RGCB ANNUAL REPORT 2018 - 19

RGCB
DISCOVERIES FOR A BETTER TOMORROW

Four curious research scholars in their residency.

Photographed by Dr. Saraswati Nayar (DST - INSPIRE Faculty Fellow) on the campus of University of Delhi, South Campus

DIRECTOR'S NOTE

Success is a science. If you have the conditions you will get the result.
Oscar Wilde

Successful research institutes are never satisfied in maintaining status quo. They relentlessly search for the next innovation and next higher level of performance. RGCB understands this requirement for constant success. Although things are going well, the institute policy and philosophy is to keep endeavoring to search for what could be improved. Most of us have a tendency to remain in our natural comfort zones, which admittedly offers protection from scrutiny and questions. A further reflection is that it is the public whose tax payments support most of our research programs. RGCB is obligated to propagate our research findings in a form that reaches the public and in a clear language that they understand. RGCB scientists serve public interest by working on some of the critical problems that our society faces. We do not live in ivory towers and ensure that we are mandated to create discoveries, make innovations and products that will impact lives of our people. Our Annual Report is to convince our management, the government, policy makers and most importantly the people of the returns they have got from investments made and trust put into RGCB.

This year's annual report makes it apparent why RGCB has a consistently very good track record in its performance. We have showcased our productivity spanning over all 12 months of the year. RGCB has made its mark in fundamental research, applied research and translational health research. Our scientists have made significant discoveries in cell biology. We have contributed to health policy changes made by World Health Organization. Our drug discovery program had a noteworthy development. A plant derived compound identified to have specific anti liver cancer activity was finally chemically synthesized which showed similar range of activity. Following successfully overcoming this first hurdle in the drug development pipeline, results coming in from xenograft models are very exciting. Agreements are in place with an international pharmaceutical industry to accelerate the program. RGCB also showed India how a biotechnology research institute can contribute to our Honorable Prime Minister's emphatic call for "Make in India". Our technology development incubator – the BioNest has 22 start up companies manufacturing biomedical devices, monoclonal antibodies, nutraceuticals, antibiotics and anti fungals. Our excellent infrastructure and technical expertise has been skillfully used to provide tens of thousands of below poverty line patients access to the best of nationally accredited international standard laboratory diagnostics so much so that RGCB is now an indispensible partner in the public health realm. Our Molecular Forensics laboratories are all set to receive NABH and NABL accreditation. RGCB has received a significant contract to do efficacy tests for India's first indegenous HPV Vaccine.

As always, I place on record my deepest appreciation and gratitude to our Governing Council and Scientific Advisory Council. I also thank my colleagues who have enabled me to bring ideas and concepts into reality including the annual report production team of Debasree Dutta, Surya Ramachandran, G. Harish, R. Ramya and R. Lekshmi.

RGCB will continue to be a focal point for new discoveries and their application to the betterment of society.

Jai Hind

Professor M Radhakrishna Pillai
FRCPath, PhD, FAMS, FNASc, FASc, FNA
Director

RGCB
DISCOVERIES FOR A BETTER TOMORROW

RGCB 2018 - 19
AT A GLANCE

RESEARCH PROGRAMS

Cancer Research
Cardiovascular Diseases & Diabetes Biology
Pathogen Biology
Regenerative Biology
Neurobiology
Reproduction Biology
Plant Biotechnology & Disease Biology
Interdisciplinary Biology

TRANSLATIONAL BIOTECHNOLOGY

Product & Process Development
Target Identification
Repositioning of Therapeutics
Development of Natural Products as Therapeutics
Vaccine Efficacy, Pre-Clinical Testing & Clinical Trials

SERVICE & TRAINING FACILITIES

Laboratory Medicine
Molecular Diagnostics
Medical Laboratory Services
Vaccine Efficacy Centre
Molecular Forensics
Research & Diagnostic Consultancy Platforms

SCIENTIST DETAILS

Core Faculty Scientists	31
Faculty Fellows (Ramalingaswami or Ramanujam or INSPIRE Fellows)	9
Program/Project Scientists	11

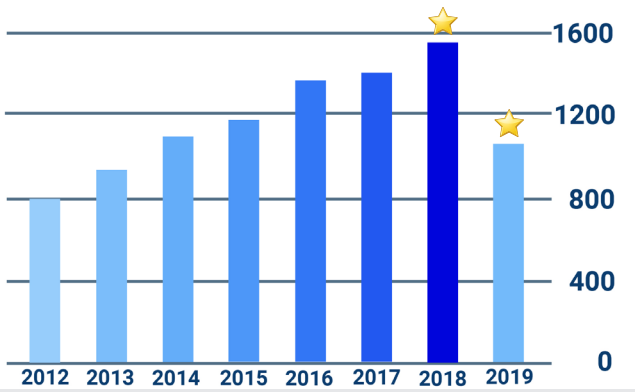
STUDENT DETAILS

Post doctoral trainees	23
MD students trained	52
PhD students	142
PhD students admitted in current year	25

Female to Male Ratio (Post Docs): 15: 8
Female to Male Ratio (PhD Students): 104:38

RGCB PUBLICATION, CITATION AND GRANTS

	All	Since 2014
Citations	12309	7719
h-index	55	41
i10-index	306	236



April 1, 2018 to March 31, 2019	
Number of Publications	124
Number of citations	2617

Number of Extra Mural Research Grants	
National	101
International	2

PRODUCT DEVELOPMENT

Mouthwash To Treat Oral Mucositis & Periodontal Disease

- Combination of ingredients from 5 plants
- Clinical trial done for oral mucositis in oral cancer patients undergoing radiation
- Clinical trial done for periodontal disease
- Significant efficacy in both disease indications showing following therapeutic properties: Anti-inflammatory, Analgesic, Anti-bacterial, Anti-plaque
- Filed Patent in India (November 4, 2010) : still in process
- Commercial formulation: patient friendly & stable product formulation
- Commercialization partnership restricted to companies specializing in food/natural products (No immediate pharma commercialization route)
- Technology Transfer Completed to Ceego Labs Pvt Ltd, Chennai
- Ceego's contribution: Prepared 3 stable product formulations:
- Combination of the whole dried plants, powdered and blended (50gm powder sachet)
- Aqueous, high temperature, plant extracts blend (60 ml liquid)
- Aqueous extract blended and spray dried from all 5 plants (30 mg powder sachet)
- Clinical validation of the three formulations in progress.

PRODUCT DISCOVERY

Uttroside B: Candidate Molecule for Liver Cancer
Discovery: Uttroside B (plant derived compound) effective against liver cancer cells (significantly more potent than Sorafenib – the only FDA approved drug for liver cancer). Isolated, purified to a single active entity; established in-vitro biological activity
Inventor: Dr. Ruby John Anto
Key problems: Uttroside B has never been synthesized; Isolation from plants is not scalable and causes QC problems.
Key development: Successful chemical synthesis of Uttroside B
Current Status: Synthetic product and analogs undergoing pre clinical evaluation

ILS - IBSD - RGCB CLUSTER PROGRAM

Institute of Life Sciences, Bhubaneswar
Institute Of Bioresources & Sustainable Development, Imphal
Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram

A comprehensive approach to etio-pathogenesis and treatment outcome in Gall Bladder Cancer (GBC)
GBC is a malignancy with a very high incidence in North and North-East India compared to South India. It is twice more common in women than in men and is the commonest digestive tract cancer in women.

GOALS AND OBJECTIVES

Defining descriptive & molecular epidemiology of GBC
Understanding the etio-pathogenesis of Gall Bladder Cancer
Development of clinically relevant models for mechanistic and translational studies
Creation of bio-banks for storing bile, serum and tissue from GBC and gallstone disease patients
Development of screening strategy and early diagnosis protocols for GBC through minimally invasive techniques

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APRIL 2018

Ruby John Anto, PhD, FNASc

Minakshi Saikia, Archana P.R, Shabna A, NP Anto, Rashmi Mittal, Shabna S, Kavya S Pillai, B S.Vinod, Vidya Peter, Reeba Thomas and **Ruby John Anto**, Heteronemin, a marine natural product, sensitizes acute myeloid leukemia cells towards cytarabine chemotherapy by regulating farnesylation of Ras, ***Oncotarget, 2018, 9, 18115-18127***

Cytarabine is a conventionally used chemotherapeutic agent for treating acute myeloid leukemia (AML). However, chemoresistance, toxic side-effects and poor patient survival rates retard the efficacy of its performance. The current study deals with the chemosensitization of AML cells using heteronemin, a marine natural product towards cytarabine chemotherapy. Heteronemin could effectively sensitize HL-60 cells towards sub-toxic concentration of cytarabine resulting in synergistic toxicity as demonstrated by MTT assay and [3H] thymidine incorporation studies, while being safe towards healthy blood cells. Flow cytometry for Annexin-V/PI and immunoblotting for caspase cleavage proved that the combination induces enhancement in apoptosis. Heteronemin being a farnesyl transferase inhibitor (FTI) suppressed cytarabine-induced, farnesyl transferase-mediated activation of Ras, as assessed by Ras pull-down assay. Upon pre-treating cells with a commercial FTI, L-744,832, the synergism was completely lost in the combination, confirming the farnesyl transferase inhibitory activity of heteronemin as assessed by thymidine incorporation assay. Heteronemin effectively down-regulated cytarabine-induced activation of MAPK, AP-1, NF-κB and c-myc, the down-stream targets of Ras signaling, which again validated the role of Ras in regulating the synergism. Hence we believe that the efficacy of cytarabine chemotherapy can be improved to a significant extent by combining sub-toxic concentrations of cytarabine and heteronemin.

TEAM: Mohan Shankar G, Vijay Alex, Jannet S, Aiswarya U S, Padma K, Shabna A, Swetha M, Archana P R, Liju V B

AWARDS

Syed Khaja Mohieddin, PhD student of Dr. Debasree Dutta was awarded the best poster presentation at Manipal Academy of Higher Education (MAHE) Research Colloquium, Manipal, Karnataka, 2018.

OUTREACH

Schools students and officials from UAE visited RGCB organized by Science India Forum - UAE - SPC 2017.

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MAY 2018

Tessy Thomas Maliekal, PhD

Cancer Meeting-Precision Medicine in Oncology –"Self-renewal ability of cancer cells"- NCBS, Bangalore - May 4th, 2018.

Among the heterogeneous cancer cells, a small subset called cancer stem cells (CSCs) influences the prognosis of cancer by regulating tumor initiation, metastasis, treatment response and recurrence. The importance of tumor microenvironment in the regulation of tumor properties is well-established. Recent evidence suggest that this tumor microenvironment in relation to CSCs, called "CSC niche", is essential to impart self-renewal ability to these cells. Since disruption of "CSC niche" results in loss of self-renewal ability, it is an attractive target to eliminate CSCs. So it is essential to understand the molecules defining "CSC niche". Our research with SILAC based phosphoproteomic analysis identified several signaling pathways in "CSC niche" regulating self-renewal of oral cancer cells. Since several reports show that ALDH1A1 marks self-renewing population in several forms of cancer, we selected this molecule as reporter for CSCs. An ALDH1A1 reporter vector was constructed by subcloning a PCR-amplified ~1Kb promoter region of ALDH1A1 into DSRed2-N1, replacing the CMV promoter. The expressions of BMI1, KLF4, NANOG and SOX2 were analyzed by RT-PCR, and the results confirmed that the expressions of stemness genes are markedly high in ALDH1A1-DS Red2 + population than ALDH1A1-DS Red2 - population. Further, enhanced tumor initiation ability of ALDH1A1-DS Red2 + cells over ALDH1A1-DS Red2 - cells were validated in a xenograft assay. Oral cancer cells expressing this reporter were used for screening chemical inhibitors that targets CSC population. We selected a few of the pathways from our phosphoproteomic analysis like, EGFR,TGF-β, ERK, MEK, mTOR, PI3K, SHH, NOTCH and WNT pathways for our further analysis. We used an array of small molecule inhibitors and three of their combinations to test the efficacy to reduce CSCs. Our results revealed that one of the combinations, Comb1, is very effective, as it reduced CSC population to 34%. At the same time, Comb1 did not significantly alter the stem cell activity of murine hematopoietic stem cells. We conclude that ALDH1A1-DS Red2 is a useful tool to screen drugs that target CSCs and Comb1, a cocktail of inhibitors, with half concentration of each, abolishes CSCs without affecting normal stem cells.

TEAM: Amrutha Mohan, Soumya Krishnan U, Nivethika R, Anitha Vimal

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MAY 2018

AWARDS

US Patent Granted for invention entitled “Assay for detection of transient intracellular Ca2+” by Omkumar, R. V., Rajeev kumar, R., Mathew Steephan, Mayadevi, M. and Suma Priya, S., Patent No.: 9,958,462; Date of issue: May 01,2018

OUTREACH

Students and faculty from Indira Gandhi National Open University visited RGCB

Harikumar K B, PhD

Lankadasari MB, Aparna JS, Mohammed S, James S, Aoki K, Binu VS, Nair S, **Harikumar KB**. Targeting S1PR1/STAT3 loop abrogates desmoplasia and chemosensitizes pancreatic cancer to gemcitabine. ***Theranostics. 2018;8(14):3824-3840.***

Pancreatic cancer is associated with poor prognosis with a 5-year survival rate of less than 6%. Approximately 90% of pancreatic cancer patients harbor somatic mutations in the KRAS gene. Multiple lines of evidence suggest a persistent activation of STAT3 in KRAS-driven oncogenesis contributing to desmoplasia and gemcitabine resistance. Sphingosine 1-phosphate receptor 1 (S1PR1) is an integral component of tumor progression and maintains an activated state of STAT3. FTY720 is an approved drug for multiple sclerosis and acts as a functional antagonist for S1PR1. Here we explored the potential utility of FTY720 to target S1PR1/STAT3 and other major signaling pathways in pancreatic cancer, and sought proof-of-principle for repurposing FTY720 for the treatment of pancreatic cancer. We examined the activity of FTY720 in the proliferation, apoptosis, and cell cycle assays in human and mouse pancreatic cancer model systems. Further, we studied the efficacy of using a combination of FTY720 and gemcitabine as opposed to individual agents in vitro as well as in vivo. Treatment of human and mouse pancreatic cancer cells with FTY720 resulted in inhibition of growth, increased apoptosis, and cell cycle arrest. FTY720 in combination with gemcitabine breached the mitochondrial membrane potential, altered the S1PR1-STAT3 loop, and inhibited epithelial to mesenchymal (EMT) transition. Data from murine models exhibited a marked reduction in the tumor size, increased apoptosis, inhibited NF-κB, S1PR1/STAT3, Shh signaling and desmoplasia, modulated the expression of gemcitabine-metabolizing transport enzymes, and restored the expression of tumor suppressor gene PP2A. Taken together, our results established FTY720 as a propitious molecule, which increases the efficacy of gemcitabine and represents a promising agent in the management of pancreatic cancer.

TEAM: Yadu Vijayan, Sreesha S Kumar , Namitha N N, Shirley James, Sabira Mohammed, Anu B, PrameelaKumari T K, Manendra Babu L

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JUNE 2018

Sabu Thomas, PhD

Karthika S, Joby John, Megha P.R, George.S and **Sabu Thomas**. Metataxonomic approach to decipher the polymicrobial burden in diabetic foot ulcer and its biofilm mode of infection. ***Int Wound J, 2018;15:473–481***

Chronic diabetic foot is a global burden affecting millions of people, and the chronicity of an ulcer is directly linked to the diverse bacterial burden and its biofilm mode of infection. The bacterial diversity of 100 chronic diabetic ulcer samples was profiled via traditional culturing method as well as metagenomic approach by sequencing the 16S rRNA V3 hyper-variable region on an Illumina Miseq Platform. All the relevant clinical metadata, including duration of diabetes, grade of ulcer, presence of neuropathy, and glycaemic level, were noted and correlated with the microbiota. The occurrence and establishment of bacterial biofilm over chronic wound tissues was revealed by Fluorescent in situ Hybridization and Scanning Electron Microscopy. The biofilm-forming ability of predominant bacterial isolates was studied via crystal violet assay and Confocal Laser Scanning Microscopy. The dominant phyla obtained from bacterial diversity analysis were Firmicutes, Proteobacteria, and Actinobacteria. The dominant aerobic pathogens identified by culture method are Pseudomonas, Proteus, Enterococcus, and Staphylococcus, whereas high-throughput sequencing revealed heightened levels of Streptococcus and Corynebacterium along with 22 different obligate anaerobes. The biofilm occurrence in chronic diabetic ulcer infection is well analysed. Herein, we illustrate the comprehensive pattern of bacterial infection and identify the community composition of chronic wound pathogenic biofilm.

TEAM: Lekshmi N, Merin Paul, Karthika S, Akhila V S, Sudha B Nair, M VidhyaLakshmi, Saritha K L, Megha P R, Aparna Sankar

AWARDS

Sowmya Gunasekaran, Ph. D. student of Dr RV Omkumar was awarded the Stanley Foundation scholarship to attend a Cold Spring Harbor workshop entitled “Workshop on Schizophrenia and Related Disorder” in Cold Spring Harbor, USA, June 2018

Arun Surendran of the Proteomics facility of RGCB was awarded the prestigious “ Have a Heart Bursary Program Awards” to attend the 2018 Canadian Cardiovascular Congress (CCC) in Toronto

TALKS

Malini Laloraya PhD : Invited lecture in the Sino-American Joint Meeting of Reproductive Immunology, the 38th Annual Meeting of the American Society for Reproductive Immunology, and the 6th Annual Meeting of the Chinese Society for Reproductive Immunology, June 28th-July 1st, 2018 Shangai, China.

