci hide within immune cells to escape killing, Immunofluorescence image showing the presence of pneumococci (green) localized inside infected human dendritic cells stained in red with phalloidin red.

SELECTED PUBLICATIONS

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REPROGRAMMING OF HOST GLUTAMINE METABOLISM DURING CHLAMYDIA TRACHOMATIS INFECTION AND ITS KEY ROLE IN PEPTIDOGLYCAN SYNTHESIS

KARTHIKA RAJEEVE, Ph.D

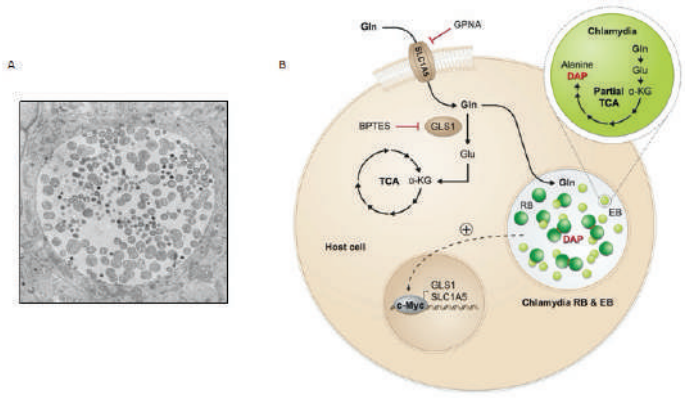
Scientist E-I, Pathogen Biology Program

Ph.D: University of Wuerzburg, Germany

Post-Doc: University of Wuerzburg, Germany, Uni Klinikum, Wuerzburg, Germany

Obligate intracellular bacteria such as Chlamydia trachomatis undergo a complex developmental cycle between infectious, non-replicative elementary-body and non-infectious, replicative reticulate-body forms. Elementary bodies transform to reticulate bodies shortly after entering a host cell, a crucial process in infection, initiating chlamydial replication. As Chlamydia fail to replicate outside the host cell, it is unknown how the replicative part of the developmental cycle is initiated. In our study, we show, using a cell-free approach in axenic media, that the uptake of glutamine by the bacteria is crucial for peptidoglycan synthesis, which has a role in Chlamydia replication. The increased requirement for glutamine in infected cells is satisfied by reprogramming the glutamine metabolism in a c-Myc dependent manner. Glutamine is effectively taken up by the glutamine transporter SLC1A5 and metabolized via glutaminase. Interference with this metabolic reprogramming limits the growth of Chlamydia. Intriguingly, Chlamydia failed to produce progeny in SLC1A5-knockout organoids and mice. Thus, we report on the central role of glutamine for the development of an obligate intracellular pathogenic bacterium and the reprogramming of host glutamine metabolism, which may provide a basis for innovative anti-infection strategies. This part of the study is published in Nature Microbiology (Rajeeve et al 2020). Since my studies are focused on host-pathogen interface and how the bacterial infection predispose the infected tissue towards carcinoma, my group will focus to investigate the direct evidence of bacterial virulence factors and how the bacteria evade immune cells, that might support transformation in human tissue. Moreover we also started a host pathogen interaction studies in Mycobacterium tuberculosis, one of the major cause of mortality. Our study will focus on the mechanism by which the pathogen remains latent, and how it reactivates in human macrophages.

From Left: Pooja K R, Safvana A T, Smitha R P, Nijisha M



A. Figure shows the transmission electron microscopy of Chlamydia inclusion. B. The figure shows the graphical abstract. Chlamydia retransforms the host tissue by increasing the glutamine uptake via upregulating the glutamine transporters on the cell surface in a c-Myc dependent manner. Host glutamine is taken up by the bacteria for peptidoglycan synthesis which is critical for bacterial replication. A glutamine inhibitor could be used an effective antibacterial drug to control Chlamydia infection.

SELECTED PUBLICATIONS

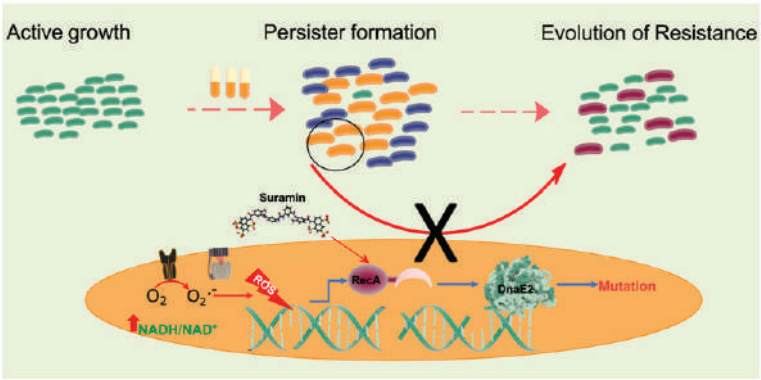
- **Rajeeve K, Vollmuth N, Janaki-Raman S, Wulff T F, Baluapuri A, Dejure F R, Huber C, Fink J, Schmalhofer M, Schmitz W, Sivadasan R, Eilers M, Wolf E, Eisenreich W, Schulze A, Seibel J, Rudel T.** Reprogramming of host glutamine metabolism during Chlamydia trachomatis infection and its key role in peptidoglycan synthesis. Nat Microbiol. 2020; 5(11):1390-1402.

THE ERROR-PRONE POLYMERASE DNAE2 MEDIATES THE EVOLUTION OF ANTIBIOTIC RESISTANCE IN PERSISTER MYCOBACTERIAL CELLS

KRISHNA KURTHKOTI, Ph.D
DBT-Ramalingaswami Faculty Fellow, Pathogen Biology Program
Ph.D: IISc, Bengaluru
Post-Doc: Sanford Burnham Medical Research Institute, San Diego, CA, USA, Rutgers University, Newark, NJ, USA

Application of antibiotics to susceptible bacterial culture generates a minor population of persisters that remain susceptible to antibiotics but can endure them for extended periods. Recently, antibiotic persisters (APs) of mycobacteria were reported to experience oxidative stress and develop resistance when treated with lethal doses of ciprofloxacin or rifampicin. However, the mechanisms driving the de novo emergence of resistance remained unclear. In our study, we demonstrated that mycobacterial APs display redox imbalance resulting in high levels of reactive oxygen species (ROS) within the persister cells. ROS inflicts DNA damage that culminated in activating the SOS response causing up-regulation of the error-prone DNA polymerase DnaE2. The sustained expression of dnaE2 in APs resulted in the rapid evolution of resistance to antibiotics and negatively impacted the proliferation of APs during the recovery phase. Whole genome sequence analysis revealed that induction of DnaE2 resulted in genome wide mutagenesis and resulted in evolution of multiple drug resistance. To counter this antibiotic induced drug resistance, we considered to target RecA protein, that is the master regulator of bacterial SOS response and is conserved in important pathogenic bacteria. Inhibition of RecA by suramin, an anti-Trypanosoma drug, decreased the conversion rate of persisters to resistors in a diverse group of bacteria. Our study highlights suramin's novel application as a broad-spectrum agent in combating the development of drug resistance.

From Left: Sinchana G Bhat, Salini S



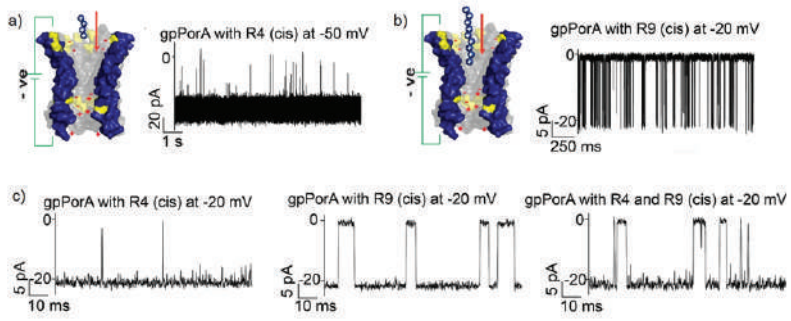
Mechanism of antibiotic induced drug-resistance in M. smegmatis. Lethal dose kills majority of the bacteria (blue cells) leaving behind a population of APs (orange cells). The APs display disturbed redox balance leading to generation of ROS. The high levels of ROS in APs inflict DNA damage activating RecA and triggering the SOS response. DnaE2 an effector protein of the SOS response induces mutagenesis resulting in emergence of drug resistance. Presence of suramin- a RecA inhibitor mitigates the antibiotic induced drug resistance in persisters.

BUILDING ALPHA-HELICAL PORES FOR NANOTECHNOLOGY AND MEDICINE

MAHENDRAN K R, Ph.D
Scientist E-I, Transdisciplinary Biology Program
Ph.D: Jacobs University Bremen, Germany
Post-Doc: Jacobs University Bremen, Germany, University of Oxford, UK

Protein pores are used as effective nanopore sensors for the single-molecule detection of a wide variety of biological and chemical molecules. While beta barrels and DNA nanopores have been engineered extensively, alpha-helical bundles remain relatively under-explored. They are attractive targets, as they can be engineered to build new pores with sophisticated architecture and specific functionality. Here we assembled a large octameric transmembrane pore from 40 amino acid synthetic alpha-helical peptides based on the pore-forming protein PorAcj from Corynebacterium jeikeium. Remarkably, these peptides self-assembled to a 36 KDa preoligomer in the SDS-PAGE. The gel extracted preoligomer rapidly inserted in the DPhPC bilayer to form a large stable pore with high cation selectivity. We studied the interaction kinetics of cationic peptides with gpPorA and resolved the differently sized and charged arginine repeat peptides. Here we could differentiate RRRR, RRRRRR and RRRRRRRRR based on the residence time of each peptide inside gpPorA at specific applied voltages. Further, we deduced the asymmetric charge distribution in the pore lumen based on the asymmetry in RRRRRRRRR binding kinetics with respect to the side of the addition. We also found that the gPporA added to the cis side of the bilayer more likely results in the pore insertion with the dense negatively charged terminal exposed towards the cis side. This study demonstrated a new class of alpha-helical pores that are advantageous in chemical synthesis, purification, modulating ion selectivity and substrate specificity. We are also focusing on a biological beta-barrel pore, CymA, a specialized substrate selective nanopore with unique structural geometry for the selective uptake of cyclic sugars.

From Left: Amina H Shaji, Mangaiyarkarasi R, Devika Vikraman, Smithadevi S, Anjali Das



Interaction of nonaaarginine with gpPorA.a) Electrical recordings showing R4 interaction with single gpPorA at -50mV and b) electrical recordings showing R9 interaction with single gpPorA at -20 mV. c) Competitive interaction of the gpPorA with R4 (10 QM, cis) and R9 (both 100 nM, cis) at -20 mV

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- **Scott A J, Niitsu A, Kratochvil H T, Lang E J M, Sengel J T, Dawson W M, Mahendran K R, Mravic M, Thomson A R, Brady R L, Liu L, Mulholland A J, Bayley H, DeGrado W F, Wallace M I, Woolfson D N.** Constructing ion channels from water-soluble α-helical barrels. Nat Chem. 2021;13(7):643-650.
- **Mahendran K R.** Building Synthetic Transmembrane Peptide Pores. Methods Mol Biol. 2021;2186:19-32

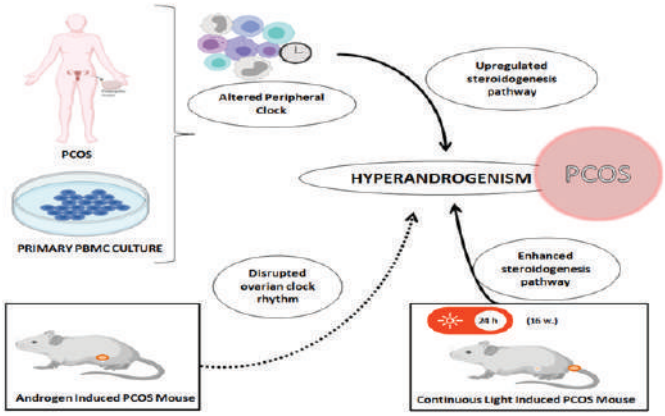
CROSS-TALK OF CIRCADIAN RHYTHM AND STEROID METABOLISM-A POSSIBLE CUE FOR PCOS PATHOGENESIS

MALINI LALORAYA, Ph.D, FNASc
Scientist G, Reproductive Biology Program
Ph.D: Devi Ahilya Vishwavidyalaya, Indore.
Post-Doc: The Rockefeller University, New York, NY, USA,
University of Virginia, Charlottesville, VA, USA,
University of Florida, Gainesville, FL, USA

Polycystic ovary syndrome (PCOS) is primarily a hyperandrogenic condition along with frequent oligo/anovulation, and polycystic ovaries seen in 5%–10% of reproductive aged women. Sleep disorders, type 2 diabetes and depression are comorbidities associated with PCOS which are thought to accompany circadian disruption. Circadian rhythm was identified as a significantly affected pathway in a global miRNA profiling conducted in peripheral blood of PCOS patients in our lab. The mechanism underlying the association of the circadian system and PCOS had been insufficiently addressed.Human peripheral blood mononuclear cells (PBMC's) contain an operative clock work and are peripheral site for steroid metabolism leading to the synthesis of potent androgen. Through real-time PCR analysis, we demonstrated downregulation of genes in the positive loop of the circadian pathway and higher expression of the negative regulators of the circadian pathway in peripheral blood of PCOS women, which further attenuates the core clock gene expression. Our results also revealed an altered expression of steroidogenesis related genes, StAR, CYP17A1, SRD5A1&2,and CYP19A1 in PCOS v/s control women.BMAL1/ CLOCKknockdown in PBMCs was also found to affect steroidogenesis through altered SRD5A1/2 and CYP19A1expression, involved in testosterone to DHT and estradiol synthesis respectively. We could also demonstrate decreased amplitude of core clock genes oscillations in ovaries of dehydroepiandrosterone (DHEA) induced PCOS mouse model when compared to the control

From Left: Rahul Singh, Betcy Susan Johnson, Vani Manoharan Nair, Anagha Balakrishnan, Renjini A P, Deeptimayee Guru, Lipika Priyadarsini Patra, Ajay Kumar Dhyani

group, indicating the responsiveness of ovarian clock genes to excess androgens. Modulation of circadian rhythm in mice by continuous light-treatment developed PCOS features. Dysregulated clock genes and increased expression of steroidogenesis genes was also observedin ovaries of continuous light induced mice. Thus, our study found that impaired circadian clock could hamper regulation of steroid metabolism in PCOS women. Our results also indicate an entwined association ofcircadian misalignment and hyperandrogenism in PCOS.



Pictorial abstract: Clinical study conducted using peripheral blood of PCOS patients revealed an altered clock genes expression that resulted in enhanced peripheral steroid metabolism. Animal studies using DHEA-induced and continuous light-induced mice models of PCOS also showed a disrupted ovarian clock rhythm and enhanced steroidogenesis pathway.

SELECTED PUBLICATIONS

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- **Johnson B S, Laloraya M.** A cytokine super cyclone in COVID-19 patients with risk factors: the therapeutic potential of BCG immunization. Cytokine Growth Factor Rev. 2020;54:32-42.

EXPLORING THE POTENTIAL OF 'DEFENSE PRIMING' AS A CROP PROTECTION STRATEGY IN PIPER NIGRUM

MANJULA S, Ph.D
Scientist F, Plant Biotechnology & Disease Biology Program
Ph.D: University of Kerala, Thiruvananthapuram

Our earlier and ongoing attempts on deciphering P.nigrum x Ph.capsici pathosystem, have led to the inference that 'Priming' by defense elicitors is a potential strategy that could be adopted for protecting P.nigrum plants from the devastating oomycete pathogen Phytophthora capsici.It was observed that pretreatment of leaves with the defense elicitor Glycol chitosan (GC) delays disease symptoms by inducing more robust defense response like Hypersensitive Response (HR)and ROS burst. This was evident by ROS assay and Real Time PCR validation of HR genes. We have identified key genes and metabolic pathways that are preferentially upregulated by defense priming. The genes identified are- Caffeic acid-methyl transferase, Chalcone synthase, Cinnamoyl CoA reductase, and Phenyl ammonia lyase, to mention a few. Results from studies conducted on P.nigrum seedlings also provide evidence that some major secondary metabolites including Piperine are preferentially accumulated in response to priming. More experiments are under way to provide molecular insights into the beneficial effect of defense priming in P.nigrum.A bioactive peptide was synthesized based on sequence of Piper colubrinum Osmotin protein through our earlier studies. The protein showed inhibitory activity towards P.capsici. Microscopic analysis of infected P.nigrum leaves pretreated with synthesized Osmotin peptide resulted in significant pathogen hyphal breakage and and a three fold reduction in pathogen DNA evidenced by FungiQuant Real Time assay. A number of key genes in the phenyl propanoid and Hypersensitive Response (HR) pathways were also significantly overexpressed by Osmotin peptide treatment. The results indicate that Osmotin peptide also effectively primes the innate immunity of P.nigrum, which suggests its potential use in crop protection.

Back Row From Left: Geethu S Nair, Liya Kurian, Gayathri G S
Front Row From Left: Saranya V, Meera B

Figure 1 a
Pre-treating seedling leaves of Piper nigrum with Glycol chitosan b- Pre-treated seedlings

Figure 2a
Pre-treated leaf of P.nigrum after infection with P.capsici (24hpi), b- Control (untreated) leaf 24hpi

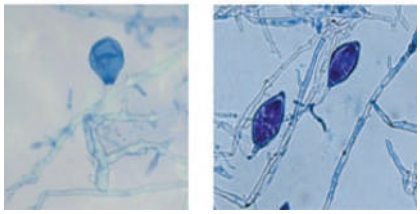

Figure 3
Deformed empty sporangium of P.capsici formed in response to Osmotin peptide treatment (left) Control normal spore (right)

SELECTED PUBLICATIONS

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PROFILING METHYLATION PATTERN OF TREATMENT RESPONSE IN SCHIZOPHRENIA

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Scientist G, Neurobiology Program
Ph.D: M.L.Sukhadia University, Udaipur
Post-Doc: AIIMS, New Delhi, CCMB, Hyderabad

In schizophrenia 30% of the individuals fail to respond to antipsychotic medications. The objective of the study was to identify methylation signatures in antipsychotic-responsive. We performed 850K MWAS in treatment responsive and non-responsive patients. We identified 9 probes hypermethylated and 87 probes were hypomethylated in nonresponders. The sites of hypermethylated genes were involved in the regulation of cytokine production, methionine metabolic process, glial cell development, oligodendrocyte differentiation etc.. Among hypomethylated probes 28% were associated with TSS site, 33% were in the body region and 25% were in the inter genomic regions (IGR). The study identifies key differential methylation sites for non-response.

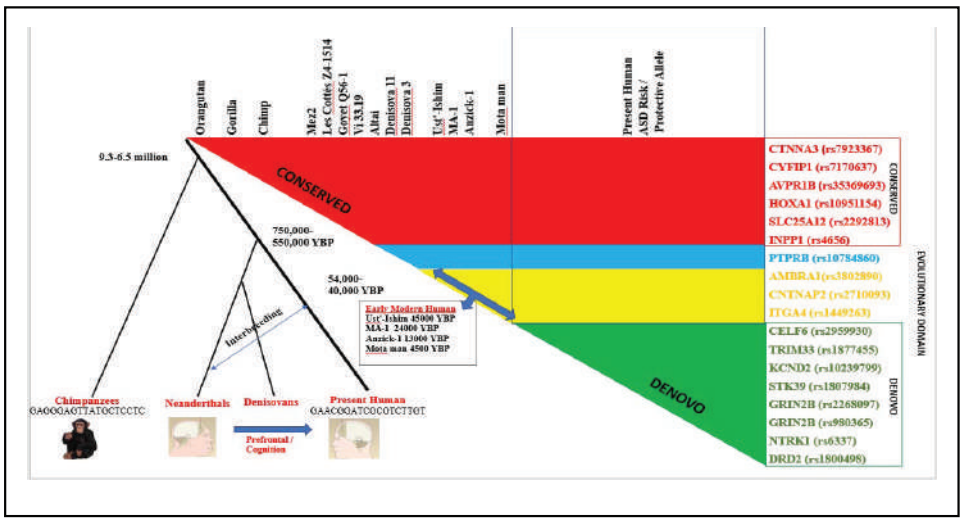
Evaluating an integrative model for phenotypic variations in autism spectrum disorder

Autism Spectrum Disorder (ASD) is a heterogeneous neurodevelopmental disorder characterized by paradoxical phenotypes of deficits in brain function and gain in brain function. A tradeoff hypothesis, was tested in ASD risk common SNPs. The positively selected ASD risk SNPs were found in the genes that are involved in cognition, memory, learning, behavior, neuronal development and other nervous system processes. The evolutionary pattern of these genomic tradeoff signature genes imply that ASD might be a casualty of higher order brain function as evident from De Novo Evolutionary Selection Domain (emergence within ~ 4000 YBP). The phenotypic variation in gain or loss also indicate a cognitive genomic tradeoff for ASD risk SNPs.

From Left: Neethu Mohan, Alfiya F, Anil Prakash, Krishna Priya E K, Binithamol K P

Genetic predisposition to Non-Syndromic Deafness: An immunogenetic perspective

Non syndromic deafness (NSD) contributes to 70% of hearing loss patients. We find only 15-25% of NSD patients carry common mutations in GJB2 and MYO6 genes. We suspect a strong role for the immune pathway in modulating the genes critical for inner ear development. Our study demonstrate the role of cytokine variants in the etiology of NSD hearing loss. We suggest imbalance in cytokine responses mediated by high producer alleles of proinflammatory and low producer alleles of anti inflammatory cytokines during the prenatal development may contribute to risk of NSD.



Evolutionary domain of positively selected Autism Spectrum Disorder loci

REGULATION OF GLUTAMATERGIC CALCIUM SIGNALING UNDER NORMAL AND DISEASE CONDITIONS

OMKUMAR R V, Ph.D
Scientist G, Neurobiology Program
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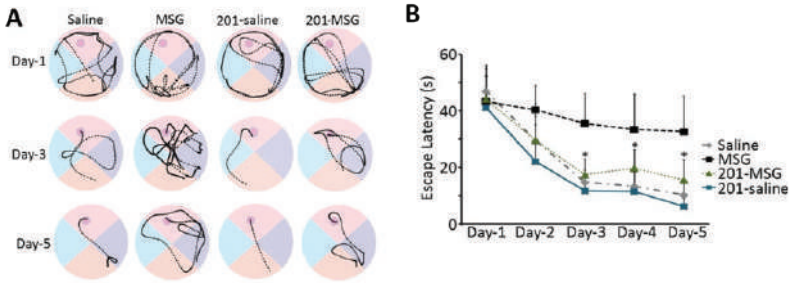
Post-Doc: Purdue University, West Lafayette, IN, USA,
California Institute of Technology, Pasadena, CA, USA

Cellular signaling mechanisms involving calcium ions underlie several brain functions. Coordinated functioning of the calcium conducting NMDA receptor (NMDAR) and the calcium activated enzyme, CaMKII, is essential for learning and memory. We have created mutants of CaMKII that are defective in undergoing biochemical regulation by NMDAR. These mutants are being incorporated into adeno-associated viral (AAV) vectors for knock-in experiments to test the role of the biochemical regulation of CaMKII in learning and memory. Altered function of NMDAR is known to be a major cause for neurodegenerative and neuropsychiatric diseases. Changes in expression of NMDAR mediated by microRNAs (miRNAs) is proposed to underlie schizophrenia. We have identified several miRNAs that could downregulate NMDAR subunits in pharmacological animal models of schizophrenia. In the MK-801 treatment model and in the methylazoxymethanol acetate (MAM) treatment model of schizophrenia, certain common miRNAs are upregulated that caused translational repression of GluN2A and GluN2B subunits of NMDAR. Further, when some of these miRNAs are overexpressed in the hippocampus in vivo using AAV constructs, GluN2A and GluN2B proteins were downregulated leading to cognitive impairments. These findings show for the first time, the potential of these miRNAs in regulating NMDAR in vivo. We have been developing new methods for calcium channel activity assays that are simple and less expensive. HEK-293 cells were found to express L-type voltage gated calcium channel (L-VGCC) endogenously. Methods were developed to detect the activity of endogenous L-VGCC and thus HEK-293 cells could be used for L-VGCC activity-based drug screening. Several rodent models have been established for studying calcium signaling mechanisms and also to test the efficacy of neuroprotective drug candidates in vivo. Intraperitoneal injection of monosodium glutamate (MSG) was used as a chronic excitotoxicity model, while intracerebroventricular (ICV), intracortical and intrahippocampal injections of NMDA were used as acute excitotoxicity models. Pharmacological models of schizophrenia have also been developed. These models exhibited behavioural impairments as well as molecular changes in the brain tissue.Overall, work from the laboratory has contributed towards basic understanding of brain functions as well as towards translating it to therapeutic approaches.

From Left: Veluthai G, Amata Sara Boban, Reena Sara Jacob



Neuroprotection in vivo by multi-target directed ligand (MTDL), 201.The efficacy of 201 was assessed using Morris water maze (MWM) behavioral test. Animals were subjected to treatment with saline or monosodium glutamate (MSG) along with 201 or vehicle. A: Representative trajectories of selected animals in each group in the MWM test on days 1, 3 and 5 are shown. B: Escape latency values from Day1 to Day5 are also shown (represented as mean3SD, n=6-7. * p value <0.05 compared to MSG treatment alone).

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- **Madhavan M, Mohanan A G, Jacob R S, Gunasekaran S, Nair R R, Omkumar R V.** Glu60 of α-Calcium/calmodulin dependent protein kinase II mediates crosstalk between the regulatory T-site and protein substrate binding region of the active site. Arch Biochem Biophys. 2020;685:108348.

MOLECULAR REGULATION OF GERMLINE STEM CELL DIVISION AND DIFFERENTIATION IN MAMMALIAN TESTIS

PRADEEP KUMAR G, Ph.D

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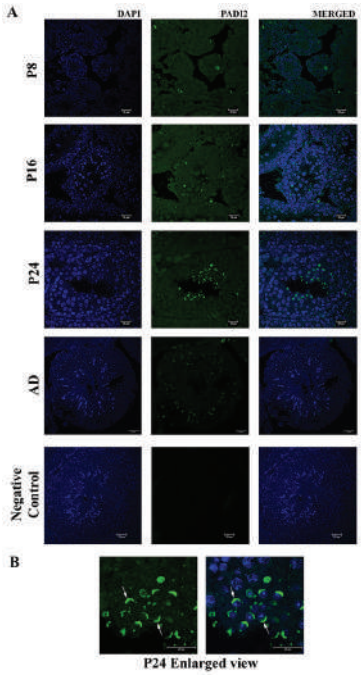
University of Florida, Gainesville, FL, USA

Our lab had reported earlier that Cyclin M1 (CNNM1) is a possible stemness determining gene in spermatogonial cells in the mouse. Though Cnnm1 expression was noted in mouse testes from post natal day 8 onwards, it could not be detected in embryonic testes till day 13, implying that the expression of this gene starts in embryonic testes during the third trimester of development. We evaluated the expression of Cnnm1 expression in two different immortalized mouse spermatogonial cell lines. The expression of Cnnm1 was significantly higher in C18-4 cells which represented undifferentiated spermatogonia when compared to GC-1spg cells which represent the differentiating spermatogonia. Cnnm1 expression was upregulated by GDNF in C18-4 cell. GDNF brought about elevations in the expression of cMyc as well. The induction of Cnnm1 expression in response to c-Myc overexpression using an OSKM construct strongly suggested that GDNF acts through Src-PI3K/Akt/Myc pathway in regulating Cnnm1 expression.

Back Row From Left: Mahitha Sahadevan, Susha Kutteyil, Keerthi Baliga, Fathima N S, Sai Sindhu Gudiboina
Front Row From Left: Vysakh G, Irfan Khan, Sabith Raj K, Jeeva S E

We identified minimal promoter activity at -256/+139 region of mouse Cnnm1 promoter in both spermatogonial cell lines. We located a CpG island at the proximal promoter of Cnnm1 which supports the notion that Cnnm1 expression may be regulated by epigenetic mechanisms, which will be studied using reporter assays with stable clones of reporter constructs.Complementing our previous observation that silencing of TDP43 brought about an enhancement in the expression of Cnnm1, we demonstrated that over-expression of TDP-43 resulted in the suppression of Cnnm1 expression, confirming that TDP43 is a negative regulator of Cnnm1 expression and could be a switch triggering germline stem cell differentiation. Further, the transdifferentiation potential of spermatogonial stem cells into somatic cell lineages has also been established.We have evaluated the regulation of the expression of 14 common target genes of miR34c and miR449a in mouse testis during the first wave of spermatogenesis and in GC1-spg cells. These included Gabra3, Heyl, Nono, Padi2, Pkia, Tbc1d2b, Vat1, Figf, Met, Ppp2r5a, S1pr3, Akap2, Marcks and Nav1. We have also profiled proteome level changes in GC1-spg cells treated with inhibitors of miR34c and/or miR449a.



Expression of PADI2, one of the common targets of MiR34c and miR449a, in mouse testis during the first wave of spermatogenesis (A) Immunolocalization of PADI2 in Postnatal day 8 (P8), 16 (P16) 24 (P24) and Adult (AD) mouse testes and negative control. PADI2 was localized in both the somatic and germ cell of the testes, with prominent localization observed in prospective acrosomal region of round spermatid in P24 testis. PADI2 appears in green and DAPI-stained nuclei in blue. (B) A portion of PAD12 staining in postnatal 24 mouse testes (enlarged view). The white arrow illustrates spermatids with robust PAD12 staining in the prospective acrosomal region.

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- **Sahadevan M and Kumar P G.** Peptidyl Arginine Deiminase 2 (PADI2) is expressed in post-meiotic germ cells in the mouse testis and is localized heavily on the acrosomal region of spermatozoa. J. Endocrinol. Reprod. 2021, 25(1), 53-65.

ROLE OF ER-α IN BRCA-1 STEERED DNA DAMAGE REPAIR (DDR)

PRIYA SRINIVAS, Ph.D
Scientist F, Cancer Research Program
Ph.D: University of Kerala, Thiruvananthapuram

BRCA1mutation carriers have much higher rate of developing cancer in hormone responsive tissues such as breasts and ovaries. BRCA1 can inhibit ER-α in a ligand dependent and independent manner. However, it is not analyzed whether E-ER signaling has any influence on BRCA1 mediated DNA repair events. Conversely, the multi-channel regulatory connection existing between ER-α and BRCA1 further suggest the definitive role of E-ER signaling in BRCA1 dependant DDR pathways and maintenance of genome integrity. Hence, we analyzed the influence of ER-α /E2-ER signaling in BRCA1 mediated DNA damage repair and its association with breast tumorigenesis to seek an explanation for tissue specificity of carcinogenesis by BRCA1 defectiveness.The influence of E-ER signaling on BRCA1 mediated DDR pathways like Base Excision Repair (BER), non-homologous end joining (NHEJ) and Homologous Recombination Repair (HRR) were analyzed by specifically designed assays in the presence and absence the ligand of 17-β estradiol. We have demonstrated that E2/E2-stimulated ER-α can augment BRCA1 mediated high fidelity repairs like HRR and BER in breast cancer cells (Fig 1)

From Left: Vinitha B K, Sheeja B, Arathy V Warrier, Neethu Krishnan, Neetha R L, Aswathy Ashokkumar, Dipyaman Patra

Conversely, a condition of ER-α deficiency itself or any interruption in ligand-dependent ER-α transactivation resulted in delayed DNA damage repair, leading to persistent activation of γH2AX and retention of unrepaired DNA lesions fueling tumor progression. ER-α deficiency not only limited the HRR in cells but also facilitated the DSB repair through error prone DNA repair pathways like alternative-NHEJ (alt-NHEJ).Together, these results infer clues to the indispensible role of ER-α in BRCA1 mediated DNA DSB repair. Further understanding of the cross-talk between ER-α and the BRCA1 dependant DNA damage processing will provide critical information to steer drug development, radiation therapy, and hormone combination treatment of breast cancer patients. The current study acts as basic evidence in understanding the molecular biology behind the predisposition of BRCA1 mutations to the breast or the ovarian cancers, which otherwise remains elusive.

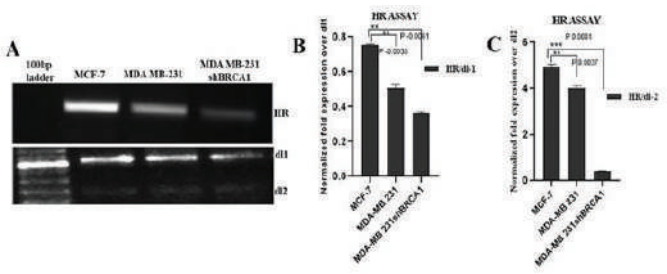

Figure.1: ER-α deficiency impairs BRCA1 mediated HRR. Figure represents Homologous recombination (HR) assay: The two defective plasmids dl1 and dl2 once co-transfected into cells, undergoes homologous recombination to generate a functional HR product. The recombinant product can be isolated and the HR efficiency of transfected cells can be further analyzed by PCR based amplification using set of specific primers. (A) HR efficiency of ER-α positive MCF-7, ER-α negative MDA MB-231 and BRCA1 deficient MDA MB-231ShBRCA1 breast cancer cells as analyzed by HR assay. (B, C) HR product formed upon recombination is quantified and normalized to backbone plasmids dl1 and dl2.

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- **Krithiga K, Arathi Rajan, Geetu Rose Varghese, Neetha R L, Dipyaman Patra, Neethu Krishnan, Arathy Warrier and Srinivas S.** Partial genome analysis of Cox1 subunit-I region in mitochondrial DNA of canine mammary tumours. J. Vet. Anim. Sci. 52(1); 2021; 95-98

DECIPHERING BREAST CANCER METASTASIS

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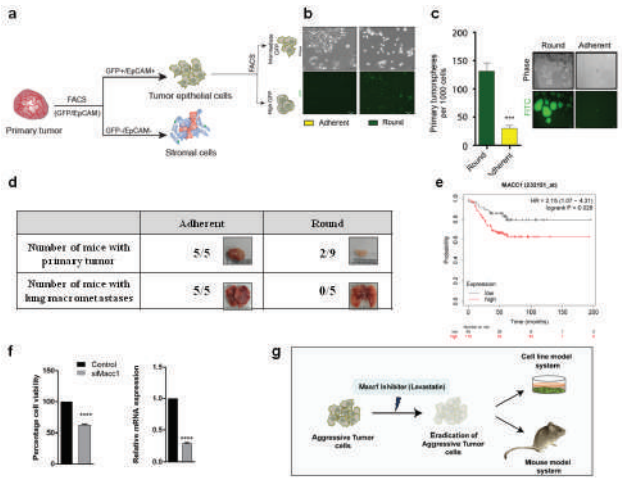
Ph.D: NII, New Delhi
Post-Doc: MRC Hutchison cancer unit, Cambridge, UK

Metastasis or the spread of cancer from the primary site to other parts of the body is a silent killer in breast cancer, with 90% mortality rate for women with metastatic disease. Therapeutic targeting requires a deeper understanding of this complex cascade of events eventually leading to metastasis. I aim to comprehend the cell intrinsic and extrinsic mechanisms (1, 5, 6) that allow a tumour cell to survive, remain in a state of dormancy and then thrive in a hostile new environment of a distant metastatic organ.

Approach 1- Investigating the role of known molecular mediators of metastasis in breast cancer
I have focused on the Inhibitor of differentiation (or Id) family of bHLH transcriptional repressor proteins which play a critical role in the metastatic spread of breast cancer cells to distant organs especially the lung (4). I have gone onto identify two potential pathways by which Id proteins control key cancer phenotypes – via negative transcriptional regulation of the Robo1 pathway (3) and cell cycle pathway by impacting Kif11 and Aurka (1).

Approach 2: Identifying the molecular mediators involved



Archana PT

in breast cancer metastasis using an unbiased approach I plan to expand this work to identify pathways which are critical for the metastatic phenotypes hardwired into the metastatic cells with the aim of discovering new potential therapeutic targets. I have isolated two phenotypically distinct tumor cell populations with differing metastatic potential. Resolving the molecular drivers behind the intratumoral heterogeneity revealed critical players which are druggable (manuscript under preparation). Using a validation cohort of 20 matched primary and metastatic tumors will allow me to further understand the genetics underlying the metastatic process and drive my work into more translational avenues in an Indian context.

Unbiased approach in identification of key drivers of metastatic progression. a,b,c, Strategy used to isolate morphologically distinct cell types from a heterogenous tumor with differing self-renewal abilities. d, The cells had different disease propagating and metastatic capacity. e, Macc1 was identified as the top candidate driving the aggressive phenotype observed in one cell type and high Macc1 expression correlated with poor survival in clinical cohort analysis. f, Macc1 knock down leads to a significant loss in aggressive tumor cell viability. g, Identification of Macc1 allows us to now target the aggressive fraction of tumor cells with Lavostatin, a small molecule inhibitor against Macc1.

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PREDICTION OF DISEASE PROGRESSION & SURVIVAL IN PATIENTS WITH ACUTE RENAL DISEASE: A TARGET-BASED GENOMIC STUDY

RADHAKRISHNAN R NAIR, Ph.D
Scientist F, Laboratory Medicine and Molecular Diagnostics Program
Ph.D: University of Kerala, Thiruvananthapuram

I joined RGCB on October 2010 as Scientist EI, Head of the division, Laboratory Medicine and Molecular Diagnostics which was under ICMR Virology Network Program. When I joined the division was performing molecular diagnostics of H1N1, HBV, HCV and Dengue samples. We developed the list of parameters form 4 to nearly 226 parameters both infectious and non-infectious diseases. The diagnostics include most of the infectious diseases such as virus, bacteria, fungi and parasite and non-infectious diseases like cardiovascular diseases, cancer markers, transplant medicine and many other life style disorders. The lab received NABL ISO 15189-2012, NABH, and ILAC accreditation in 2016 and presently maintains the accreditation status to date.

From Left: Vineetha P T, Sanughosh K, Heera Pillai R, Karthika V

RESEARCH

1 Association of gene encoding APRIL and BAFF with IgA Nephropathy, A case-control study, ICMR, 2020-2023

IgA nephropathy (IgAN) is a common cause of end-stage renal disease. In India, IgAN is characterized by marked severity in a younger population. Elevated serum levels of B cell activation factor (BAFF) and a proliferation-inducing ligand (APRIL), two critical factors for B cell homeostasis, coded by TNFSF13B and TNFSF13 genes, have been reported in IgAN. The study's main objective is to find the association of TNFSF13B and TNFSF13 genes with susceptibility and severity of IgAN in our Indian population. We will also look for the association of APRIL and BAFF levels with IgAN in a smaller patient subset. A case-control study will be performed to investigate the effect of genetic variants in TNFSF13 and TNFSF13B genes involving 220 IgAN patients and an equal number of ethnically matched normal healthy controls. The results of the present study will provide evidence for the involvement of TNFSF13 and TNFSF13B in the pathogenesis and severity of IgAN. It will help to identify the potential causal variants related to the development, severity, and progression of IgAN in our population and will aid in predicting the pathogenesis and severity of the disease

2. Development of a point of care Lateral Flow Diagnostic Platform to detect viral antigens and antibodies, IgG & IgM, of Corona Virus SARS-CoV-2 enabling efficient and swift diagnosis and mass screening, BIRAC, 2020-2021. (Co-investigator)

SARS CoV 2 (COVID-19) is a global pandemic. Millions of the world population are affected by this deadly disease. Lakhs of people have lost their lives because of this disease. It is necessary to detect the disease as early as possible and start treatment. The lateral flow device for rapid antigen detection is a point of care testing for identifying antigens within 20 minutes. This can be used for bedside screening, screening at airports, schools, colleges, and significant public gatherings to prevent the outbreak's recurrence. The rapid antibody test kit will help to identify the post-COVID-19 diseases like cardiovascular diseases. The antibody test kit will also help in detecting people who were asymptomatic Covid positive patients. The lateral flow device was developed in collaboration with Ubio systems and submitted to ICMR for validation.

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EXOSOME BASED CANCER THERAPY

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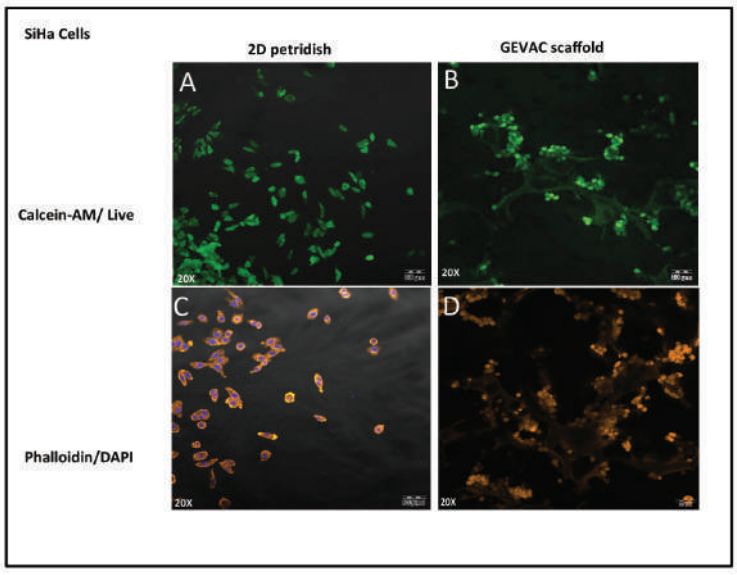
Cancer Research Program
Ph.D: University of Barcelona, Spain
Post-Doc: University of Zurich, Zurich, Switzerland
University of Lausanne, Lausanne, Switzerland.

Cervical cancer (CC) is the third leading cause of cancer mortality amongst females. The early metastasis of the primary tumor results in poor prognosis and poor therapeutic outcomes. Specifically, an increasing amount of research has revealed that long-lasting infections of high-risk human papillomavirus (HPV), such as HPV-16 and HPV-18, mainly compose the majority of CC cases, however, the infection alone may not be sufficient to induce malignancy. About 45% of women with CC are diagnosed at an early stage. If CC is metastasised to the surrounding tissues, organs or the regional lymph nodes, the 5-year survival rate is 56%3. The therapy prospect for CC patients has not improved significant and treatment regimens for CC are highly toxic, and patients with metastatic disease are rarely cured. Strategies to deliver small RNA molecules such as miRNAs (miRs) are an exciting and potential therapeutic option for controlling the growth of malignant CC.

From Left: Sreebharathi R, Kavitha UK

The ability of miRs to down regulate expression of genes involved in cancer progression makes them an excellent candidate for developing a miR based therapeutic strategy. Delivery of these molecules to the target site is another area of concern since most of the carriers such as gold nanoparticles, viral vectors etc. cause immunogenicity and lack inherent targeting ability. We focus on delivering those miRNA molecules using engineered non-toxic carriers such as extracellular vehicles which will exhibit inherent targeting ability and deliver the miRNAs to the target site. We will also elucidate the mechanism of entry of extracellular vesicle loaded miRNA to the target cells. In parallel, we are also developing a physiologically relevant scaffold based CC metastasis model which recapitulates the in vivo environments. The 3D scaffold based CC model will help in distinguishing more invasive or migratory phenotypes which will aid in the diagnosis or drug discovery.



SiHa cells grow in 3D scaffolds and form tumoroids. Live/ dead and Phalloidin fluorescence images of SiHa cells in 2D tissue culture plates (TCP) and in GeVAc scaffolds.

RNA-MEDIATED GENE REGULATION: IMPLICATIONS IN CARDIOVASCULAR GENE PROGRAM

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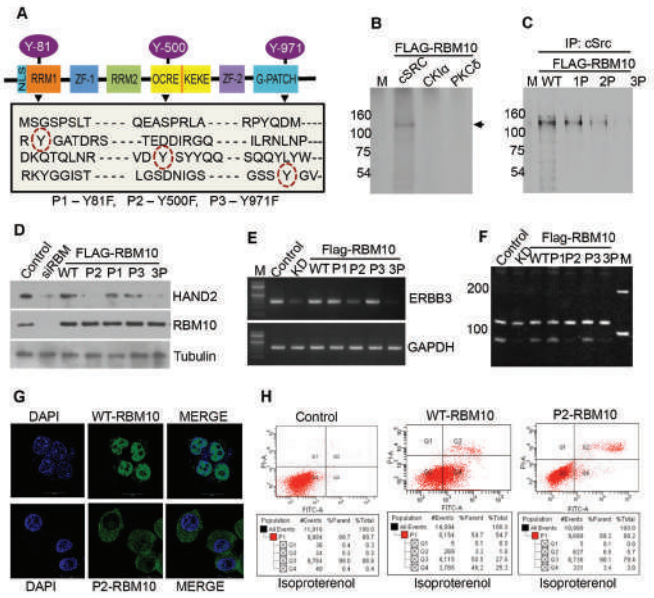
Cardiovascular Diseases & Diabetes Biology Program
Ph.D: CDFD, Hyderabad
Post-Doc: University of Wisconsin-Madison, MI, USA

Processing at the 3′-end is an essential step in the generation of all eukaryotic mRNAs and long non-coding RNAs. It is an important molecular mechanism involved in the regulation of heart function and conditions including cardiac hypertrophy (CH) or heart failure (HF). Genes encoding various pro- and anti-hypertrophy factors are controlled through their 3′-untranslated region (UTR). We have identified a variant poly(A) polymerase, Star-PAP (Speckle targeted PIPKIalpha regulated PAP) that regulates mRNAs involved in the hypertrophic gene program. We have shown that regulation of hypertrophy regulators involves alternative polyadenylation where the UTR length difference causes differential gene expression. We have shown that Star-PAP functions with an associated protein RNA binding motif protein 10, RBM10 that is required for the Star-PAP mediated PA-site selection. Both Star-PAP and RBM10 and down regulated during cardiac hypertrophy leading to global UTR shortening that results in increased expression of pro-hypertrophy geens and down regulation of anti hypertrophy genes. Concomitantly, in a physiological model, re-expression of RBM10 but not

From Left: Dhanya R, Neeraja K M, Malaya Ranjan Behera, Feba Shaji, Ciji Varghese, Nimmy Francis

Star-PAP rescued the isoproterenol-induced hypertrophy in cardiomyocytes

Progression of hypertrophic heart to heart failure involves massive myocyte apoptosis in the heart. We identified a proto-oncogene c-Src kinase mediated tyrosine (Tyr, Y) phosphorylation on RBM10 that triggers apoptosis of hypertrophic cardiomyocytes. We confirm c-Src phosphorylation of RBM10 (Y81, Y500 and Y971) by in vitro kinase assay and Immunoprecipitation experiments using phospho-Tyr specific antibody. Of the three cSrc sites, mutation of Y500F but not Y81F or Y971F compromised splicing and 3′-end processing of target mRNAs. Strikingly, expression of RBM10 triggers apoptotic cell death of isoproterenol-treated hypertrophic cardiomyocyte that was attenuated on mutation of Y500F or inhibition/knockdown of cSrc kinase in the cell. Our results establish RBM10 as a central regulator of CH and progression to heart failure.



cSrc-mediated phosphorylation of RBM10 triggers apoptosis of hypertrophic cardiomyocyte. (A) Schematic of RBM10 protein sequence indicating three cSrc target three tyrosine phosphorylation sites. Phospho-deficient mutations (P1 – Y81F, P2 – Y500F, and P3 – Y971F) are indicated. (B) In vitro kinase assay using purified RBM10 and cSrc kinase and control PKC and CKI kinases. (C) In vitro kinase assay with cSrc kinase of Wild type RBM10 of various tyrosine mutants of RBM10 (1P - Y81F, 2P – Y81F and Y500F, and 3P - Y81F, Y500F and Y971F). (D) Western Blot analysis of RBM10 target HAND2 protein after mutation of cSrc sites on the RBM10 in the cell. (E) 3′-RACE assay of RBM10 target mRNA ERBB3 and control GAPDH under similar condition as in D. (F) Assay of alternative splicing (exon skipping) of RBM10 target gene FAS under similar conditions as in D. (G) Immunofluorescence analysis of RBM10 localization in the cell in the presence and absence of Y500F mutation. (H) FACS analysis of H9C2 cells after isoproterenol treatment in the presence and absence of ectopically expressed Wild type and Y500F phosphor-mutant RBM10.

PROTEO-TRANSCRIPTOMICS ANALYSIS IDENTIFIES SUMO2 AS A PROMISING TARGET IN GLIOBLASTOMA MULTIFORME THERAPEUTICS

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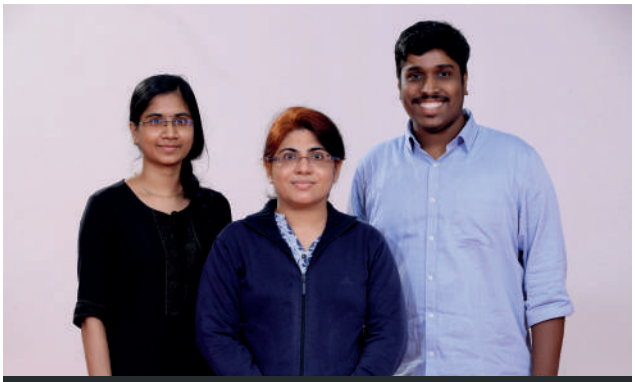
Ph.D: NBRC, Manesar
Post-Doc: Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany, Curie Institute, Paris, France

Proteo-Transcriptomics analysis identifies SUMO2 as a promising target in glioblastoma multiforme therapeutics

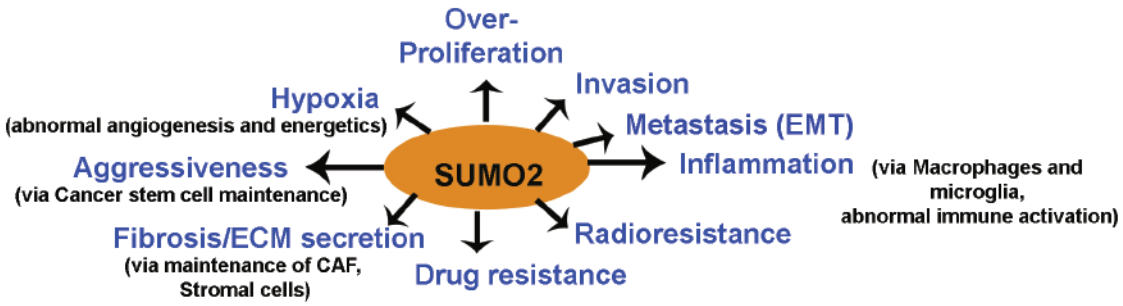
Glioblastoma multiforme (GBM) is a deadly brain tumor with minimal survival rates due to ever expanding heterogeneity, chemo and radioresistance. Kinases are known to crucially drive GBM pathology, however a rationale therapeutic combination that can simultaneously inhibit multiple kinases has not yet emerged successfully. Here, we analyzed the GBM patient data and deduced hub GBM kinases, most of which were identified to be targets of SUMO2/3 isoforms. Intriguingly, a significant proportion of upregulated genes in GBM involved in proliferation, metastasis, invasion, epithelial mesenchymal transition, stemness, DNA repair, stromal and macrophages maintenance were also identified to be the targets of SUMO2/3 isoforms.



From Left: Gayathri K G, Sebastian John

However, high expression of SUMO2 alone was found to be significantly associated with poor patient survival. SUMO2 was found to enable unique nuclear pro-proliferative functions of many tumor associated kinases. Although, many natural products and drugs are evidenced to inhibit general SUMOylation, our data strongly calls for the need to design SUMO2/3 or even better SUMO2 specific inhibitors for universally potential, physiologically non-toxic anti-GBM drug therapy. The extended patient data analysis showed that this anti-tumor strategy is well applicable to lung, breast and colon cancers as well.

SUMO2 is a master regulator of glioblastoma multiforme(GBM) pathology and a promising anti-GBM drug target



The schematic representation sums up the findings in this study which suggest that SUMO2 isoform by itself may be a key player in GBM development and progression, via exercising its control on the genes involved in the hallmarks of cancer. Hence, SUMO2 is a promising target for anti-GBM therapeutics in all GBM subtypes.

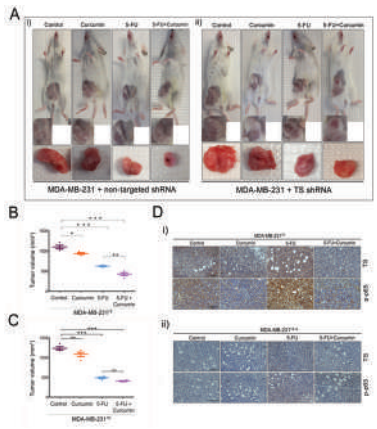
EVALUATION OF NATURAL PRODUCTS AS CHEMOTHERAPEUTICS, CHEMOPREVENTIVES AND CHEMOSENSITIZERS

RUBY JOHN ANTO, Ph.D, FNASc
Scientist G, Cancer Research Program
Ph.D: Amala Cancer Research Centre, Thrissur
Post-Doc: RGCB, Thiruvananthapuram,
UT M.D. Anderson Cancer Center, Houston, TX, USA

Recently, we proved, with molecular evidence that tryptanthrin, a compound we isolated in the lab is an effective suppressor of non-melanoma skin cancer (NMSC) using DMBA/PMA-induced skin carcinogenesis model in Swiss albino mice. In mice, topical application of tryptanthrin suppressed skin carcinogenesis, attenuated inflammation, impeded the proliferation of hair follicle (HF) cells and sup-pressed the activation of β-catenin, a major driver of HF cell proliferation. Additionally tryptanthrin suppressed the activation of ERK1/2 and p38, both of which promote β-catenin activation and lowered the expression of c-Myc and cyclin-D1. Tryptanthrin suppressed the proliferation of the human NMSC cell line, A431 and abrogated EGF-induced activation of β-catenin and subsequent cytoskeletal rearrangement (Shankar et al, 2020)

Back Row From Left: Swetha M, Shabna A, Rayginia P Tennyson
Front Row From Left: Aiswarya U S, Keerthana C K, Devika M Kumar, Jannet S

In another study, we demonstrated, utilizing two independent murine breast cancer models, the ability of curcumin in chemosensitizing BC to 5-Fluorouracil (5-FU) chemotherapy, independent of their receptor status. Furthermore, we authenticated the pivotal role of thymidylate synthase (TS) in regulating the 5-FU–curcumin synergism using the TNBC pre-clinical model. Our study also confirmed the pharmacological safety of this chemotherapeutic plus phytoactive combination using acute and chronic toxicity studies in Swiss albino mice. Subsequently, the molecular docking analysis of curcumin binding to TS demonstrated the affinity of curcumin towards the cofactor-binding site of TS, rather than the substrate-binding site, where 5-FU binds. Our in vivo and in silico evidence substantiate the superior therapeutic index of this combination. This is the first-ever pre-clinical study portraying TS as the critical target of a combinatorial regimen for mammary carcinomas (Haritha et al, 2021).



The role of TS in regulating the synergism of 5-FU and curcumin.
[A (i, ii)] Representative images of animals from each experimental group, bearing tumor produced by orthotopic injection of both sets of transduced cells and tumors excised showed a reduction in tumor size upon completion of treatment. (B, C). Graphs showing a comparison of tumor volume of MDA-MB-231TS and MDA-MB-231TS- xenografts, respectively upon completion of treatment. Significant reduction in tumor volume is observed in animals bearing MDA-MB-231TS xenografts, upon treatment with combination while no significant reduction in tumor volume is observed in animals bearing MDA-MB-231TS- xenografts. Data represent two independent sets of experiments and results are shown as the mean 3 S.D. P-values were calculated with one-way ANOVA. ***P-values ≤0.001, **P-values ≤0.01 and *P-values ≤0.05; ns represents non-significance. [D (i, ii)] Immunohistochemical analysis of expression status of TS and p65 sub-unit of NF-κB in different treatment groups of MDA-MB-231TS and MDA-MB-231TS- xenografts, respectively.