EVENTS


Using multiple sclerosis drug to treat pancreatic cancer

SCIENCE

Using multiple sclerosis drug to treat pancreatic cancer

Aswathi Pacha

JUNE 23, 2018 20:20 IST
UPDATED: JUNE 30, 2018 18:22 IST

SHARE ARTICLE

KB Harikumar and team were featured in The Hindu for their findings published in the Journal *Theranostics*.

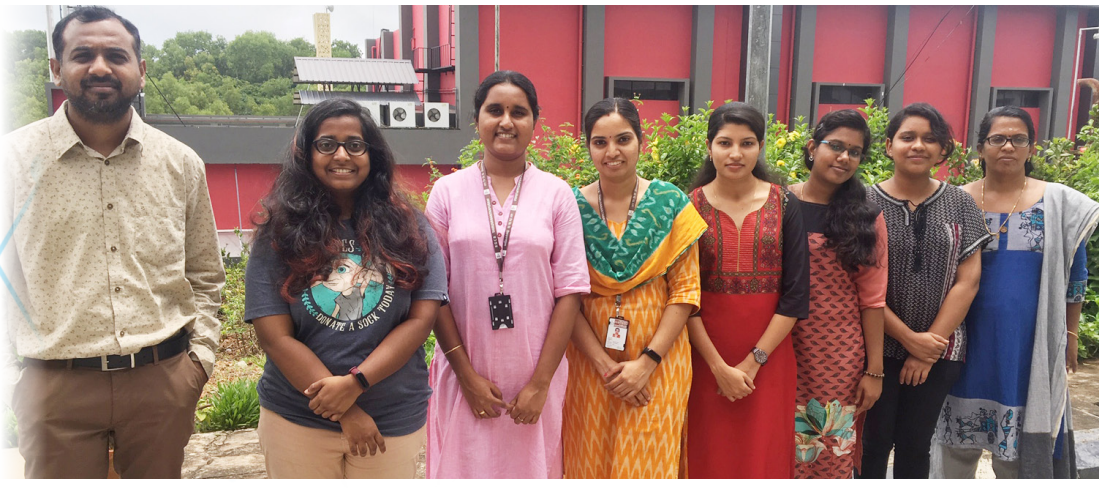
RGCB signs MoU with DBT guaranteeing performance evaluation compliance

15 JULY 2018

Mahendran K R, PhD

Remya S, Smrithi Krishnan R, **Mahendran KR**. Controlling Interactions of Cyclic Oligosaccharides with Hetero-oligomeric Nanopores: Kinetics of Binding and Release at the Single-Molecule Level. ***Small. 2018. 14 (32), 1801192***

Single molecule sensing with membrane protein pores were developed to identify the size and chemical composition of macromolecules ranging from peptides, polysaccharides to nucleic acids. Here, we use a novel approach to control the transport of cyclodextrins (CDs) across the asymmetrically shaped and charged hetero-oligomeric protein pore for the peptide sequencing. Further, we engineer and build transmembrane pores from short synthetic alpha-helical peptides. The porin ACj is an α-helical porin that spans the mycolic acid outer membrane of Gram-positive mycolate, Corynebacterium jeikeium. Here, we report that a 40-amino acid, synthetic peptide, pPorA corresponding to porin PorACj inserts into the lipid bilayers and form well-defined pores. We measured the single channel properties that revealed the autonomous assembly of large conductance ion selective synthetic pores using single-channel electrical recordings. We characterized a cysteine peptide mutant pPorA-K24C that showed remarkably higher conductance than that of WT revealing the large pore size of cysteine mutant. Further, we described the functional properties by blocking the peptide pores by cyclodextrins of different symmetries. We deduced the subunit composition and putative structure of the pore by site-specific chemical modification in single channel electrical recordings and gel electrophoresis. Based on these findings, we suggest that this is a large functional uniform transmembrane pore built entirely from short synthetic α-helical peptides. Accordingly, we propose a model demonstrating structural assembly of large α-helix based peptide pores for understanding the action of antimicrobial peptides. The significance of this work is that no one has assembled a large stable synthetic transmembrane pore with a single oligomerization and a steady large conductance state. The peptide pore demonstrated in this work is a highly original system due to the unique protein architecture, the significance of transmembrane pores, and their potential applications for nano biotechnology.



TEAM: Neethu P, Smrithi K R, Remya S, Amina H Shaji, Greeshma S Nair, Devika V, Smitha R P

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JULY 2018

Devasena Anantharaman, PhD

Abrahão R, **Anantharaman D**, Gaborieau V, Abedi-Ardekani B, Lagiou P, Lagiou A, Tommasino M, Scelo G, Brennan P. The influence of smoking, age and stage at diagnosis on the survival after larynx, hypopharynx and oral cavity cancers in Europe: The ARCAGE study. ***Int J Cancer. 2018 Jul 1;143(1):32-44.***

Cancers of the oral cavity, pharynx and larynx are predominantly squamous cell in origin and grouped together as head and neck cancers (HNSCC). Despite being a preventable disease, HNSCC is often detected late and remains the leading cause of mortality. HNSCC management is heavily dependent on pathological stage, the ability of staging to predict prognosis is limited. Patients with tumors of the same clinical and pathologic staging have heterogeneous response to clinical treatment, and different probability of recurrence and survival. We examined the predictors of survival after larynx, hypopharynx and oral cavity (OC) cancers with particular emphasis on long-term (10 year) survival. Data from the Western European multicenter study (ARCAGE) and the Carolina Head and Neck Cancer Study were used to estimate overall survival by the Kaplan–Meier method and Cox proportional models to test the association between survival and patient factors. Five-year survival was 65% for larynx, 55% for OC and 35% for hypopharynx cancers. We observed an increased mortality among older (≥71 years) versus younger (≤50 years) patients, current versus never smokers [HR 2.67, 95% CI 1.40–5.08 (Larynx) and HR 2.16, 95% CI 1.32–3.54 (oral cavity)]. Survival was not associated with sex, alcohol consumption, education, oral health, p16 expression, presence of HPV infection or body mass index 2 years before cancer diagnosis1. These results demonstrate that despite modern detection methods, most patients in Europe are still diagnosed with advanced disease. Similarly, ten year overall survival was 69%, 67% and 72% for oral cavity, larynx and oropharynx respectively. Among HPV positive cases, the hazard ratio for death was 1.5 (95% CI 0.7-3.1) for smokers and 2.4 (95% CI: 0.7-8.8) for nonsmokers, while smoking did not affect the risk of death in HPV negative cases. Stage at diagnosis remained the strongest predictor of HNSCC survival. These data suggest that HNSCC survival continues to decline after 5 years and this is not explained fully by differences in smoking, disease stage or HPV status.

TEAM: Edwin S, Professor M -Radhakrishna Pillai, Jyothi Narayana, Jinu Austin, Abitha Thomas, Lekshmy S R, Subha Sankaran, Divya Jayalakshmi, Pretty Mary, Rintu Varghese, Vivek Ashok Kumar, Kannan T R, Aparna G J, Deeksha Suganan, Ahalya Sreekumar, Purnima Kartha, Manju V, Nithin R

AWARDS

Mr. Umer Ali, PhD student of Dr. John Johnson won Newton Bhabha Ph.D. Exchange Fellowship (July 2018 to October 30 2018)

EVENTS

RGCB has its own "Skygreen" organic farm which serves fresh vegetables in the cafeteria to its faculty, staff and students . Director, Professor Pillai and Mr. George Varghese take Additional Secretary, DBT, Shri. Anand Balagopal on a walk across the greens.

Asha Srinivasan who did her PhD at RGCB under the mentorship of Dr EV Soniya receiving ICAR Jawaharlal Nehru Award for outstanding doctoral research thesis in agricultural and allied subjects 2017 from Honorable Union Minister for Agriculture, Sri Radha Mohan Singh and Minister of State Sri Gajendra Singh Shekhawat.

OUTREACH

LAB VISIT

SCT College of Engineering, Pappanamcode	20 Students
Vellalar College for Women Thindal, Erode	45 Students
Bharatiya Vidya Bhavan, Thiruvananthapuram	57 Students

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AUGUST 2018

Professor M Radhakrishna Pillai FRCPath, PhD, FASc, FNASc, FAMS, FNA

Sankaranarayanan R, Joshi S, Muwonge R, Esmy PO, Basu P, Prabhu P, Bhatla N, Nene BM, Shaw J, Poli URR, Verma Y, Zomawia E, Pimple S, Tommasino M, Pawlita M, Gheit T, Waterboer T, Sehr P, **Pillai MR**; ***Vaccine. 2018 Aug 6; 36: 4783-479***

An increase in worldwide HPV vaccination could be facilitated if a single dose of the vaccine be as effective as three doses. We examined vaccine efficacy in terms of the concentration of binding antibodies against the major capsid protein L1 and neutralizing antibodies specific for vaccine targeted HPV types and incident/ persistent HPV infections. Albeit inferior to that of 3- or 2-doses, the one dose recipients demonstrated a robust and sustained immune response against HPV 16 and 18 over a 4-year period. The proportion of persistent infections against HPV 16 and 18 infections was low in all the vaccinated study groups throughout the 7-year follow-up period compared to the age-matched unvaccinated cohort. These results indicate that a single dose of the quadrivalent HPV vaccine is similar to the three- and two-dose vaccine schedules.

Extending two-dose recommendations of HPV vaccine to girls up to 18 years will reduce program cost and improve compliance. To address this, we examined the immunogenicity outcomes of L1 binding antibody titres, neutralizing antibody titres and vaccine targeted HPV infection outcomes. 1795 girls aged 15-18 years receiving two doses were compared against 1515 15-18 year old girls receiving three doses (standard of care) and the 2833 10-14 year old three dose recipients (best response group). The 7-month L1-binding antibody titres of 15-18 year old two-dose recipients were non-inferior to 15-18 year old and 10-14 year old three-dose recipients. The seven month L1-binding antibody titres and neutralizing antibody titres of 15-18 year old two-dose recipients were non-inferior to 15-18 year old and 10-14 year old three-dose recipients. At a median follow-up of 7 years, no persistent HPV 16 infection was observed.

TEAM: Bharani Devi T, Professor G B Nair, Remya V S, Vinitha Richard, Sanjay D, Raji Prasad, Sara Jones, Santanu Chattopadhyay, Iype Joseph, Vishnu V M, Deepak Chauhan, Retnakumar R J

Santanu Chattopadhyay, PhD

Iype Joseph, MBBS, MPH

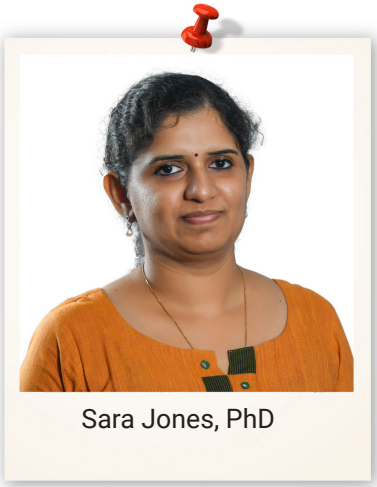
Helicobacter pylori infection is associated with gastric cancer and peptic ulcer. Interestingly, only 10–20% of the *H. pylori* infected individuals suffer from gastric diseases and rest of the infected individuals remain asymptomatic. The roles of other gastrointestinal bacteria are unknown. To understand gastrointestinal microbial interplay in gastric health and diseases, we took following metagenomics and culture based approaches. Gastric biopsy and stool samples were collected from 200 patients suffering from various gastric disorders.Of them, 44 (22%) were infected with *H. pylori*. Most *H. pylori* strains are sensitive to amoxicillin and clarithromycin, while most of them are resistant to metronidazole.PCR- genotyping showed that 96.2% of the patients are infected with toxigenic vacAs1 strains, which also carry the virulence associated cagA gene. RAPD fingerprinting reveals a panmictic population structure.Phylogenetic analysis showed that the vacA of Kerala clusters with Kolkata and Bangladesh. while the cagA of Kerala clusters with Western cagA. Overall, no association between gastric diseases and *H. pylori* virulence alleles were observed suggesting that other factors like gastrointestinal microbiome may play a role.

Field epidemiology support for Measles, Influenza, Anti Microbial Resistance (AMR) and DNA Fingerprinting research groups continued to be effectively provided. The Influenza Research group received 291 samples from three private hospitals in Kollam and one Government Medical College in Trivandrum, Kerala. Of these, 99 were found to be due to Influenza A pH1N1. An outbreak was detected by RGCB and it was reported State Health authorities. The Measles Research group received 107 samples. Of these, 90 were found to be due to Measles. The samples were from Palakkad, Kollam and Thiruvananthapuram districts. An outbreak was detected by RGCB at Thiruvananthapuram and it was reported State Health authorities. As the Measles group requires Mother-Child blood samples for another branch of their study, 206 pairs of such samples were collected.

The AMR Research group aims to investigate the spectrum of bacteria found in common community acquired infections and resistance pattern of the isolates. The group received 25 samples and 8 bacterial isolates from 12 Government hospitals in Thiruvananthapuram district.

Regional Facility for DNA Fingerprinting (RFDF) aims to create a genetic database and for this 250 blood samples were collected for this purpose.

A collaborative study on seroprevalence of Leptospirosis was done with College of Veterinary and Animal Sciences, Mannuthy. A total of 41 human serum samples were collected from apparently healthy cattle care-takers from Mannancherry panchayat in Alappuzha district. Of these, seven were found positive by Microscopic Agglutination Test (MAT) - Autumnalis(3), Sejroe(2), Pomona(1) and Multiple (1).



Sara Jones, PhD

Measles is a global public health problem and a leading cause of childhood mortality preventable by vaccination. Despite an active two-dose vaccine program in developed nations, outbreaks continue to occur, affecting tens of thousands of individuals. While most of the cases are of unvaccinated individuals, measles vaccine failure does play a role in these outbreaks as observed in the most recent outbreaks were 10-50% cases were pre-vaccinated. Our investigation among southern Indian children demonstrated that >6% remain unprotected even after two doses of measles vaccine. With the goal of eradicating measles from India, a phased supplementary immunization activity using measles-rubella (MR) vaccine targeting children aged 9 months–14 years commenced in 2017 in the South-East Asia Region including India. Despite increased vaccine coverage measles outbreaks persists mainly due to exposure of vaccine-exempt populations to imported and primary or secondary vaccine failed cases. With this background, our study aims to better understand measles vaccine failure in Southern India by recruiting two cohorts of children (vaccinated or measles virus infected) and their mothers. A total number of 206 serum samples were collected till date from children (4-12 yrs) who had received 2-3 doses of measles vaccine, including 99 female (48.06%) and 107 male (51.94%). Of the total vaccinated subjects screened for antibodies against measles virus, 93.20% showed reactivity to measles antigens, while 4.37% children failed to develop immunity from the first dose. It has been widely suggested that immunization with the clade A measles vaccine strain is protective against members from other clades. Recent studies have challenged the ability of clade A measles virus vaccines to be pan-protective. Phylogenetic analysis of isolates from Kerala obtained during the study revealed segregation with clade D, genotype D8, against which clade A Edmonston strain of measles vaccine may only elicit suboptimal protection. Measles incidence in India and other regions increased sharply in 2018 when compared to 2017. Our data shows that 77.36% of infection occurred in children before the EPI-recommended immunization age of 9 months and 92.47% occurred in adolescents and/or young adults. Among the positive adult cases only 23.26% were vaccinated and 76.74% were not sure of their vaccination status. Our data points to a pattern that children under 9 months of age, are highly susceptible to measles virus infection and more importantly waning in measles specific antibodies occurs with time in those vaccinated. 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 measles virus.

21 AUGUST 2018

Soniya E V, PhD

Dr. E. V. Soniya, was awarded National Academy of Biological Sciences (NABS) - Best Woman Scientist Award 2018

Black pepper is a major spice in India which also has a wide array of medicinal properties. Our team focuses on the regulation of defense and development in black pepper. As the major threat to black pepper cultivation is quick wilt caused by the oomycete Phytophthoracapsici, we investigated plant responses towards *P. capsici* infection. Metabolite profiling of the leaves of infected plant revealed the involvement of phytohormones like salicylate (SA), jasmonate (JA), and abscisic acid (ABA) in defense. The impact of hormone production in the development of quick-wilt was analysed by pre-treatment with hormones followed by a challenge with *P. capsici*. This revealed the susceptibility of plant to *P. capsiciin* the case of pre-treatment with ABA. It was found that ABA antagonises SA-mediated defense in *P. nigrum*, where ABA-treatment increased the susceptibility to *P. capsici* by suppressing the SA-mediated defense gene expression. Another aspect of our study emphasizes on the small RNAs derived from tRNAs and their role in development and defense. From the small RNA profile, the number of candidate tRFs was narrowed-down based on the sequence conservation of tRNAs among plants. These were majorly classified as 5'tRFs and 3'tRFs, and named accordingly with the help of genomic tRNA database. In silico target and structure predictions of these tRFS resulted in fishing out crucial tRFs whose targets are important genes of plant defense network. The medicinal activity of black pepper is attributed to the secondary metabolites in the berries. We carried out a high-throughput metabolic profiling which provided a comprehensive data regarding these bioactive compounds. Transcriptomic analysis unveiled that the majority of these molecules are synthesized through the phenyl propanoid pathway. The real-time expression study of crucial transcription factors and enzymes responsible for phenyl propanoid biosynthesis was carried out. The key miRNAs targeting them were identified from miRNA profiling. Functional validation of these miRNAs is currently in progress.

TEAM: Sora S, Divya Kattupalli, Sinsha Prakashan, Maimoonath Beevi Y P, Mallika V, Sweda Sreekumar, Aswathi U, Sruthi Bharathan, Lekshmi R S, Preetha Chandran P

22 AUGUST 2018

Asha V V, PhD

Tom G, Philip S, Isaac R, Praseetha PK, Jiji SG, **Asha VV**.Preparation of an efficient and safe polymeric-magnetic nanoparticle delivery system for sorafenib in hepatocellular carcinoma. ***Life Sci. 2018 Aug 1;206:10-21.***

Super paramagnetic iron oxide nano particles (SPIONs), as drug delivery vehicles, offer to eliminate the concerns associated with hydrophobic anti-cancer agents. The current study was intended to fabricate a SPION based delivery system for sorafenib that can simultaneously enable targeted delivery of sorafenib and expand its therapeutic index against hepatocellular carcinoma (HCC). Co-precipitation and physical entrapment methods were employed for the synthesis of sorafenib loaded PVA coated SPIONs. Physicochemical characterizations were done using TEM, XRD, FTIR, Raman spectra and VSM measurements. The superior activity of nanoconjugate was demonstrated by AO/EB staining, FACS, immunofluorescence and Western blot. The safety of the sorafenib conjugated nanoparticles were verified in Wistar rats. The synthesized nanoparticles were in the size range of 5-15 nm. The adsorption of PVA to the SPIONs and the conjugation of sorafenib to the nanocarrier were confirmed by XRD, FTIR and Raman spectra analyses. VSM study ascertained the superparamagnetic nature of the nanoconjugate. Cellular uptake studies suggested its efficient entrapment in HepG2 cells. MTT assay showed that the cytotoxicity of sorafenib loaded PVA/SPIONs was comparable or higher than free sorafenib. The activation of apoptosis and autophagy pathways in HepG2 by the nanoconjugate was evidenced. Acute toxicity testing in Wistar rats supported the safe administration of the nanoconjugate and established its localization in animal tissues by Perl's Prussian Blue reaction. The novel combination of sorafenib with PVA/SPIONs showed better anticancer efficiency than free sorafenib demonstrative of its potential in cancer chemotherapy.

TEAM: Sreeja, Gayathri L T

23

AUGUST 2018

AWARDS

Ruby John Anto Elected as Fellow of Kerala Academy of Sciences

RGCB Technical Officer, Arun Surendran won the Research Manitoba Master's Studentship for 2018

EVENTS

Director of RGCB Thiruvananthapuram handed over a contribution of Rupees 25 Lakhs to the Honourable Chief Minister of Kerala towards the Distress Relief Fund. This was from donations received from Staff and Services. RGCB also promised all scientific and technical expertise at no cost towards handing of health related issues that were anticipated after the flood waters recede.

Khaja Syed, first PhD student of RGCB Thiruvananthapuram to graduate from Manipal Academy of Higher Education, Institute of Eminence, with an MR Das Research Excellence Award, gold medal, cash prize and a citation. This award is given for the best overall performance in the PhD program, every year, in terms of quality of publications, points gathered based on presentations (oral & poster) in National and International symposia and patents generated.

OUTREACH

LAB VISIT

S.B. College, Changanacherry, Kerala	28 Students

24 SEPTEMBER 2018

Rakesh S Laishram, PhD

Mohan, N., Kumar, V., Kandala, D., Kartha, C.C. and **Rakesh S. Laishram**. Anew splicing independent function of RBM10 controls specific 3-UTR processing to regulate cardiac hypertrophy in the heart. ***Cell Reports. 2018, 24:3539-3553***

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 putative master switch, RNA binding motif protein 10 (RBM10) that acts at the 3'-UTR of keyCH regulators mostly down regulated during CH. RBM10 expression is enriched in the heart and functions with the variant poly(A) polymerase (PAP) Star-PAP (Speckle targeted PIPKI alpha regulated PAP). RBM10 binds target pre-mRNA and guides Star-PAP polyadenylation complex to specifically regulate 3'-end processing of cardiac mRNAs. In both cellular (rat cardiomyoblast, H9C2) and in animal (rat)heart models for CH, RBM10 expression is down regulated resulting in reduced expression of target anti-hypertrophic genes. RBM10 depletion resulted in the generation of molecular events of hypertrophic response. Ectopic re-expression ofRBM10 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 andY971) by in vitro kinase assay and Immunoprecipitation experiments using phospho-Tyr specific antibody. Of the three cSrc sites, mutation of Y500F but not Y81F orY971F 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 acentral regulator of CH and progression to heart failure.

TEAM: Gowri V P, Sneha Sandra P S, Neeraja K M, Anurag Babu, Nimmy Mohan, Nimmy Francis, Ciji Varghese, Sudheesh AP

25 SEPTEMBER 2018

Hari Krishnan K, PhD

Pillai, A. B., Kumar, A. J. and **Kumarapillai, H**. Enhanced production of poly(3-hydroxybutyrate) in recombinant Escherichia coli and EDTA-microwave-assisted cell lysis for polymer recovery. ***AMB Express 2018, 8:142***

Production of bioplastic (poly[3-hydroxybutyrate]) in recombinant Escherichia coli and a novel eco-friendly method for the biopolymer recovery Polyhydroxy alkanoates (PHAs) are a group of polyesters accumulated in microorganisms as intracellular granules in response to unbalanced growth conditions. Poly(3-hydroxybutyrate) (PHB) is the most common kind of PHA produced by bacteria, having physical properties similar to that of polypropylene and has tremendous application potential in various fields. PHAs are regarded as a green-substitute for synthetic plastics due to their biodegradability, possibility to produce from renewable resources, and plastic-like properties. But their wide spread application as commodity plastics is hampered due to high cost of production. PHB productions from wild bacterial strains are uneconomical due to low yields, as they harbour PHA depolymerases enabling self-utilisation of the polymer. E. coli lack PHA depolymerases and hence a recombinant plasmid system was established in E. coli for improved polymer yield, utilising the PHB biosynthetic genetic elements from a high yielding environmental bacterial isolate Bacillus aryabhattai PHB10. The recombinant bacterial cells filled with polymer granules were observed by Transmission Electron Microscopy. The cells accumulated 6.22±0.08 g/L polymer which corresponds to 83.18% of cell dry mass (w/w) and the material was confirmed as PHB by Gas Chromatography-Mass Spectrometry and Nuclear Magnetic Resonance Spectroscopy analyses. A novel eco-friendly method was developed for cell lysis and the recovery of polymer granules, based on EDTA-microwave treatment and was found to be efficient on the recombinant cells. The new method yielded 93.75% polymer with a purity of 97.21% from recombinant E. coli. The PHB obtained through this method showed 2.9 fold improvements in molecular weight and homogeneity in comparison with polymer obtained through the conventional sodium hypochlorite treatment method. The study recorded the highest polymer accumulation rate ever reported through a batch fermentation system in a recombinant strain engineered solely with the genes from a Bacillus sp. Optimization of the production and recovery processes with this recombinant system and scaling up in large fermenters will reduce the cost of production yielding PHB with superior polymer properties.

TEAM: Geetha S L, Priya P, Athira S S

26 SEPTEMBER 2018

Ananda Mukherjee, PhD

Mukherjee A, Patterson AL, George JW, Carpenter TJ, Madaj ZB, Hostetter G, Risinger JI, Teixeira JM. Nuclear PTEN expression contributes to DNA damage repair in Endometrial Adenocarcinoma and could have a diagnostic benefit for therapeutic management of the disease. ***Mol Cancer Ther. 2018 Sep;17(9):1995-2003.***

Clinical response of a patient's tumor depends on its molecular characteristics. A guided therapy by targeting the molecular features is the way to reduce unwanted cellular toxicity and develop more effective treatments. The inadequate knowledge of candidate targets is the rate limiting to unleash the full potential of the guided therapy.

Currently, we have taken an in *silico* approach to identify a few candidate genes in endometrial carcinoma. It is among the few cancers, whose rate of incidence is increasing globally, and has a strong positive correlation with obesity of post-menopausal women. At the molecular level, tumor suppressor PTEN is the most mutated gene in endometrial cancer. Here, we utilized The Cancer Genome Atlas (TCGA) patients' data set and the Cancer Cell Line Encyclopedia (CCLE) to analyze the correlation of DNA damage response (DDR) genes with the alteration of PTEN in endometrial cancer. We used a curated list of the 276 DDR genes that are encompassing all major DNA repair pathways for the study. The analyses suggest that nucleotide excision repair (NER) pathway is enriched, and Damage Specific DNA Binding Protein 2 (DDB2), a UV-induced DNA damage sensor protein of NER signaling is significantly upregulated in endometrial cancer with altered PTEN expression.

We will validate results by assaying the level of gene expression, and setting up functional experiments to understand biological roles of DDB2 in development, progression, and therapy of endometrial tumors.

TEAM: Neethu Krishna

27 SEPTEMBER 2018

Omkumar R V, PhD

Arunkumar, R. C., Steephan, M., Rajeevkumar, R., Suma Priya, S. D., Kumar, M., Paul, M., Mayadevi, M., and **Omkumar, R. V**. A Simple End-point Assay for Calcium Channel activity. ***Cell Calcium 201874, p 73-85***

Earlier we have shown that the neuronal enzyme, CaMKII gets allosterically modulated by the NMDA receptor (NMDAR) subunit, GluN2B. Hypofunction of NMDAR that is known to cause neuropsychiatric diseases such as schizophrenia could be due to impaired regulation by microRNAs (miRNAs). We have identified several miRNAs that could down regulate NMDA receptor subunits in primary neuronal cultures. Excess glutamate treatment of primary neuronal cultures causes cell death mimicking excitotoxic neurodegeneration in vivo.Expression of semaphorin 3A, an axonal guidance molecule and its receptor neuropilin 1 were increased during excitotoxicity. 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. These models exhibited behavioural impairment as well as down regulation of cell survival signals such as pAkt and pCREB. A series of structurally related compounds and a plant extract that were inhibitory to NMDAR were found to be neuroprotective in vitro and in vivo. Patent applications have been filed in case of the tacrine derivatives. The plant extract was found to inhibit NMDA receptor dependent epileptiform activity in a rat brain slice model. Astrogliosis and several biochemical changes induced by MSG were prevented upon feeding with the extract. Our work has revealed new mechanisms underlying learning and memory as well as neurodegeneration. We have developed new tools as well as molecules to address demands related to r treatment of neurological diseases.

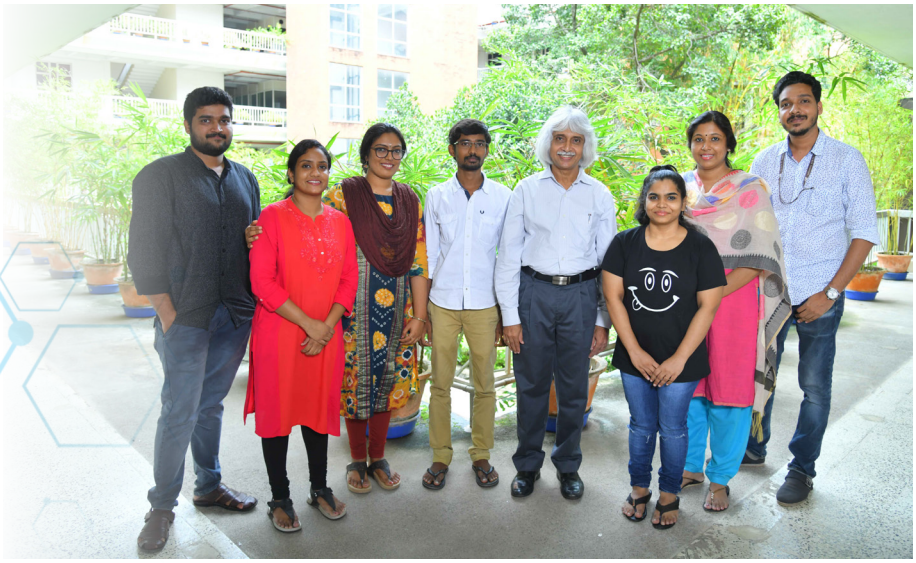
TEAM: G Sheela, Lakshmi K, Mayadevi M, Sowmya Gunasekaran, Reena Sara Jacob

28 SEPTEMBER 2018

Pradeep Kumar G, PhD

19th Royan International Research Award (RIRA), 2018
Best research project in Genetics field (shared winner)
"'Epigenetic regulation of coding and non-coding RNA expression during the 1st wave of spermatogenesis"

Autoimmune regulator (AIRE) is one of the differentially displayed sperm proteins identified in our laboratory to be associated with impaired spermatogenesis in men. We had amplified and cloned full length Aire from mouse testis and have established the presence of AIRE in mouse testis. AIRE is undisputedly known for its involvement in autoreactive T-cell deletion in thymic epithelium. Though extrathymic expression of AIRE is well documented, the functional relevance of AIRE in non-thymus tissues is recently emerging. AIRE is expressed in neonatal and adult testis, and has been implicated in sporadic germ cell apoptosis in developing testis. AIRE deficient mouse showed compromised fertility rates and reduced litter size. A reduction in the number of apoptotic cells in testis at an early phase of germ cell apoptosis is a notable feature of Aire-/- mouse. Apoptotic events operating at various stages of germ cell development are critical to a developing testis and caspase activation is known to play a crucial role in regulating the processes. AIRE has a Caspase Recruitment domain and it has been shown to induce cell death in HEK 293 cells. We examined whether AIRE has any role in inducing apoptosis in cultured spermatogonial cells. We report that C18-4 cells which are derived from As spermatogonia expressed AIRE, while GC1-spg which is closer to Type B spermatogonia was negative for AIRE expression. Overexpression of AIRE or CARD domain of AIRE induced Caspase-3 expression in GC1-spg cells. Silencing of AIRE in C18-4 and 12 day old mouse testis inhibited Caspase-3 expression. When overexpressed, AIRE and CARD brought about a very negligible increase in germ cell death and resulted in altered cell cycle pattern with a reduction in G1 phase. This was not associated with any increase in activation of Caspase-3. These results suggest that the CARD domain of AIRE enhances caspase-3 expression through possible direct DNA binding and triggers non-apoptotic downstream signalling in cultured spermatogonial cells.



TEAM: Shabith Raj, Susha Kutteyil, Mahitha Sahadevan, Jeeva S E, Devi A N, Vysakh G

29 SEPTEMBER 2018

Ani V Das, PhD

Significance of sub cellular localization of piwi homologs in cancer stem cells: correlation with chromatin modifiers. EMBO workshop on piRNAs and PIWI proteins, Le Corum, France.

Virtually all cervical cancers are caused by HPV infections, but not all the HPV infections lead to tumorigenesis. The most interesting question is that why all the HPV infections do not lead to tumorigenesis. We hypothesize that there are a few factors, in association with which HPV oncogenes that cause induction of cancer. Piwi, a subfamily of Argonaute proteins, could be one such factor since they have been known to act as carriers for many proteins. Evidence indicates that Piwi proteins are aberrantly expressed in cervical cancer. In the present study, we are trying to understand the correlation of Piwi homologs with HPV oncoproteins. For our study, we selected three cervical cancer cell lines based on the HPV integration: C33A (HPV-ve), CaSki (HPV+ve High Copy) and SiHa (HPV+ve low copy). We observed that all the four homologs of Piwi proteins were present in these cervical cancer cell lines (Hiwi/PiwiL1, Hili/PiwiL2, PiwiL3 and Hiwi2/PiwiL4). Except PiwiL2, all the other Piwi homologs showed high expression in CaSki (HPV+ve, high copy) than SiHa (HPV+ve, low copy) and C33A (HPV-ve) suggesting a positive correlation with HPV oncoproteins. But PiwiL1 showed more expression than other homologs. In silico docking analysis using ClusPro predicted a possible physical interaction of E6/E7 with Piwi L1. We found that PiwiL1 was co-expressed with both E6 and E7 in CaSki cells. Not only E6 and E7 physically interacted with PiwiL1, but also they accentuated its expression in cervical cells. Further, using an in silico approach, from small RNA Sequencing Data, 663 known piRNAs have been predicted from cervical tissue samples of which 76 piRNAS were in control and 333 piRNAs in cancer samples. Our data suggest that Piwi proteins and associated piRNAs may have important role in HPV-associated tumorigenesis in cervical cells.

TEAM: Joby Issac, Jayasree R , Midhuna Raj K, Mary Angelin

30 SEPTEMBER 2018

AWARDS

Haritha H.Nair : Budding scientist award for Best oral presentation at the 3rd International Conference on Nutraceuticals and Chronic Diseases held at Rishikesh, Dehradun, Sep 14th-16th 2018.

OUTREACH

220 students from schools and colleges of Trivandrum visited RGCB for an outreach program as part of India International Science Festival (IISF) 2018. School and college students visited stalls put up by RGCB to showcase the institute research activities.