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ELUCIDATION OF DETERMINANTS PERTAINING TO ANTIBIOTIC RESISTANCE AND BIOFILM FORMATION IN PATHOGENS BY GENOME ANALYSIS

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Antimicrobial resistance and biofilm formation are two major hindrances in the treatment of bacterial infections and identification of determinants is need of the time to come up with suitable solutions. Cholera, caused by the Gram-negative bacterium Vibrio cholerae, remains a serious threat in underdeveloped countries. Although rehydration therapy has been the mainstay of disease management, antibiotics are also being used as an adjunct treatment, resulting in an increase in the circulation of antimicrobial-resistant strains. In the present study, adaptive laboratory evolution, whole-genome sequencing and molecular docking studies were performed to identify putative mutations related to doxycycline resistance in V. cholerae on constant exposure to the antibiotic. Of the various single nucleotide polymorphisms (SNPs) identified by comparative SNP identification of the sensitive and evolved V. cholerae strains, V57L mutation in the RpsJ protein was identified to be important in conferring doxycycline resistance. As revealed by molecular docking studies, the mutation was identified to alter the ribosome structure near the doxycycline binding site (Fig 1). Doxycycline stress also induced co-resistance to colistin, a last-resort antibiotic to treat extensively drug-resistant bacteria (Narendrakumar et al., 2020). The study illustrates for the first time a possible mechanism of doxycycline-selected resistance in V. cholerae as well as its co-resistance, warranting strict restrictions on the indiscriminate use of antibiotics.

From Left: Akhila V S, Karthika S, Sudha B Nair, Aparna Shankar, Merin Paul

Enterococcus faecalis is an emerging nosocomial pathogen, owing to its robust biofilm forming ability and the inherent antimicrobial resistance. Genome sequencing and analysis of a biofilm forming E. faecalis strain SK460 which is devoid of fsr two component system, a well-known factor influencing biofilm formation, revealed a set of virulence and surface adhesion factors associated with pathogenicity and biofilm formation. Comparative genome analysis among pathogenic biofilm forming E.faecalis strains and nonpathogenic non-biofilm forming strains identified a set of accessory genes encoding polysaccharide lyase, sugar phosphotransferase system, transporter proteins, certain phage associated proteins and transcriptional regulators exclusively present in pathogenic biofilm formers (Suryaletha et al., 2021). These identified genes can act as targets, which in turn help to develop future treatment strategies against enterococcal biofilm infections.

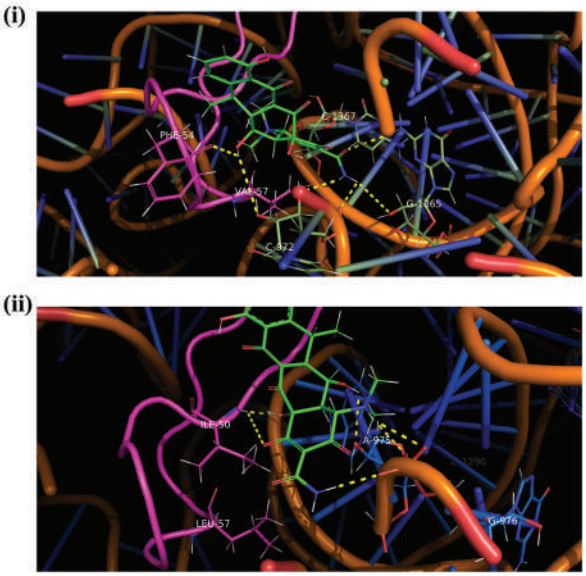

Figure. 1: Docking conformation of doxycycline with (i) RpsJ(V57, wild type) and (ii) RpsJ(L57, mutant). Residues interacting with ligand are represented with lines.

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SYNERGISTIC EFFECT OF FROG SKIN ANTIMICROBIAL PEPTIDES IN COMBINATION WITH ANTIBIOTICS AGAINST MULTI-HOST PATHOGENS

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Ph.D: Mahatma Gandhi University, Kottayam

Cationic Host Defence Peptides are considered natural alternatives to chemical antibiotics. The synergistic effect of AMPs with common antibiotics is a promising area. Although combination therapy with various antibiotics is a standard treatment for drug resistance infections, using AMPs and antibiotics in combination is often under investigation, despite the promising effects. The present study examines the synergistic action of parent peptides and their modified analogs (Fig. 1) with the conventional antibiotics, their killing kinetics, hemolytic potential, serum stability, the effect of pH and cations on the activity against G- and G+ bacteria, and possible mode of membrane interaction of the peptides.

The parent peptides were active against V. vulnificus, but their modified analogs did not improve the activity. In P. aeruginosa, the parent peptides showed weak activity, but their modified analogs showed increased activity. The activity of both the peptides against V. vulnificus depends on Rana Box as its elimination resulted in decreased activity but no change in the activity in P. aeruginosa. A synergistic interaction was observed when combining the peptides with traditional antibiotics resulted in an overall increase in the activity in low doses of both peptides and antibiotics. As a result, the percentage of hemolysis and the time needed for the bacterial killing were reduced notably with retained activity in different cation, pH, and serum concentrations.
The effect of enhancing charge, hydrophobicity, and removal of 'Rana Box' on brevinin-2 peptide is evaluated against G- and G+ pathogens. These modifications result in increased activity against both bacteria than their parent peptides. The results indicate the redundant role of Rana box in brevinin two peptides. This study also showed that a peptide-antibiotic combination effectively produces synergy or additivity which remarkably reduced the time needed for bacterial killing and was stable in varying cation, pH, and serum concentrations.

From Left: Akhilnath P G, Anoop V S

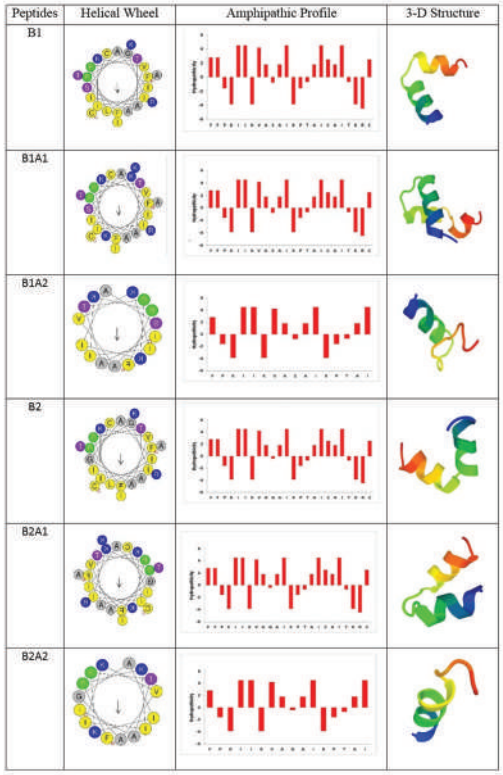

Fig.1: Helical wheel, Amphipathic profile, and 3-D structure of peptides- Column 2 shows the peptide's helical wheel projection. Yellow represents hydrophobic residues; green represents basic residues & blue represents hydrophilic residues. Arrow indicates the direction of a hydrophobic moment. Column 3 represents the amphipathic profile calculated using Expasy. The positive axis shows hydrophobicity, and the negative axis shows hydrophilicity. Column 4 demonstrates the 3D structure of peptides, analyzed by PEPFOLD.

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ANTIBIOTICS RESISTANCE PROFILE OF HELICOBACTER PYLORI AND GUT RESISTOME ANALYSIS IN THIRUVANANTHAPURAM POPULATION

SANTANU CHATTOPADHYAY, Ph.D

GN Ramachandran Fellow, Pathogen Biology Program
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Post-Doc: Lerner Research Institute, Cleveland Clinic, OH, USA,
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Cold Spring Harbor Laboratory, New York, NY, USA,
Albert Einstein College of Medicine, New York, NY, USA

Helicobacter pylori is a gastric pathogen causing gastritis, peptic ulcer and gastric cancer, which result in over a million annual deaths globally. Treatment for all H. pylori infected people are recommended, but the antibiotic sensitivity profile of H. pylori and its mechanism has not been reported from Kerala. In this study, we tested the antibiotic resistance pattern of 42 H. pylori strains isolated from Thiruvananthapuram against metronidazole, clarithromycin, amoxicillin, tetracycline and furazolidone.

We also studied the genetic basis of resistance and intestinal resistome in H. pylori +ve and –ve individuals. The antibiotics resistance profile of the H. pylori strains is shown in Figure 1A. Overall, we observed 26 metronidazole resistant strains, 2 clarithromycin resistant strains, 18 amoxicillin resistant strains, 23 tetracycline resistant strains and 15 furazolidone resistant strains. 40.4% of the strains were resistant to more than two antibiotics (Figure 1B). In strain TMC269, the deletion of a single nucleotide at the 1836th position of pbp1 gene alters the reading frame resulting in truncated protein and amoxicillin resistance (Figure 1C). The intestinal resistome was derived from the stool whole genome metagenome data of 8 H. pylori +ve and 8 H. pylori –ve individuals. We found that the resistance determinants against macrolides [ermT, mef(A)], tetracycline [tetL and tetW], beta-lactams [cfxA3, cfxA6] and streptomycin [aadS] were dominant in Thiruvananthapuram population (Figure 1D). The resistance

Retnakumar R J

determinants to macrolides, tetracycline and β-lactam were in higher proportion for the H. pylori-positive individuals as compared to the H. pylori-negative individuals (Figure 1E). Macrolide resistance was seen almost exclusively in H. pylori-positive individuals (Figure 1E). Our study revealed that that clarithromycin resistance among H. pylori strains is very low in Thiruvananthapuram. Conversely, high prevalence of macrolide resistance genes in the gut resistome of the H. pylori infected individuals is a matter of concern for the antibiotic therapy.

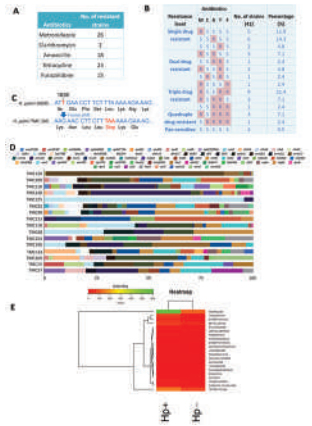

Figure 1. (A) Frequency of antibiotics resistance among H. pylori strains isolated from Thiruvananthapuram. (B) Single, dual, triple and quadruple antibiotics resistance patterns of H. pylori strains isolated from Thiruvananthapuram. (C) Deletion of thymine at 1836th position of pbp1 gene in H. pylori TMC269 leads to introduction of stop codon prior to the actual termination site. The frame shift mutation resulted in a truncated protein. (D) Relative distribution of various antimicrobial resistance genes in the intestinal microbiota of patients from Thiruvananthapuram. (E) Heat map showing the distribution of genetic determinants of antimicrobial resistance among H. pylori +ve and –ve individuals, derived from intestinal resistome analysis using ABricate tool. The relative distribution of resistance determinants to macrolide, tetracycline, vancomycin and beta-lactam, differ considerably between H. pylori +ve and –ve individuals.

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HYPOXIA INDUCED MITOCHONDRIAL REDOX HETEROGENEITY CONTRIBUTES TO DYNAMIC CHANGES IN CANCER STEM CELL LIKE POPULATION WITH RESISTANCE AND INVASINESS

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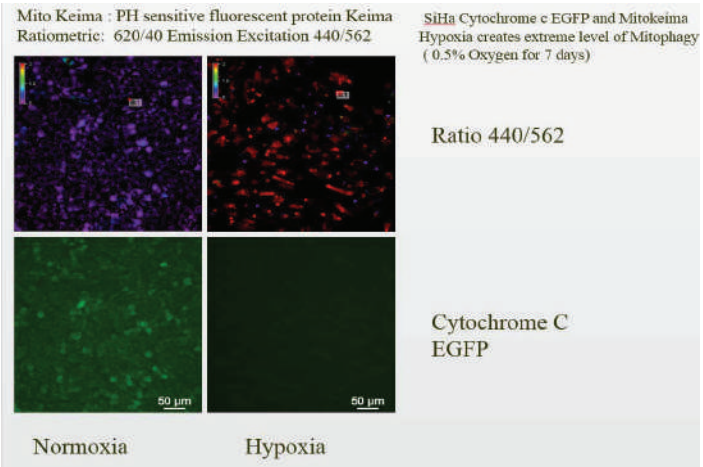
Ph.D: SCTIMST, Thiruvananthapuram

Hypoxia induced Mitochondrial redox heterogeneity contributes to dynamic changes in cancer stem cell like population with resistance and invasiness

Identification and characterization of rare tumor initiating cancer stem cells offers a unique opportunity to target them for effective cancer therapy. Cancer cells especially cancer stem cells are highly dynamic and are able to interconvert to multiple states that govern tumorigenesis process. We have addressed the impact of hypoxia and other forms of physiologic stress, on the dynamics of cancer stem cells and its functional implications in drug resistance and invasion. Cancer cells expressing genetically encoded real-time probes of cell death, cell cycle and redox status were generated in diverse cancer cell lines and exposed them to both chemical and physiological hypoxia to understand the long-time fate and cancer stem cell functional dynamics. The results revealed an unusual modulation of mitochondrial redox during hypoxia that generates distinct cell population with differing cellular and mitochondrial ROS. The acquired mitochondrial redox heterogeneity favors expansion and longtime maintenance of cells with cancer stem cell functional properties such as low reactive oxygen species (ROS) level, increased invasion and resistance.

Back Row From Left: Aparna G J, Aneesh C, Shianshu Kumar Tiwari
Front Row From Left: Aswathy S, Jain Tiffe P J, Pramod Darvin

Both short-term and long term hypoxia altered the equilibrium of stem cell and non-stem cell compartment in established cancer cell lines. Functional analysis of populations with low mitochondrial ROS as well as high mitochondrial ROS reveals secondary acquisition of distinct levels of resistance and invasion during Hypoxia-oxygenation process. In addition the study further revealed the critical role of PARKIN in the regulation of cell survival during hypoxia. Cell expressing mitophagy sensor Mitokeima and cytochrome c EGFP confirmed that hypoxia generated mitophagy cells evolve with slow mitochondrial biogenesis during re-oxygenation creating complex functional heterogeneity. The importance of this complex functional heterogeneity in metastasis and drug resistance is under evaluation.



Cervical Cancer cells stably expressing mitophagy sensor Mitokeima and Cell death Sensor Cytochrome c EGFP under normoxia and Hopoxia

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UNDERSTANDING MEASLES VACCINE FAILURE (AND SUCCESS) IN SOUTHERN INDIA

SARA JONES, Ph.D
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Ph.D: Dr. Babasaheb Ambedkar Marathwada University, Aurangabad
Post-Doc: Emory University, Atlanta, GA, USA

Measles is a global public health problem and a leading cause of childhood mortality. Although there are active immunization programs against the measles virus, India still accounts as a significant contributor to the total burden of the measles virus worldwide. Our investigation among southern Indian children demonstrated that children under the recommended vaccination age of nine months are highly susceptible to measles. More importantly, the waning of measles-specific antibodies occurs with time in those vaccinated with a single dose of vaccine. We also observed rare cases of measles in those who have had multiple doses of vaccine. We screened for measles-specific IgG antibodies to understand the seroconversion rate in children who had received two doses of measles vaccine. IgG titers in the children ranged between 3.5 to 58.2 NTU. 90.5% were seropositive, 5.1% were equivocal, and 4.4% were seronegative. IgG titers in the mothers ranged from 1.9 to 49.3 NTU. 94.9% of the subjects were seropositive, 0.6% were equivocal, and 4.4% were seronegative. These data suggest that the majority of the mothers have existing immunity to measles, despite the lack of vaccination records. The higher titers in the mothers compared to the children may reflect immune boosting due to measles exposure. We also observed an epidemiological shift of measles infections to the older population presenting a new public health challenge because of the increased severity of the disease, especially in vulnerable people and immunocompromised patients. In-depth investigations into the immune profile of these individuals will provide us a unique opportunity to understand the basis of measles vaccine failure strengthening our efforts to eradicate the measles virus.

From Left: Remya V S, Remya Raveendran, Vishnu V M

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CHARACTERIZATION OF A MADS BOX TRANSCRIPTION FACTOR IN MICROALGAE COCCOMYXA SUBELLIPSOIDEA C-169

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Ph.D: University of Delhi, New Delhi

The functions of MADS-box transcription factors have not been explored in unicellular green microalgae. A MADS-box transcription factor from Coccomyxa subellipsoidea C-169, a unicellular green micro-alga, strongly expressed in the lag phase of growth. This MADS-box transcription factor (CsubMADS1), unlike Type II MADS-box proteins of streptophytes which have MADS, Intervening, K-box and C domains, only has a MADS and Intervening domain. CsubMADS1 forms part of a sub-clade that groups with the Type II MIKCC proteins. CsubMADS1 needs to form homodimers to precisely localize to the nucleus. The monomer form has non-specific localization in the cell.

CsubMADS1 consists of two nuclear localization signals: one in the N terminal end and another in the overlapping region between the DNA binding and dimerization interface. CsubMADS1 overexpression led to slow growth of the algal culture. The overexpressors contained large polyploid multinucleate cells looking like autospore mother cells (Figure 1A). This suggests that the release of autospores may be delayed. Thus, CsubMADS1 is probably playing a role in slowing down growth during the lag phase. The role of starvation was studied in two-month-old colonies in solid media. The wild type colonies produced substantial amounts of mucilage in response to the starvation stress, whereas the overexpressors produced significantly less mucilage (Figure 1A). These results show that CsubMADS1 is negatively regulating this process. Thus, CsubMADS1 probably has a prominent role in governing stress tolerance during the lag phase. Hence CsubMADS1 has a significant role in regulating development and stress tolerance in this unicellular green micro-alga (Figure 1B).

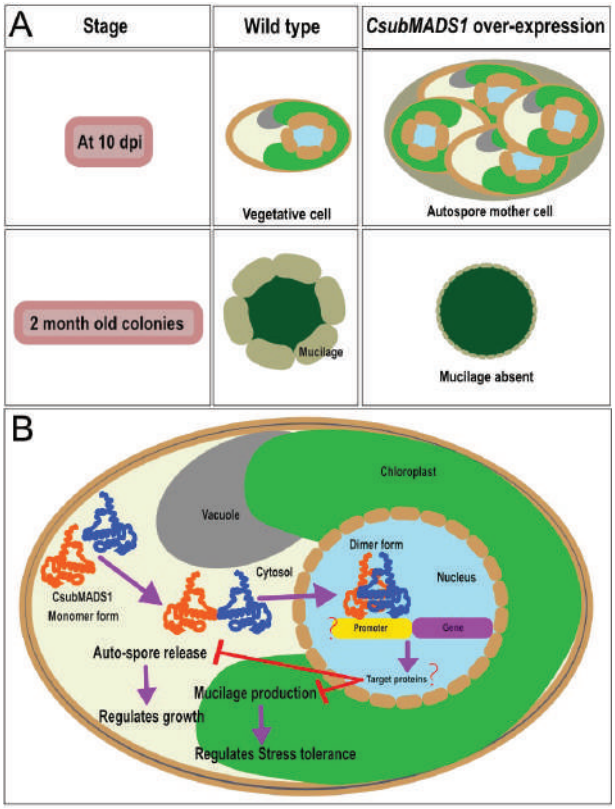

Figure. 1: Graphical representation of the regulation of growth and stress tolerance in Coccomyxa subellipsoidea C-169 by CsubMADS1. (A) Summary of CsubMADS1 OX phenotype. (B) Hypothetical model for regulation of Coccomyxa subellipsoidea C-169 development by CsubMADS1.

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COMPARATIVE PERFORMANCE OF CDC MODIFIED COVID-19 REAL-TIME PCR ASSAY WITH FOUR COMMERCIAL ASSAYS AND ITS EVALUATION USING CLINICAL SPECIMENS IN KERALA, SOUTH INDIA

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Post-Doc: Apollo Hospitals Educational and Research Foundation, Hyderabad, Howard University, Malawi, South East Africa

Comparative Performance of CDC modified COVID-19 Real-Time PCR assay with four commercial assays and its evaluation using clinical specimens in Kerala, South India

The COVID-19 pandemic has emerged as a global public health crisis and the surge of ongoing second-wave cases in India. Manage to reduce its spread the need for fast and reliable diagnostic assays for the detection of SARS-CoV-2 is a demand of the hour. The objectives of the study were to develop CDC modified qualitative real-time reverse transcriptase PCR (RT-PCR) assay and compare with other commercially available RT PCR assay (Altona, Seegene,BD and GBC) to detect to detect Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). RT-PCR will remain the gold standard for all viral infections. We used serial dilutions of viral RNA to establish PCR efficiency. Furthermore, out of 1,70,942 patients' we have selected randomly and ran a panel of SARS-CoV-2-positive clinical samples (n = 156) negative clinical samples (n = 52) for a primary clinical evaluation. Two hundred and nine patient's samples data of the Ct readings for target genes of five assays 100% sensitive for Ct values. Mean Ct values for N1, N2, RdRp, S and E of the positive controls in CDC assay, RealStar®, Allplex, GBC, and SD Biosensor were 17.5 30.49, 16.930.51, 203 0.49, 21.730.38, and 23.130.43, respectively. All assays showed an efficiency<120 % and R squares were<0.99, which are both well above the pre-defined required level (Figure 1). Thus, when taking the CDC modified assay as a gold standard, the other four assays demonstrated a Concordance at 100% and a Kappa at 1. 000.We conclude that all RT-PCR kits assessed in this study may be used for routine diagnostics of COVID-19 in patients by experienced molecular diagnostic laboratories.

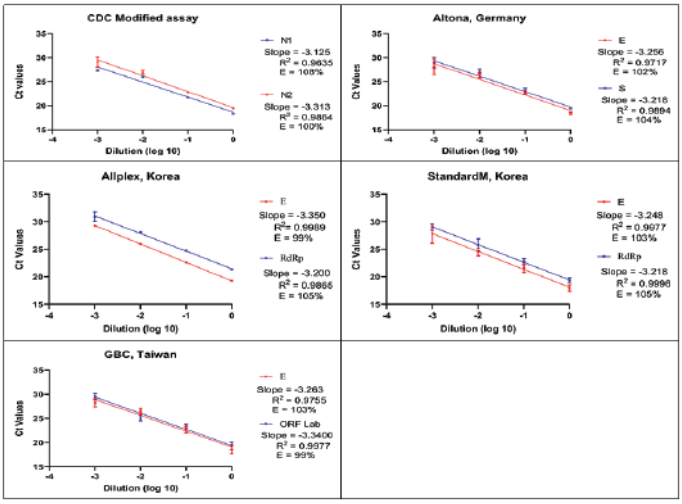

Figure 1 PCR efficiency for five RT-PCR kits for the detection of SARS-CoV-2 RNA. PCR efficiency (E) for each target gene was assessed using four replicates with dilution series of SARS-CoV-2 viral RNA.

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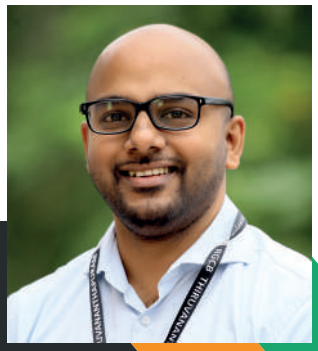


THE STRUCTURE AND EVOLUTION OF ENVIRONMENTAL RESISTOMES

SHIJULAL NELSON-SATHI, Ph.D

Scientist C, Transdisciplinary Biology Program

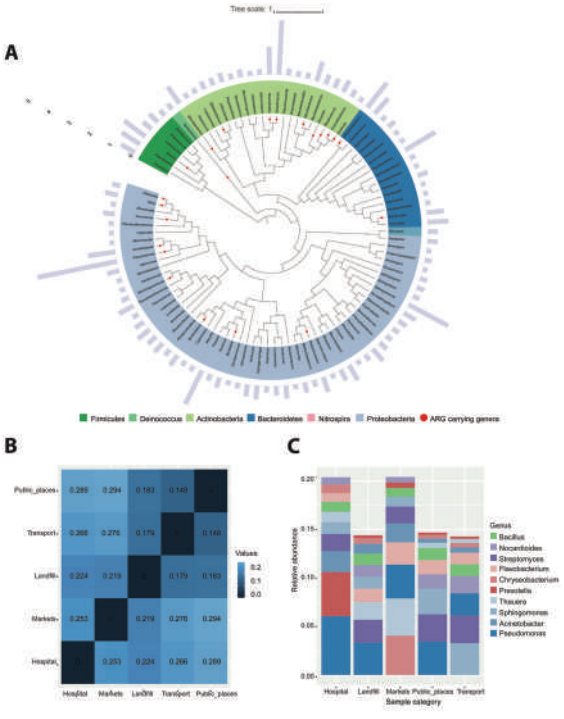
Ph.D: Heinrich Heine University (HHU), NRW, Germany
Post-Doc: Heinrich Heine University , NRW, Germany,
Christian-Albrechts-University of Kiel, Kiel, Germany

Impact of antimicrobial-resistant microbes in the environment influencing the flow of resistant genes within pathogenic bacteria is largely remains unknown. By using high throughput sequencing technologies and evolutionary bioinformatics approaches, our laboratory study focuses on understanding the origin, adaptation, transmission and evolution of antibiotic resistance genes within pathogenic bacteria and develop strategies to slow down its further spread.

Front Row From Left: Greeshma S Nair, Vinitha P V, Jiffy John, Pratik Kumar Behera
Back Row From Left: Anand Mohan, Malootty S, Jamiema Sara Philip

The Structure and Evolution of Environmental Resistomes

We studied the resistome of different polluted settings of an urban system. Using a combination of culture based and metagenomics approaches, we have identified more than 10,000 bacterial species and confirmed higher abundance of faecal contamination indicators such as Escherichia coli and Enterococcus in the urban settings. The resistome of urban settings contains a total of 454 antibiotic resistance genes that belongs to almost 11 major drug classes. We found a higher prevalence and a more diverse repertory of antibiotic-resistant genes in hospital, landfills and markets whereas the ARGs in public places and transport systems are ubiquitous. Further, the functional metagenomic study revealed almost 38 ARGs responsible for multidrug (Ampicillin and Tetracycline) resistance in environmental bacteria encoding plasmids and other mobile genetic elements that are having 100% identity to genes from diverse human pathogens. Many of these genes come from pathogenic bacteria such as Acinetobacter johnsonii, Shigella sonnei, Shigella boydii, Klebsiella pneumoniae etc. Our study helps in long term infectious disease surveillance, bioterrorism threat action planning and health care management of fast growing urban structures of Kerala.



Bacterial diversity profile of urban ecosystem. (A) Circular plot showing the taxonomic distribution of top 100 genera present in the urban settings. The genera are sorted based on the 16S reference phylogeny and the red dot on the branches indicates the genera having ARGs. The bars on the outermost circle show the relative abundance of each genus in the urban settings. (B) Heat map showing the beta diversities (dissimilarity between urban categories) calculated from relative abundance profiles of bacterial communities. (C) Stack plot showing the relative abundance of top 10 genera present in different categories of urban ecosystem.

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ELUCIDATION OF MOLECULAR MECHANISM OF STRESS REGULATION IN BLACK PEPPER DURING BIOTIC STRESS RESPONSES

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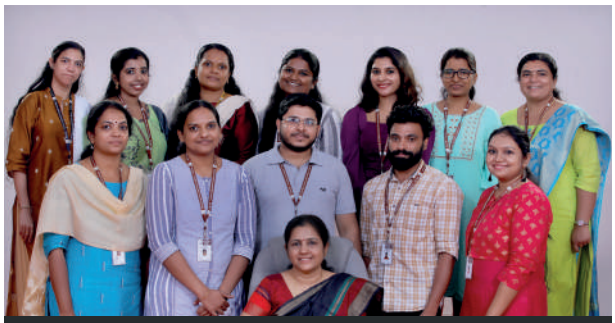
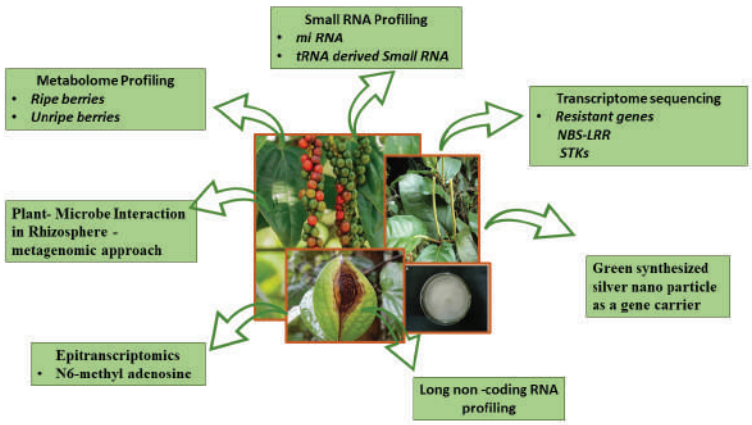
Ph.D: University of Kerala, Thiruvananthapuram

Black pepper is one of the most valued and widely used spices in the world. Quick wilt disease in black pepper (Piper nigrum L.) is caused by Phytophthora capsici against which no resistant varieties have been characterised. Non-coding RNAs are found to be important regulators of protein coding genes involved in developmental processes and various stress responses in plants. A high-throughput systematic analysis of the small RNAome revealed the predominance of 5 tRFs in the infected leaf and root. Our findings uncovered the diversity, differential expression and stress responsive functional role of tRNA-derived small RNAs during Phytophthora infection in black pepper. The preliminary cloning and sequencing of the sRNA enriched library, from Phytophthora infected black pepper plants, revealed three tRNA-derived small RNAs such as 5 ArgTCGtRNA, 5 AlaAGCtRNA, and and3 GlyTCCtRNA. Furthur we have done analysis of components related to the tRNA transcription during stress response and identified the role of tRNA modification during stress response. We also identified microRNAs belonging to conserved miRNA families and 4 novel candidate miRNAs from the sRNAome data. Using a combined experimental–in silico approach we characterized two conserved miRNAs, miR166 and miR171, from black pepper. We studied the role of miRNAs, transcription factors and genes involved in the bioactive compound formation in black pepper berries using integrated omics approach. This is expected to be of great significance for accumulating these compounds through metabolic engineering methods.