31 SEPTEMBER 2018

OUTREACH

LAB VISIT

Periyar University, Salem 46 Students

Sreekumar E, MVSc, PhD

Singh S, Anupriya MG, Modak A, **Sreekumar E**. Denguevirus or NS1 protein induces trans-endothelial cell permeability associated with VE-Cadherin and RhoA phosphorylation in HMEC-1 cells preventable by Angiopoietin-1. ***J Gen Virol. 2018 Oct 24***

Host cellular proteins are important targets to modify the disease pathogenesis caused by dengue virus. In dengue patients a transient increase intrans-endothelial cell permeability leads to vascular leakage and shock syndrome. We analyzed the molecular mechanisms that cause permeability changes using a direct dengue virus (DENV) infection model or treatment with NS1, a secreted DENV non-structural protein in human dermal microvascular endothelial cells (HMEC-1).Both the treatments increase permeability in the monolayer culture of these cells with a concordant increase in the secretion of Angiopoietin-2 (Ang-2). We detected that at the protein level, there is phosphorylation and loss of the junction protein VE-Cadherin from the inter-endothelial cell junctions and phosphorylation of RhoA. Wecould also identify difference between the two treatments. Direct virus infection results in activation of Src by phosphorylation, whereas NS1 treatment alone doesnot lead to Src activation. Addition of recombinant Ang-1, a physiological antagonist of Ang-2, in the treated cells prevents Ang-2 release, VE-Cadherin phosphorylationand internalization, and phosphorylation of RhoA and Src, resulting in restoration of barrier function. The permeability increase could also be prevented by blocking theAng1/2 signaling receptor, Tie-2 or using a Rho/ROCK-specific inhibitor. Dasatinib, a Src-family kinase (SFK) inhibitor that prevents Src phosphorylation, alleviated enhanced permeability induced by direct DENV infection whereas in NS1 protein-treated cells its effect is less significant. The results from our study stress that there are possibilities of therapeutic use of recombinant Ang-1 or Src phosphorylation inhibitors in order to prevent vascular leakage in dengue.

TEAM: Navya Pious, Parvanendhu P, Sreeja S, Srishti Rajkumar Mishra, Rahna A, Anupriya M G, Ayan Modak, Rebu Varghese,

Surya Ramachandran, PhD

Indian Council of Medical Research, Chaturvedi Kalawati Jagmohan Das Memorial Award for Research in Cardiovascular Diseases.

Macrophage apoptosis and the ability of macrophages to clear dead cells, known as efferocytosis, are crucial determinants of atherosclerosis lesion progression. Prolonged ER stress with Unfolded Protein Response (UPR) activation stimulates apoptosis. Cyclophilin A, a secretory monocyte protein, induces foam cell formation in high glucose activated macrophages. In this study we hypothesize that cyclophilin A increases apoptosis and impairs efferocytosis under high glucose conditions. We developed an in vitro model of monocyte derived macrophages cultured in 20mM (high) glucose in the presence and absence of extracellular cyclophilin A. Flow cytometry was used to identify apoptotic cell death using Annexin V-FITC/PI staining. Increased apoptotic cell population by annexin FITC staining was observed by flow cytometry and immunofluorescence assay. DNA fragmentation assay also confirmed that cyclophilin A induces THP 1 macrophage apoptosis in high glucose conditions. Addition of cyclophilin A led to mitochondrial depolarization and a loss of TMRM fluorescence intensity. The levels of mitochondrial superoxide anion were significantly increased in the presence of cyclophilin A. Cyclophilin A activated the ER stress inducers such as IRE-1, elf 2 and ERK in high glucose conditions. Further treatment with cyclophilin A significantly increased the phosphorylation of IRE 1alpha indicating that cyclophilin A induces prolonged UPR activation which leads to apoptosis of high glucose primed macrophages. To explore the impact of cyclophilin A on the efferocytic capacity of phagocytic cells, we performed efferocytosis assays in the presence and absence of cyclophilin A using cocultured THP 1 macrophages and apoptotic smooth muscle cells. The results of flow cytometry and confocal microscopy assays demonstrated that apoptotic HCASMCs were cleared less efficiently by cyclophilin treated phagocytes compared to professional phagocytes. Thus cyclophilin A impairs efferocytosis and increases apoptosis in high glucose activated macrophages.

TEAM: Jithin Das, Sangeetha Vijay, Jayalekshmi V S, Vinitha A, Thushara Thulaseedharan

Debasree Dutta, PhD

Best Poster Award
at Women Conclave
in India International
Science Festival (IISF),
Lucknow, October 2018.

In our earlier study, we demonstrated that Histone cell cycle regulator A (HIRA), a histone chaperone, regulates hemogenic to hematopoietic transition involved in normal hematopoiesis. Abnormal proliferation and disrupted differentiation of hematopoietic progenitors mark the emergence of leukemia. Mechanistically, HIRA is involved in the dynamics of nucleosomes and have been associated with other regulatory stages during development. But, its role remains unexplored in leukemia, a case of dysregulated hematopoiesis. In this year, we studied the role of HIRA in dictating the proliferation vs. Differentiation of leukemia cells. The Cancer Cell Line Encyclopedia database analysis showed enhanced HIRA mRNA expression in cells of hematopoietic and lymphoid origin with maximal expression in the chronic myeloid leukemia (CML) cell line, K562. This observation was further endorsed by the induced expression of HIRA in CML patient samples. Downregulation of HIRA in K562 cells displayed cell cycle arrest, loss in proliferation, presence of polyploidy with significant increase in CD41+ population thereby limiting proliferation but inducing differentiation of leukemia cells to megakaryocyte fate. Induced megakaryocyte differentiation of mouse Hira-knockout hematopoietic progenitors in vivo further confirmed the in vitro findings in leukemia cells. Molecular analysis showed the involvement of MKL1/GATA2/H3.3 axis in dictating differentiation of CML cells to megakaryocytes. Thus, HIRA could be exploited for differentiation induction therapy in CML and in chronic pathological conditions involving low platelet counts.

TEAM: Bindhu M S, Debparna Nandy, Dhanalakshmi J, Ishita Baral, Sruthy M R, Pallavi Chinnu Varghese, Arya T Dharan

AWARDS

Malini Laloraya PhD elected Fellow of The National Academy of Sciences, India (NASI), 2018

TALKS

Divya Kattupalli: PhD student of Dr EV Soniya. "Phytophthora Infected Transcriptome and Metabolome Reveals Insight into Biotic stress Responses of Piper nigrum L." at *National Conference on Next Generation Sequencing & Rational Drug Designing*, jointly organized by DBT-BIF Centre, SIUCEB & AICADD at DCBB, University of Kerala on 8th October, 2018.

Aswathi U, PhD student of E V Soniya (Oral presentation). "An insight into a novel group of gene regulators in the small RNA cartel of Black pepper" in the *National Conference on Next Generation Sequencing and Rational Drug Designing*, jointly organized by the DBT-BIF Center, SIUCEB &AiCADD at the Department of Computational Biology and Bioinformatics, University of Kerala on 8th October 2018 .

Archana PT, Binitha Anu Varghese, Nitheesh K, Radhika Nair Studying the role of microenvironment in breast cancer metastasis; *14th Indo-Australian Biotechnology Conference on 'Emerging modalities to improve cancer outcomes'* held on 22nd and 23rd October 2018 at ACTREC-Tata Memorial Centre, Kharghar, Navi Mumbai-410210 Maharashtra, India.

Sweda Sreekumar PhD student of EV Soniya (Oral presentation). "De novo transcriptome analysis of black pepper berries brings out critical genes and transcription factors in secondary metabolism" in the One day *National Conference on Next Generation Sequencing & Rational Drug Designing* jointly organized by the DBT-BIF Center, SIUCEB & AICADD at the Department of Computational Biology and Bioinformatics, University of Kerala on 8th October 2018.

OCTOBER 2018

OUTREACH

RGCB participated in the India International Science festival (IISF) in Lucknow with active involvement of young investigators, women scientists, faculty and staff. Students from different schools of India visited the RGCB stall at the MEGA SCIENCE AND TECHNOLOGY & INDUSTRY EXPO

Jackson James, PhD

J. James, R. Ann Paul, L. Soundararajan, S. Parvathy, S. Surya, V. Meera, S. Dhanesh, B. Budhaditya. Differential mode of Hes-1 activation maintains neural stem cells and promotes its transition into radial glial cells during neocortical development. Neuroscience 2018, Society for Neuroscience meeting, 3-7 November 2018, San Diego, USA

Notch signaling pathway and its downstream effector Hes-1 are well known for their role in cortical neurogenesis. Despite the canonical activation of Hes-1 in developing neocortex, recent advances have laid considerable emphasis on Notch/CBF1-independent Hes-1 (NIHes-1) expression with poor understanding of its existence and functional significance. Here, using reporter systems and in utero electroporation, we could qualitatively unravel the existence of NIHes-1 expressing neural stem cells from the cohort of dependent progenitors throughout the mouse neocortical development. Though Hes-1 expression is maintained in neural progenitor territory at all times, a simple shift from Notch-independent to -dependent state makes it pleiotropic as the former maintains the neural stem cells in a non-dividing/slow-dividing state, whereas the latter is very much required for maintenance and proliferation of radial glial cells. Therefore, our results provide an additional complexity in neural progenitor heterogeneity regarding differential Hes-1 expression in the germinal zone during neocortical development.

TEAM: Sreedevi L R, Meera V, Lalitha S, Riya Ann Paul, Surya S, Budhaditya Basu, Biju S Nair, Parvathy S

Ajay Kumar R, PhD

Sajith Raghunandanan, Leny Jose, Vipin Gopinath and Ramakrishnan **Ajay Kumar** (2019). Comparative label-free lipidomic analysis of Mycobacterium tuberculosis during dormancy and reactivation. ***Scientific Reports 2019, 9:3660 DOI:10.1038/s41598-019-40051-5.***

Mycobacterium tuberculosis (MTB) is an intracellular pathogen and employs several strategies to adapt to adverse conditions inside the host. The bacterium undergoes many physiological changes to enter into a dormant state and then to get reactivated when the conditions become favourable. Our previous work has demonstrated significant changes in the proteomes of normoxially growing, dormant and reactivated MTB. One of the significant observations was the variations in the proteins involved in the lipid metabolism in MTB. To get an insight into the changes this might cause in the lipid content of the bacterium, we employed a comparative lipidomic analysis, to profile the changes in lipid content in MTB during normoxia, dormancy and reactivation. In parallel to the changes in the proteomic profile, we observed an enhanced degradation of cell wall-associated and cytoplasmic lipids during dormancy, and their gradual restoration during reactivation. After 144 h the lipid profile was similar to that of normoxially grown bacteria. This study reveals how MTB modulates its lipid content to tide over dormancy and during reactivation.

Isoniazid (INH) is a first-line drug used to treat tuberculosis because of its ability to inhibit mycolic acid synthesis, an integral lipid component of the mycobacterial cell wall. Non-replicating MTB is phenotypically resistant to INH. Inability of dormant MTB to convert the pro-drug into its active form is thought to be one of the reasons for this resistance. Employing targeted metabolomic approach, we showed that dormant MTB can metabolize INH into its active INH-NAD+ adduct form. Further we showed that the dormant bacteria have similar levels of expression of katG and inhA(INH metabolizing enzymes) as in actively growing bacteria. Levels of drug efflux pump proteins do not increase in response to INH treatment during dormancy. These findings point to an alternative mechanism for INH resistance in dormant MTB.

TEAM: Salini, Jijimole G R, Aravind Madhavan, Krishna Kurthkoti, Nijisha M, Laiza Paul, Ranjit Ramachandran, Mini, Balaji M, Sreejith, Akhil Raj P, Arun K B

Krishna Kurthkoti, PhD

It is widely recognized that biofilm formation is a widespread phenomenon across the bacterial domain and infections involving bacterial biofilms are extremely resistant to antibiotic therapy. Previously, we had observed there is increased expression of an error-prone DNA polymerase dnaE2 in Mycobacterium smegmatis biofilms resulting in increased mutation rate compared to the planktonic culture. Using the promoter fusion reporter strains we further showed that expression of dnaE2 was induced when the strains were subjected to lethal doses of drugs and also during starvation condition indicating that dnaE2 could be a part of the stress induced mutagenesis system in mycobacteria. To further probe the role of dnaE2, a knockout strain was constructed in M. smegmatis and initial characterization revealed that the strain was sensitive to UV radiation. Additionally, the mutant strain displayed reduced persistence when subjected to lethal doses of antibiotics and lower mutation rate than the parental wild-type strain in biofilm cultures.

To determine the proteins that interact with DnaE2 and to identify the DNA binding sites of the enzyme, we generated a FLAG tagged DnaE2 construct and expressed it in a dnaE2 mutant strain. The FLAG tagged strain was functionally active as it could complement UV sensitivity phenotype displayed by the mutant strain. Currently, conditions for immunoprecipitation are being standardized to identify DnaE2 interacting proteins.

TALKS

Institute Foundation Day Lecture - 2018
"S & T in India through the ages and for the future" by Dr. Shekhar C Mande, Secretary, Government of India, Department of Scientific and Industrial Research and Director General, Council of Scientific and Industrial Research (CSIR), November 18, 2018.

L. Soundararajan, V. Meera, S. Surya, R. Ann Paul, S. Parvathy, B. Basu, A. Bhattacharjee, NM. Abraham and J. James. Guiding Retinal Ganglion cell axons to brain visual centres: Is Pax6 the key molecule?.Neuroscience 2018, Society for Neuroscience (SFN) meeting, 3rd to 7th November 2018, San Diego, USA

R. Ann Paul , S. Parvathy , L. Soundararajan , T. Thomas Maliekal , S. Nelson Sati , J. James. Recapitulating developmental cues of neural stem cells into cancer stem cell maintenance: Is pleiotropic Hes-1 responsible Neuroscience 2018, Society for Neuroscience (SFN) meeting, 3rd to 7th November 2018, San Diego, USA

EVENTS

Regional Children's Science Congress 2018 organized by Navodaya Vidyalaya Samiti Hyderabad region at RGCB

AWARDS

Nimmy Fathima Francis, PhD student of Dr. Rakesh S. Laishram was awarded the RGCB Student Merit Award 2018 by Dr Shekhar Mande, DG CSIR, India on the RGCB Foundation Day

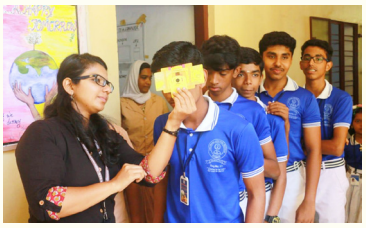
Riya Paul, student of Dr. Jackson James was awarded the joint Second Prize for the RGCB merit award 2018

Mantosh Kumar, Ph.D. student of Dr RV Omkumar was awarded with Trainee Professional Development Award (TPDA) 2018 by Society for Neuroscience (SFN), USA for presenting poster at Society for Neuroscience meeting held on 3-7 November 2018 at San Diego, USA

Nimmy Mohan, Ph.D. Student, Best Poster Award: "A Splicing Factor RBM10 controls 3'-UTR Processing to regulate Cardiac Hypertrophy" at the 87th meeting of the Society of Biological Chemists (India) from 25th-27th November, 2018 held at School of Life Science, Manipal Academy of Higher Education, Manipal, Karnataka

Tapas Pradhan, student of Dr Asha Nair was awarded the joint Second Prize for the RGCB merit award 2018

OUTREACH



Team Foldscope of RGCB conducting workshops and creating awareness about the simple affordable and durable paper microscope

LAB VISIT

Shanthiniketan School, TVM	100 Students
Hyderabad Cluster	59 Students
Govt.Girls H.S.S, Karamana	51 Students
Salvation Army, TVM	50 Students
ViswadeepthiCentral School, Kattakada	45 Students
Sree Narayana Trust H.S.S, Chenganoor	36 Students

Saraswati Nayar, PhD

Saraswati Nayar, Overexpression of a cytokinin related gene (CRG) in Chlorella extends its life in culture. *4th International Plant Physiology Congress.* Lucknow. December 2nd -5th, 2018

Functional characterization of a MADS box transcription factor in unicellular algae. We are currently working on a MADS box transcription factor in a unicellular green algae. The presence of this MADS box transcription factor has been confirmed by BLAST analysis wherein proteins from Arabidopsis and Rice were used as reference sequence. It is already known that MADS box transcription factors are present in green algae belonging to Charophyceae. Further studies will reveal whether this isolated MADS box transcription factor is similar to that of land plants. One of the first objectives was to find the full length cDNA of this transcription factor. Using 5' RACE and 3'RACE we found that the sequence available on the database was complete and it did not contain the I, K, C domains like the MADS box transcription factors of seed plants. Localization study has revealed that this transcription factor is unable to localize to the nucleus specifically though it has a monopartite nuclear localization signal (NLS). To check if this protein is able to homo dimerize it was cloned into YFPn and YFPc(bimolecular fluorescence; BiFC) vectors. According to the BiFC results it was observed that this protein is able to homo-dimerize as well as localize to the nucleus specifically. Thus this protein needs to dimerize for localization in the nucleus indicating the requirement of two NLSs. Further studies were done to delineate the NLS and the dimerization interface of this transcription factor by mutation studies. When the NLS was mutated the specificity to the nucleus was lost and the dimer was seen to localize in the cytoplasm thus confirming the function of the NLS. When the dimerization interface was mutated, dimerization efficiency was affected as the dimer was not able to localize in the nucleus and expression was seen mainly in the cytoplasm. Further studies using the overexpression and knock down lines will reveal the exact role of this transcription factor.

Suparna Sengupta, PhD

Suparna Sengupta
"α-Fodrin is essential for the organization of functional microtubules during mitosis" - Indian Society for Cell Biology conference, Goa, India, December 2018

Fodrin is mostly known for its role in the maintenance of cytoskeletal structure integrity of plasma membrane. Its role as a functional protein is rarely known except for a few reports in apoptosis and TGF-β signaling. To check more of its functional involvement in mitosis, we are depleting fodrin by shRNA treatment in glioblastoma and neuroblastoma cell lines where it is present in plenty. Our earlier studies show that depletion of fodrin gives rise to mitotic delay, metaphase arrest and mitotic errors like uncongressed chromosomes and multipolarity. These defects are accompanied with increase in checkpoint proteins at the kinetochores as measured by timely mitotic completion by the inhibition of checkpoint protein MPS1 and measuring the checkpoint protein BubR1 and CREST ratio. We find that lesser number of kinetochore attached microtubules are generated in a mitotic cell upon fodrin downregulation. We are also checking the role of fodrin depletion on mitotic motors such as CENP-E which would cause the improper alignment of the chromosomes during mitosis that causes mitotic delay. Further, reports published earlier from our lab detail the presence of fodrin as a component of the γ-TuRC (gamma tubulin ring complex) derived from neuronal tissue and neuronal lineage cells. The major objective of this study is to understand the contribution of fodrin in γ-TuRC mediated functions in the cells. γ-TuRC is a complex association of proteins, utilized in the cells as a major tool for microtubule formation and organisation from the centrosome. Our earlier studies by two methods showed that fodrin interacted directly with gamma tubulin - by far western analysis, and by immunoprecipitation studies in HEK 293 cells overexpressed with fodrin. We have further checked experimentally the domain of fodrin involved in the interaction with fodrin by cloning different fragments and found that a C-terminal fragment is involved in the binding. We have also checked the role of fodrin on microtubule nucleation by analysis of microtubule assembly. Turbidometric and electron microscopic analysis of microtubule polymerization induced by γ-TuRC in presence of fodrin showed that fodrin's interaction with gamma-tubulin is responsible for its inhibitory effect on γ-tubulin mediated microtubule nucleation.

TEAM: J S Sreeja, Athira Jyoti, Dhrishya Dharmapal, Krishnatej Pammi

Sumi S, PhD

N Radhakrishnan, Deepu George, R Jayakrishnan, **Sumi S** , CC Kartha. Vein size and disease severity in chronic venous diseases. ***International Journal of Angiology 2018 Dec;27(4):185-189.***

Chronic venous disease (CVD) of lower limbs is characterized by the presence of varicose veins, edema, skin hyperpigmentation, and venous ulcers. Blood reflux in larger veins was hitherto considered the key factor for morbid manifestations of CVD. We conducted a retrospective study comprising 6350 patients with CVD to find the relationship between the size of veins with blood reflux and clinical manifestations. Our study revealed that reflux and varicosity in incompetent reticular veins and vein tributaries is associated with severe manifestations of CVD, rather than the truncal saphenous veins. Our studies also indicate a prominent role of altered hemodynamics in venous remodeling resulting in CVD. Hence we are aiming to define the role of altered shear stress during disturbed blood flow on venous wall remodeling. In an in vitro study using integrated BioDiagnostics flow system, human umbilical vein endothelial cells (HUVEC) were exposed to non-uniform shear stress mimicking the vein vasculature in CVD and laminar shear stress comparable to normal venous flow. The magnitude of shear stress was maintained at 6 dyn/cm2 which represents venous pressure. Gene expression analysis demonstrates that the exposure to disturbed flow resulted in endothelial dysfunction in vein cells. A sustained laminar shear stress in a physiological range induced the expression of anti-inflammatory and anti-proliferative genes (eNOS, Klf2) that exert a vasoprotective effect. Disturbed flow induced the expression of several pro-inflammatory genes (HuR, BMP4). Cells exposed to disturbed flow became inflammatory and proliferative phenotype. We also found the overexpression of Snai1, N cadherin, α SMA and vimentin in the endothelial cells exposed to disturbed flow indicating the activation of Endothelial mesenchymal transition (EndMT). All the above shear stress and EndMT markers were seen upregulated in human varicose veins as well, suggesting a role of disturbed flow induced EndMT in such patients. Our study highlights the role of altered blood shear stress in the development of endothelial dysfunction and venous remodelling leading to development of CVD.

TEAM: Karthika C L

DECEMBER 2018

John Bernet Johnson, PhD

"Complement mediated neutralization of a potent neurotropic human pathogen, Chandipura virus, is dependent on C1q."
Centre for Infectious Disease Research, Indian Institute of Science & Infosys Foundation,Symposium on Viral Diseases,13th December, 2018

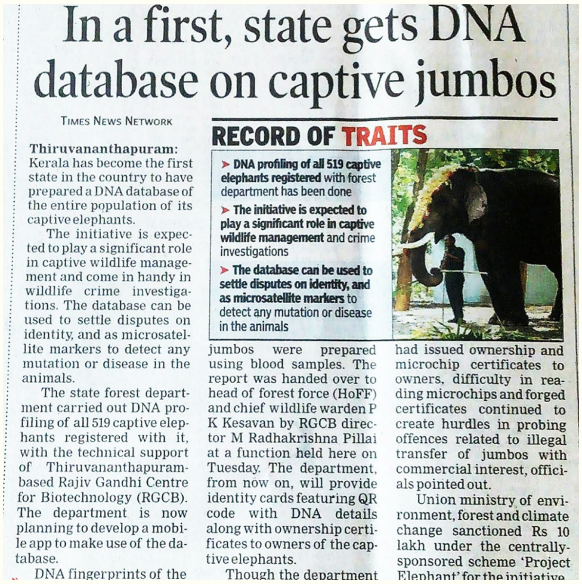
Rhabdoviruses are RNA viruses of significance to both animals and humans and include Chandipura virus and rabies virus. Pathogenesis associated with Rhabdoviruses is manifested upon dissemination to the CNS. The primary barrier faced by these viruses is the innate arm of the immune system which includes the complement system. The complement system lacks memory and can target pathogen via three major pathways, classical (CP), mannose binding lectin (MBL) or alternative pathway (AP). A finely choreographed group of proteins called as regulators of complement activation (RCA) minimizes unprecedented complement activation. This study aims to unravel the underlying mechanism of complement activation and evasion by Rhabdovirus, using the prototypic vesicular stomatitis virus (VSV). The only surface glycoprotein,the G protein of VSV, activated complement resulting in sensitization of the virus to CP mediated neutralization. However VSV was found to limit complement dependent neutralization by employing a novel strategy of recruiting the host RCA's, CD46 and CD55. The virion associated CD46 and CD55 was capable of inactivating C3b or accelerating the disassembly of complement convertases (C4b2b, C3bBb, C4b2b3b and [C3b]2Bb). CD55 protein levels were maintained in infected HeLa cells between 0 – 24 h while a steady decline in CD46 levels was observed after 11h suggesting greater protective role for CD55 over CD46. However, transcriptional down regulation of both the RCA's was observed,with marked delay in CD55 down-regulation. Virus harvested at select checkpoints including 12, 18 and 24h showed increased RCA incorporation most importantly CD55 at early time points. The potency of the biological activity and protection conferred correlated with the time of egress and levels incorporated, with CD55 having a dominant role than CD46. With increasing efforts to exploit VSV as an oncolytic or vaccine vector it is highly essential to understand the molecular modulation of complement to develop potent yet safe vectors.

TEAM: Joydeep Nag, Nisha Asok Kumar, Umerali K, Sreenath MS, Reshma K M

AWARDS

Reena Sara Jacob, Ph. D. student of Dr RV Omkumar was awarded the second prize for 'Best Poster in Research Category at *3rd IBRO/APRC Chandigarh Neuroscience School* organized by University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh from 25 November - 2 December, 2018

EVENTS



In a first, state gets DNA database on captive jumbos

TIMES NEWS NETWORK

Thiruvananthapuram: Kerala has become the first state in the country to have prepared a DNA database of the entire population of its captive elephants.

The initiative is expected to play a significant role in captive wildlife management and come in handy in wildlife crime investigations. The database can be used to settle disputes on identity, and as microsatellite markers to detect any mutation or disease in the animals.

The state forest department carried out DNA profiling of all 519 captive elephants registered with it, with the technical support of Thiruvananthapuram-based Rajiv Gandhi Centre for Biotechnology (RGCB). The department is now planning to develop a mobile app to make use of the database.

DNA fingerprints of the jumbos were prepared using blood samples. The report was handed over to head of forest force (HoFF) and chief wildlife warden P K Kesavan by RGCB director M Radhakrishna Pillai at a function held here on Tuesday. The department, from now on, will provide identity cards featuring QR code with DNA details along with ownership certificates to owners of the captive elephants.

Though the department had issued ownership and microchip certificates to owners, difficulty in reading microchips and forged certificates continued to create hurdles in probing offences related to illegal transfer of jumbos with commercial interest, officials pointed out.

Union ministry of environment, forest and climate change sanctioned Rs 10 lakh under the centrally-sponsored scheme 'Project Elephant' for the initiative

RECORD OF TRAITS

- DNA profiling of all 519 captive elephants registered with forest department has been done
- The initiative is expected to play a significant role in captive wildlife management and crime investigations
- The database can be used to settle disputes on identity, and as microsatellite markers to detect any mutation or disease in the animals

Kerala's Captive Elephants Get Own Genetic IDs. Director RGCB handed over DNA fingerprinting reports of 519 captive elephants to the Kerala Forest Department.

OUTREACH

LAB VISIT

S.N. College, Varkala 37 Students

Professor Rakesh Kumar, PhD

Rahul Sanawar, Vipin Mohan, Thankayyan R Santhoshkumar, **Rakesh Kumar** and M. Radhakrishna Pillai. Estrogen receptor-α regulation of microRNA-590 targets FAM171A1—a modifier of breast cancer invasiveness, ***Oncogenesis, 2019 8:5***

The development of human cancer, as a polygenic disease, involves co-dysregulation of multiple cellular pathways and underlying regulatory molecules for manifestation of a battery of cancerous phenotypes. Examples of dysregulation of critical biologic processes shared across multiple cancers include: proliferation, inflammation, energy metabolism, chromatin and cytoskeleton remodeling and immune response. Though some cancers are driven by mutant versions of certain genes and/or addicted on certain genes, the majority of cancer-types are dependent on multiple gene/protein modules for maintaining the abnormal cellular proliferation. These facts fundamentally argue against the notion of cancer-dependency on a single gene unless the cancer-type in question is absolutely addicted on it. Further, the lateral regulatory approval of cancer drugs after an initial approval is also primarily driven by the reasoning of shared pathways. Recently, Kumar's team has postulated that cancer being a polygenic disease could be best tackled by pursuing a polygenic hypothesis. In this context, the laboratory has discovered: a) a set of over two dozen genes that are coordinated co-overexpressed across multiple cancer-types, including breast, ovarian, lung, head & neck, glioma, colon, pancreatic, liver, gastric; b) over expression of these genes in is not necessarily associated with their genomic amplification; c) these genes exhibit shared transcriptional factor binding motifs and modified histone marks across their regulatory regions; d) encode proteins belonging to diverse known or predicted functions; e) a sub-set of genes are components of cancer stem cell elements as well as of exosomes etc. Because of co-dysregulation of multiple genes with diverse established or predicted functions, we hypothesized that persistent co-upregulation of these genes will lead to dysregulation of complementary functions that might be shared across multiple human cancer-types. In brief, these studies are allowing us to gain new insights into the pathobiology of human cancer, build new pathways, present new strategies for an unavoidable acquired therapeutic resistance, and for tackling more than one cancer types by shared approaches by design.

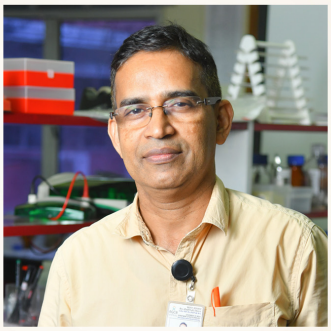
TEAM: Amjesh Ravi, Aswathy Mary Paul, Bijesh George, Rajeswari Raghuraman

Santhosh Kumar T R, PhD

Chandrasekharan, A., S. N. Varadarajan, A. Lekshmi, S. S. Lupitha, P. Darvin, L. Chandrasekhar, P. R. Pillai, **T. R. Santhosh kumar** and M. R. Pillai. A high-throughput real-time in vitro assay using mitochondrial targeted roGFP for screening of drugs targeting mitochondria. ***Redox Biol, 2019, 20, 379-389.***

The thrust area of my research group is to generate cell and tissue resources for understanding tumor progression and generate in vitro and preclinical models to enable cancer drug screening and identifying target specific drugs. The laboratory has developed patient derived xenografts from breast cancer patients as a resource for tumor progression studies and drug discovery. A 3D in vitro and ex vivo tissue based real time approach was developed to quantitate drug efficacy at single cell level. Glutathione depletion is a typical hallmark of apoptosis and changes in the intracellular thiol-disulfide (GSH/GSSG) balance is a determinant of the redox status/signaling of the cell. The GSH/GSSG based roGFP shows dual excitation peaks at 405 nm and 488 nm. Oxidation-dependent disulfide formation leads to an increase of emission signal from 405 nm excitation and a reduction in 488 nm excitation. Based on this , the laboratory has engineered a reliable cell based indicator of redox potential of mitochondria using ratio imaging. The tool consists of stable cell expressing roGFP targeted at mitochondria (mt-roGFP) and nuclear H2B-mCherry that enable real-time imaging of mitochondrial oxidation induced by cytotoxic compounds in a high-throughput manner. The study showed that mitochondrial oxidation is an universal marker for mitochondrial permeabilization. This event can be detected at the single-cell level using mitochondrial targeted redox sensing GFP with high spatio-temporal resolution. Simultaneous imaging of redox alterations of mitochondria and mitochondrial permeabilization of dying cells revealed that mitochondrial oxidation is an initiator of mitochondrial permeabilization and mitochondria undergoes rapid secondary oxidation upon completion of mitochondrial permeabilization. The assay is highly sensitive, easy to adapt to high-throughput screening platforms and is a valuable resource for identifying cytotoxic agents that target mitochondria and also for dissecting cell signaling events relevant to redox biology.

TEAM: Shivanshu Kumar Tiwari, Minsa M , Aswathy S, Sanoj Namdev Patil, Pramod Darvin, Shine V J, Aneesh Chandrasekharan, Halikar Aman Munirpasha



Abdul Jaleel K A, PhD

Vijayakumar G, Manghat S, Vijayakumar R, Simon L, Scaria LM, Vijayakumar A, Sreehari GK, Kutty VR, Arun R, **Jaleel A**. Incidence of type 2 diabetes mellitus and prediabetes in Kerala, India: results from a 10-year prospective cohort. ***BMC Public Health. 2019;19(1):140***

The major research theme of my laboratory is metabolic adaptations towards the onset of type 2 diabetes Mellitus (T2DM), and that too focused on the population in Kerala. T2DM is now highly visible across all sections of society within Kerala. Majority of the data on burden of T2DM in India is derived from the prevalence estimates. Though incidence studies could provide more valid estimates of disease trend, such studies on T2DM are limited and none from Kerala. Last year, my laboratory in collaboration with Medical Trust Hospital, Kulanada completed a 10 year prospective cohort study estimating the incidence of T2DM in two adjacent Wards of Venmony Panchayat of Pathanamthitta District in Kerala State. The individuals who participated in the baseline survey 10 years ago were again invited for a follow-up study. Logistic regression analysis was used to estimate odds ratios and 95% confidence intervals. Findings are based on the 10 year follow-up data from 869 participants from the cohort. The overall follow-up and response rate of the study was 68.9% and 86.9% respectively. During the follow-up period, 190 people (21.9%) developed T2DM. The incidence rate of T2DM and impaired fasting glucose (IFG) were 24.5 per 1000 person years and 45.01 per 1000 person years respectively. Nearly 60% of participants with baseline IFG were converted to T2DM group in the follow-up period. Age >45 years, family history of T2DM, BMI≥25 and presence of central obesity emerged as important risk factors for incident T2DM. The population attributable risks for overweight/obesity and central obesity were 27.2 % and 21.8% respectively. High incidence of prediabetes over diabetes observed in this study shows an epidemic trend of T2DM in Kerala, India and solicit for an immediate public health action.

TEAM: Mahesh Chandran, Mahesh Krishna, Kalaivani V, Akhila Suresh, Gopika Satheesh, Deepa Mathew, Aneesh Kumar A

Arumugam Rajavelu, PhD

Jabeena CA, **Rajavelu A**. Epigenetic players of chromatin structure regulation in *Plasmodium falciparum*. ***Chem Bio Chem.2019 Jan 10, 20. 1 – 7.***

The *P. falciparum* carries unique epigenetic signatures like the absence of linker H1, RNAi and carries unusual histone methylation marks. Importantly, the DNA cytosine methylation and its functions in P. falciparum remain enigmatic. Moreover, stage-specific gene expression is poorly characterized in P. falciparum. It has been proposed that the nature of chromatin structure fine-tunes the gene expression in malaria parasite. The regulators of chromatin organization/plasticity in various developmental stages of parasite remain elusive. Our focuses are to explore the various novel histone methyl modifications and its role in nucleosome organization, chromatin plasticity. We have identified methyl mark at unconventional positions at H3K64, H3R48 and H4K44 on histone globular domains of *P. falciparum*. Further, we found that H3K64me3 is deposited in stage-specific manner, the methyl mark present in ring and trophozoite stages but reduced in schizont stage. This suggests a strong role of core histone methylation in regulation of dynamic chromatin structure in the parasite. To identify the methyltransferases which introduces H3K63me3 in *P. falciparum*, we cloned, expressed, purified 9 SET domains from P. falciparum as recombinant proteins. The in vitro methyltransferase assays identified only two SET proteins of parasite methylates at H3K64 position. Most importantly, we have found that these two SET proteins prefer intact nucleosome as substrate and do not methylate free histones. This is very interesting findings as this mark lies close to DNA contact point on the nucleosome and it might have strong role in regulation of chromatin dynamics. To identify the potential function of H3K64me3, we have performed global ChIP analysis and found that the methyl mark dynamically mark the family of genes belong to exported proteins that are essential to maintain the RBC integrity and antigenic variation. A detailed study on PfSET4 and PfSET5 proteins would help us to find unique drug targets in *P. falciparum*.