Back Row From Left: Kalapriya V S, Pooja Viswam, Preetha Chandran P, Aswathi U, Sruthi Bharathan, Kattupalli Divya, Sinsha Prakasahan
Front Row From Left: Lekshmi R S, Asha S, Akash P, Santhoshkumar R, Sora S

Integration with transcriptome, miRNA and degradome profiles uncovered critical genes, transcription factors and miRNAs whose expression and functional validation was carried out.Long noncoding RNA sequencing of P.capsici infected Piper nigrum identified large number of novel lncRNAs. Differential expression and target prediction analysis revealed regulatory roles of lncRNAs in plant defense. Further we conducted me-RIP sequencing which identified N6-methyl adenosine (m6A) mediated epitranscriptomic regulation in biotic stress responses of black pepper. Preliminary data support the dynamics of m6A post infection with Phytophthora capsici, causative agent of quick wilt of black pepper. Work is also progressing using green synthesized nanoparticle for controling this Oomycete.



Overview of ongoing research on Black pepper in our lab

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27-HYDROXYCHOLESTEROL, THE ENDOGENOUS SERM, INDUCES THE DNA METHYLATION CHANGES

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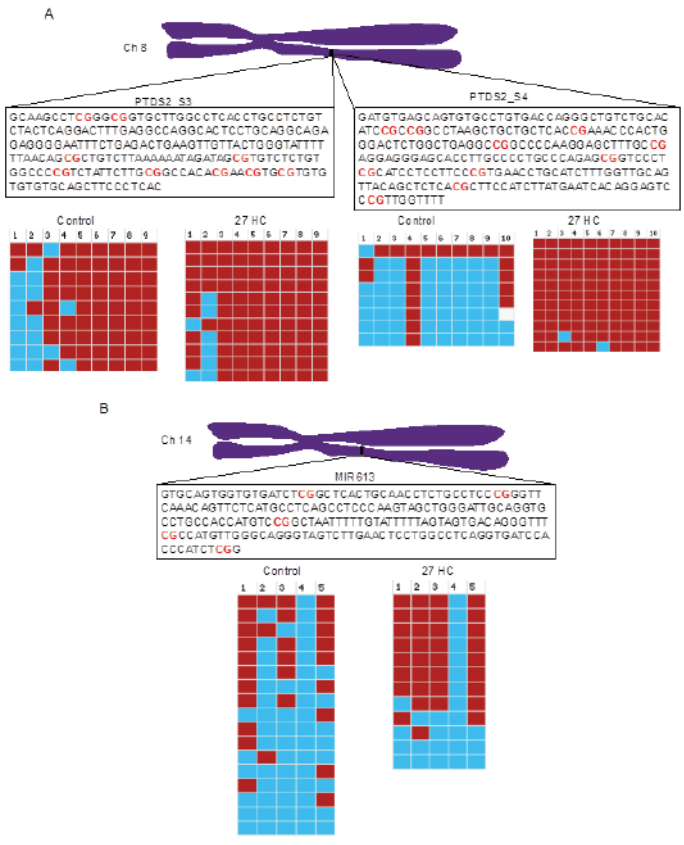
Ph.D: University of Kerala, Thiruvananthapuram

27-hydroxycholesterol (27-HC) is the first known endogenous selective estrogen receptor modulator and its elevation from normal level is strongly associated with the many chronic diseases including breast cancer. A plethora of evidences suggests aberrant epigenetic signatures in the breast cancer cells can result in differential responses to the chemotherapeutics and development of resistant cancer cells. The microenvironment strongly dictates the development and outcome of breast cancer cells and it is proposed that aberrant epigenetic landscape in the breast cancer cells are due to the microenvironment conditions. The local concentration of oxygen and the metabolites in the microenvironment of breast cancer are known to influence the development of breast cancer. The metabolites in the category of oxysterols such as 27-HC, an endogenous SERM, has been shown to induce breast cancer progression.

Back Row From Left: Susmi T R, Savitha R K, Ayswarya R S, Sajitha T
Front Row From Left: Viji Remadevi, Vini Ravindran, Anjana S S

There are ample evidences showing aberrant DNA methylome signatures in breast cancer cells but it is unknown whether 27-HC mediates the epigenetic alteration in breast cancer cells. For addressing the same, we treated the Estrogen Receptor positive cells with 27 HC and identified DNA hypermethylation on a subset of genes by performing bisulfite sequencing. The genes which showed significant DNA hypermethylation were phosphatidylserine synthase (PTDSS2), MIR613, indoleamine 2,3-Dioxygenase 1(IDO1), thyroid hormone receptor alpha (THRA), Dystrotelin (DTYN), Mesoderm induction early response 1, family member 3 (MIER). Among these, BISMA analysis after Sanger sequencing showed significant hypermethylation majorly in two genes, PTDSS2 and MIR613. PTDSS2 is involved in the synthesis of phosphatidylserine from phosphatidylethanolamine (PE) while miR-613 is generally identified as a tumor suppressor in multiple cancers. 27-HC mediated hypermethylation at PTDSS2 lead to transcriptional down regulation, whereas hypermethylation at the promoter of MIR613 leads to biogenesis of miR-613. The DNA hypermethylation might help in cancer progression in addition to altering immune responses and increasing proliferation via ERα and metastasis via LXR receptor.



Validation of promoter DNA methylation by bisulfite sequencing:
(A)Schematic representation of PTDSS2 promoter region. (B)The bisulfite sequencing analysis for MIR613. The red box indicates methylated CpGs and blue box indicates the unmethylated CpGs. Each row represents individual clone and the number at the top denotes the CpG sites of the corresponding amplicons.

EXPANDING HOST-DIRECTED ANTIVIRAL APPROACHES AGAINST EMERGING RNA VIRUSES

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Ph.D: University of Kerala, Thiruvananthapuram
Post-Doc: Johns Hopkins Bloomberg School of Public Health, Baltimore, MA, USA

Our laboratory continued studies on chikungunya virus (CHIKV) and dengue virus (DENV) during the year. We also initiated a new research program on Severe Acute respiratory Syndrome Corona Virus -2 (SARS CoV-2). The major focus of our studies is on developing a host-directed antivirals (HDA), an emerging paradigm in antiviral therapy. Our targets of interest are those proteins that exerts a potential antiviral effect by modulating specific pathways selectively used by these viruses. We had previously identified a host protein Nucleophosmin (NPM1/B23) that is differentially expressed in chikungunya virus infected cells and exerts antiviral effect. In continuation, our recent studies defined both the viral and cellular partners interacting with NPM1, and studies are in progress to decipher how these interactions exert the antiviral function against CHIKV.

Back Row From Left: Srishti Rajkumar Mishra, Parvanendhu Pradeep, Ariya Ajay, Seethalakshmi S
Front Row From Left: Ayan Modak, Guhan K S, Sreeja S

In another approach, we explored the possibility of targeting cap-dependent translation as an antiviral strategy. We identified that inhibitors targeting of p38 MAPK pathway leads to reduction in CHIKV infection; and as in the uninfected cells, the other supporting pathways of cap-dependent translation such as the Akt-mTOR and RAF-MEK-ERK pathways remains functional, it is possible that the effect of p38 MAPK inhibitors selectively affects the infected cells (Fig.1; J.Gen.Virol.; Manuscript in Press). Another group of molecules of our interest is Interferon-stimulated genes (ISG). Many of them have been reported to function as antiviral effectors. We have initiated studies on these molecules such as DDX60, USP80, MNDA and IFITMs in CHIKV infection and in pseudovirion- based models of SARS CoV-2 infection. Along with these studies, we also work on molecules that can be used as disease modifiers, while they lack the antiviral activity. In this aspect, we focus on endothelial kinase inhibitors that can alleviate enhanced endothelial cell permeability, a major cause of vascular shock and mortality caused by dengue virus (Fig.2).

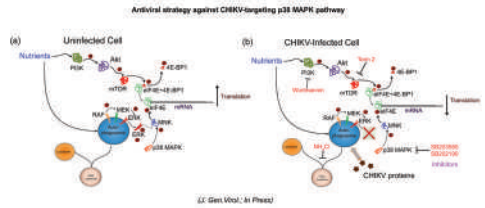

Fig.1 Pathways affected by CHIKV infection (a) Extracellular nutrients in normal, uninfected cells activate PI3K-Akt-mTOR pathway and the two arms of the MAPK pathway (the p38 MAPK and the RAS-RAF-MEK-ERK pathways) leading to eIF4E phosphorylation and translational activation. (b) In infected cells, replication of CHIKV induces autophagy which causes selective degradation of phospho-ERK and inactivate RAS-RAF-MEK-ERK pathway. This makes virus infected cells selectively sensitive to p38 MAPK inhibitors resulting in decreased translation of capped cellular and viral RNA (J.Gen.Virol.; In press)

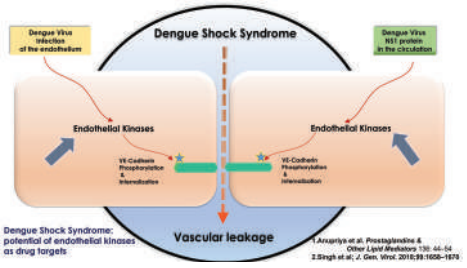

Fig.2 Direct dengue virus infection of endothelial cells or the effect of soluble plasma factors such as viral NS1 protein can activate intra-endothelial cell pathways that lead to VE-cadherin phosphorylation. VE-Cadherin, that maintains adherens junctions and thus barrier integrity, is internalized once it get phosphorylated. This causes barrier disruption, increased permeability and vascular leakage. Identifying and targeting the specific endothelial cell kinases that are activated during this process and pharmacologically targeting them offer a potential therapeutic approach to alleviate dengue shock syndrome.

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ALTERED HEMODYNAMIC SHEAR STRESS INDUCED ENDOTHELIAL TO MESENCHYMAL TRANSITION IN CHRONIC VENOUS DISORDERS

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Post-Doc: RGCB, Thiruvananthapuram

Despite the global prevalence of chronic venous diseases and associated complications, molecular mechanisms underlying the pathogenesis of this disease remains uncertain. It is believed that hemodynamic factors play a major role in the disease progression along with genetic and inflammatory factors. In the vasculature, endothelium in the tunica intima controls various biomechanical signals to maintain selective permeability and vascular tone. Even though altered shear stress (ASS) induced mechanotransduction is being investigated in arterial endothelium, no reports are available about the hemodynamic signalling in the vein vasculature. Mechanosensing studies in arterial vasculature indicates that a low flow and ASS alters endothelial cell (EC) phenotype by processes such as endothelial-to-mesenchymal transition (EndMT), wherein, ECs lose their endothelial specific features and morphology and acquire mesenchymal characteristics. Venous system operates on very low shear stress system. We speculate that altered shear stress rather than physiological low flow, result in endothelial dysfunction in any vasculature. Using an IBIDI flow system, Human Umbilical Vein Endothelial Cells (HUVECs) were exposed to minute non-uniform shear stress mimicking the vein vasculature in the early stages of venous disorders and laminar shear stress comparable to normal venous flow.

From Left: Sreelakshmi B J, Karthika C L, Vani Venugopla, Ahalya Sreekumar

We investigated the role played by TGF-β and BMP4-mediated signalling in ASS-induced EndMT. Studies of cultured ECs exposed to various venous flow regimens revealed that ASS induced the expression of EndMT-associated Snail, Slug, Twist, N-cadherin, α-SMA (Figure 1). These EndMT markers were overexpressed in veins collected from patients with varicose vein implying a role of EndMT in this disease. We are currently focussing on studies to determine whether therapeutic targeting of TGF-β and BMP4 can be used in the therapeutic management of venous remodelling by reversing EndMT. This study would, in future, pave the way to identify potential agents which can modulate this dysfunction at an earlier stage of chronic venous disease.

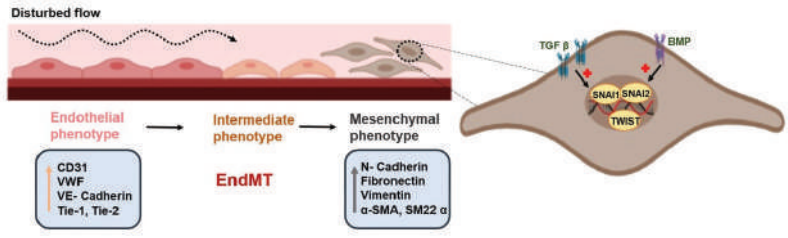

Figure 1: Endothelial to mesenchymal transition (EndMT) in venous endothelium exposed to disturbed flow regime. A decreased expression of endothelial markers VE-cadherin, CD31, and a gain of mesenchymal markers such as αSMA, N-cadherin, vimentin, fibronectin etc., was observed in venous endothelial cells exposed to minute altered venous shear stress. EndMT-associated TGF-ß1 and BMP4 signalling was highly activated. These results corroborated well with the findings in vein tissues collected from patients with varicose veins compared to healthy vein tissues.

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α-FODRIN AS MITOSIS MODULATOR AND MICROTUBULE NUCLEATION REGULATOR

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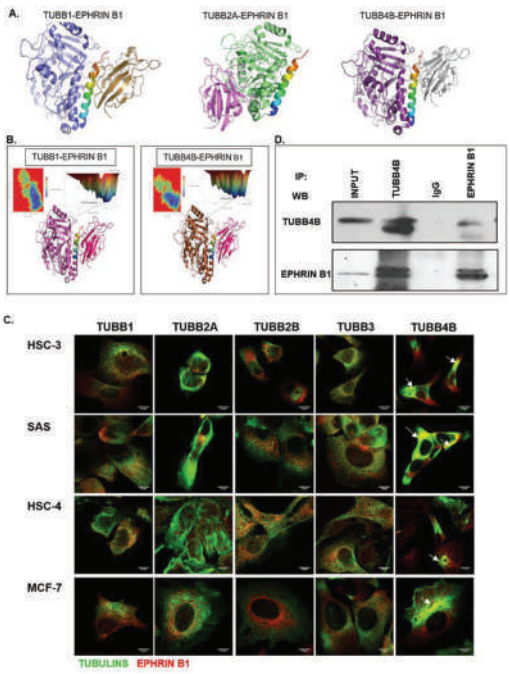
Scientist F, Cancer Research Program
Ph.D: Bose Institute, Kolkata
Post-Doc: University of Kansas, Lawrence, KS, USA

The nucleation competent form of γ-tubulin is the γ-tubulin ring complex (γ-TuRC) which is concentrated at the centrosome that acts as the primary microtubule organizing centre (MTOC) in most eukaryotic cells. Our previous work has showed that fodrin, a cortical cytoskeleton protein is present in brain derived γ-TuRCs and regulates mitosis. Through the present study, we can conclude that fodrin being a cortical protein, is important in various cellular functions besides supporting the plasma membrane. It is an important regulator of microtubule nucleation. It is significant in maintaining the optimal concentration of γ-tubulin and CDK5RAP2 at the centrosome thereby preserving the centrosome functionality to form microtubules in interphase and mitosis. A proteomic approach has also showed that fodrin is vital to the activity of a few key kinesins such as KIF2B, KIF3C and KIF23 and the maintenance of certain important cytoskeletal proteins and apoptotic proteins. Further, based on our results that fodrin regulates chromosome congression and mitosis, it's effect on cancer and apoptosis is being studied.

From Left: Dhrishya Dharampal, Athira Jyothy, Ghorai Sayan



II β-tubulin isotype TUBB4B in the maintenance of cancer stem cell self-renewal

In a background study to identify proteins differentially expressed in sphere culture as opposed to monolayer culture, a few β-tubulin subtypes were found to be upregulated in the membrane fraction of sphere culture. Hypothesizing the up-regulation of tubulin subtypes is to facilitate the transport of membrane receptors essential for stemness to plasma membrane, our work aims to prove that in self renewing cancer stem cells. The expression of stemness markers like SOX2, NANOG and ALDH1A1 were seen to decrease when TUBB4B was downregulated. The involvement of the tubulin isotype in stemness was linked to Ephrin B1, a membrane expressing ligand, previously shown to aid in the maintenance of stemness of cancer stem cells with increased expression in the membrane of sphere culture. In-silico analysis, involving docking studies and dynamic simulation implied a favorable interaction between TUBB4B and Ephrin B1 in contrary to other isotypes. Also, immunofluorescence studies showed a membrane co-localization of TUBB4B with Ephrin B1 in various cell lines. The interaction between Ephrin B1 and TUBB4B was further corroborated by Immunoprecipitation (Figure 1).

Interaction of tubulin isotypes with Ephrin B1. (A) Protein-Protein docking images of β-tubulin isotypes and Ephrin B1. (B) Images showing dynamic simulation between TUBB1 or TUBB4B and Ephrin B1. (C) Colocalization of TUBB4B with Ephrin B1 in different cell lines. Oral cancer cell lines and a breast cancer cell line were immuno-stained with antibodies against five β-tubulin isotypes (green) and Ephrin B1 (red). (D) Direct interaction between Tubulin β-4B and Ephrin B1 in HSC3 cells by immunoprecipitation.

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CYCLOPHILIN A INDUCES MACROPHAGE APOPTOSIS AND ENHANCES ATHEROSCLEROTIC LESIONS IN HIGH-FAT DIET-FED HYPERGLYCEMIC RABBITS

SURYA RAMACHANDRAN, Ph.D

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Ph.D: RCC, Thiruvananthapuram
Post-Doc: RGCB, Thiruvananthapuram, Oklahoma Medical Research Foundation, Oklahoma City, OK, USA

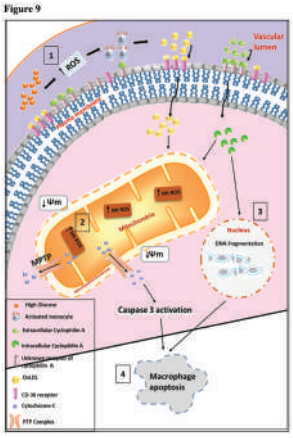
Macrophage apoptosis is a key contributor to the progression of atherosclerosis. It is mainly depends on the stage and severity of the lesion. Apoptosis is considered beneficial for early lesions because it suppresses the progression of the fatty streak, whereas in advanced lesions it results in lesion cellularity and severity. Vascular disease associated with type 2 diabetes is known to have more severe and extensive lesions. Our studies suggest that cyclophilin A can contribute to atherosclerotic lesion progression and severity through its ability to induce apoptosis in macrophages under high glucose conditions using both in vitro cell culture system and in vivo system using New Zealand White rabbits fed with high fat diet (HFD) containing 0.5% cholesterol and 3% saturated fatty acids. This action is by increasing mitochondrial superoxide levels and impairing mitochondrial membrane potential thus resulting in the opening of the MPTP pore and caspase activation. HFD fed rabbits also had higher levels of plasma cyclophilin accompanied by higher serum lipids and glucose levels compared to the ND group. There was a modest increase in the levels of proinflammatory cytokines such as TNF alpha, MCP 1, IL 1 beta and IL6 were also seen in the animals of the HFD group compared to ND group.

Back Row From Left: Aswathy S., Jagannath R S, Jeeva Prasannan, Vinitha A.
Front Row From Left: Jayalekshmi V S, Rajeswari Gopal G.

Sufficient engulfment of apoptotic cells by macrophages, a process called efferocytosis, is important to endure the formation of atherosclerotic lesions. An increased load of apoptotic cells in atherosclerotic lesions suggests either increased apoptotic cell death or inadequate efferocytosis for the removal of such cells in the lesions. Cyclophilin A is possibly a key player in increasing the apoptotic cell load and/or hindering normal efferocytotic mechanisms.

Although advances in understanding macrophage apoptosis in atherosclerotic lesions, it remains to be seen whether the apoptotic process can be manipulated in a way that it can be made useful for preventing atherothrombosis. Identifying and understanding the mechanism of action of pro-inflammatory molecules such as cyclophilin A, their receptors and inhibitors may provide us tools and targets for such manipulations.

Figure 9



Cyclophilin A induces apoptosis of high glucose activated macrophages through mitochondria-mediated intrinsic death signaling pathways. (a) High glucose induces ROS in the aortic vascular lumen which increases secretion of cyclophilin A by activated monocytes leading to increased uptake of OxLDL by overexpressing CD 36. (b) Intracellular cyclophilin A increases mitochondrial ROS resulting in both mitochondrial membrane potential loss and mPTP opening leading to the induction of cytochrome C and activation of caspase 3. (c) Intracellular cyclophilin A induces chromosomal DNA fragmentation in the presence of high glucose. (d) Both the nuclease activity of cyclophilin A and the induction of mitochondria-mediated death signaling pathways induce macrophage apoptosis.

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EPH/EPHRIN SIGNALING REGULATES CANCER STEM CELLS IN ORAL CANCER

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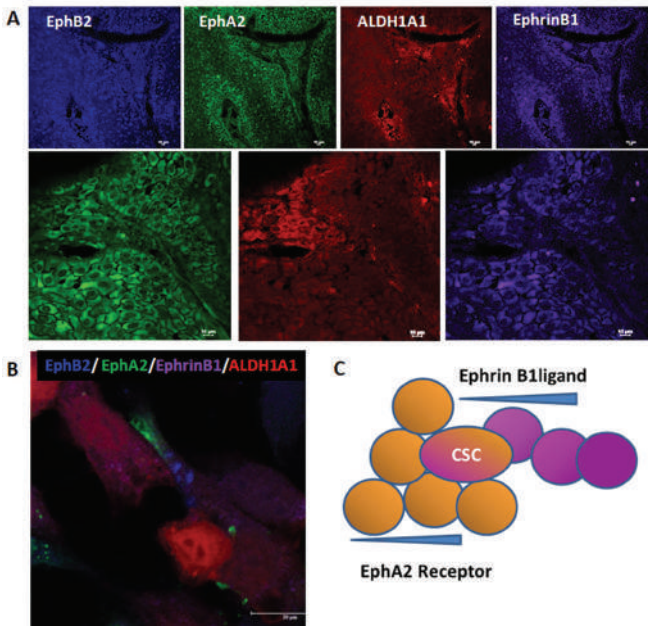
Ph.D: RGCB, Thiruvananthapuram
Post-Doc: RCC, Thiruvananthapuram, NCBS, Bengaluru

Though screening programs and improved treatment modalities have improved the cancer management, there still remain certain lacunae in our understanding of the biology of cancer. "Why does cancer come back after treatment?" The simplest answer is "There are certain cancer cells that are resistant to therapy, and they acquire stem-like characteristics to regenerate cancer". All these stem-like cancer cells, cancer stem cells (CSCs), may not have the stem-like characteristics by birth; they acquire it. The tumor microenvironment or the "CSC niche" plays a pivotal role in that.

Signaling pathways initiated in the "CSC niche" are critical in the regulation of CSCs. Our earlier attempts to discover the signaling pathways and their intermediates, using phosphoproteomic analysis identified Eph/Ephrin signaling as an important regulator of CSCs. Although the significance of this pathway in the "CSC niche" is not addressed so far, its relevance in normal stem cell niche is well-established in intestinal crypts. Eph/Ephrin signaling pathway is bidirectional, where both the ligand (Ephrin) and the receptor (Eph) are membrane bound, and mediate signaling events. So, when two cells come in contact, there is a forward signaling initiated in the receptor-bearing cell, as well as a reverse signaling happening in the ligand-bearing cells. Since the intermediates of both these signaling are different, the two cells might attain different cell fates.

From Left: Anitha Vimal, Amrutha Mohan, Gayathri Mohan, Reshma Raj R, Padmaja K P



We found that the important components of the Eph/Ephrin pathway in oral carcinoma are EphrinB1, EphA2 and EphB2. While EphA2 and EphrinB1 take part in constituting the "CSC niche", EphB2 is probably responsible for other functions related to cancer progression. We found that both EphA2 and EphrinB1 regulate CSC population marked by ALDH1A1. A reverse gradient of the ligand and the receptor formed in the "CSC niche" regulates the balance of self-renewal and differentiation of CSCs.

Eph/Ephrin signaling in the regulation of the "CSC niche" in oral carcinoma. A. Oral carcinoma sections were stained for the expression of indicated molecules. Although the expression of EphB2 was uniform throughout the sections, EphA2 and EphrinB1 were highly expressed where ALDH1A1-positive CSCs were found. B. High resolution image of the expression of indicated molecules in oral cancer cells. In ALDH1A1 expressing cells, the EphrinB1 ligand specifically engages to EphA2 of the neighboring cell, even though EphB2 is also expressed on the cell. C. Schematic representation of the CSC niche regulated by the gradient of EphA2 and EphrinB1.

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REGULATORY MECHANISMS OF CLATHRIN-MEDIATED ENDOCYTOSIS

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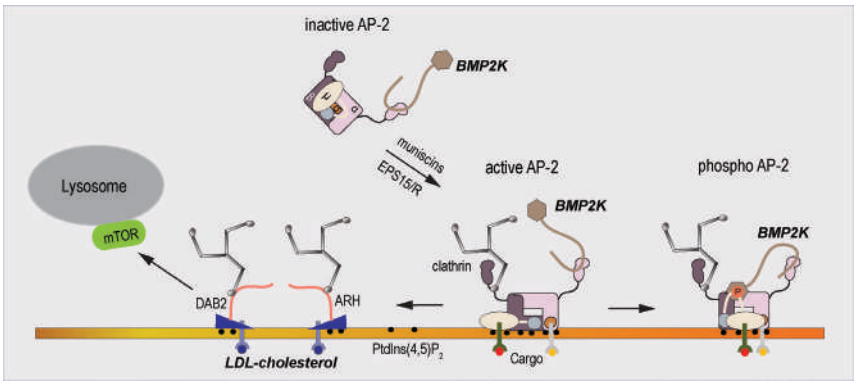
Transdisciplinary Biology Program
Ph.D: NCCS, Pune
Post-Doc: University of Pittsburgh, Pittsburgh, PA, USA

Clathrin-mediated endocytosis (CME) is vital for the internalization of most transmembrane proteins (cargo) in eukaryotes. Aberrations in this process are hall marks of cancer, metabolic and neurological diseases. Furthermore, viruses and intracellular pathogens hijack CME for cellular entry and dissemination. Yet how the process initiates in vertebrates remains poorly understood. Our lab seeks to identify the initiation mechanisms of CME with the hope of designing novel inhibitors and activators that could regulate the process. The heterotetrameric clathrin adaptor complex, AP-2 is the core organizer of CME. AP-2 recruits accessory proteins and clathrin to form clathrin-coated pits (CCP) into which cargo is sorted. Earlier we had discovered the pioneer muniscin-EPS15/R protein duo which can activate AP-2 for CCP inception. Phosphorylation of AP-2 is considered a critical regulatory step in CME. We have now identified a novel kinase, BMP2K that reversibly phosphorylates AP-2 and promotes CME in cells and organisms. By integrating reverse genetic, pharmacological and biochemical approaches in genome-edited cells and D. rerio (zebrafish) embryos, we demonstrated that BMP2K phosphorylates T156 residue on the Q subunit of AP-2. Further, we found that the kinase uses its unique C-terminus to interact with AP-2 and that this interaction is pivotal for its recruitment, stability and function. Currently, we are investigating how BMP2K interacts with the initiation complex to regulate its functions.