TEAM: Dhakshmi S, Devadathan V S, Jabeena C A, Gayathri G

JANUARY 2019

Radhika Nair, PhD

"Phenotypic heterogeneity as a driver of cancer progression", presentation at Indian Institute of Science, January 6, 2019.

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. We aim to comprehend the cell intrinsic and extrinsic mechanisms 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. We are interested in defining the cellular and molecular mechanisms of metastasis by translating our in vitro findings into a more complex physiologically relevant setting. We also focus on deconvoluting the tumour-metastatic niche microenvironment in an effort to understand the role of the stroma in tumor progression. Such studies are integral to developing new drugs to target metastatic spread of a cancer and eventually alleviate the suffering in patients. The main aim of this work is to delineate the key molecular players involved in the cell autonomous control of metastatic cells. We have shown that Id1 which is a negative bHLH transcriptional factor controls the Mycself renewal program in cancer stem cells via Robo1. We continue to leverage this work in a translational aspect by using small molecule inhibitors against Id1 targets Kif11 and Aurka in order to ablate the cancer cells more effectively. The importance of the micro environment in cancer progression and metastasis is also being increasingly recognized. We have successfully built ex vivo models of the stroma from lung, liver, bone marrow and brain of metastatic and normal samples which will be interrogated to understand why cells home to a particular organ.

TEAM: Archana P T, Reshma Murali

AWARDS

Arumugam Rajavelu; Kerala State Young Scientist Award – 2018, , for the work carried out in RGCB on "Epigenetic players as novel drug targets in *P. falciparum*" by Kerala State Council for Science, Technology and Environment, Thiruvananthapuram, Government of Kerala.

Manendra Babu L, PhD student of Dr. KB Harikumar, won best oral presentation on Abrogation of Pancreatic Cancer Using a Brain Malady Drug, presented at International Conference on Biomedical Engineering, Bioscience, Bioinformatics, Biochemistry, Cancer Biology, Molecular Biology and Applied Biotechnology (BCM-2019) organized by Krishi Sanskriti, New Delhi on 12-01-2019 at Jawaharlal Nehru University, New Delhi.

Vysakh G, student of Dr Pradeep Kumar G- 3rd prize in Poster Presentation at the 37th Meeting of the Society for Reproductive Biology and Comparative Endocrinology and International Conference on Reproduction, Endocrinology and Development, Navrachana University, Vadodara, January 18-21, 2019

Devadathan VS, PhD Student: Awarded the EMBO Short term fellowship to work at CRICK Institute, UK for 3 months.

Debasree Dutta was invited to deliver a talk on "Induced pluripotent stem cells- a classic example of union of basic and translational research" at International conference on Advances in Therapeutic molecules and drug design held at Karpagam Academy of Higher Education from 9-11 January 2019, Coimbatore, India

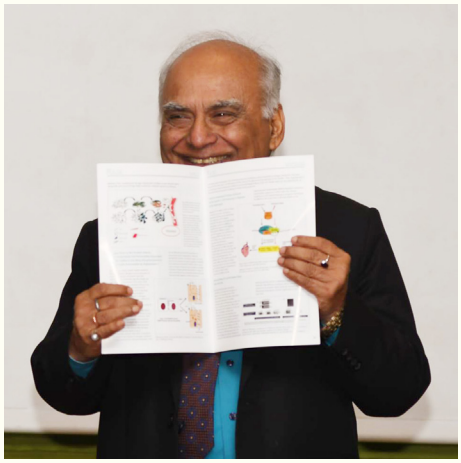
EVENTS

RGCB and PHD chamber of Commerce and Industry, in collaboration with the Office of the Controller General of Patents, Designs and Trademarks, Ministry of Commerce and Industry, Government of India, conducted a One-day awareness programme on Importance of Intellectual Property Rights. The program was hosted by the Office of Technology Ventures, RGCB

JANUARY 2019

70th India Independence Day lighting at RGCB Thiruvananthapuram.

Professor M Radhakrishna Pillai, Director RGCB Thiruvananthapuram hoisting the Indian National Flag on the 70th Republic Day. Jai Hind.



Professor NK Ganguly launching "PULSE" the quarterly official newsletter of RGCB during the 14th SAC meeting. PULSE contains glimpses of scientific & outreach activities of RGCB, staff stories and special features

Members of the 14th Scientific Advisory Council meeting of RGCB

OUTREACH

LAB VISIT

U.P.G. School, Kollam	44
Mercy College, Palakkad	29
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J.N.V University	23
J.J.College of Arts & Science	28
Govt.Victoria College, Palakkad	25

Malini Laloraya, PhD, FNASc

Joseph A, Nair LCR, Johnson BS, Thomas PL, Padmanabhan RA, Puthumadathil N and **Laloraya M**.Transcriptional regulation of Nos2 via STAT5B binding to Nos2 gene promoter mediates nitric oxide (NO) production : Relevance in beta cell maintenance. ***Cell Physiol Biochem 2019, 18:52(1):141-155***

Type 1 Diabetes (T1D) (Juvenile diabetes or insulin-dependent diabetes) is a chronic condition when pancreas fail to produce insulin. It occurs early in life and hence children and young adults form the major affected population. Although it constitutes 5% of the diabetic population, the only option for survival is life-long insulin injection/pump. T1D involves autoimmune attack on insulin-producing pancreatic beta cells. We had reported an unique mutation C1462A (L327M) in Stat5b on chromosome11 within a previously mapped T1D susceptibility interval (Idd4) in the nonobese diabetic (NOD) mice leading to weakened STAT5B binding to the promoter. This mutation plays a central role in T1D pathogenesis, by affecting cytokine signaling, T-cell selection, lymphoid-cell apoptosis and Regulatory T cells(Treg) insufficiency. Although reactive oxygen species are considered to orchestrate the immune attack, nitric oxide's (•NO) role is unclear. JAK-STAT pathway is known to induce Nos2. In this report, we prove that STAT5B binds to the candidate gamma-interferon-activated (GAS) element in Nos2 promoter thereby inducing Nos2 mRNA transcription and $NO^{\cdot}$ generation in mouse pancreatic beta cell line, MIN6. To detoxify excess superoxide due to lowered Nos2, an overexpressed SOD2 in Stat5b silenced cells results in massive H_2O_2 production. Pancreatic islets are unable to cope up with excess H_2O_2due to reduced H_2O_2 metabolizing enzymes. Thus we suggest that oxidative stress is brought about by amassed H_2O_2 upon Stat5b silencing culminating in reduced AKT expression – a prosurvival signal. Thus, we propose that β-cell destruction is aggravated by STAT5B's incapability to induce Nos2 resulting in H_2O_2 accumulation and the ensuing oxidative stress enhances β-cell death in addition to the already known inadequacy of regulatory T-cells due to mutant STAT5B in NOD mice. STAT5B deficiency in T1D patients shows strong association to T1D susceptibility. Thus, further studies are needed to clarify the STAT5B's role in human T1D pathogenesis.

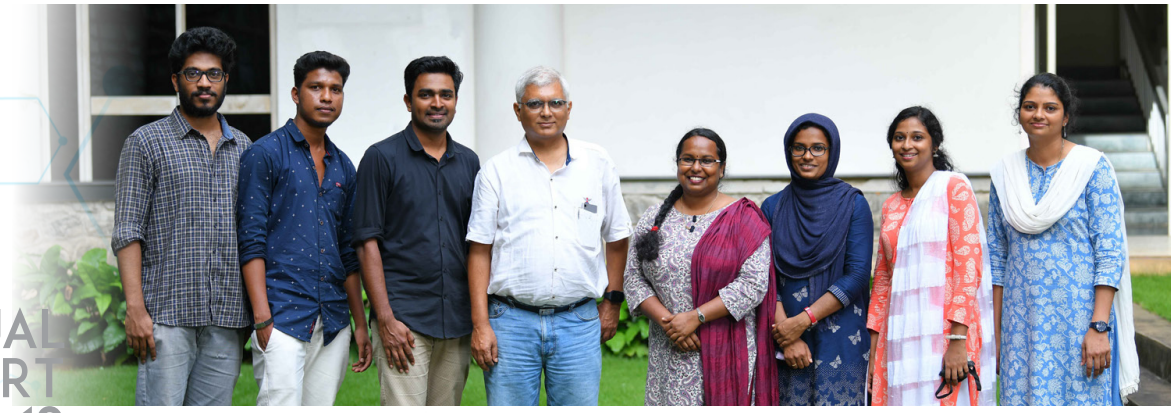
TEAM: Renjini A P, Betcy Susan Johnson

FEBRUARY 2019

Moinak Banerjee, PhD

Alex AM, Saradalekshmi KR, Shilen N, Suresh PA, **Banerjee M**. Genetic association of DNMT variants can play a critical role in defining the methylation patterns in autism. ***IUBMB Life.2019 Feb 20.doi: 10.1002/iub.2021***.

Autism spectrum disorder or autism includes a range of conditions with varied characteristic features being difficulty in social communication and expression of repetitive or stereotype movements. The symptoms and severity changes among individuals. Early identification of the condition is a crucial factor in the prognosis of the disorder. Various genetic and epigenetic factors have been linked to autism. Results from linkage mapping, genome wide association studies, candidate gene studies, whole exome sequencing have implicated more than 600 loci in the etiology of autism. Different factors in the social, chemical, nutritional and physiological dimensions contribute to the epigenetic influence over autism development. Majority of the phenotypes associated with autism converge at the monoamine biosynthesis pathway and the action of its metabolites. This pathway is in turn under the regulation of the circadian rhythm pathway and also the epigenetic machinery. The aim of our study was to understand the genetic contribution of monoamine biosynthesis pathway, circadian rhythm pathway and the epigenetic machinery in the development of autism from a population perspective. We screened nine genes in the monoamine synthesis pathway, of which TH, COMT and MAOA were found to be associated with autism in our population. This is the first report of a positive association of TH gene with autism. The associated genes and the functional prediction of the SNPs correlate with the reported altered biochemical level of these molecules. In the epigenetic machinery, the DNA methyltransferase genes were selected for our study. A positive association was observed for SNPs in DNMT1 and DNMT3A genes. This was the first study exploring the association of variants in the DNMT genes, which are central in controlling the methylation, with ASD. Our result when compared to genetic associations in schizophrenia from the same population point towards same genes being involved in the etiology but different variants associated with each condition. This suggests a possibility of a disease specific signature in the genes associated with the two similar neuropsychiatric disorders. Phylogenetic analysis of the studied pathways suggests pathway specific evolutionary relationship. In case of monoamine biosynthesis pathway Kerala population was more similar to the East Asians and for the DNA methyltransferases, Kerala was closer to the European population. This suggests the role of different environmental factors influencing the evolutionary drive of different pathways.



TEAM: Anil Prakash, Lijin john J, Shafeeque CM, Binithamol K Polakkatil, Alfiya F, Sindhura K P, Aswathi P M

AWARDS

Smrithi Krishnan R, PhD student of Dr K Mahendran: Best paper presentation award in *International Conference on Nanomedicine* (ICON-2019) held at Madurai Kamaraj University, Madurai on 25th and 26thFebruary 2019.

CL Karthika, student of Dr. S Sumi: Conference Travel Award at *International conference on Translational Research in Cardiovascular Disease* held from 15 to 17 February 2019 at NIMHANS, Bangalore

Kalaivani V Postdoctoral Fellow of Dr. Abdul Jaleel won the Devendra K Agarwal Young Investigator Award in the international conference *Translational Research in Cardiovascular Sciences" held by the International Academy of cardiovascular Sciences* (India Chapter) in Bangalore, 15 – 17 February 2019

Aneesh Kumar A, PhD student of Dr. Abdul Jaleel won the CC Kartha Travel Award in the *International Conference Translational Research in Cardiovascular Sciences* held by the International Academy of cardiovascular Sciences (India Chapter) in Bangalore, 15 – 17 February 2019

Vinitha A, student of Dr. Surya Ramachandran received Naranjan Dhalla Best Poster Award for *Cyclophilin A induces apoptosis and impairs efferocytosis of high glucose activated macrophages* in the *International Conference Translational Research in Cardiovascular Sciences* held by the International Academy of cardiovascular Sciences , Bangalore, 15-17 February, 2019.

Jayalekshmi VS, student of Dr. Surya Ramachandran, received the CC Kartha Travel Award for her poster ""Changes in expression of low density lipoprotein (LDL) receptors and transporters in HTR-8/SVneo placental cell line treated with oxidized-low density lipoprotein" in the *International Conference of Academy of Cardiovascular on Translational Research in Cardiovascular Sciences*, Bangalore, 15-17 February, 2019.

Soumya A, PhD student of Dr. Pradeep Kumar G won Best Poster Award at *ISSRF-2018* to for her work "Proteomics of sperm membrane rafts during epididymal maturation and capacitation".

Karthika Radhakrishan -PhD student of Dr. Pradeep Kumar G won Dr. Mridula Kamboj Young Scientist Award -2019 of *Indian Society for the Study of Reproduction and Fertility* (ISSRF)

TALKS

Dr. Debasree Dutta was invited to deliver a talk on stem cells in the *Indian Society for Study of Reproduction and Fertility (ISSRF)*, at Jawaharlal Nehru University, February 2019.

Dr. Surya Ramachandran was invited to deliver a talk on "Metformin attenuates lipid uptake in monocytes and represses atherogenesis in patients with diabetes" in the *International Conference of Academy of Cardiovascular on Translational Research in Cardiovascular Sciences* at Bangalore, February 2019.

Dr. Suparna Sengupta was invited to deliver a talk on 'The ginger product 6-Shogaol shows promise in breast cancer treatment by inhibiting Breast Cancer Cells and Stem Cell like Spheroids" International Symposium of Tumour Microenvironment and Cancer Prevention & Therapeutics, Jawaharlal Nehru University, India

EVENTS

Gifted students of the Travancore National School, Vattavila, Poojapura a leading learning hub for special kids spent an exciting day at RGCB

RGCB celebrated National Science Day 2019 by opening its gates to excited young students from schools of Trivandrum. Scores of children celebrated science with the correct aptitude, creativity and temperament.

OUTREACH

LAB VISIT

Ayya Nadar Janaki Amma College, Sivakasi	50
Travancore International School , Poojappura	43

MARCH 2019

George Thomas, PhD

Nath, V. S., Koyyappurath, S., Alex, T. E., Geetha, K. A., Augustine, L., Nasser, A.and **Thomas, G**. Transcriptome-based mining and expression profiling of Pythium responsive transcription factors in Zingiber sp. ***Functional Integrative Genomics 2019 19: 249-264***.

Cell wall fortification and suppression of cell wall loosening mediate *Pythium myriotylum* resistance in Zingiber zerumbet. Almost 15 species of the soil-borne necrotrophic oomycete genus Pythium cause soft rot disease in spice crop ginger (Zingiber officinale Roscoe). Although certain accessions of a wild congener of ginger namely *Z. zerumbet* is immune to soft rot,little is known about the mechanisms that produce resistance in these accessions. We examined transcriptional reprogramming and histochemical changes occurred in resistant accessions of Z. zerumbet following *P. myriotylum* inoculation. We identified expression changes in a total of 903 transcription factors particularly belonging to WRKY, AP2, bZIP, MYB, bHLH and NAC families that are known toplay a crucial role in host defense. The high differential modulation was evident for transcription factors that are involved in lignin biosynthesis and cell wall fortification. Expressions of the genes involved in the biosynthesis of phytohormones that regulate cell elongation were suppressed. Similarly the genes that have different role in the elongation and loosening process of cell walls were also suppressed. However, several genes involved in monolignol biosynthesis were up-regulated. Histochemistry of the collar region of the aerial stem revealed significant increase in total lignin content, H_2O_2 accumulation and increased lignification of the mesophyll cells surrounding vascular bundles in the leaf sheaths, especially in the peripheral whorl of leaf sheath. The hyphae of the pathogen penetrated the host tissues intracellularly. The hyphal growth were restricted to the peripheral leaf sheath whorl indicating that the cell wall fortification by lignin deposition prevented the pathogen spread into the pith of the aerial stem. The data highlight a coordinated transcriptional reprogramming to render the host cell wall less amenable to pathogen penetration. Further, the study depicts cell wall fortification in the host to prevent pathogen colonization in the pith through which the principal vascular tissues pass, thus ensuring the transport system remains unaffected by the pathogen invasion.