From Left: Shikha Ramesh T, Navyasree K V



Schematic depicting possible working model of clathrin-mediated endocytosis based on our investigations

Another major project in the lab investigates involvement of initiation complex in the endocytosis of AP-2 independent cargo. For this, we are using LDL receptor as a model. LDLR internalizes via DAB2 and ARH clathrin adaptor proteins. Recently, we discovered that LDL-cholesterol endocytosis activates mTOR signaling on lysosomes for cell growth. Currently, we are analyzing the transport of LDL-cholesterol and associated mTOR activation in inititation complex knockout cells. We are also trying to understand how this process goes awry in Niemann-Pick type-C patients having aberrant cholesterol accumulation in lysosomes.

DEVELOPMENT OF DRUG RELEASING IMPLANT SYSTEMS FOR POST-SURGICAL TREATMENT OF GLIOMA

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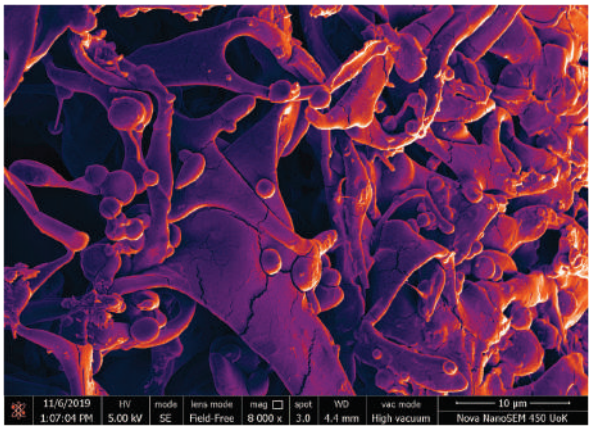
Scientist E-II, Cancer Research Program
Ph.D: Mahatma Gandhi University, Kottayam

Cancer free prognosis for glioblastoma is not more than 12-18 months in spite of current available therapies (Surgery, radiation and chemotherapy) which can be attributed to frequent relapse in patients. Previously, we have developed a self-assembling glycolipid nanomicelles decorated with a targeting peptide (TGN) as drug delivery system for crossing the Blood Brain Barrier (BBB) (Biomater. Sci.,2019,7,4017). Major hindrance in treating brain cancer is the aggressive nature and recurrence of tumor post surgery and presence of (BBB) that allows selective passage of drug. To compensate this, very high doses of drug have to be given, which remains in circulation and cause non specific systemic toxicity. In this work we have developed a polymeric implant system to bypass the BBB obstacle in treatment and release combination of drugs in-situ as a part of post-surgical glioma chemotherapy. By use of an implant system, we can expect direct drug delivery into the surgical site, timely release of required amount of drug; thus eventually decreasing peripheral toxicity.

From Left: Teena Jacob Chirayil, Akhil K Mohan, Vipin C L, Laiju C K

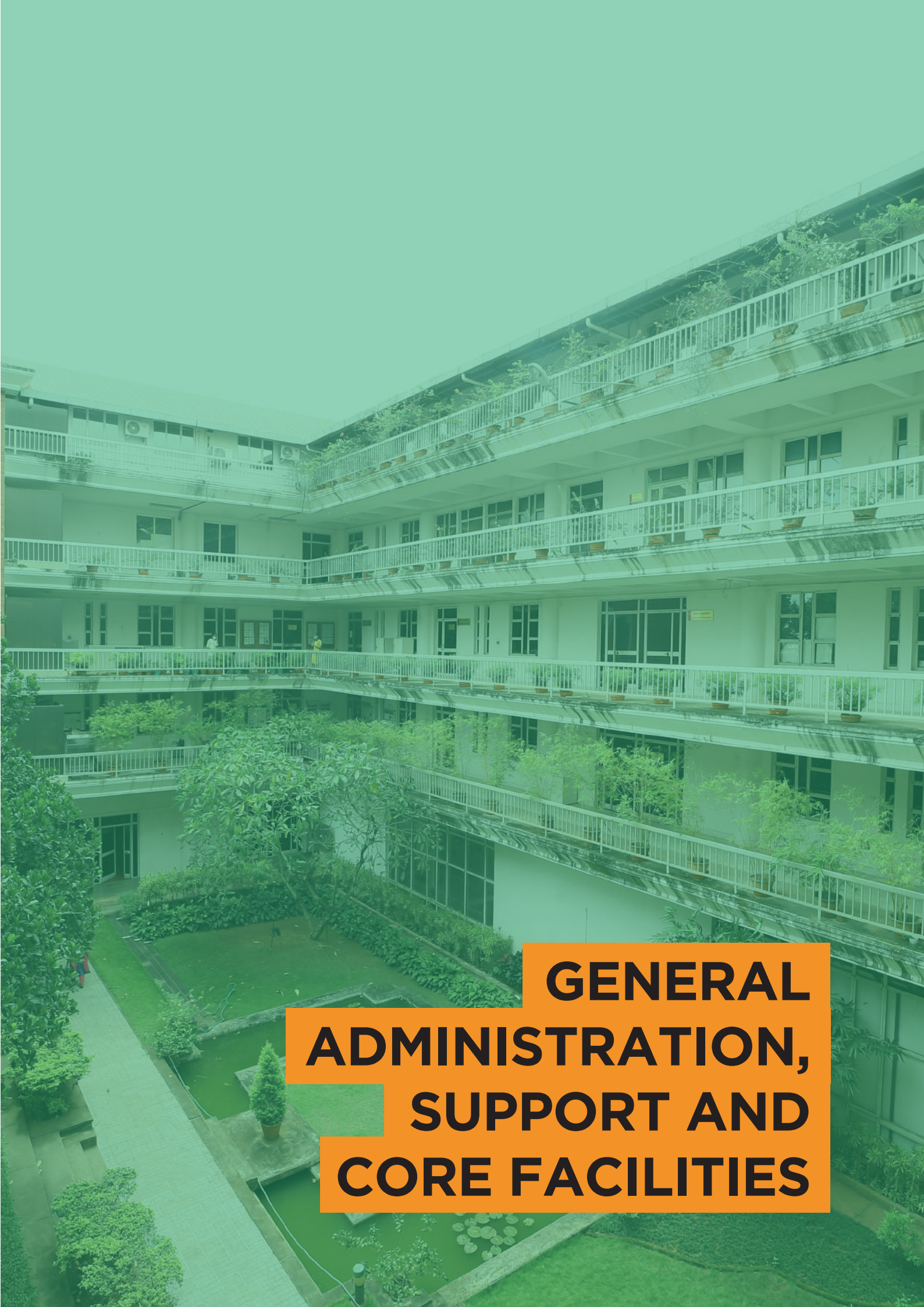


A Hyaluronan based polymeric system designed for the encapsulation and controlled release of chemotherapy drug such as 5-fluorouracil (5FU). Hyaluronan is the most biocompatible polymer that can swell and form a hydrogel. This system crosslinked with gelatin is a substrate for Matrix metalloproteinases (MMP) secreted by tumor cells in the process of migration. We use the brain micro environment to our advantage; as most of the cells in cortex are terminally differentiated whereas the tumor cells are undergoing aggressive mitosis. Hence we can entrap cell cycle dependent chemotherapy drug such as 5FU which will specifically kill the multiplying cells. This system is further enhanced with Redox sensitive PLGA nanoparticles which carry DNA alkylating drug and are targeted with peptide to kill the quiescent glioma cells. This system is in the form of lyophilised cottony-structure which is easy to handle and implant. We have characterised the copolymer and in vitro and in vivo efficacy studies are being performed. We are verifying its biocompatibility in Sprague Dawley rat brain cortex and evaluating it based on histological studies.

Scanning electron micrograph of HA-GEL cottony matrix with redox sensitive PLGA nanoparticle (arrows) dispersed (Mag: 8000X).

SELECTED PUBLICATIONS

- **Amritha Vijayan, Nanditha C K and Kumar G S V.** ECM-mimicking nanofibrous scaffold enriched with dual growth factor carrying nanoparticles for diabetic wound healing.Nanoscale Advances, 3, 2021, 3085–3092



GENERAL ADMINISTRATION, SUPPORT AND CORE FACILITIES

OFFICE OF THE DIRECTOR

Back Row From Left: Venugopalan J, Priya R, Jayalakshmi U S
Front Row From Left: Professor Chandrabhas Narayana, Mohanan Nair S

The Office of Director is responsible for successful leadership and management of the organization according to the strategic directions set by the institute management. This office develops the vision and strategic plan to guide the organization, develop an operational plan which incorporates goals and objectives that work towards the strategic direction of the organization, ensures that the operation of the organization meets expectations of its stakeholders and funding agencies. The Office of the Director also oversees efficient and effective day-to-day operation of the organization, draft policies for approval of the Governing Body; prepare procedures to implement organizational policies; review existing policies and recommend changes as appropriate; ensure that programs and services offered by the institute contribute to its mission; monitor day-to-day delivery of programs and services to maintain or improve quality, determine staffing requirements for organizational management and program delivery, recruit, interview and select staff that have the right technical and personal abilities to help further the organization's mission. The Office also is responsible to supervise preparation of a comprehensive budget and work with the Governing Body to secure adequate funding for the operation of the organization.

GENERAL ADMINISTRATION

The management of research and development (R&D) and innovation has emerged as a specialized area within both research and higher education institutions. New modalities of research and innovation have evolved over the last 10 to 20 years against a backdrop of major changes in the tertiary research and education sector as a whole. The Administration Group is backbone of any such organization. An effective administrator is an asset to an organization. The Administration Group is the link between various units and sections of the organization and ensures the smooth flow of information from one part to the other. The Administration Group also provides administrative & technical support in the areas of human resources management, budgetary, strategic planning, legal affairs, pay and allowances, medical benefits, leave management, purchase procedures, management of stores and facilitates security.

THE CONTROLLER OF ADMINISTRATION

Mohanan Nair S

Directs and coordinates the administrative, finance, purchase & stores activities at the Institute, business service functions & procedures of the institute and ensures compliance with all applicable regulations & policies. The Controller of Administration is the primary link between the general administration groups and the Office of the Director. The Controller also provides leadership & supervision of business services, administrative duties, all recruitment & promotions, compilation and monitoring of revenue, expenditures etc. The Controller manages all procurements and provision of stores/stock. All legal matters are also supervised by the Controller. The Security, Vigilance, Disciplinary matters are all dealt with by the Controller of Administration.

GENERAL ADMINISTRATION DIVISION

Back Row From Left: Dileep Kumar, Anil Kumar R, Vishnu P, Akhiljith S, Edwin S, Vishnu T S, Subash K
Central Row From Left: Preetha J, Reena Prasad, Asha R Nair, Priya R, Jayalakshmi U S, Sujitha S
Front Row From Left: Jayakrishnan N, Mohanan Nair S, Jayachandran Nair R

The main responsibility of general administration group is to ensure all requirements are implemented for the efficient performance of all research related services at RGCB. The General Administration Group serves as the connecting link between the senior management and employees. The major mandates of general administration include good coordination among all the departments ensuring attainment of organizational goals; optimum utilization of resources, minimization of cost, human resources and payroll, transportation, fulfilment of social and economic needs of the employees and organization as well as development and growth of the institute. The General Administration also implements work related to Estate Affairs, House Keeping & Welfare, Legal matters and implementation of various Acts (including RTI), Building Engineering & Construction, Security & Surveillance, Vigilance & Disciplinary matters and official language.

SUPPORTING STAFF

Back Row From Left: Hariharan S, Baiju R, Ashok Kumar S, Pradeep Kumar B S
Central Row From Left: Suresh Kumar S K, Harikumar S, Anil Kumar B, Ratheesh R, Vijaya Kumar S

INSTITUTE PROJECT PERSONNEL

Back Row From Left: Briji S, Harikrishnan S, Akshay Kumar Nair, Vaisakh V R, Sarath S N, Dinesh Kumar S, Renjit Kurup, Navajith Nair

Central Row From Left: Sajeesh T V, Vinu S Nair, Priya R, Meena H, Athira V L, Asha V S, Vishnu Priya, Pradeep Kumar T M, Abilal G O

Front Row From Left: Kumari Geetha T R, Sreevidya R C, Ambika P Kumar, Anithakumari O, Neethu S D, Aryasri P, Jyothisree V T, Athira Chandran, Chithra G S, Smitha L R

PURCHASE & STORES DIVISIONS

From Left: Sandhya S J, Kumar R, Mohanan Nair S, Jayakrishnan N, Vishnu S

The Purchase & Stores Group occupies a vital and unique position in RGCB. This unit ensures procurement of the right material in right quantities and of appropriate quality. The section ensures procurement from right and reliable source or vendor as well as procurement of the material economically, i.e., at right or reasonable price. The RGCB Central Stores serves all four campuses of the institute. The most common yet major responsibilities that are carried by stores include receipt of incoming goods, inspection of all receipts, storage and preservation, identification of all materials stored, materials handling, packaging, maintenance of stock records, inventory control and stock-taking.

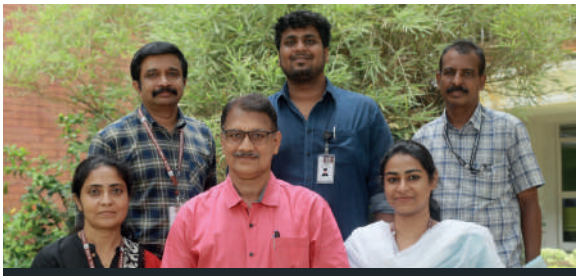
FINANCE & IFC DIVISIONS

From Left: Nidheesh Raj R, Sathichandran S, Mohanan Nair S, Kumar R, Sreejith S

The Finance Division of RGCB has been inventive in budget planning and its real-time reporting, always in absolute synchronization with the scientific fraternity of the Institute. Preparation & Monitoring of Budget and Resource Generation are always aimed to acclimatize the available resources' utilization in achievement of its mandated science, thereby paving the way for productive application of all available resources. Prompt generation and submission of internal management information by the Finance Division always facilitates RGCB in taking accurate and apt decisions. Matters related to RGCB's Finance Committee, audit, processing of payments, TDS/GST and returns, accounting of receipts & disbursements, revenue refunds, reconciliation of bank accounts and rendition of utilization certificates and statements of expenditure are always promptly implemented by the Finance Division. The Final Accounts along with Audit Report are placed on the tables of both Houses of Parliament through the Department of Biotechnology. The dynamic contributions of Finance Division have always resulted in building organizational strength, enthusiastic and motivated personnel and hence a robust institution.

A dedicated IFC supports in all Financial as well as Administrative/Establishment works related to extra-mural funded projects of the Institute, all matters related to Ph.D, MSc, Summer training programs, Post-Doctoral Fellows etc. Accounting in respect of all service facilities of the Institute are exclusively done by this Group. This specialized Group plays an extremely important management role of all extramural and institute generated funds. It is the connecting link between all funding agencies and RGCB. The vital duties of IFC includes implementation of procedures related to accounting, payment, preparation and rendition of Utilization Certificates and Statements of Expenditure in respect of all cases except the Core Grants, Ph.D Fellowships, Post Doctoral Fellowships, Program Scientist Fellowships and fund management of Extra Mural Projects. The IFC is the internal link group in respect of all matters pertaining to purchases in utilisation of such extra-mural funds.

OFFICE OF ACADEMIC AFFAIRS (OAA)



Back Row From Left: Hareesh G, Bharat Krishanan J C, Edwin S
Front Row From Left: Beena Nair L, Dr. Santhosh Kumar K, Parvathy Prasad

The Academic Council is the body looking after all the academic activities of RGCB. They are responsible for structuring the course syllabus, the mode of evaluation, admission procedures, academic calendar, course instructors and coordinators, the duration and timing of the internship and facilitate the Director and Administration with regard to the academic activities of the students enrolled in RGCB.

Office of Academic Affairs (OAA) supports the management of academic programs at RGCB including Ph.D and MSc program, short and long term training programs, Post-doctoral training, biotechnology skill development programs and other specialized training programs. This year along with the IT section, they conducted all the MSc and Ph.D course work classes and the semester examinations in the online mode to make sure that the academic program will not be affected by the Covid19 pandemic. The OAA assists the Academic Council to provide leadership in development of a strong academic program, policy formulation and program planning and student research progress evaluation. OAA under the advice of the Academic Council, keeps abreast of trends and changes in higher education; works for institutional vision, stability, growth and excellence; provides a connection between administration and faculty; serves as catalyst to create a climate conducive to scholarly research in an atmosphere committed to the mandates of the institute and the Dept. of Biotechnology. Other responsibilities includes maintenance all official records, conducting screening tests and examinations for selection of various positions in the research projects. The OAA's ensures coordination and collaboration to guarantee quality learning for students and excellence in academic administration.

Constitution of the Academic Council		
Name	**Position**	**Designation**
Professor Chandrabhas Narayana	Director	Chairman
Dr. Santhosh Kumar T R	Scientist G & Dean (Research Administration)	Vice Chairman
Dr. Soniya E V	Scientist G & Dean (Academic Affairs)	Member
Dr. Ajay Kumar R	Scientist G	Member
Dr. Jackson James	Scientist F & Associate Dean	Member
Dr. Sreekumar E	Scientist F & Associate Dean	Member
Dr. Debasree Dutta	Scientist E-II	Member
Dr. Santhosh Kumar K	Senior Consultant, Academic Administration	Special Invitee
Dr. Surya Ramachandran	Program Scientist	Special Invitee

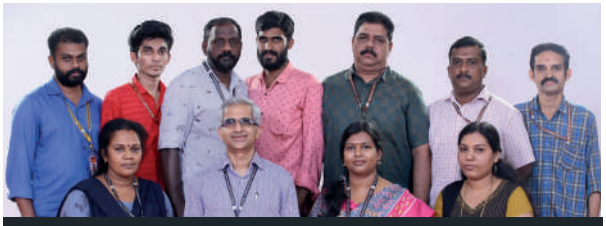
ANIMAL RESEARCH FACILITY

Animal Research Facility (ARF) at RGCB is involved in planning and conducting animal experiments by providing good quality animals and veterinary expertise. The facility is registered with the "Committee for the Purpose of Control and Supervision of Experiments on Animals"(CPCSEA)for Research for Education purpose, Breeding for in-house use, Breeding for the purpose of trade. The facility operates at main campus and also at Bio Innovation Centre at KINFRA campus so the investigators from both campuses can make use of the services. Our's is a laboratory rodent facility that currently maintains 27 strains of mice, 3 strains of rat and one strain of rabbit. To support our scientific community in its response to understand and contain the COVID- 19 pandemic, ARF has expanded the available mice strains with one more strain, hACE2 – KI which are susceptible to SARS -CoV-2, and are useful for studying antiviral therapies to COVID-19. All the animals are maintained in controlled environment specific for each species. The Institutional Animal Ethics Committee convenes 4 times a year and reviews the animal research proposals. During the year 2020-2021 IAEC, RGCB approved 55 research proposals.

In addition to routine breeding and maintenance of various strains, the service provided by the facility includes designing of in-vivo studies and animal models, execution of animal studies, import of animals based on the requirement of researchers, hematology and serum biochemistry analysis. Last year ARF issued 1078 animals including mice, rats and rabbits for various research proposals at RGCB. The facility has Certificate course in Laboratory Animal Science for Ph.D students, Msc students and other project staffs who needs to do research using laboratory animals. 72 students were trained during the year 2020-2021. ARF is also involved in the development of a cryopreservation facility. The facility is well equipped with stereo microscopes, fiber optic illuminator, biosafety cabinets, CO2 incubator, electronic balance and water bath. Cryopreservation reduces maintenance costs and safeguards valuable mouse lines against loss through infection, breeding failure and genetic drift. The procedures are being standardized in the facility. A zebra fish facility was set up in the Animal Research Facility at RGCB Bio-Innovation Centre, KINFRA campus. The zebra fish (Danio rerio) of the AB strain are reared in Recirculating Stand Alone Housing system. Activities like breeding and collection of fish embryo, growing the healthy embryos to adults and feeding of live Artemia brine shrimps are currently undertaken for establishing the zebra fish colony.

The new equipments installed and fully functional in the facility includes Veterinary Haematology Analyser (MEK6510; Nihon Kohden, Japan), Animal Biochemistry Analyzer (Dry Chem NX-500; Fuji Film), Rodent Colonoscope (Karl Storz, Germany), Advanced Animal Imager (Perkin Elmer, IVIS Spectrum) with 3D surface topography.

Despite the pandemic Covid -19, the facility is providing an uninterrupted support to the researchers without any compromise in the quality of work, which is possible with the whole hearted support of the RGCB management and staff.

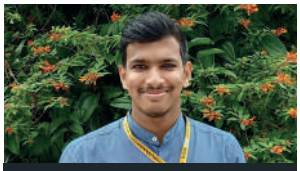


Back Row From Left: Alex Anto A, Govind V, Rajeev R V, Siva Kumar A S, Anwar K Y, Vinod V M, Vinod G
Front Row From Left: Sumaja V, Dr. Sreekumar E, Dr. Archana S, Rejani C S

Dr. Arya Aravind

Dr. Vishnu Sunil Jaikumar

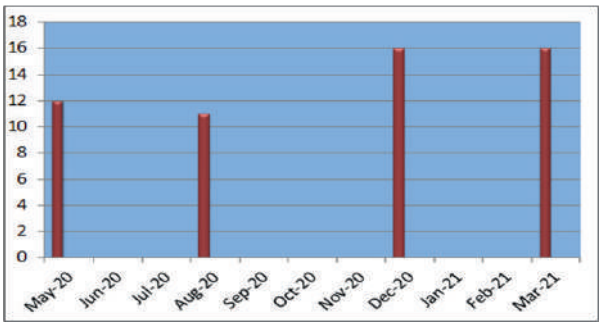
Anand B



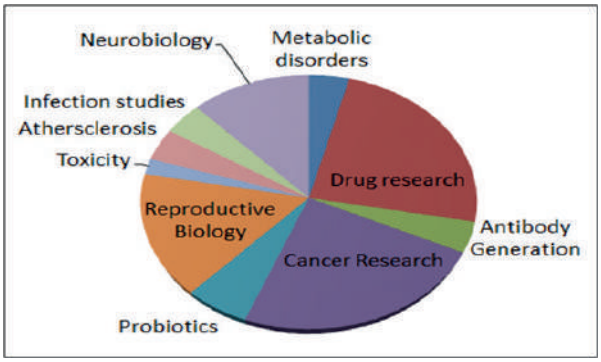
Anandhu B

Neethu S M

An overview of the activities in ARF during the year 2020-2021.
Details of IAEC meeting conducted and B forms approved.



Distribution of the purpose of animal use



GENOMICS SERVICE FACILITY

Genomics facility is doing Sanger sequencing and Genotyping various bacterial, viral, plant and human samples using Multicapillarry systems 3730 & 3730 XL DNA analyzers, for both in-house and external samples. The samples from research labs, such as Human molecular genetics lab, Plant disease Biology lab (microsatellite screening, marker screening), Infectious disease Biology lab, cholera lab, cardiovascular disease lab, Mycobacterium lab, Molecular virology lab, and Laboratory medicine and molecular diagnostics are sequenced. For genescan analysis, samples of plants / animals were processed for SSR analysis, SNP genotyping and microsatellite analysis for various research laboratories. The facility is extensively used by the institutes in and around Kerala as well as by universities from all over the country. For Q-PCR applications, the facility equipped with RTPCR 7500, 7900HT and Quantstudio 5. Gene expression studies with Real Time PCR 7500, 7900 HT systems, & Quantstudio are used in SNP analysis, absolute quantitation, relative quantitation, Allelic discrimination & Taqman low Density (TLDA) array applications using SYBR green/Taqman chemistry, for various research labs of both internal and external investigators. Microarray platform using the affymetrix genechip technology has been fully utilized with human and mouse arrays. The facility is also equipped with droplet digital PCR (BioRad) for copy number variation studies and genomic library quantitation.

Dr. Manoj P

Dr. Barath Kumar T R

BIO-IMAGING FACILITY, FLOW CYTOMETRY CORE AND HISTOLOGY CORE

The Bio-imaging Core Facility offers state-of-the-art imaging equipment for basic and advanced imaging applications. The facility is also available for external users from Academia & Industries.

1. Spectral Confocal Microscope with Resonance Scanner for Fast Live Cell Imaging (A1Rsi)
   A1R si, NIKON is the most advanced and fully automated spectral confocal microscope from Nikon, capable of capturing high quality confocal images with high speed and sensitivity. This machine includes a 32 array spectral detector and high speed resonance scanner

2. Confocal Laser scanning Microscope with high sensitivity spectral detector (Olympus FV3000)
   Olympus FV3000 is equipped with a high sensitivity spectral detector (HSD) with GsAsP PMTs which enables it to view samples having weak emission. The desired emission range can be selected using the spectral detectors. The Diode Laser lines available are 405nm, 488nm, 514nm, 561nm and 640nm with 4x, 10x, 20x, 40x and 60x objectives.

3. Confocal Laser Scanning Microscope with GaAsP Detector for Multifluorescence and Live Cell Imaging (Leica SP8 WII Confocal Microscope)
   Leica SP8 Spectral Confocal with WLL is an advanced confocal microscope from Leica Microsystems, Germany. This equipment is configured with white light laser (WLL) that can support any laser lines between 470-670nm and AOBS for filter less emission tuning, in addition to the highly sensitive GaAsP detector.

4. LEICA TCS SP8 STED 3 X FALCON LIFETIME IMAGING UNIT WITH WLL (470- 670 nm) & AOBS
   Features: Multi line Argon with 488, 456, 515 nm laser lines and 405nm laser is provided for imaging as well as photomanipulation applications. Dual colour SMD HyD for life time imaging. High Resolution Imaging : Life time based Tau STED .
   NIKON SPINNING DISC CONFOCAL MICROSCOPE (MODEL CSU-W1 WITH DUAL CAMERA)
   Omnicron Laser Combiner Model (405/120mW, 445/100mW , 488/100mW, 515(100mW), 561(80mW), 638(100mW), Yokogawa Main Unit (CSUW1), 2 Camera system with 10pFW
   Andor EMCCD Camera and NIS Element software.

GENOMICS SERVICE FACILITY

Genomics facility is doing Sanger sequencing and Genotyping various bacterial, viral, plant and human samples usingMulticapillarry systems 3730 & 3730 XL DNA analyzers,for both in-house and external samples. The samples from research labs, such as Human molecular genetics lab, Plant disease Biology lab (microsatellite screening, marker screening), Infectious disease Biology lab, cholera lab, cardiovasculardisease lab, Mycobacterium lab, Molecular virology lab, and Laboratory medicine and molecular diagnostics are sequenced. For genescan analysis, samples of plants / animals were processed for SSR analysis, SNP genotyping and microsatellite analysis for various research laboratories.The facility is extensively used by the institutes in and around Kerala as well as by universities from all over the country. For Q-PCR applications, the facility equipped with RTPCR 7500, 7900HT and quantstudio 5.Gene expression studies withReal Time PCR 7500, 7900 HT systems,& Quantstudio are used in SNP analysis, absolute quantitation, relative quantitation, Allelic discrimination &Taqman low Density (TLDA) array applications using Sybr green /Taqman chemistry,for various research labs of both internal and external investigators. Microarray platformusing the affymetrix genechip technology has been fully utilized with human and mouse arrays. The facility is also equipped with droplet digital PCR (BioRad) for copy number variation studies and genomic library quantitation.


Dr. Santhosh Kumar T R


Jiji V


Indu Ramachandran


Bindu Asokan


Saravana kumar M


Anurup K G


Vishnu S Sanjeev


Surabhi S V


Tilak Prasad


Arya V S


Gopikrishnan K


Viji S


Tanima Toni

LABORATORY MEDICINE AND MOLECULAR DIAGNOSTICS

LABORATORY MEDICINE AND MOLECULAR DIAGNOSTICS

Laboratory Medicine and Molecular diagnostic (LMMD), ICMR Viral Research and Diagnostic Laboratory (VRDL) grade 1 Laboratory of Rajiv Gandhi Centre for Biotechnology (RGCB) is one of the significant laboratories in India which handles more than 220 infectious and noninfectious disease diagnostics. The only lab in India under the Dept of Science and Technology, Govt of India with NABL ISO 15189-2012, NABH, and ILAC accreditations since 2016. The reports generated for this Division are approved by all the medical councils around the world. The Division handles research and diagnostics hand in hand. The Division is expertise in translational research, which will be helpful for the society, which consists of point of care testing technology.