TEAM: Lini Varghese, Vinitha M R, Lal kumar, Sajeesh Kappachery, Velthai G, Shaifaly Parmar

Sreeja S, PhD

Lathika, Lakshmi Mohan, Jagathnath Krishna Kumarapillai Mohanan Nair, Valliamma Neelakandapilla Saritha, Kunjuraman Sujathan, and **Sreeharshan Sreeja**. Role of phospho–ezrin in differentiating thyroid carcinoma. ***Scientific reports 2019 9, 1: 6190***

The mechanism behind estrogen induced metastasis of thyroid cancer is less explored. For the first time, here, we report the role of estrogen in inducing the expression of ezrin, a metastatic determinant in follicular thyroid cancer cells. We studied the clinical applications of ezrin and p ezrin in all types of thyroid carcinomas and it was observed that the ezrin was expressed in all thyroid carcinoma lesions. p-ezrin (T567)was found to be intensely stained in follicular thyroid carcinoma and follicular variant of papillary thyroid carcinoma while the follicular adenoma (FA), papillary thyroid carcinoma and goiter lesions were negatively stained. Strikingly, the 'H' score for ezrin was also observed to be higher in FTC and FVPTC compared to PTC and benign FA. In case of goiter lesions, p ezrin (T567) was negatively stained like staining in adjacent benign tissue of thyroid carcinoma. The papillary area was unstained for p ezrin indicating that p ezrin is the marker for follicular differentiation in PTC. Moreover all the papillary thyroid carcinoma lesions taken for the study were negative for p ezrin.Further, to identify the upstream kinases responsible for the phosphorylation of ezrin using pharmacological inhibitors, it was observed that PI3K and ROCK-2 are among the kinases responsible for Estrogen induced phosphorylation of ezrin. Either Estrogen activated PI3K or ROCK-2 can directly activate ezrin or activated PI3K can activate ROCK-2 and thus activating ezrin. This study has thrown light into the dilemma of differentiation of follicular neoplasms like benign FA, FTC and FVPTC in which the follicular morphology overlaps and the differentiation based on the cytology is challenging for the clinicians and cytopathologists. The over-expression of p ezrin in FTC and FVPTC and its exclusive absence in benign FA; 100% sensitivity and specificity in the histological correlation between FTC and benign FA, FVPTC and benign FA enables us to suggest p ezrin (T567) as a diagnostic marker to differentiate between the follicular neoplasms.

TEAM: Anjana S S, Vini Ravindran, Viji Remadevi, Lakshmi M L, Savith R K, Ayswarya R S

Vinod Kumar G S, PhD

Amritha Vijayan, Pinky Prabha James, CK Nanditha, **GS Vinod Kumar**, Multiple cargo deliveries of growth factors and antimicrobial peptide using biodegradable nanopolymer as a potential wound healing system. International Journal of ***Nanomedicine 2019 14, 2253–2263.***

Treatment of wounds with the help of nanoparticles (NPs) is more effective and superior in comparison to traditional wound healing methods as it protects and sustains active drug release at the wound site thus enhancing the safety of the drug and reducing the possibility of side effects. This is enabled by the fact that the entire amount of the encapsulated drug does not come into direct contact with the skin surrounding the wound site in one instance. The wound is instead, exposed to it gradually in small doses. This process also helps to prevent biological degradation of loaded drugs thus ensuring enhanced stability and sustained release. The advantages of this method are the possibility of allowing a reduction in administered dose, limiting toxicity levels to the minimum and increasing safety of topical delivery of the drug. We report the synthesis of a novel Poly (lactic-co-glycolic acid) [PLGA] nanoparticle based multi-cargo delivery system for growth factors and antimicrobial peptide. Vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) were entrapped in PLGA nanoparticles by solvent diffusion method and an antimicrobial peptide (K4) was conjugated to the nanoparticle by carbodiimide chemistry. The developed multiple cargo delivery systems with growth factors (VEGF and bFGF) and an antimicrobial peptide (K4) was investigated and optimized for potential wound healing. The system showed a sustained release of growth factors and was evaluated for cytotoxicity by MTT and live/ dead assay which revealed that the bioactivity of the growth factor entrapped nanoparticles was higher than that of free growth factors, and it also induced enhanced cell proliferation in vitro. The development of a system for the co-delivery of growth factors (VEGF and bFGF) and an antimicrobial peptide (K4) was investigated for potential wound healing application. The entrapment of growth factors with very high efficiency is an advantage in this method along with its sustained release from the nanoparticulate system which will enhance the angiogenesis. Our system also displayed broad-spectrum antimicrobial activity against both gram-positive and gram-negative bacteria.

TEAM: Gourav Chakravarty, Nanditha CK, Teena Jacob Chirayil, Mrunal Vitthal Wanjale, Akhil K Mohan

Shijulal Nelson Sathi, PhD

Wonders of Small 2.0, *National Conference on Recent Trends in Microbiome Research*: Exploring the Microbial Diversity, March 20-21, 2019, Pondicherry University, India

Phylogenomic analysis reveals the evolutionary route of antibiotic resistant genes in *Staphylococcus aureus* Multi-drug resistant *S. aureus* is a leading cause of concern worldwide. Coagulase- Negative Staphylococci (CoNS) are claimed to be the reservoir and source of important resistant elements in *S. aureus*; however, the origin and evolutionary route of these elements remain unknown. Herein, we performed a detailed phylogenomic analysis of 152 completely sequenced *S. aureus* strains in comparison with 7,353 reference bacterial genomes. Our results revealed that *S. aureus* has a large open pan-genome with 70% (124) of its resistant genes belonging to the core part of its genome. Among 177 resistant genes, 47 (27%) are located within the Staphylococcal Cassette Chromosome (SCCmec), which is responsible for resistance against major classes of antibiotics, including beta-lactams, fluoroquinolones, and aminoglycosides, and are highly diverse within the selected 152 strains of *S. aureus*. However, the physically linked core gene structure (MecA-MecR-MecI) of *S. aureus* that is essential for the maintenance of SCCmec element is well conserved. Gene distribution pattern and maximum likelihood phylogenies of mec-box genes reveal that the core resistance machinery of the SCCmec element might have originated within the Bacillales lineage and assembled into its current structural form in one of the early linages of Staphylococcus species, which later got horizontally transferred to S. aureus. Interestingly, we found that at least 89% of SCCmec encoded and 63% of non-SCCmec encoded resistant genes in *S. aureus* were influenced by horizontal gene transfers from both closely and is tantrelated species, which might have influenced the evolution of antibiotic resistance in *S.aureus*.

TEAM: Govind Krishnadas, Soumya JD, Jamemia Sara Philip, Padma Cheredy, Jiffy John

MARCH 2019

Asha S Nair, PhD

Tapas Pradhan, Padmanabhan. K, Prasad. M, Chandramohan K , **Nair AS** Augmented CD133 expression in distal margin correlates with poor prognosis in colorectal cancer. ***Jounal of Cellular Molecular Medicine 2019, DOI 10.11/1/JCMM 14284***

It is known that around 20% to 40% of patients undergoing curative resection of CRC develop loco regional recurrence or distant metastasis Pathological assessment of excised tumor and surgical margins in colorectal cancer (CRC) play crucial role in prognosis after surgery. Molecular assessment of margins could be more sensitive and informative than conventional histopathological analysis. Cancer stem cells are known for their role in therapy failure and disease recurrence. Considering this view, we evaluated the distal surgical margins for expression of cancer stem cell markers. Here, we have analyzed distal resection margin, which is the closest lower edge of the tumor for expression of cancer stem cell marker expression CD133, CD44 and Ep-CAM and compared with distant normal and tumor tissues. This study revealed that pathologically (H & E staining) negative distal tissues harbor cancer stem-like cells. Further, follow up study revealed an interesting correlation between cases with CD133 enriched distal tissue with lower disease-free survival. In addition, mRNA sequencing for distal and tumor tissues showed a significant similarity in mutations between distal and tumor tissues. The commonly altered genes were found enriched for Wnt, Notch, and HH pathways. Nuclear expression β-catenin and oct4 stem cell regulatory proteins were found enriched in distal tissues suggesting their possible role in stem-like cell enrichment in CRC. This study is the first one to demonstrate the presence of CRC associated mutations and cancer stem cell enrichment in pathologically negative margin tissues and their prognostic importance. Most importantly, our study has revealed that tumor surrounding tissue may harbor cancer stem cell signatures in colorectal cancer. Our work also suggest possibility of tumor field effect and/or presence of residual cells, in both cases these signatures could be crucial in patients prognosis.

TEAM: Samu John, Tapas Pradhan, Rajshree R Nair, Meera Nair, S K Vijayalakshmi, Anjana Soman, Ketakee Mahajan,

MARCH 2019

Priya Srinivas, PhD

Sengodan SK, Hemalatha SK, Nadhan R, Somanathan T, Mathew AP, Chil A, Kopczynski J, Nair RS, Kumar JM, **Srinivas P**. β-hCG induced mutant BRCA1 ignites drug resistance in susceptible breast tissue. ***Carcinogenesis. 2019 DOI: 10.1093/carcin/bgz070***

Human Chorionic Gonadotrophin (hCG) is the glycoprotein hormone well studied as the pregnancy hormone. However, the isoforms, β-hCG, reigns the cancer research realms with its controversial reports supporting both protective and tumorigenic effects. It has been already reported that if a woman is BRCA1 mutation carrier, the risk of breast cancer at an early age will be increased with full term pregnancies. We have already unveiled that the levels of β-hCG are higher in BRCA1 defective breast cancer cells, which is reduced once BRCA1 is restored. Further, BRCA1 transcriptionally reduces the levels of β-hCG by binding to the β-hCG promoter. β-hCG directly binds to TGFBRII and induces TGFBRII mediated cell proliferation, thereby inducing tumorigenicity in BRCA1 defective cells. In this study, we have analyzed the mechanism of action of β-hCG on BRCA1 expression and its influence on drug sensitivity in breast cancer cells. We reveal that β-hCG induces mutant BRCA1 protein expression in BRCA1 mutant cells; however, in BRCA1 wild type cells, β-hCG reduced wild type BRCA1 protein expression. β-hCG could induce Slug/LSD1 mediated repression of wild type and mutant BRCA1 mRNA levels by transcriptional regulation. However, β-hCG induces HSP90 mediated stabilization of mutant BRCA1, which causes the over expression of mutant BRCA1 protein, resulting in partial restoration of homologous recombination (HR) repair of damaged DNA. Subsequently, in BRCA1 defective cancer cells, the presence of β-hCG contributes to drug resistance to 17AAG, which is an HSP90 inhibitor. A combination of HSP90 inhibitor and TGFBRII inhibitor has shown to sensitize β-hCG expressing BRCA1 defective breast cancers to drugs. Henceforth, targeting the β-hCG-HSP90-TGFBRII axis could prove to be an effective treatment strategy for BRCA1 mutated breast tumors.

TEAM: Revathy Nandhan, Geetu Rose Varghese, Arathi Rajan, Neetha R L, Vinitha R K, Neethu Krishnan, Dipyaman Patra

Santhosh Kumar K, PhD

Best Poster Presentation Award at National Seminar on Advanced Functional Materials for Analytical, Environmental and Biomedical Applications- NSAFM-2019 at University of Kerala, Kaiavattom

The major drawback of the commercially available chemotherapeutic drugs against cancer is their lack of specificity and narrow window of therapeutic efficacy. Multifunctional, globular structured poly-lysine dendritic nanocarrier incorporated with target specific moieties, cytotoxic drugs and solubilising agent was synthesised on a polymer support for targeted cancer chemotherapy. This targeted drug delivery system can improve the solubility, specificity, biodistribution, half-life in blood and bring down the toxic side effect of drug. After each generation of the dendrimer, enzyme Cathepsin B sensitive peptide linker GFLG was incorporated to pre-defined functional sites and the drug doxorubicin was incorporated. Several novel peptide ligands to target the over expressed EGFR and VEGFR in maligned cells were designed using Bioinformatics tools. Free energy score after Rosetta FlexPep ab-initio docking (RMS BB) were identified and Molecular Dynamics simulation of those ligands with EGFR and VEGFR were carried out. There docking score and binding energy (kJ/mol) were compared with the respective natural receptors. Those ligands that showed better scores were chemically synthesised on the surface carboxylic moieties of the G4 dendrimer. The polylysine dendrimer containing drug and targeting moieties were cleaved from the solid support using TFA and cleavage cocktails, purified by HPLC and characterised by mass spectrometry. MTT and RBC haemolytic assays showed that the dendrimer is non-toxic, biocompatible and their interaction with the cell wall was minimum. Dendrimer showed dose dependent hemolysis character which is significantly less compared to commercial dendrimers. In vivo acute and 28 days' sub-acute toxicity studies using Swiss albino mice showed no mortality upto 75mg/Kg dose. The haematological, biochemical or histopathological changes showed only insignificant differences upto this dose. In vivo bio-distribution studies showed that free doxorubicin was cleared from the systemic circulation within 24 h while the nano delivery system provided prolonged action even after 48h showing that Cathepsin B releases the drug at a steady rate. G4-dendrimer provided high tumor specificity compared to other organs as the drug accumulation was high in tumor. Comparative analysis of in vivo bioluminescent imaging of mice tumor cells after single dose doxorubicin i.v. administration showed decreased bioluminescent intensity after 7 days while its drug equivalent showed better bioluminescent intensity.

TEAM: Anju Krishnan A, Pratibha Narayanan, Neethu Ajayakumar, Archana Sivan, Smitha Devi S, Aswathi, Aswani Kumar, Anandu B, Mohammed A, Johney Philip, Manu N M

MARCH 2019

AWARDS

Betcy Susan Johnson, Meera Krishna B, Sathy M Pillai and Malini Laloraya. 'Best Poster Presentation Award' Aberrant Circadian Rhythm Genes in Polycystic Ovary Syndrome Patients" in "*International Symposium on Biological Rhythms*" during March 11-13, 2019 at the Department of Zoology, Chaudhary Charan Singh University, Meerut, India. .

TALKS

Debasree Dutta delivered an invited talk on "Histone chaperones in induced pluripotency" at *Modern perspective of research and development in Biochemistry and Biophysics* held at University of Kalyani, West Bengal

EVENTS

International Women's Day

Nurturing is the basic instinct of all women. RGCB KINFRA and main campus celebrated womanhood by planting saplings, because when you plant a tree, you grow life.

OUTREACH

LAB VISIT

Sacred Heart College, Kochi	11
N.S.S.College , Nilamel	25
Christ College, Bangalore	20
L'ecole Chempaka, Edavacode	35
Al Amen College, Aluva	67

Sanil George, PhD

C-terminally amidated Brevinin-1 peptides (Brevinin-1 HYba1 & Brevinin-1 HYba2) are salt-resistant. C-terminally amidated analogs of brevinin-1 peptides identified from the skin secretion of Hydrophylax bahuvistara, an endemic frog of Western Ghats, were analyzed to understand the antimicrobial activity in the presence of varying salt concentration (NaCl, KCl, MgCl2 & CaCl2) and pH. There was no significant change in activity of the peptides against Gram-positive bacteria under salt challenge. However, a maximum of 15 fold changes in activity observed for Gram-negative bacteria. The peptides were also resistant to changes in pH in the tested range. Both the peptides showed strong antimicrobial activity throughout the range of pH tested (5-8). The MICs were almost stable at neutral and acidic media, minute differences were observed in highly basic media. The small differences in MICs observed in the tested range were not significant. The results indicate that these peptides may act on Gram-positive bacterial membrane independent of cation binding sites, while they depend on cation binding sites on Gram-negative bacterial membrane. These data illustrate that amphibian skin secretions continue to provide a suitable template for designing novel therapeutic agents. A small lectin-like peptide was also identified from the skin secretion of an endemic frog, Hydrophylax bahuvistara. Lectins are sugar-binding proteins and considered as attractive candidates for drug delivery and targeting. Here, we report the identification of a smallest lectin- like peptide (odorranalectin HYba) from the skin secretion of Hydrophylax bahuvistara which is being the shortest lectin- like peptide identified so far from the frog skin secretion, with 15 amino acid residues. The peptide lacks antimicrobial activity but strongly agglutinate intact human erythrocytes. The sequences at the L-fucose recognizing region is conserved as in other lectins reported from frog skin secretion and could be exploited for specificity and drug targeting properties.

TEAM: Reena R, Anoop V S

Manjula S, PhD

Phytophthora capsici, which is a highly dynamic and destructive plant pathogen with an extensive host range, is a significant threat to black pepper (*Piper nigrum L*) cultivation. The infection strategy of *P. capsici* involves an asymptomatic biotrophic phase of infection followed by a hemi-biotrophic transition phase leading to a sporulating necrotrophic phase . Even though the high success rate of pathogenicity of these pathogens is attributed to such a multi-phased developmental process, the exact molecular mechanisms that regulate these pathogenicity stages are largely unknown. We optimized a de novo transcriptomics strategy for categorical identification of putative pathogenic determinants as well as novel transcripts differentially expressed in *P. capsici* early in the infection process based on the hypothesis that the biotrophic to hemi-biotrophic switch if distinctly elucidated, could be the key to developing a targeted disease control strategy for *P. capsici*. From the expression data, we infer that there is a tight temporal regulation of multiple pathogenic determinants that help colonise, establish disease and complete the pathogenic lifecycle in black pepper. It was observed that the biotrophic to necrotrophic switch involves dynamic regulation of critical pathogenic determinants such as CAZymes, proteases, effectors, peroxidases, HSPs and several other regulatory proteins, the exact mechanisms of which are yet to be resolved. We also validated the active expression of fifteen novel pathogenic determinants which were previously unknown for their roles in causing pathogenicity in black pepper. These genes could be used as potential markers for the early detection of *P. capsici* in planta. Our study confirms that pathogenic determinants are the key players which modulate the outcome of this spice-oomycete interaction. The data also present potential targets that could be explored further for redesigning a more holistic disease management strategy like “oomyceticides against oomycetes” in *P.nigrum*.