History

ICMR initiated the lab under Viral Research and Diagnostic Laboratory (VRDL) in 2011. The lab was credited as Grade 1 laboratory and the 7th laboratory established in India by ICMR. LMMD was initially started to screen H1N1 epidemic samples and perform tests such as HBV, HCV, Dengue, etc. The Division used to receive samples from all medical colleges and government hospitals in and around Kerala. The Division gradually started expanding its portfolio from 4 parameters to other infectious diseases on gastroenterology, transplant medicine, respiratory medicine, neurology, ophthalmology, Pediatrics, Oncology, and Gynecology. The lab also developed in-house panel-based testing for respiratory disease, Encephalitis panel, Bacterial pathogen screening, etc. In 2013, the Division stepped on to noninfectious diseases diagnostics, the first mutation analysis performed by the Division was on cardiovascular disease, Hypertrophic Cardiomyopathy in collaboration with KIMS hospital. The findings were published in The American Journal of Cardiology (Hypertensive Hypertrophic Cardiomyopathy -Is it a Part of Systemic Hypertension or Genetic Abnormality; Suman Omana Soman, Govindan Vijayaraghavan, Ramesh Natarajan, Radhakrishnan Nair, Heera Pillai, Kartha CC, Volume 115, Supplement 1, March 16, 2015, Pages S139). The Division gained its NABL ISO 15189 2012, NABH, and ILAC (International Laboratory Accreditation Cooperation) accreditations in 2016. It became the first lab in the Dept of Science and Technology, Govt of India to gain this achievement.

Epidemic and Social Services

Kerala has faced different types of epidemics over a while. There was a Dengue outbreak in Kerala in 2012 and 2016, H1N1 outbreak in 2010-2011, 2016, Nipa outbreak in 2019, and SARS Covid2 outbreak in 2020-present. LMMD was always a frontline worker for the diagnosis and prevention of all these epidemics in Kerala. Samples used to come from all parts of Kerala to the Division for timely reporting, which helped state and central government for policy decision making. The technologists of the Division used to have peripheral posting for sample collection and point of care testing. The samples were brought back to the lab for detailed study such as genotyping, whole-genome sequencing, etc. The lab has published the Dengue serotype four whole genomes in NCBI, Seven GenBank®, accession numbers KJ938501 through KJ938507 awarded for Dengue 4.2013, 4 papers were published in international journals from the Division based on the samples collected during epidemics. More than 6000 samples for Dengue, 7000 samples for H1N1, and More than 1 Lakh, 80 thousand samples of SARS Covid 2 were screened in the lab so far, and the Division maintains a vast repository of these samples.

Infectious and Noninfectious Disease Diagnostics

The lab performs nearly 220 different molecular as well as serological diagnostics. The Division has facilitated the clinicians to provide appropriate treatment and design proper treatment strategies for acute and chronic HBV, HIV, HCV, CMV, EBV, etc. The viral load determination of these chronic diseases helps the clinicians to start/ manage the antiviral treatments. The Division also has introduced new parameters for the molecular screening of ocular pathogens such as gram-positive gram-negative, fungal, and viral. The preliminary screening results are issued within 24 hours from sample reception, and the detailed screening report is provided with 72 hours. The Division has included tests that are relied upon in identifying emerging infections, antibiotic resistance, exposure to toxic substances, and detection of chemical and biological threats into thrust areas of laboratory support. Another advance, made possible by discoveries about the human genome, has opened the door to personalized medicine approaches that can tailor medical treatments to individual patient needs, transforming modern medicine, which is being utilized in the pharmaco-genomic test for optimizing drug dosage. Except for five tests, all the remaining tests are developed and validated in-house. Noninfectious diseases such as genetic disorders like Cardiovascular Diseases, Cancer markers, Autoimmune disease, transplant medicine, etc., are also screened. The major highlight of the Division is the TAT and cost-effective testing facility. Genotyping of HBV and HCV was an initiative by LMMD, which sheds light on antiviral therapy resistance. ELISA and Immunofluorescence assays were launched as testing platforms to rapidly detect major diseases such as scrub typhus and the Hantavirus. A cloud-based result reporting system has been established in the lab for accurate and timely reporting of the results. The Laboratory Management system (LIS) states that the art technology is used in the laboratory as part of the cloud-based reporting system.

SARS CoV2

The lab initiated the SARS CoV 2 as soon as the first case was reported in Kerala. The testing was started by March 2020, and the Division is working 24 x 7 so far without any holidays. A total of 1 lakh 86 a thousand samples were processed in the Division to date. The Division maintains approximately 10,000 positive samples in the repository. The lab also helps the government understand the dominant strains and the genetic variations based on whole-genome sequencing. The Division has expertise in sequence-based studies. LMMD, RGCB is the only participant from Kerala on INSACOG (Indian SARS-CoV-2 Genomic Consortia (INSACOG), coordinated by the Department of Biotechnology (DBT) along with MoH & FW, ICMR, and

CSIR. The Division actively participates in discovering new variants of SARS-CoV-2 in the country by doing more than 3000 next-generation sequencings per month.

Validation Centre

LMMD is among the 7 VRDL labs under ICMR that are authorized to validate PCR, Antigen, Antibody, and VTM kits supplied in the country to screen SARS CoV 2. The Division is also allowed to validate disinfectants and instruments for disinfection. ICMR and Govt approve the validation reports generated from this Division of India. The devices and reagents validated by this Division are sold worldwide.

Research

The Division has diagnostics and research hand in hand. The Division concentrates on translational research, mainly focusing on the point of care testing devices. The lab has developed a lateral flow assay to detect snake bites, SARS CoV 2 antigen and antibody kits, etc. The lateral flow assay for snakebite was approved by the Govt of India for technology transfer. The VTM, RTPCR kit, RAT kit, and RNA isolation kits jointly developed by the LMMD and industry partner for COVID-19 detection are approved by ICMR and CDSCO and are currently available in the market. Now, the lab has an ICMR study on the Association of genes encoding APRIL and BAFF with IgA Nephropathy (2020-2023)

Revenue Generated

Month	Revenue
April 2020	838400
May 2020	2805100
June 2020	4852600
July 2020	6767500
August 2020	7407900
September 2020	6627600
October 2020	6303700
November 2020	3663000
December 2020	3674200
January 2020	3173050
February 2020	3582650
March 2020	3639200
Total	**5,33,34,900 INR**

Training

LMMD is an MCI approved rotation center for medical PG students; 155 Medical Postgraduate students (MD Biochemistry, MD Microbiology, MD Pharmacology, MD Pathology, and MD Transfusion Medicine) have completed their training in this Division so far. The staff of LMMD is involved in the MSc program of RGCB by imparting teaching and training in the Molecular Diagnostics elective.

Achievements

Concerning the extensive work and research done by the Division on SARS CoV 2 pandemic, the Dr. Radhakrishnan R Nair of LMMD is an expert committee member for SARS CoV 2 management in Kerala State Planning Board, Task Force member, and an expert committee member for SARS CoV 2 related projects, and validation of new kits, BIRAC, DBT, Government of India.

Back Row From Left: Johny G, Ragil Krishnan R G,
Seetha Dayakar, Vivek Hari S, Rahul J L,
Heera Pillai R,
Irfan Hussain, Karthika V, Vineetha P T

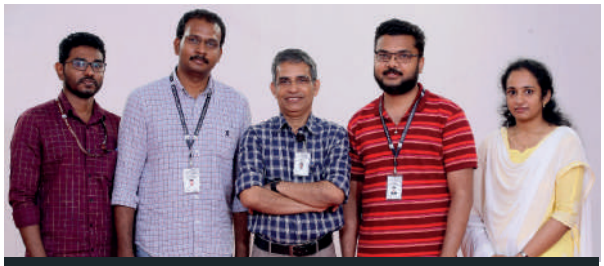
Front Row From Left: Rajalakshmi S,
Sree Lekshmi S,
Archana R S, Dr. Radhakrishnan R Nair,
Sanughosh K, Lekshmy Srinivas, Midhula S U,
Arya S Nair

MASS SPECTROMETRY & PROTEOMICS CORE FACILITY

The Mass Spectrometry and Proteomic Core Facility at RGCB provides cutting edge mass spectrometry technology available to RGCB researchers as well as the wider academic and life science industry community across the country. While being a core facility, a major goal of the facility is to become a research environment for multidisciplinary research that utilizes mass spectrometry and other related technologies to understand the disease biology and molecular medicine in the post-genomic era. The facility has an ESI-LC/MS/MS (Acquity nanoLC-Synapt G2 HDMS Quadrupole-TOF mass spectrometer) from Waters Corporation and a MALDI-TOF-TOF (Ultraflextreme) from Bruker Daltonics. The MALDI-TOF/TOF occupied with mass determination, polymer analyses and protein identifications from gel bands. LC/MS/MS is employed for high throughput proteomics protein profiling, relative quantification or protein expression, determination of post-translational modifications and non-targeted metabolomics. While the primary emphasis of the core is geared toward supporting proteomics research, the facility also provides basic MS support for a broad range of research and sample types, such as polymers, natural products, small synthetic molecules, and large intact proteins and nucleic acids.

- During the year 2020-21, just around 900 samples were analysed on various services mentioned above.
- The facility has served several students and faculties across India, including industries
- The facility also generates income from services of external as well as internal samples
- 13 papers published during 2020 and 2021 which used the facility are listed below

1. 2020, Chandraprabha VR et al Frontiers in Oncology
2. 2020, Kumar AA et al Metabolomics
3. 2020, Kumar AA et al Scientific Reports
4. 2020, Kumar V et al. Molecular and Cellular Biochemistry
5. 2020, Sobha K. et al Asian Journal of Microbiology and Biotechnology
6. 2020, Surendran A et al JACC: Basic to Translational Science
7. 2021, Chandel S et al Journal of Cell Science
8. 2021, Anandan V etal FASEB BioAdvances
9. 2021 Riyaz A et al, Toxicon
10. 2021 Tamhane VA et al Proteome Science
11. 2021, Jabeena CA et al Journal of Biological Chemistry
12. 2021, Kumar AA et al Metabolomics
13. 2021, Kumar AA et al Genes



From Left: Anoop Krishna P N, Mahesh Chandran V R, Dr. Abdul Jaleel, Arun Surendran, Lekshmi Padmakumar

LIBRARY AND INFORMATION SERVICES

Back Row From Left: Balagopal S, Meera N V, Suma S Nair, Gopakumar G, Shibin S B
Front Row: Dr. Priya Srinivas

RGCB Library is well equipped and dedicated to cater to the needs of its diverse subscribers of its research/academia/general domains. The library with its committed aim of providing physical and online library & information associated services is always harmonious in all respects to the contemporary and envisioned educational and research information needs of RGCB Community.

The library hosts nearly 8500 documents, printed journals, digital media references, back volumes, Ph.D thesis, protocols, standards, manuals, reports and reprints. These were facilitated globally through Online Public Access Catalogue (OPAC/ Web OPAC). New Ph.D thesis, manuals, digital content media etc., were also included. Major e-resource materials were obtained through DBTs e-Library Consortium (DeLCON). This year DeLCON facilitated fifteen new open access journals. More than thousands of e-journals, e-books, databases etc. were obtained regularly. Further, any additional requirements related to the queries of subscribers were addressed by means of resource sharing from other institutes.

Database of all contents were updated by adding new additions of books and related materials. Institutional repository of RGCB functioning as part of Science Central was updated by uploading all available research articles from RGCB. Library also extends its assistance in Bibliographic analysis, citation analysis of RGCB publications for the year consideration. Media clippings from newspapers, journals, magazines, periodicals, web resources etc. were conveniently categorized and displayed in the library for the benefits of users.

MEDICAL LABORATORY SERVICES

Rajiv Gandhi Centre for Biotechnology (RGCB) is an autonomous institution under the Department of Biotechnology, Government of India. RGCB in collaboration with the Department of Health and Family Welfare, Government of Kerala, implements Public Health and Research Service Programme all over the State. A major activity under this programme is the establishment of Medical Laboratory Service (MLS) units in the Government Hospitals. MLS is conducting Clinical Diagnostic Services on approved CGHS rates.

The MLS Unit provides clinical investigation services in the area of Biochemistry, Immunology, Virology, Hematology, Molecular Diagnostics and Microbiology with the help of high end imported equipments and fully automatic analyzers, reagents and well trained Technicians. The results of investigations are reported through cloud based software system for ensuring a speedy delivery which helps to augment the process of the treatment of the patients. Needless to say that the investigation process is very quick and less time consuming as the equipments are designed for speedy processing of samples using automatic analyzers.

Medical Laboratory Service Units in Thiruvananthapuram

RGCB established Medical Laboratory Service Units in Government Medical College Hospital Thiruvananthapuram, General Hospital Thiruvananthapuram, District Hospital Nedumangadu, General Hospital Neyyattinkara ,Taluk Hospital, Chirayinkeezhu, The Kerala Government Secretariat, The Kerala Government Legislature Complex, A full-fledged Laboratories functioning in the Techno Park Campus, Thiruvananthapuram.

We have “collection and report” units functioning at 64 CHCs/PHCs/FHCs in Thiruvananthapuram District .We also have C&R units at Vikas Bhavan and Thozhil Bhavan. ESI hospital Peroorkada, Kerala state Ayurveda Hospital, Panchakarma Hospital, Homoe Medical College, Siddha Ayurveda Research Centre etc . We are participating as a diagnostic partner in many projects conduct by Ayurveda/ Ophthalmic hospitals in Thiruvananthapuram.

RGCB MLS was awarded NABH accreditation for 5 main Centers separately on September 2018 and NABH and QAI accreditation ISO 15189-2012 for major 3 Centers on December 2018. Labs are registered with Clinical Establishment Act 2018 also

COVID-19

Special mention is made regarding the RTPCR and Antigen Investigations done to detect the covid-19 virus infection. RGCB have established the testing facility during the beginning of the outbreak itself under the guidance of Government of India protocol with the approval of ICMR. MLS is having a dedicated team of field sample collection unit who collects samples for Hematological Investigations as well as Antigen/RT-PCR Testing.


Dr. Ashok R


Padmavathy Amma B


Ambili S Nair


Dr. Vishnu T S


Dr. Bobby R G


Dr. Jenish Joseph


Vineetha Vijayakumar


Arathi S


Roshna P V

OFFICE OF TECHNOLOGY VENTURES (OTV)

The objectives of Office of Technology Ventures include encouraging and managing research leading to innovation and translation with a view to facilitate economic development. This is envisaged through the transfer of intellectual property and by offering consultancy services. OTV is managed by a Chief Scientific Officer supported by a Research Assistant.OTV acts as a legate for all IP related matters and various other agreements related to the research work. It includes preparation, negotiation and administering of the agreements such as Confidential Disclosure Agreements, Material Transfer Agreements, Memorandum of Understandings for both national and international collaborations, sponsored research/consultancy services and Technology Transfer Licensing Agreements to the in-house scientists/researchers.

RGCB is processing currently fourteen patent applications, both National and International. RGCB has been granted patent applications with jurisdictions of grant in various countries including India, USA, Japan and Canada.In 2020-2021, two Indian Patents and one US patent were granted to RGCB. We also filed five patent applications in the Indian patent office in this financial year. OTV manage the correspondences with patent attorneys and patent offices for all these applications which are presently under process in various Patent Offices including India, Canada, Japan, Republic of South Korea and USPTO. OTV also manage applications of RGCB scientist's with National Biodiversity Authority (NBA), Government of India for attaining the approval for research involving materials from biodiversity origins. This year we processed two applications pertaining to the approval of NBA, which is required prior the grant of Patent Application in India. Apart from this OTV executed eighteen Material Transfer Agreements (MTA), eight Confidential Disclosure agreements (CDA) and eleven MoUs for various research collaborations. We also licensed out the technology called 'COVID-Anosmia Checker', which is a fast and low cost tool for Covid-19/olfactory dysfunction screening.

Dr. Sreekumar E

Hima Sithul

RESEARCH ENGINEERING AND TECHNICAL SERVICES

Research Engineering Service Department has been playing an important role since inception of the Institute, and its contributions in the growth of the Institute are not neglectable. Having operations in three campuses, it ensures uninterrupted supports, with no compromise on quality and standards at any level of its functioning, which directly contributes to the outcome of the various Research activities. The ultimate goal of the department is to support all divisions, striving to achieve the Mission & Vision of the Institute, impartially and upholding the highest standards of integrity.

The prime responsibility of The Department encompasses installation, care & maintenance as well as service of all sophisticated and general research Equipments, including that of Central Instrumentation Facilities at Main Campus and Bio Innovation Centres.

This Division also maintains a well equipped engineering workshop with facilities for repair of sophisticated instrumentation systems. It helps to curtail, the down time of the sophisticated instruments and heavy repair costs. Inhouse Engineer's expertise to fix highly complicated hardware issues helps the institute to save heavily on AMC and CAMC's to be signed with respective suppliers of the equipments. On top of the above, the Division also undertakes customisation by designing, fabrication & modification of components of research automations to meet end users requirements and convenience.

It also extends its support in procurement, by analysing the need of the user department, understanding the currently available technology, features and future upgradation/ customisation possibilities, and prepare necessary technical specifications within the budget, to initiate purchase processes through out the years.

Division has well equipped inhouse Calibration facilities, mainly for pipettes, electronic balances, centrifuges, autoclaves, freezers, incubators, PCRs etc., . This facility includes standards and measuring instruments with proper calibration certificates from Govt. recognised National Calibration and Acreditation Agencies. Department has been calibrating and certifying instruments of various laboratories aspiring for NABL accreditation.

Research Engineering Services has also been offering training programs for students of Engineering Degree & Diploma, on operation, application, calibration and maintanance of various instrumentation systems used in Biotechnology and Life Science Research.

Apart from the above, the division also maintains computers and security surveillance systems, biometric time attendance recorders, online conferencing facilities, communication systems, liquid nitrogen plant, auditoriums, convention centre, 11KV electrical substation & 340 ton AC plant which includes power transformers, distribution transformers, DG sets, protection & control equipments, medium & high voltage switchgears, chillers, UPS & batteries, passenger lifts and elevators. Department also takes a role in automation with PLC/DCS/Scada Control Systems.

Research Engineering services plays an instrumental role in recognizing and adapting cutting edge technologies to facilitate instrumentation systems to reduce man machine interface.

Research Engineering Services have set up new precedents and a bench mark for similar departments in other institutions in the country and this division can set up new goals while contributing silently and significantly to grow the institution to new heights in the days to come.

Back Row From Left: Ancy Prince T S, Prem Kumar V, Sajan I X, Aneesh B, Akhilkumar T, Siddharth A, Gowrisankar S P, Mohan Nallath, Ullas Chandran C D

Central Row From Left: Radhika U, Sreelekshmi A S, Aswathy G Raj, Amal V, Ajith Kumar R, Shaji V, Soumya S P, Parvathy L

Front Row From Left: Ajith Kumar S, Rajasekharan K, Rajeev S

SUPPORTING STAFF

Back Row From Left: Bibin Dev, Aji Shaji, Desingh, Ajun Babu, Aneesh R, Ajeesh S S, Ajay S Kumar
Central Row From Left: L to R: Jacob B, Ajeesh R, Sreenath, Arun, Vijeesh T, Sajin G S, Sreekanth S L
Front Row From Left: Ajith Kumar S, Rajasekharan K, Ancy Prince T S

BIC CAMPUS

Back Row From Left: Anup ML, Unni Raj S, Vijayakumar A S
Front Row From Left: Renadeep CS Nair, Lekshmi C, Rahul C S Nair, Manoj Kumar K

INFORMATION TECHNOLOGY, AND DATA MANAGEMENT GROUP

The IT infrastructure of RGCB's main campus includes 9 Servers, more than 400 Desktops, and Laptops, Network Printers, etc., and houses of one of the best computing networks with constant up-gradation in a bid to provide the students and staff with state-of-the-art facilities. The Institute has been connected to the National Knowledge Network, which provides a 1Gbps leased line with multiple redundant backups.

The highly distributed computing environment at RGCB uses sophisticated computer simulation to solve staff and research scholars' problems. It is managed and actively supported by experienced engineers in the IT Department. IT department is also responsible for maintaining and administrating Mail Servers. IT department provides technical support to staff and students within the Institute on LINUX, WINDOWS platforms and includes software development for research groups.

IT department develops, maintains, host and support online admission portal, leave management system for Ph.D students/ project staff, online training portal, conference websites, RGCB Website, intranet applications for various administration and scientific activities, yearly portals for updating annual reports and integrating payment gateway for various web applications. In the mid of Covid-19 pandemic, IT team supports the smooth functioning of online classes for MSc and Ph.D students via moodle, hosted and fine tuned by IT Team.

Internet facilities are provided throughout the campus through 1 Gbps, and 100 Mbps leased lines from NKN and BSNL. RGCB has invested in a high-speed Fibre Optic Backbone with high-end security for networking across the campus. Wireless connectivity is provided at strategic locations to provide Internet access to the faculty.

The Information Technology Division of Bio-innovation Centre at KINFRA, Kazhakuttom, uses cutting-edge technology to provide high-quality services and capabilities to different research groups. It includes servers with active directory domain infrastructure, secured network with state of the art firewall system, 100Mbps leased line, and 100Mbps broadband line with failover backup connection.

Back Row From Left: Ramya Rajan, Radhika U, Amal V, Gowrisankar S P, Durga Prasad C, Lekshmi R

Front Row From Left : Rajasekharan K, Muralidhara Kurup

BIOINFORMATICS SERVICE FACILITY

The RGCB-Bioinformatics Facility is located at the Bio-innovation Centre (Campus-II) of Rajiv Gandhi Centre for Biotechnology. Considering the growing demand for computational approaches to solve biological problems, the facility is offering various bioinformatics services and training programs to students and researchers from RGCB and academia. We provide i. Computational infrastructure (Servers and Storages) for performing large scale biological data analysis ii. Short term (1 day) and long term (6-months/1year) training programs (The facility is conducting the training programs in online format) iii. Essential bioinformatics services to students and researchers from academics iv. Academic projects (Bioinformatics) to both internal and external students

RGCB Bioinformatics Facility

Bioinformatics activities offered at the facility

Services

1. Molecular Docking (proteins/ small molecules/ nucleic acids)
2. Protein Mutation design and Structural analysis
3. Protein Structure modelling (Comparative /fold recognition/ ab-initio)
4. Molecular Dynamic Simulations of Proteins/Small molecules
5. Functional annotations (GO.KEGG, COG)
6. NGS analysis and denovo assembly
7. RNA-Seq analysis
8. Phylogenetic analysis
9. Metagenomics
10. Heatmaps /3D plots/ Interactive charts

Training :

- Biological sequence analysis . Computer programming (Python & R)
- Structural Bioinformatics (Docking and Simulation) . Phylogenetics
- NGS Data analysis (Genomes and RNAseq) . Basics of data science
- Trainings to RGCB MSc & Ph.D students

Infrastructure

20 x computer terminals

1 x Server cluster with 64GB RAM and 5TB HDD

1 x DELL Power Edge T630 with 128GB and 28TB

Back Row From Left: Jamshaid Ali, Sivakumar K C
Front Row From Left: Anand Mohan, Dr Shijulal Nelson-Sathi, Meena Vinay, Aswathi Mary Paul, Bijesh George

REGIONAL FACILITY FOR DNA FINGER PRINTING (RFDF)

RFDF offers DNA fingerprinting services to legal bodies, crime investigating and law enforcing agencies. The samples analysed at RFDF relates to maternity/paternity disputes, crime, rape incidents and cases involving man missing. CO1-based molecular identification and DNA barcoding of fauna especially for species identification in wildlife forensics is yet another service offered by RFDF. Other services offered by this facility include DNA fingerprinting of plants and animals in case-by-case manner using RAPD, AFLP or microsatellite markers and DNA barcoding of animals using CO1 gene and plants using matK and rbcL. The facility also offers hands on training on DNA fingerprinting and DNA barcoding techniques. Details about various DNA fingerprinting/barcoding services and training programmes are provided in our website.

In 2020-2021 we analysed more than 61 samples related to identification, maternity/paternity and relationship disputes forwarded by courts from different districts of Kerala, Child welfare Committee and Kerala Women's Commission. In addition, we have analysed 8 forensic samples to identify body parts recovered from crime sites.

We have also received more than 339 samples related to animal poaching forwarded from various forest range offices through court. Animal poaching is one of the major threats to the animals in wild. It is imperative to punish the offenders to prevent illegal poaching. Samples confiscated by forest officers in Kerala Forest Department are forwarded to our lab for identification of species, so as to enable them to charge the case and punish the offenders.

One candidate was given training in DNA fingerprinting/barcoding during this period. We have received more than 1242 samples for DNA Barcoding/Fingerprinting/Sequencing analysis from various research institutions, colleges, and universities from all over India.

Back Row From Left: Suresh kumar U, Vinod Kumar S, Abhilash M K, Anandhu A, Anil Kumar P, Renju Krishnan R V
Center Row From Left: Saptharshi Biswas, George Varghese, Preetha V Rajan, Remya R C, Rintu Varghese, Ratheesh R V
Front Row: Dr. Soniya E V

CAFETERIA

An exclusive well- maintained cafeteria is available in all our RGCB campuses offering tasty and hygienic food. In order to cater to all the students /staff and visitors from different parts of India and abroad, South Indian, North Indian and Chinese dishes are offered. Food quality and hygiene are the two most important factors in the cafeteria. There is regular quality control and quality checks at the cafeteria to ensure highest standards of hygiene. There is never a compromise on food quality, cleanliness, and overall hygiene at the cafeteria. Be it kitchen or raw materials used for preparation of food, everything goes through a stringent quality check. The "onam" feast with more than 20 different dishes is just one example of the culinary skills of the cafeteria chefs. We aim to minimize the impact of catering operations on the environment and promote sustainable practices and consumption. The RGCB cafeteria runs on a "no profit no loss basis"

AKKULAM CAMPUS

Back Row From Left: Rajesh Kumar P S, Anoop K C, Manoj S
Front Row From Left: Baby saraswathy L, Bindhu, Jayakumari S, Prathush P

MAIN CAMPUS

Back Row From Left: Shivankutty Nair K, Sajith C, Sureshkumar R, Manoj Kumar R
Central Row From Left: Najeem M, Sunil Kumar, Gopakumar M S, Abinandh P S, Arun Kumar, Deepu RV Nair
Front Row From Left: Sandya R, Sailakumari I, Meena R P, Remadevi Amma B R, Prasanna T R

BIC CAMPUS

Back Row From Left: Rahul S, Anandhkumar, Baiju, Chandra Raj
Front Row From Left: Praveen Mohan, Nandha Kumar

KRIBS-BioNest – Biotech Park – Kochi

Bio-Nest is the 3rd off site center of RGCB, functioning jointly with Kerala Startup Mission within the Kerala Technology Innovation Zone, Kochi. The facility currently is in the 4th year of operation, since RGCB started nurturing. The facility provides infrastructure and scientific support to enable researchers, investors and entrepreneurs looking to translate biological research, innovations and medical technologies into mature business ventures. Spanning over 44,000 sq.ft, it provides bio incubation space of over 17,000 sq. ft, and a common 1000 sq, ft laboratory to the startups housed within the facility. Presently, the facility has 29 physical incubates, 9 virtual incubate and 1 YIP fellow. Figure 1A and Figure 1B represents the growth of the facility in terms of incubates over the 4 years and their phase of incubation. New applications and enquires for biotechnology based incubation has increased considerably and at present, the center is working on 100 percent occupancy in terms of incubation space.

The broad business verticals/laboratories include Analytical Biochemistry, Phytotechnology, Cell and molecular Biology and Bioprocess Engineering conducts industry relevant research, supports upstream, downstream and testing facility to incubates and contract research operations. BioNest has been able to collaborate with a number of industries to set up Corporate Research Operations (Table 1 & 2). The center also attracts students for curriculum based project training and pre-employment training (Table 2). The facility over the 4 years has witnessed growth in terms of number of incubates, creating employment opportunities, training students, and conducting industry based contract research projects. Incubates have also made progress in terms of patents, products launched and technology transfers (Table 4) (Figure 2).
Figure 1A: Number of incubates over the years

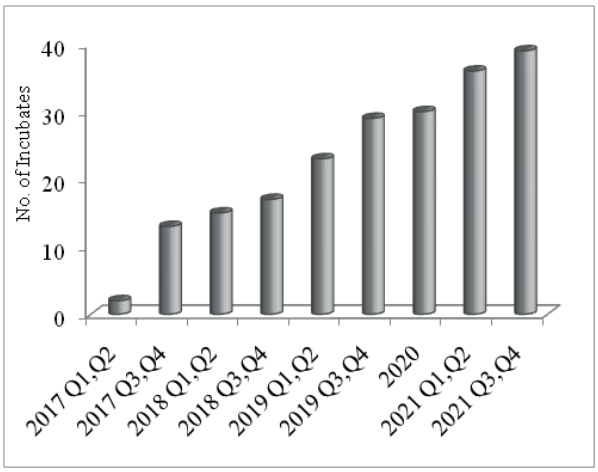


Figure 1B: Number of incubates in various phase of incubation

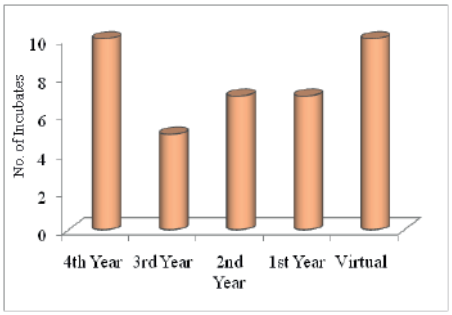


Table 1: CRO agreement with BioNest

Sr. No	Company	Project	Status
1.	M/s Western India Cashew Co, Kollam	Valorization of Almond Meal by Proteases	Completed
2.	M/s Scigenics (India) Pvt. Ltd	Demo process development center	Ongoing
3.	M/s Avisa Biotech Pvt Limited, Mumbai	Production of Melanin using Gliocephalotrichum simplex	Ongoing
4.	M/s Phytocom Pharmaceuticals Pvt. Ltd, Thiruvananthapuram	Production of Lactobacillus plantarum MTCC 1407 for formulation of aquatic feed probiotic	Ongoing
5.	M/s Zeus Biotech Pvt. Ltd., Mysore, India	Evaluating the levels of anabolic steroids in equine feed supplements	Ongoing

Table 2: Research Activities of BioNest

Industrial USP/DSP Scale-up:	
BioNest - Bioprocess development	Pneumocandin B0, Staurosporine, Echinocandin B, Methionine
Bioprocess development – RGCB projects	Production of Osmotin a phytodefense protein using recombinant E.Coli
Analytical Chemistry – Testing:	
Standardization and measurement of Biomolecules on LC-MS/MS	Serum Homocysteine and MMA Urolithin – in Anaerobic culture and Human faecal samples Steroids in various matrices
Standardization and measurement of Biomolecules on GC-FID	Tryptanthrin, Curcumin, Piperine, Pneumocandin B0, Staurosporine, Echinocandin B
COVID-19 testing	
Testing for Antimicrobial activity	3 Companies
Surface/Space/Gadget sterilization equipment testing	16 Companies

Table 3: Student training program

	Qualification	Students enrolled	students completed
Academic year (2018 – 2019)	B.Sc/M.Sc Biotechnology/ Biochemistry/Microbiology; B.Tech/M.Tech Biotechnology	59	59
Academic year (2019 – 2020)	B.Sc/M.Sc Biotechnology/ Biochemistry/Microbiology; B.Tech/M.Tech Biotechnology	27	18
Academic year (2020 – 2021)			
Project Training (3 months)	M.Sc/M.tech Biotechnology/ Microbiology/ Biochemistry	15	13
Project Training (6 months)	M.Sc/M.tech Biotechnology/ Microbiology	8	8
Internship-Training (3 months)	B.Sc/M.Sc Biotechnology/ Biochemistry/Microbiology B.Tech/M.Tech Biotechnology	3	3
Internship Training (6 months)	B.Sc/M.Sc Biotechnology/ Biochemistry/Microbiology B.Tech/M.Tech Biotechnology	3	3

Enclosed but discontinued due to COVID-19.

Table 4: Incubate Achievement

Patent	Incubate
Provisional patent number: 201941007160; 2019	M/s. Phytocom Pharmaceutical (P) Ltd
Provisional Patent Application No. 201841044627; Trademark registered – 4008443, 2019	M/s OmicsGen Life Sciences Pvt. Ltd
A process for production of water soluble melanin using a strain of the fungus gliocephalotrichum; Indi :IN2545/MUM/2008; PCT : WO2010064262A3	M/s. Avisa Biotech Pvt. Ltd
US Provisional Patent for applications of our Melanin for Radiation Protection; USSN 63/000, 273;Docket No. AVMK.003P; 2020	M/s. Avisa Biotech Pvt. Ltd
Provisional Patent for IoT enabled and pulse oximeter integrated high-flow nasal cannula (HFNC) oxygen therapy device, 202141019595; 2021	Heka Biomedicals Pvt. Ltd
Technology Transferred	
To Dettol a brand of © Reckitt Benckiser. 2020	M/s OmicsGen Life Sciences Pvt. Ltd
Seed Fund	
Production of Melanin using Gliocephalotrichum simplex utilisisng the fermentation and Bioprocess facility of BioNest. A 200,000 USD seed fund for application development from US base Biotech Accelerator Indiebio	M/s. Avisa Biotech Pvt. Ltd

Unnikrishnan V R

Dr. Uma Subramanian Unni

Jayakrishnan K S

Roshna R Nair

Front Row From Left: Charutha, Smitha S, Surya Rose K Johnson
Central Row From Left: Dr. Saji George, Joby Jose
Back Row From Left: Rajeev Reghunath, Manoj A, Dr. Pradipta Tokdar, Rijo George, Antony K P

Figure 2: Products developed by Incubates

BEATING THE PANDEMIC : COVID-19 INITIATIVES AT RGCB

In a quick response to the emergence of the COVID-19 pandemic, Rajiv Gandhi Centre for Biotechnology formed acore Corona virus Research & Intervention Group consisting of scientists from infectious disease biology, cell biology, immunology, diagnostics services, public health epidemiology and technology development group, who are currentlyinvolved in all research &development / service activities on Covid-19. A brief description of these activities and outcomes inspecific areas are highlighted below.

NEW DIAGNOSTICS DEVELOMENT

CoVID-19 diagnostic product developed by Sperogenx Biosciences, Bangalore and POCT Service, New Delhi, in Collaboration with RGCB

RGCB's industry academic collaboration brought us many advantages including deep tech scientific knowledge sharing and in-house product validation to support and improve various diagnostic products for the detection of CoVID 19. This could improve and deliver various diagnostic products as shown in the flyer at affordable price to the society. Under RGCB's support and guidance, following products were developed and launched into the market as molecular/classical products for CoVID-19 diagnosis

Q-line ER CoVID-19 RT-PCR kit:

We have developed Q-Line® Molecular nCoV-19 RT-PCR Kit is designed to detect Novel Coronavirus (nCoV-19) based on single tube multiplex real-time RT PCR (rRT-PCR) assays in respiratory and serum specimens. We have utilized CoVID-19 virus target genes such as E-gene, RdRP gene and internal control RNaseP (IPC) for CoVID-19 detection. The developed kit was validated and approved by National Institute of Virology-ICMR, Pune with the sensitivity of 98.7% and specificity of 100% for commercial use. As far as now, we have sold more than 1.5M test kits to CoVID-19 screening centers both government organization as well as private hospitals.

In order to improve the CoVID-19 screening accuracy, we have developed highly sensitive three gene RT-PCR kit which uses CoVID-19 virus specific target genes such E gene, RdRP gene and N gene that improves the testing sensitivity and specificity. Currently, our three gene kit is under the in-house validation and in the process of submitting to ICMR approval for commercial use.

Q-line Viral RNA extraction kit:

We have developed Viral RNA extraction method using silica column chemistry for the isolation of highly pure RNA from CoVID-19 patient sample that will be used for downstream process such as RT-PCR analysis for screening the CoVID-19. The silica column-based RNA extraction system is lysis enzyme proteinase-K free and it can be performed in room temperature that will help and increase the users experience which is not possible in other extraction methods available in the market. Further, we have designed a lysis and working reagents specific to the CoVID-19 viral RNA isolation from the nasal-swap samples and showed better viral RNA quality and quantity as compared to the other available extraction methods. The developed kit was in-house validated at RGCB and performed well as compared to gold standard methods. Further, our viral RNA isolation kit was validated and approved by NIV-ICMR with 98% analytical performance for commercial use.

DIAGNSOTICSERVICES

Laboratory Medicine & Molecular Diagnostics (LMMD) is an ICMR Grade 1 National Virology Network laboratory, operating under DBT since 2011. LMMD is accredited by both NABL and ILAC and certified by NABH since 2016. LMMD is currently performing over 65 viral diagnostics, all bacterial, fungal, and parasitic infection diagnosis using molecular diagnostic methods. The PCR based testing has a speedy turn-around time of under 8 hours, which goes a long way in early diagnosis.

During the current nation-wide crisis of COVID-19, LMMD started testing extensively for COVID-19 on 27th March 2020. The department has been accepting samples every day without holiday and operates 24x7 for the past seven months. LMMD has a declared testing capacity of 2000 samples per day. During peak COVID testing times in July-August, the department has processed over 2500 samples per day.

LMMD was of support to the State by analyzing 3 Districts samples in the beginning, when the State machinery was not equipped. Currently, LMMD caters to the need of the biggest district of Kerala State daily and takes in surplus samples from other Districts in times of need. LMMD also fulfills a National Institute's social relevance by performing COVID analysis of staff from various Governmental and private institutions on demand.

KIT VALIDATION AND ANTIVIRAL TESTING

RGCB is one of the DBT and ICMR approved centres to perform test kit validation for VTM, RNA isolation kits, PCR kits, LAMP assay kits, Rapid antigen, and Rapid antibody test kits. The kits submitted by commerical agenices are validated, and results are sent to ICMR for further decision on the kits' usability for public use. In addition, RGCB supports industries and academia with innovative SARS CoV-2 pseudovirion assay for antiviral testing. So far RGCB has tested morethan 200 samplesusing a unique pseudovirion assay developed at RGCB.

COVID-RELATED OUTREACHACTIVITIES AND OTHER RESPOSNIBILITES BY RGCB

There is a separate public outreach program carried out by RGCB for COVID-19, where RGCB infectious disease group and LMMD are invovled. Faculty scientists from these divisions participated in several TV discussions and radio programmes as a panelists for COVID-19 awareness for the public, both in National television and privately owned television channels. One of our infectious disease scientists (Dr. E.Sreekumar) is a memebr of the Kerala state Government expert group on COVID-19 involved in providing scientific inputs to the Governemnt for COVID-management in the state.In additon, RGCB LMMD and medical laboratory services (MLS) staff carries out COVID-19 awareness campaigns and sample collection for state local bodies. They are also involved in regular monitoring of our own staff and students for COVID detection.RGCB Jagathy and BIC campuses conducted rapid antigen screening tests for all asymptomatic staff as a preventive measure to contain the spread of novel coronavirus.

RESEARCH AND DEVELOPMENT

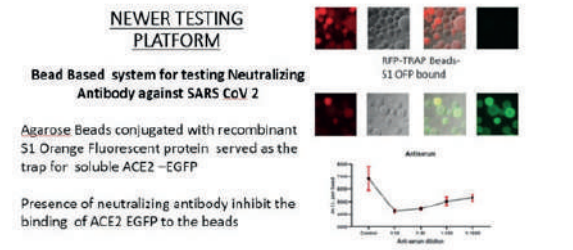
Molecular Determinants for Virus-Host Interaction

SARS-CoV-2, the causative agent of COVID-19 pandemic is an RNA virus prone to mutations. Formation of a stable binding interface between the Spike (S) protein Receptor Binding Domain (RBD) of SARS-CoV-2 and Angiotensin-Converting Enzyme 2 (ACE2) of host actuates viral entry. Using a high fidelity bioinformatics pipeline, we analysed 31,403 SARS-CoV-2 genomes across the globe, and identified 444 non-synonymous mutations that cause 49 distinct amino acid substitutions in the RBD. Molecular phylogenetic analysis suggested independent emergence of these RBD mutants during pandemic. We identified that interfacial interaction involving amino acid residues N487 and G496 on either ends of the binding scaffold are indispensable to anchor RBD and are well conserved in all SARS-like corona viruses. All other interactions appear to be required to locally remodel binding interface with varying affinities and thus may decide extent of viral transmission and disease outcome. COVID-19, so far the worst hit pandemic to mankind, started in January 2020 and is still prevailing globally. Our study identified key molecular arrangements in RBD-ACE2 interface that help virus to tolerate mutations and prevail.

Publication : Nelson-Sathi S, Umasankar PK, Sreekumar E, Radhakrishnan Nair R, Joseph I, Nori SRC, Philip JS, Prasad R, Navyasree KV, Ramesh S, Pillai H, Ghosh S, Santosh Kumar TR and Pillai MR. 2020. Mutational landscape and in silico structure models of SARS-CoV-2 Spike Receptor Binding Domain reveal key molecular determinants for virus-host interaction. bioRxiv. doi: 10.1101/2020.05.02.071811.

A bead based assay kit for rapid detection of COVID -19 neutralizing antibody

Quantitative determination of neutralizing antibodies against SARS-CoV-2 viral protein is of paramount importance in immunodiagnosis, vaccine efficacy testing and convalescent plasma therapy. Scientist from Rajiv Gandhi Centre for Biotechnology have developed bead based assays that utilizes recombinant protein immobilization on beads with affinity tag or nanobody. Nanobody mediated bead capture of orange fluorescent protein tagged Spike (SI) protein of SARS-CoV-2 showed rapid binding of soluble recombinant EGFP ACE-2 that is inhibited by neutralizing antibody

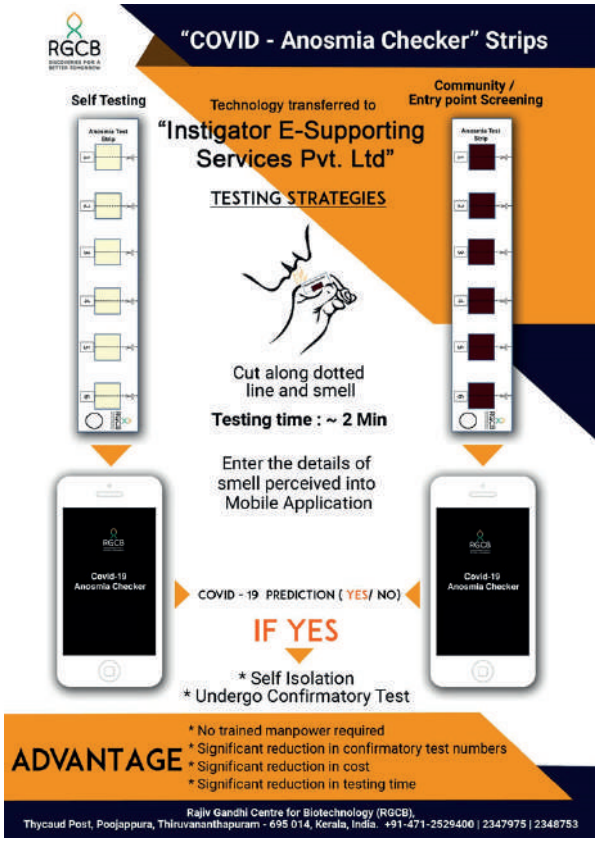


A more simplified system utilized recombinant RBD bead to trap soluble ACE2 EGFP. Both the assays are rapid, cost effective, sensitive and adaptable for multiple detection platforms such as fluorescence readers, microscopy and HTS imaging systems.

RGCB has transferred the technology of "COVID-Anosmia checker"

RGCB has transferred the technology of "COVID-Anosmia checker", a tool for Covid-19/olfactory dysfunction screening, developed by Dr. Jackson James, Scientist F, RGCB to INSTIGATOR e-SUPPORTING SERVICES PRIVATE LTD, Thiruvananthapuram. Loss of smell is reported as a major symptom of COVID-19. The odor strip, "COVID-Anosmia checker", is spotted with

gradients of coffee and lemon grass oil and can be used for mass screening of COVID-19. No special training is required to use this tool.



GENERAL RESOURCES FOR COVID RESEARCH

ACE2 HA Stable cells for SARS CoV2 Research

Human Angiotensin Converting Enzyme 2 is the natural receptor for SARS CoV-2 to enter host cells. Since most established cell lines lacks this receptor , cells expressing human ACE2 are on high demand for the maintenance of live virus and SARS CoV2 pseudovirions.To support his RGCB has developed the following cell lines and validated their utility using pseuodvirion assay and fluorescent RBD & S1 protein. These cell lines are currently available from Layog Life Sciences Pvt astart-up company incubated at RGCB BioNest.

1. HEK293 Stably expressing human ACE2 HA
2. HEK 293 stably expressing human ACE2 –myc
3. DLD cells stably expressing h ACE2

KEY ONGOING RESEARCH PROGRAMMES

RGCB COVID-research team has initiated major research programs on COVID-19. A few of them have already been approved by external funding agencies and others are under consideration for funding. One such program is on 'Development of a rapid and reliable in vitro screening platform based on fluorescent reporter knock-in targeting host cell IFITM gene to identify phytochemical immunomodulators against SARS-CoV-2'. Another approved programme is on " "New Therapeutics against SARS Cov2: Analyzing small molecule chemical libraries by establishing targeted cell-based assays for inhibitors of viral entry and viral protease." Apart from these, we have submitted R&D proposals on new SARS CoV-2 antibody engineering approaches; novel antibody testing platforms and also clinical collaborative programmes on understanding host-cellular responses to SARS CoV-2. Our public health epidemiology scientists have also submitted requests to the state governemnt for initating projects by being part of the state level surveillance activities with respect to SARS CoV-2 immunity assessment in response to natural infection or vaccination.

BSL3 plus FACILITY FOR COVID 19 research @ RGCB

Our major handicap initiating some key projects realted to COVID in the current pandemic was not having a BSL-3 facility to hanlde live virus. However, RGCB with special support from DBT is establishing a dedicated BSL3 plus facility for COVID- 19 research and Development activities. A fully equipped, pre-fabricated, modular facility is expected to be commissioned within 4 months at RGCB. This facility will support all live virus-dependent research and testing activities as per the regulatory requirements and will be a major boost to the R&D activities on all BSL-3 pathogens including SARS CoV-2 in the region.

NURTURING THE YOUNG MINDS TOWARDS FUTURE BIOTECHNOLOGIST AND ENTREPRENEURS RGCB'S FLAGSHIP M.Sc PROGRAM IN BIOTECHNOLOGY

RGCB launched a highly innovative M.Sc Biotechnology Program with three unique specializations - Disease Biology, Molecular Diagnostics & DNA Profiling and Genetic Engineering in August 2019. The M.Sc program is affiliated to the Regional Centre for Biotechnology (RCB) an "Institution of National Importance" providing education, training and research established by the Department of Biotechnology, Government of India under the auspices of the UNESCO, a specialized agency of the United Nations (UN) based in Paris. Dr. Renu Swarup, Secretary to Government of India, Department of Biotechnology, India launched the program and welcomed forty one new students of first year M.Sc along with Shri B Anand, IAS, Additional Secretary; Dr. Sudhanshu Vrati, Executive Director, RCB and Professor M Radhakrishna Pillai, Director RGCB.

The forty one students were selected from all over the country after an entrance examination conducted in 17 centers across India. The M.Sc program at RGCB is unique as it covers the fundamentals of Biotechnology fundamentals of Biotechnology, while focusing on laboratory exercises and industrial as well as research applications. The students will be introduced to concepts of "Enterprise and Entrepreneurship". This allows students who wish for a career beyond the laboratory in an existing biotechnology industry or for those who dream of starting a new biotechnology enterprise. Students get trained in a real business & technology development bio-incubator where startup companies function.

Among the first batch of M.Sc, 2019-2021, 2 received CSIR-JRF, 2 qualified CISR-NET-LS, 2 received Khorana Fellowship, 1 received INSA fellowship. Almost all of them qualified GATE 2021. After the completion of the course, 3 students have been enrolled in Ph.D program at University of Chicago, Illinois, University of Liverpool and Max Planck Research School-IMPRS while one student each has been selected for the NCBS, NBRC and ACTREC Ph.D program. The students completed their 2 years curriculum on 30th July 2021 and were officially given a send off on 1st August 2021.

The second batch of RGCB M.Sc students were admitted through the basis of marks scored in GAT-B exam conducted by RCB. Top rank students enrolled into the program, but only 31 students were selected for the 2020 batch. These students are presently in their 2nd semester.

Professor Chandrabhas Narayana, Director RGCB is addressing the gathering during the farewell function

Ms. Athira Menon received the best outgoing student award (2019-21 batch) from the RGCB director in presence of Dr. Santhoshkumar T R and Dr. Soniya E V. The award consists of Rs.10,000 cash and a certificate.

RGCB M.Sc Biotechnology Batch (2020-2022) with tutors and supporting staff

Back Row From Left: Swarnabha Chowdhury, Ashik Francis, Victor Samuel, Atriya Mazumder, Ratulananda Bhadury, Sahil Md, Jaskirat Singh Sandhu, Irfan Shafi Malik, Arvind Jangra, Akshit Jain, Aswani Kumar, Yetcheria Raja Arvind, Yashasvi Sharma

Central Row From Left: Kartik Rangari, Ajay Pradhan, Aman Grewal, Lakshay Garg, Diksha Shandilya, Priyanshu Priya, Saumya S K, Aakriti Langeh, Andhela Leela Sairam, Thene Harikrishna, Vandana Sharma, Vicky Kumar, Anandhu B.

Front Row From Left: Sulagna Adhikary, Neha Bera, Ashmita Dutta, Bhawna Kangotra, Baishali Chakraborty, Sanjai D, Dr. Mahesh Krishna, Dr. Lekshmy Srinivas, Dr. Rajeswari G, Dr. Aparna Shankar, Smithadevi S, Aleena Marian Shaji, Archana Praveen, Sindhu V

AS WE BID ADIEU....

During this period three of our esteemed members were retired and due to COVID-19 pandemic, we could not arrange a formal farewell function.

Dr. Santhosh Kumar K retired as Scientist G and Dean after 24 years of service at RGCB. He joined RGCB in 1996 after completing his Ph.D and played major roles in establishing the chemical biology R&D program and a key role in RGCB's journey from a state institute to a national institute. He also made an outstanding contribution to M.Sc program and guided several students in their Ph.D program. We wish him the very best for the future and thank him for all his contributions over two decades.

Mr. Jeevan Chacko retired as Senior Chief Manager (Purchase) joined RGCB in 1997 and was managing the important department of Stores and Purchases. He was the brain behind finalizing the purchase procedures at RGCB which have helped the institute to rise to where it is today. We greatly acknowledge his contribution to our overall purchase procedures, strategy, and daily operations of the division. We wish him the very best in his future endeavors

Mrs. Lathika K retired as Senior librarian, joined RGCB in 1995. She was instrumental in establishing a central library and currently is a depository of a valuable collection of many sought after international books and journals on life sciences. We sincerely acknowledge the contribution in transforming the RGCB library into a knowledge resource center with state of art facilities. The Nobel laureate Dr. James D Watson visited the central library during her term and presented autographed copy of his famous book “The Double Helix”. We wish her the very best for the future.

SOCIAL INTERVENTION ACTIVITIES AT RGCB

TECHNOLOGY INTERVENTIONS FOR TRIBAL HERITAGE RESILIENCE OF KERALA

Project Investigators:

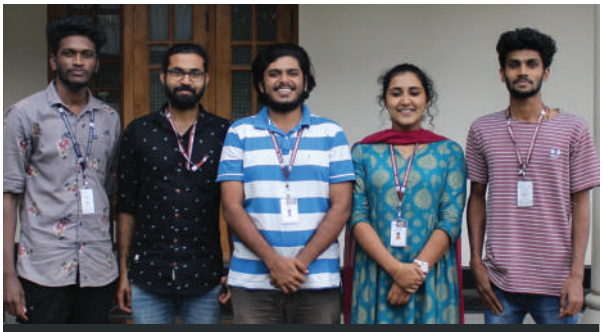
- Professor Chandrabhas Narayana, Director, RGCB
- Dr. Soniya E V, Scientist G & Dean
- Dr. Anish N P, Scientist C & Assistant Registrar
- Dr. Archana S, Veterinary Medical Officer

Department of Science and Technology's SHRI program has supported us to conduct studies on Tribal Heritage of Kerala. We have achieved significant progress to document the traditional knowledge and to identify and mobilize the tribal communities in the two targeted districts, Idukki and Wayanad. Ethno-veterinary formulation for wound healing has been successfully evaluated using in vitro, in silico and in vivo models. We have created 9 tribal community groups (Self Help Groups/Societies) for establishing various social enterprises for the empowerment of tribal communities and also to protect their rich heritage. Social Enterprises on Traditional Pepper Nursery (with 26 varieties) by Mala Arayan Tribes, two Bamboo Craft Units by Urali tribes at Idukki and Field Distillation of Essential Oils by Ulladan tribal community at Idukki, Kurichya and Paniya communities at Wayanad were established under the project. Regarding the traditional paddy varieties, as of now, we have documented 34 landraces and collected samples for genetic and nutritional analysis which are progressing in the lab. Moreover, we have distributed seeds of 19 traditional paddy varieties to establish around 4 hectares of field gene bank in various parts of Wayanad district.

OUTREACH ACTIVITIES

- DBT- RGCB has celebrated the National Science Day 2021 with students of tribal colonies in Idukki and Wayanad. The team of scientists visited the tribal colonies and demonstrated various experiments for the students to inculcate scientific temperament among students.
- "Azadi Ka Amrit Mahotsav" is an initiative of the Government of India to celebrate and commemorate 75 years of independence of progressive India and the glorious history of its people, culture and achievements. As part of the programme, DBT-RGCB is conducting various programmes like popular lecture series etc. for the public (https://www.rgcb.res.in/india75.php).

WAYANAD TEAM
From Left: Arun Rajagopal, Roshni S, Syam Sankaren, Abin Abraham



IDUKKI TEAM
From Left: Rajesh K T, Harikrishnan P, Mohsin Nayeem, Anu Theresa Antony, Jishnu Janardhanan

THIRUVANANTHAPURAM TEAM
From Left: Dr. Archana S, Dr. Soniya E V, Aparna M, Dr. Anish N P, Kattupalli Divya, Dr. Asha S, Dr. Aneeshkumar A L
Along with Director RGCB Professor Chandrabhas Narayana

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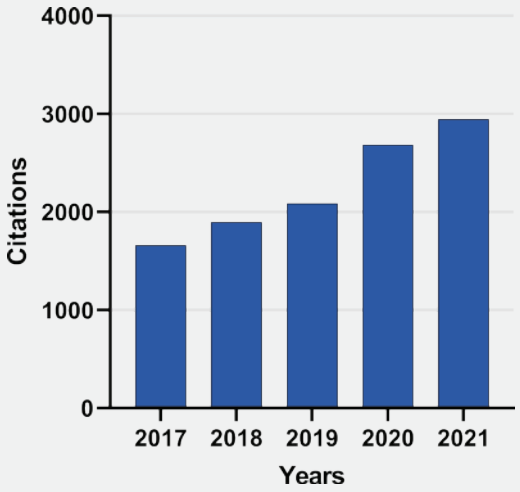


EXTRAMURAL PROJECTS ACTIVE BETWEEN APRIL 2020 AND MARCH 31, 2021

ABDUL JALEEL

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Metabolic Profiling of Normal Healthy people in Kerala: Impact of Family History of Diabetes	DBT	PI	2017-2021
2	Genome India: cataloguing the genetic variations in Indians	DBT	Co-PI	2020-2023
3	Does maternal hypercholesterolemia influence cholesterol transport mechanisms across the placenta during gestation?	ICMR	Co-PI	2019-2022

ANANDA MUKHERJEE

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Studies on noncanonical role of tumor suppressor PTEN in endometrial adenocarcinoma	DBT-Ramalingaswami fellowship	PI	2018-2022
2	Domain-specific role of tumor suppressor PTEN in genomic stability: A systematic approach	SERB	PI	2019-2022

ANANTHALAKSHMY SUNDARARAMAN

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Role of RhoGTPases in Intracellular Trafficking of Mitochondria-Derived Vesicles (MDVs) and Angiogenesis	DBT- Ramalingaswami Fellowship	PI	2020-2025

ANI V DAS

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Deciphering the regulation of Piwil1 in cancer stem cells	SERB	PI	2021-2024

EXTRAMURAL PROJECTS ACTIVE BETWEEN APRIL 2020 AND MARCH 31, 2021

ARUMUGAM RAJAVELU

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Mechanisms and functions of methyl-binding proteins in virulence genes expression of the human malaria parasite.	DBT	PI	2021-2024
2	Elucidating the functions of CHROMO domains - H3K9me3 interactions in Plasmodium parasites with special focus on virulence genes.	SERB	PI	2021-2024
3	Study the aberrant functions of altered metabolic pathway enzymes in artemisinin drug resistant Plasmodium falciparum.	ICMR	PI	2020-2023

DEBASREE DUTTA

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Histone chaperone HIRA as a novel modulator in dictating differentiation vs. Proliferation	SERB	PI	2017-2021
2	Cellular transition in development and disease-an epigenetic perspective	DBT	PI	2017-2020
3	Evaluation of histone chaperone APLF as a novel biomarker in triple negative breast cancer	DBT	PI	2018-2023
4	RGCB Interdisciplinary Life Science Program for Research Based Learning	DBT- BUILDER	Co-PI	2021-2026

DEVASENA ANANTHARAMAN

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Human papillomavirus (HPV)-related oropharyngeal cancer burden and the natural history of oral HPV infections: an Indian perspective	DBT/ Wellcome Trust	PI	2019-2024
2	Biomarkers of oral cancer risk prediction	DBT Glue Grant	PI	2018-2023
3	HPV genotyping for efficacy testing of generic qHPV vaccine development: Serum Institute of India study	Serum Institute of India	PI	2019-2022

EXTRAMURAL PROJECTS ACTIVE BETWEEN APRIL 2020 AND MARCH 31, 2021

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
4	Accurate and satisfactory analysis of all high risk HPV types and some of the low risks including HPV 6 and 11 antibody titers for the 2-versus 3 dose HPV vaccination clinical trial in India – Follow-up study	IARC	PI	2020-2025
5	Evaluation of 10-year long term immune response to single dose of quadrivalent HPV vaccine	IARC	PI	2019-2021

GEORGE THOMAS

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Delineation and characterization of defense signaling pathways and genetic regulation of induced systemic resistance in Zingiber-Pythium pathosystems.	DBT	PI	2018 -2021

HARIKUMAR K B

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	A mechanistic evaluation of Chiravilvadi Kashayam in colitis associated colorectal cancer	SERB	PI	2018-2021
2	Understanding the role of sphingosine kinase isoforms in systemic lupus erythematosus (SLE)	CSIR	PI	2018-2021
3	Mex3C: a novel tumor suppressor in colorectal cancer	ICMR	PI	2018-2021

IYPE JOSEPH

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	(a) Impact of Climate Change on Human Health interface and studies on climate change and air pollution and its effect on respiratory health at Kavaratti Island. (b) Epidemiology, Clinical aspects and Management of Leptospirosis at Kavaratti Island, Lakshadweep.	NISCAIR, CSIR, Delhi	PI	2016-2019

EXTRAMURAL PROJECTS ACTIVE BETWEEN APRIL 2020 AND MARCH 31, 2021

JACKSON JAMES

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Regulation of stemness by Pleiotropic Hes-1 expression in neuroblastoma	National Bioscience Award, DBT	PI	2018-2021
2	Development of a low-cost Anosmia screening tool to mass screen asymptomatic COVID-19 carriers	DST	PI	2020-2021
3	Expression of Notch independent Hes-1 (NIHes-1) specifically in ES derived organoids representing developing neocortex: Understanding its functional significance.	DBT	PI	2018- 2020

JOHN B JOHNSON

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Understanding measles vaccine failure (and success) in Southern India.	NIH, USA	Co-PI	2020-2021

KARTHIK SUBRAMANIAN

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Disarming bacterial pathogens using novel peptides that target pore-forming toxins: from in silico to in vivo	DST	PI	2021-2026

KARTHIKA RAJEEVE

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	AUFF (Aarhus Universitets Forskningsfond)	AUFF	PI	2020
2	Anna og Dagny Hjerrilds Fond	Anna og Dagny Hjerrilds Foundation	PI	2020
3	Novo Nordisk Funding	Novo Nordisk foundation	PI	2020
4	SERB-POWER Fellowship	SERB	PI	2021-2024

EXTRAMURAL PROJECTS ACTIVE BETWEEN APRIL 2020 AND MARCH 31, 2021

MAHENDRAN K R

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Antibiotic translocation through porins in Gram-positive bacteria at the single-molecule level	DBT- Ramalingaswami fellowship	PI	2016-2021
2	Single-molecule biosensing with hetero-oligomeric protein nanopores.	Early career research award, SERB	PI	2018-2021
3	Structure determination and targeting of ubiquitously expressed membrane integrated form of chloride intracellular channels (CLICs) for discovery of small molecular anti-cancer therapeutics	Multi-institutional grant, Centre for excellence in membrane biology, DBT	PI	2019-2021
4	Structural Assembly of Functional Transmembrane peptide nanopores: From Synthesis to Single-Molecule Sensing	DBT	PI	2021-2024
5	Merck award travel grant.	Merck	PI	2020-2021

MALINI LALORAYA

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Investigating the role of superoxide in regulating the major events during embryo implantation.	SERB	PI	2020-2023
2	Molecular Analysis of Circadian Rhythm in Polycystic Ovarian Syndrome Patients.	DBT	PI	2020-2023
3	Ascertaining the causes of low tregs in polycystic ovarian syndrome patients.	ICMR	PI	2021-2024

MANJULA S

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Transcriptome analysis and characterization of key metabolic and hormone signaling pathway genes in Piper nigrum in response to defense elicitors	DBT	PI	2018-2021
2	Identification and functional characterization of Phytophthora capsici effectors specific to 'quick wilt' disease in black pepper (Piper nigrum)	DBT	PI	2018-2021

EXTRAMURAL PROJECTS ACTIVE BETWEEN APRIL 2020 AND MARCH 31, 2021

MOINAK BANERJEE

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Evaluating pharmaco-epigenomic response of antipsychotic drug	SERB	PI	2018-2021
2	Genetics of complex pediatric epilepsy syndromes: electro-clinico-imaging based genotype-phenotype correlations in an Indian cohort.	ICMR	Co-PI	2019-2024

OMKUMAR R V

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Investigations on the role of the biochemical bistable switch in learning and memory in vivo	SERB	PI	2019-2022

PRADEEP KUMAR G

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Inter-relationship between polymorphisms in four obesity genes, their expression and its correlation with infertility and obesity in subjects from Kerala	KSCSTE	PI	2016-2020
2	Transdifferentiation of Spermatogonial Stem Cells (SSC) into somatic cell lineages via Embryonic Stem Cell (ES) like intermediaries	DBT	PI	2017-2020
3	Evaluation of the role of AIRE in germ cell development and differentiation	CSIR	PI	2018-2021
4	Mapping of CNNM1 expression during gonocyte development in mouse	SERB	PI	2021-2023
5	Prospective study on the screening of the expression of an array of sperm proteins and its correlation with assisted reproductive technology outcome	ICMR	PI	2021-2024

EXTRAMURAL PROJECTS ACTIVE BETWEEN APRIL 2020 AND MARCH 31, 2021

PRIYA SRINIVAS

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Targeting Cancer associated fibroblasts for Metastasis Inhibition in BRCA1 defective cancer	SERB	PI	2018-2021
2	Identification of Xenoestrogen indused spontaneous mutations and changes in promoter methylation status in the Cancer causing genes BRCA1, BRACA2 and p53 in Breast, Ovarian, Prostrate and Pancreatic Cancer	CSIR	PI	2020-2023

RADHIKA NAIR

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Deciphering breast cancer metastasis	DST	PI	2015-2020

RAKESH S LAISHRAM

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Alternative polyadenylation in gene expression – implications in cardiovascular diseases	SERB	PI	2020-2025
2	Star-PAP control of 3'-end processing and alternative polyadenylation in cancer progression	SERB	PI	2020-2023

RAM MOHAN RAM KUMAR

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Therapeutic microRNA delivery mediated by exosomes targeting cervical cancer metastases in the 3D and in vivo environments	DBT	PI	2020-2025

EXTRAMURAL PROJECTS ACTIVE BETWEEN APRIL 2020 AND MARCH 31, 2021

RASHMI MISHRA

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	How galectin-3 drives pressure overload mediated cardiac hypertrophy and heart failure	ICMR	PI	2020-2023
2	Identification of the role of redox signaling pathways in the mechanobiology of glioblastoma multiforme.	DBT	PI	2018-2021

RUBY JOHN ANTO

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Evaluation and in vivo validation of tryptanthrin analogues as potent lead molecules for malignant melanoma chemotherapy	CSIR	PI	2020-2023
2	In vitro and in vivo validation of the efficacy of the synergistic combination of curcumin and 5-FU in exterminating breast cancer stem-cell like population using orthotopic breast xenograft model in NOD-SCID, gamma mice.	The Spices Board of India	PI	2020-2023

SABU THOMAS

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Development of probiotic therapy for enhancing urolithin production by using bacterial flora of human origin	SERB	PI	2018-2021
2	A study on the antimicrobial resistance pattern in Kerala	Dept. of Health and Family Welfare, Govt of Kerala	Co-PI	2019-2021

SANIL GEORGE

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Strategies for enhancing the biological activity of novel peptides identified from an endemic frog of the Western Ghats	DST	PI	2019-2021

EXTRAMURAL PROJECTS ACTIVE BETWEEN APRIL 2020 AND MARCH 31, 2021

SANTANU CHATTOPADHYAY

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Helicobacter pylori infection in Sikkim and possible use of probiotics isolated from ethnic fermented foods of Sikkim against H. pylori	DBT	PI	2018-2021

SANTHOSHKUMAR T R

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Establishment of fast life time imaging facility	DBT	PI	2019-2023
2	Design and Characterization of peptide-based cell targeting domains with live cell and animal imaging methods	DBT	PI	2019-2022

SARA JONES

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Understanding measles vaccine failure (and success) in southern Indian population	NIH, USA	Investigator	2017-2022

SHIJULAL NELSON-SATHI

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Major Gene Influxes in Microbial Genome Evolution	DST-INSPIRE	PI	2016-2021
2	The Structure and Evolution of Environmental Resistomes	DST	PI	2018-2021
3	Phylogenomic analysis of endosymbiotic genes in eukaryotic genomes	Heinrich Heine University, Germany	PI	2018-2021
4	Genome India : Cataloging Genetic Variations in Indians	DBT	Co-I	2020-2022
5	New Therapeutics against SARS Cov2: analyzing small molecule chemical libraries by establishing targeted cell-based assays for inhibitors of viral entry & and viral protease	DBT	Co-PI	2020-2021

EXTRAMURAL PROJECTS ACTIVE BETWEEN APRIL 2020 AND MARCH 31, 2021

SONIYA E V

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Genome India: Cataloguing the Genetic Variation in Indians.	DBT	PI	2020
2	Development of a disease management strategy against Phytophthora capsici utilizing an effective bio control agent and green synthesized silver nanoparticles from black pepper	DST	PI	2019
3	Centre for Excellence in Inclusive Technology Interventions for Tribal Heritage Resilience of Kerala.	DST	PI	2019-2021

SREEJA S

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Study of progesterone receptor foci and progesterone signalling in the breast cancer cells	DBT	PI	2019-2022
2	Development of probiotic therapy for enhancing urolithin production by using bacterial flora of human origin	SERB	Co-PI	2018-2021

SREEKUMAR E

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Elucidation of the role of endothelial cell signaling pathways in vascular permeability modulation in Dengue virus infection	ICMR	PI	2017-2020
2	Therapeutic targeting endothelial kinases to abrogate Dengue virus-induced vascular permeability	ICMR	PI	2019-2022
3	Design and Synthesis of Novel Iminosugar variants and their cationic amphiphiles as antiviral therapeutics against Dengue virus (DENV)	DBT	PI	2020- 2023
4	New Therapeutics against SARS Cov2: Analyzing small molecule chemical libraries by establishing targeted cell-based assays for inhibitors of viral entry & and viral protease	DBT	PI	2020 -2021

EXTRAMURAL PROJECTS ACTIVE BETWEEN APRIL 2020 AND MARCH 31, 2021

SUMI S

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Piezo-KLF2 axis in endothelial dysfunction and venous wall remodelling in varicose veins	SERB	PI	2021-2024
2	Do epigenetic alterations in shear stress regulatory genes induce endothelial mesenchymal transition in patients with cerebral arteriovenous malformations?	ICMR	PI	2019-2022
3	Do epigenetic alterations in shear stress regulatory genes induce endothelial mesenchymal transition in patients with cerebral arteriovenous malformations?	KSCSTE-YIPB grant	PI	2018-2021
4	Molecular Pathogenesis of varicose veins	Dr. N Radhakrishnan fund for Venous Research	PI	2018-2023

SUPARNA SENGUPTA

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Analysis of fodrin association with gamma-tubulin complex, the microtubule organizer	DST	PI	2017- 2020
2	Investigating the Nanomaterial Based Exosome Sensor for Cancer Prognostic: An Approach towards Liquid Biopsy for Cancer	DBT	PI	2017- 2021
3	Exploration of the role of fodrin, a protein required in functional microrubule organization, in cancer and apoptosis	ICMR	PI	2021- 2024

SURYA RAMACHANDRAN

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Does maternal hypercholesterolemia influence cholesterol transport mechanisms across the placenta during gestation?	ICMR	PI	2019-2022
2	Does Cyclophilin A, an Immunophilin under High Glucose Conditions Regulate Efferocytosis in Atherosclerotic Lesions?	KSCSTE	PI	2018-2021

EXTRAMURAL PROJECTS ACTIVE BETWEEN APRIL 2020 AND MARCH 31, 2021

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
3	Screening lead molecules identified by structure-based rational drug design methods against cytochrome b5 reductase 3 and dopamine beta hydroxylase in spontaneously hypertensive rat models for antihypertensive effects	DBT	Co-PI	2017-2020
4	Cyclophilin A and Efferocytosis in Vascular Disease Associated with Type 2 Diabetes	Madras Medical Mission, Chennai	PI	2017-2020
5	RGCB-SAgenome program on Personalized Medicine	SAgenomics Private Limited	PI	2020-2023

TESSY THOMAS MALIEKAL

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Virtual National Oral Cancer Institute	DBT	PI	2018-2022

UMASANKAR P K

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Endocytic modulation of BMP signaling: deciphering mechanistic insights into health and disease	DBT- Ramalingaswami Fellowship	PI	2016-2021
2	Uncovering mechanisms to remodel cholesterol landscape in cancer cells	SERB	PI	2018-2021
3	New Therapeutics against SARS CoV-2: Analyzing small molecule chemical libraries by establishing targeted cell-based assays for inhibitors of viral entry and viral protease.	DBT	Co-PI	2021-2022

VINOD KUMAR G S

No.	Name of Grant	Funding Agency	PI or Co-PI	Year
1	Development of a novel three dimensional self aggregating peptide fiber as an implant for brain tumors	SERB	PI	2018-2021
2	Development of cotton-like bioadhesive antimicrobial peptide based hydrogel patches for wound healing	ICMR	PI	2019-2020

PATENTS APPLIED AND GRANTED

ASHA NAIR S

The synthesis and application of 2,6, diiodo-aza -Bodipy Biotin conjugates DPR2a and DPR2b as theranostic agents.

Ref N0: QSP/Mgs/01/Pat 2020
New patent application: 0188NF2020

ASHA V V

Title of Invention: Carbon Quantum dots can act as the powerful wound healant. Application number-201941025609A.Publication date .01/01/2021
Name of the Inventor: Dr. Praseetha P K, Dr. Prakash Vincent S G, Dr. Asha V V

KARTHIK SUBRAMANIAN

Patent filed (2020):Title: Mannose Receptor-Derived Peptides For Treatment Of Pneumococcal Disease. Authors: Birgittahenriquesnormark, Karthik Subramanian, Georgiossotiriou,
Patent number: 2050805-7
Date of filing: 30/06/2020
Filing country: Swede

MAHENDRAN K R

A complete patent application (Synthetic pores) filed: India patent application no: 201941014383 from RGCB
Manjula S
Patent filed
Indian patent, No. 202041015632
PCT- PCT/IN2021/050354
Title: An antifungal synthetic peptide derived from osmotin protein

OMKUMAR R V

Indian patent No.: 351849,
Date of granting: November 20, 2021
Title: A method of detecting and quantifying the calcium -conducting activity of calcium channel proteins
Inventors: Omkumar R V, Mathew Steephan, Soumya Paul, Arunkumar R C, Mayadevi M.

RUBY JOHN ANTO

Title: Uttroside B and Derivatives Thereof as Therapeutics for Hepatocellular Carcinoma

No.	Country	Patent Application Number	Patent Application filed on	Current Status	Patent Number Granted	Date of Grant
1	USA	16/304630 [WIPO patentscope number US20190160088]	November 26, 2018	Notice of Allowance Issued dated 27th October, 2020		
2	USA	17/161,928 [US20210154220]	January 29, 2021	Published		
3	Canada	WIPO patentscope number 3,026,426	November 28, 2018	Granted	3,026,426	April 13, 2021
4	European patent office	WIPO patentscope number- EP 3463382	December 21, 2018	Examination is in progress		
5	China	WIPO patentscope number CN109496153	May 27, 2017	Published the application		
6	Korea	WIPO patentscope number KR1020190008323	May 27, 2017	Notice of Allowance Issued	Granted	June 29, 2021
7	Japan	WIPO patentscope number JP2019520425	May 27, 2017	Granted	Granted 6830153	January 27, 2021

SARASWATI NAYAR

PCT/IN2020/050888, PCT, 17th October 2020 Method for increasing biomass of photosynthetic organism by extending its life in culture

SURYA RAMACHANDRAN

NOVEL ANTI-HYPERTENSIVE CARDIOPROTECTIVE COMPOSITION COMPRISING OF DISPIRO[1H-PERIMIDINE-2(3H),2''(3''H)-[1H]PERIMIDINE
Patent number: 202111026998
Publication date:2021/6/17
Patent office: IN

TESSY THOMAS MALIEKAL

Apoptosis Inducing Peptide (SSTP1)"; 202041016382 provisional patent, India

VINOD KUMAR G S

- Indian Patent Application No. 202041024450 "SYNTHETIC HYBRID PEPTIDE FOR CHRONIC WOUND HEALING AND SKIN REGENERATION" Vinod Kumar G S & Nanditha C K (filed on June 2020)

- Indian Patent Application No. 202041024449 "THERMOSENSITIVE SPRAYABLE HYDROGEL AS A DRUG DELIVERY SYSTEM"
Vinod Kumar G S & Nanditha C K (filed on June 2020)

FACULTY AWARDS /HONORS/ RECOGNITIONS

KARTHIK SUBRAMANIAM

- DST-INSPIRE Faculty Fellowship
- DBT-Ramalingaswami Re-entry Fellowship

KARTHIKA RAJEEVE

- SERB POWER fellowship
- Anna ogDagnyHjerrilds Fond

MAHENDRAN K R

- Upcoming scientist featured in Journal of Membrane Biology (Upon invitation).

MALINI LALORAYA

- Member of DBT review committee under DBT-Task Force on Maternal and Child Health Programme from April 2020.

- Member, National Scientific Advisory Committee for ISSRF 2021 - 1st Virtual International Conference on Challenges and Strategies in Reproductive and Environmental Health during and after Covid-19 Pandemic, February 19-21, 2020.

MOINAK BANERJEE

- President: Indian Society of Human Genetics.

PRIYA SRINIVAS

- Elected as the Secretary, Indian Association for Cancer Research – IACR (for the term 2019-2022)

RADHAKRISHNAN R NAIR

- Member; INSACOG, jointly initiated by the Union Health Ministry of Health, and Department of Biotechnology (DBT) with Council for Scientific & Industrial Research (CSIR) and Indian Council of Medical Research (ICMR), is a consortium of 28 National Laboratories to monitor the genomic variations in the SARS-CoV-2.

- Nodal Officer, SARS CoV 2 Vaccine administration, Govt. of India

- Task Force member, Expert committee for SARS CoV 2 related projects and validation of new kits, BIRAC, DBT

- Expert committee member for SARS CoV 2 management in Kerala State Planning Board.

- Chairman, Board of Studies, Dept of Biochemistry, Kannur University: currently in the third consecutive term as Chairman

RADHIKA NAIR

- Featured in the TLoS annual calendar 2021 with the theme of inclusivity in Indian Science

SURYA RAMACHANDRAN

- Panelist and Resource person, Brainstorming session The Heart Failure Conflux-Virtual Confluence of Scientists and Clinicians Caring Heart Failure; ICMR Centre for Advanced Research and Excellence in Heart Failure, SCTIMST 5-7 Feb 2021

AWARDS RECEIVED BY Ph.D STUDENTS/ RESEARCH FELLOWS/POST-DOCTORAL FELLOWS

- Kalaivani V (Postdoctoral Fellow, Mentor: Dr. Abdul Jaleel) won the Best poster award in the SERB-ACS National Postdoctoral Fellows (NPDF) Online Research Poster Competition 2020

- Anu B, (Junior Research Fellow, Mentor: Dr. Harikumar K B) won the best poster award in the theme "Genomics&Health" in the International Webinar on " Advances in Genomics & Gene Technology" organized by the Inter University Centre for Genomics & Gene Technology, University of Kerala, Thiruvananthapuram from March 24-26, 2021.

- Riya Ann Paul (Ph.D student, Mentor: Dr. Jackson James) won the Best presentation award in 33rd Kerala Science Congress 2021.

- Renjini A P (Senior Research Associate, Mentor: Dr. Malini Laloraya) was awarded the Founder President Dr. T C Anand Kumar Young Scientist Award -2021 in the virtual 31st Annual Meeting of ISSRF along with International Conference on Challenges and Strategies on Reproductive and Environmental Health with Special Reference to COVID-19 Pandemic (ISSRF-2021) during February 19-21, 2021.

- Sindura K P (Ph.D Student, Mentor: Dr. Moinak Banerjee) won the following (a) the best oral presentation award (Theme: Genomics & Health) in the International webinar on 'Advances in Genomics &Gene Technology' organized by the Inter University Centre for Genomics & Gene Technology, University of Kerala from March 24th to 26th 2021; (b) RIKEN CBS Summer program fellowship 2019 'Neurotechnology-Understanding the brain in health and disease' from July 1st to July 5th, 2019 at RIKEN, Japan and (c) Second prize oral presentation in the 'Conspectus of genes, genetics and genomics'organized by the P.G. department of Biotechnology, Government Arts College, Thiruvananthapuram from November 25th to 27th 2019.

- Sowmya Gunasekaran (Ph.D Student, Mentor: Dr. Omkumar R V) was awarded (a) Department of Biotechnology-Conference, Travel, Exhibition and Popular Lectures (DBT-CTEP) travel grant from India for attending American Society for Neurochemistry (ASN) conference to be held in St. Charles, Missouri, USA (2020); (b) was selected for Oral presentation at the American Society for Neurochemistry (ASN) conference, St. Charles, Missouri, USA, April 17th -23rd, 2020. (POSTPONED to June 2021 due to COVID) and (c) was selected for the ICMR- Senior research Fellowship (2021)

- Mahitha Sahadevan (Ph.D student, Mentor: Dr Pradeep Kumar G) Awarded ICMR-SRF to work on a project entitled "Role of AIRE as a possible epigenetic regulator of PRDM9 mediated gene expression during spermatogenesis

- Vysakh G (Junior Research Fellow, Mentor: Dr. Pradeep Kumar G) Awarded ICMR-SRF to work on a project entitled "A case study to evaluate the aberrant expression of TDP-43 in the germ cells of human semen".

- Krithiga K (Ph.D student, Mentor: Dr. Priya Srnivas) won the following (a) Best Oral Presentation in National online clinical case conference 2020 conducted by the Pot-Graduate Institute of Veterinary and Animal Sciences, Akola, Maharashtra, from 12th -14th October 2020 and (b) Third best Oral Presentation in Kerala Veterinary Science Congress 2020 conducted in the online plat form from 14th – 15th November 2020 conducted by The Indian Veterinary Association (Kerala).

- Sebastian John (Ph.D student, Mentor Dr. Rashmi Mishra), selected for (a) Competitive Selection for Poster Presentation by EMBO Conference on Calcium Signaling: Molecular mechanisms to role in health and diseases, January 26 – 29, 2020, NCBS, Bangalore and (b) Olympus Junior Scientist Presentation in Olympus' Neuroscience Week organized by Olympus on October 27-29, 2020, at the Society for Neuroscience (SFN) conference (virtual mode).

- Lakshmi Narendrakumar (Ph.D student, Mentor: Dr. Sabu Thomas) won the first position in Poster presentation-Inter National Symposium on Antimicrobial Resistance. Organized by Amrita Vishwa Vidyapeedam, C-CAMP & University of California.

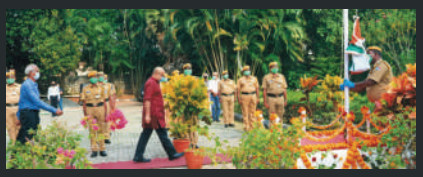
- Karthika S (Research fellow, Mentor: Dr. Sabu Thomas) awarded CSIR Research Associateship.

- Vinitha A (Ph.D student, Mentor: Dr. Surya Ramachandran) won the Global Health Travel Awards, Keystone eSymposia on Obesity, Colorado, Feb, 2021.

- Mrunal Wanjale (Ph.D student, Mentor: Dr. Vinod Kumar G S) won the best paper presentation award-student category international web conference in 'BIOINVENTIYON'20 - Advances in Biosciences' Conducted at Mahatma Gandhi University in association with Research Directorate and Internal Quality Assurance Cell (IQAC), SIAS on 5th and 6th November 2020.

RGCB EVENTS 2020-21

AUGUST 2020



Professor Radhakrishna Pillai M, Director RGCB hoisted the national flag on the occasion of 74th Independence day of our nation.

NOVEMBER 2020

Dr. Chandrabhas Narayana, Professor and Dean, JNCSAR, Bengaluru joined as the new Director of RGCB on 6th November 2020

NOVEMBER 2020

Professor Balram P , Ex.Director, IISc Bengaluru given the RGCB foundation day lecture on 25th November 2020

RGCB EVENTS 2020-21

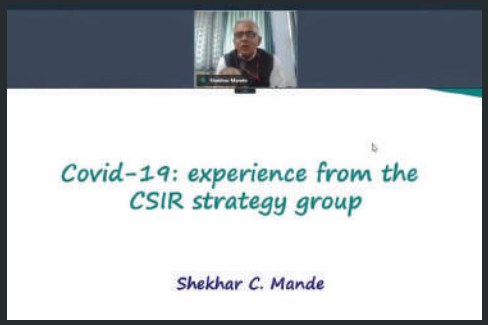
NOVEMBER 2020

RGCB celebrated Constitution Day (or Samvidhan Divas) on 26th November 2020

MARCH 2021

RGCB celebrated International Women's Day on 8th March 2021

FEBRUARY 2021



RGCB celebrated National Science Day on 28th February 2021 and arranged 3 talks and were given by Dr. Shekhar C Mande, Director General, CSIR; Shri. Kris Gopalakrishnan, Former Executive Vice Chairman, Infosys and Shri Jayant Sahasrabudhe, National Organizing Secretary, Vijnana Bharati.

RGCB's tribal heritage project camp office at Idukki also conducted an awareness program among school children as a part of science day celebrations

RGCB EVENTS 2020-21

JANUARY
2021

Professor Chandrabhas Narayana unfurled the national flag on the occasion of 72nd Republic day of our nation.

Faculty Science Club (FSC), a forum for interaction among the scientists of RGCB, and the forum is held on the 2nd and 4th Mondays of every month.

ANNUAL REPORT COMPILATION COMMITTEE 2020-2021

Dr. Santhosh Kumar T R, Scientist G
Mr. R Jayachandran Nair, General Manager
Mr. R Kumar, Senior Manager (Accounts & Audit)
Dr. Harikumar K B, Scientist E-I
Dr. Karthika Rajeeve, Scientist E-I
Dr. Shijulal Nelson-Sathi, Scientist C
Ms. Lekshmi R, Manager (Technical Services)
Ms. Ramya Rajan, Engineer (IT)

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