TEAM: Saranya V, Gayathri G S, Geethu S Nair, Deepthi S, Indu M, Meera B, Rajeswari Gopal G

Rashmi Mishra, PhD

The research focus is on understanding the Mechanobiology of Chronic Disease Development, Progression and Therapeutics. Imbalances in physiological mechanical homeostasis are emerging as the root cause of several chronic diseases. Since the plasma membrane in eukaryotes acts as the prime interface at which the mechanical microenvironmental forces are sensed and relayed to the intracellular controller for an effective adaptive response, we are trying to understand the 'link' between specialised plasma membrane assemblies called the lipid rafts and biomechanical force homeostasis in physiology and pathologies with a special attention on brain, vascular, cerebrovascular ailments and tumors of various tissue origins. We have shown that tumors biomechanical homeostasis can be specifically disturbed by causing uncontrolled hydrostatic pressure via a bioactive molecule called Bacoside A and with another approach, it was demonstrated that tumor cells can be forced to levitate off the substrate and die via excessive clustering of a tumor cell enriched glycosphingolipid-GM3. We have also found that the loss of caveolae from the human neural stem cell populations of the lateral ventricles, due to enhanced ECM stiffening, can be a seed to the origin and progressive of brain tumors. Results suggest that upon stretch, the caveolae disassemble and its resident IGFR receptors undergo SUMOylation by SUMO2 isoform that enables the receptor translocation to the nucleus. The nuclear IGFR acts as a transcription factor for upregulation of proliferation associated genes such as cyclinD1, TCF/LEF1 and beta catenin. Inhibition of SUMO2 alone or in combination with EGFR receptor inhibition promoted significant GBM cell death. The human protein atlas data shows high nuclear expression of both SUMO2 and IGFR in several other tumor types and future efforts may bring forth the inhibition of SUMOylation, especially SUMO2 as an efficient universal anti-tumor therapy. Intriguingly, a parallel pathway involving IGFR Sumoylation dependent survival pathway activation was found to inhibit mechanically stressed neurons from neurodegeneration.

TEAM: Gayathri KG, Aswani Krishna, Jain Tiffee, Sebastian John

Umasankar P K, PhD

Clathrin-mediated endocytosis (CME) is vital for the internalization of most cell-surface proteins (cargo). 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. Hence understanding this process is of utmost importance to human health and disease. 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. Phosphorylation of AP-2 is considered a critical regulatory step in CME. Yet, specific kinases and the mechanisms underpinning their recruitment and regulation are not well understood. We identified a novel kinase, BMP-2 inducible kinase (BMP2K) that phosphorylates AP-2 in cells. We demonstrated that BMP2K is a bonafide CME protein that co-localizes with AP-2 at CCP on the plasma membrane of cells. Over expression of BMP2K specifically increased phosphorylation of the μ subunit of AP-2 at CCP and in cell lysates. Interestingly, functional inactivation of BMP2K abolished AP-2 μ phosphorylation, changed CCP morphology and diminished cargo (transferrin) internalization. To further understand how kinase functions in cells, we generated BMP2K deletion mutants. Localization studies revealed that both Q/H and CT regions are necessary for the precise localization of BMP2K to CCP and for the AP-2 phosphorylation. Biochemical GST-pull down assays showed that BMP2K interacts with AP-2 and clathrin through CT. RNAi silencing of AP-2 decreased the steady state levels of endogenous BMP2K and completely abolished transferrin uptake. In addition, BMP2K protein levels were also diminished in FCHO1/2 knockout cells (fcho-/-) that possess AP-2 in closed inactive conformation (Umasankar et al, 2012, Umasankar et al, 2014, Ma et al, 2016). Together, our findings reveal that BMP2K is an AP-2 specific kinase that phosphorylates open conformation of AP-2 and is stringently regulated by AP-2.

TEAM: Anjitha A.B, Navyasree K.V, Shikha Ramesh T

BIO NEST

Saji George, MTech, PhD

Pradipta Tokdar, PhD

Uma Subramanian Unni, PhD

BioNest, the bio incubation facility jointly run by RGCB and Kerala Startup Mission (KSUM) is unique in terms of providing state of art laboratory facility and space for Biotechnology startup ventures by providing instrumentation platforms to promote & develop new entrepreneurs. It also aims to provide such instrumentation platforms for Small and Medium scale industries (SME's), academic institutions & hospitals, to further their research programs in biotechnology, life sciences and biomedical sciences. BioNest provides a four-year incubation facility for start-ups and also the required infrastructure for the new company to work independently thereafter. This year witnessed growth in terms of number of incubates, students being trained, academic research and industry based contract research projects. In order to accommodate the increasing requests, BioNest is developing larger incubation spaces, which in turn would result in greater utilization of the central laboratory facility housing the 4 sections, Molecular Biology, Fermentation Technology, Analytical Chemistry and Phytochemistry.

ANTIFATS (KERALA Remedies)
Standardized extracts of fruit rinds of MalabarTamarind (Garciniacambogia), Commiphora wightii (Guggulu), Amlamyrobalan (Emblicaofficinalis), Chebulic myrobalan (Terminaliachebula), and Beleric myrobalan (Terminaliabelerica) are homogenously blended and served as "0" Size capsules may help to induce early satiety and burn stored fat and help inhibit the conversion of excess calories into fat.

BLACUMIN (KERALA Remedies)
Alpha Linolenic (Omega 3), Linoleic (Omega 6) and Oleic (Omega 9) Fats are the most essential poly Unsaturated Fatty Acids (PUFA's) nutritionally for health and wellness. These fats are essential for healthy modulation of the physiological activities at cellular level yet generally deficient due to lifestyle changes. Omega 3 and Omega 6 fatty acids are true antioxidant and anti- ageing phyto nutrients.

GRAPELINA (KERALA Remedies)
In patients with moderate to severe hypertension, drug therapy is appropriate, but should be ideally used as a bridge therapy until dietary, lifestyle, and supplement strategies to lower blood pressure take hold. Non-drug therapies such as diet, exercise, relaxation therapies, and dietary supplements like Grape Seed Extract have been found beneficial.

ACTIVGRA PLUS (Phytocom Pharmaceuticals)
Activgra Plus, which has properties such as Anti-stress immunemodulatory, regulates blood glucose level and increase reproductive health. In helps in Relaxation and reduces symptoms of depression. Bodina markets the product.

MULTI VITAMIN GUMMIES (Ebrilive Heath Care)

Multi vitamin gummies are chewable vitamins that have a texture and taste similar to gummy candies. They are one of the most popular types of vitamins that can be used for kids and adults.

BIOSAN (BioPhoton Technologies)

BioSan is a multiple function sterilizer, which has sterilization, aromatherapy and charging functions. UV lights kills virus, bacteria and make you live safety. This machine can be used for cell phone, MP3/MP4, jewellery, socks, baby's toys, forks, knives, watches, eye glasses, toothbrushes, keys, Bluetooth earphones and other small objects.

Products/patents from BioNest:
Patent: Provisional patent number: 201941007160; Phytocom Pharmaceutical (P) Ltd
Products:

Product Name	Benefit	Incubate
ANTIFAT	HCA Obesity Management	Kerala Remedies
BLACUMIN	Overall Health Management	Kerala Remedies
GRAPELINE	Hypertension Management	Kerala Remedies
GTCAPS	Stay Young	Kerala Remedies
VEGFLAX	Omega-3Deficiency Management	Kerala Remedies
ACTIVGRA PLUS	Body Relaxer	Bodina natural (P) Ltd and Phytocom Pharmaceutical (P) Ltd
RADIANCE METER	Measurement of exposure of Phototherapy	Biophoton Technologies (P) Ltd
INFANT WARMER	Phototherapy blanket for management of Neonatal Jaundice	Biophoton Technologies (P) Ltd
TRACKVEIN	Infrared Vein viewer	Biophoton Technologies (P) Ltd
BIOSAN	UV based Mobile sterilizer	Biophoton Technologies (P) Ltd
AQUESENSE	Cholera Detection kit	Klonos Lifesciences (P) Ltd

Contract Research

Title	Value	Collaborating Company
Improving Protease activity in Aspergillus Nyzae MTCC 25131	2.69 lakhs	Zeus Biotech Pvt Ltd.

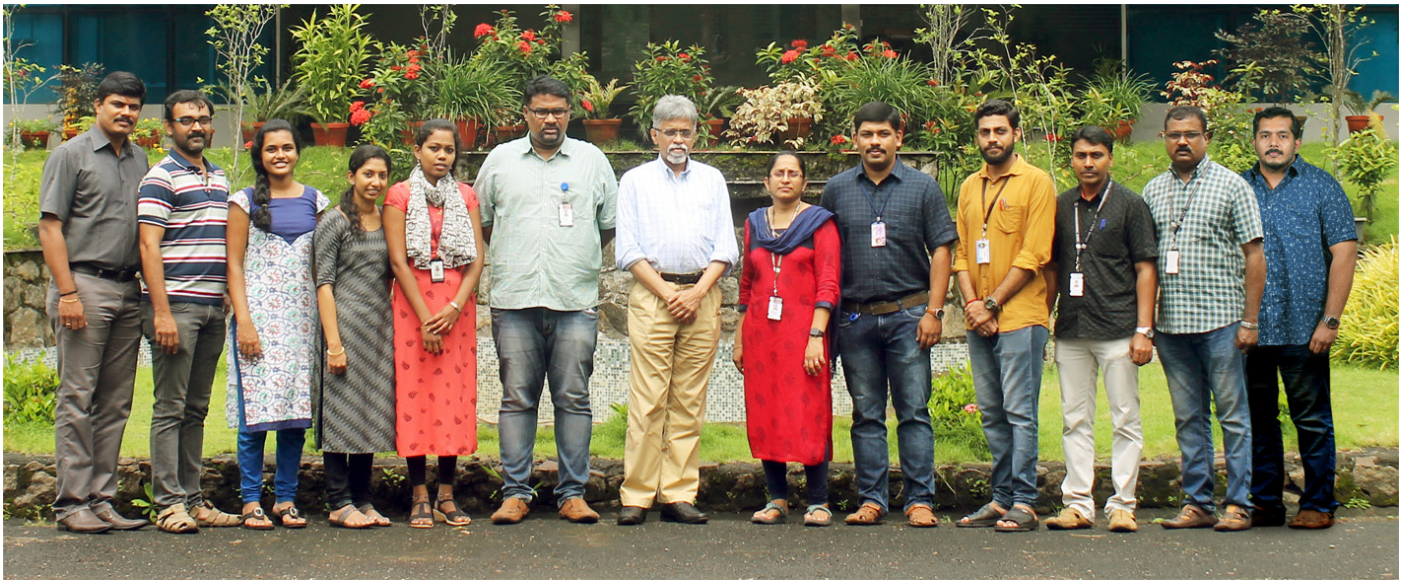
Training/Finishing School/Internship of Student

The projects given to students for internship are of industrial significance and selected as per the request from few industries. The plan is to tie up with industry/research partner when the project reaches a critical or Proof of Concept stage.

Course	Qualification	Students enrolled	Students completed/ Joined
Finishing School	M.Sc Biotechnology	5	5
Advanced Project Training (6 months)	M.Sc Biotechnology	1	1
Project Training (3 months)	B.Sc Biotechnology	14	14
Project Training (3 months)	M.Tech Biotechnology	3	3
Project Training (3 months)	M.Sc Microbiology/Biochemistry	14	14

Diagnostic Facility:

A high-end diagnostic facility is being developed for in-born error screening for neonates is being standardized and validation using neonatal samples are being done. In addition a cell free fetal DNA analysis is being set up for detection of trisomy



TEAM: Manoj, Rajeev Raghunath, Surya Rose, Dona George, Charutha, Pradipta Tokdar, Uma S Unni, Jobi Jose, Akhil Raj, Johny, Unnikrishnan, Jayakrishnan K S

PhD s AWARDED 2018 - 19

Satheesh Kumar S

Reciprocal Regulation of β-hCG and BRCA1- An in vitro study

Mentor - Dr. Priya Srinivas
April 2018

Akhilandeswaree D

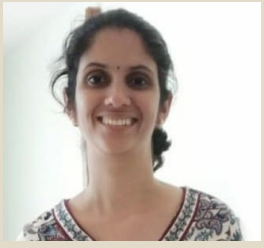
Identification of potential targents for inhibiting biofilm formation in Vibrio parahaemolyticus and Vibrio cholerae

Mentor - Dr. Sabu Thomas
April 2018

Sreelatha K H

Effect of Cancer Associated Fibroblasts on Cancer Cells: Relation to Aggressiveness

Mentor - Dr. Priya Srinivas
April 2018



Ramya R Prabhu

N-Methyl –D- Aspartate Receptor Mediated Calcium Signaling in Glutamatergic Synapses of cortical and cerebellar Neurons

Mentor - Dr. R. V.Omkumar
May 2018

Reshma R S

Studies on Regulation of Cell growth by BRCA1/2 in prostate cancer cells: Influence of certain selected Quinones

Mentor - Dr. Priya Srinivas
April 2018

Mallika V

Structural charecterisation and in silico studies on selected members of type III polyketide synthase family of proteins

Mentor - Dr. Soniya E V
May 2018

PhD s AWARDED 2018 - 19

Krishnakumar K A

Bioactivity guided fractionation and Characterization of Phyllanthus Maderaspatensis L for Anti-Liver fibrotic effects

Mentor - Dr. Asha V V
July 2018

Anupriya M G

Elucidation of Endothelial Cell Signaling Mechanisms and Vascular Permeability in Dengue

Mentor - Dr. E.Sreekumar
September 2018

Deivendran S

Identification of biological mediators of metastasis associated protein-1 (MTA1) in cancer cells

Mentor
Professor M Radhakrishna Pillai
July 2018

Subhashini C

Wnt5a signaling and its implications in cerebellar neurogenesis

Mentor - Dr. Jackson James
October 2018

Syed Khaja Mohieddin

Role of Histone Chaperones in Cellular Reprogramming

Mentor - Dr. Debasree Dutt
August 2018

Aneesh B

Cloning and Expression of Polyhydroxybutyric Acid Biosynthesis Genes from Bacteria Isolated from the Environment and the Optomized Production of the Biopolymer

Mentor - Dr. Harikrishnan K
November 2018

PhD s AWARDED 2018 - 19

Arjun J K

Generation of Metagenomic Libraries and Screening for Potential Biomolecules

Mentor - Dr. Harikrishnan K
December 2018

Revathy Nadhan

βHCG and BRCA1 in Gestational Trophoblastic Diseases

Mentor - Dr. Priya Srinivas
January 2019

Lesly Augustine

Expression profiling of phenylpropanoid biosynthetic pathway genes in Zingber spp. with contrasting response to soft-rot pathogen Pythium

Mentor - Dr. George Thomas
December 2018

Philip Litto Thomas

Molecular Mechanisms of cell differentiation and pluripotency

Mentor - Dr. Malini Laloraya
January 2019

Sneha Singh

The role of endothelial cell Angiopoietin-1(Ang-1) signalling in vascular leakage induced by Dengue virus

Mentor - Dr. E. Sreekumar
April 2018

Annu Joseph

Molecular Determinants in Pancreatic Sustenance: Implications in Type 1 Diabetes

Mentor - Dr. Malini Laloraya
January 2019

PhD s AWARDED 2018 - 19

Divya M P

A Study on Environmental Vibrio Parahaemolyticus with special emphasis on its Pathogencity

Mentor - Dr. Sabu Thomas
January 2019

Karthika S

Comprehensive analysis of biofilm forming bacterial communities in chronic diabetic ulcer and identification of biofilm associated genes in Enterococcus faecalis

Mentor - Dr. Sabu Thomas
February 2019

Haritha H Nair

Mechanistic evaluation and In vivo validation of synergistic combinations of curcumin and resveratrol with chemotherapeutics used in breast cancer treatment

Mentor - Dr. Ruby John Anto
January 2019

Vikas Kumar

Molecular basis of metabolic switch in response to hemodynamic stress in aging heart

Mentor - Dr. TR Santhosh Kumar
February 2019

Asha R

Effect of PEGylation and fatty acid acylation on the membrane perturbation activity of AMP

Mentor - Dr. Santhosh Kumar K
January 2019

Devi A N

Expression Profiling and Functional Characterization of Nephrocystin in relation to Spermatogenesis

Mentor - Dr. Pradeep Kumar G
February 2019

PhD s AWARDED 2018 - 19

Chidambareswaren M

An integrated systems biology approach for the molecular elucidation of Piper nigrum L. - Phytophthora capsici Leonian phytopathosystem

Mentor - Dr. Manjula S
February 2019

Sumitra Sankar

Application of Synthetic Nucleases for HPV Gene Editing

Mentor - Prof. Radhakrishna Pillai
February 2019

Prasanth Narayan

Evaluating the Role of FOXP3 (SCURFIN) During Embryo Implantation, An Immune Privileged Instance

Mentor - Dr. Malini Laloraya
March 2019

Sreeja R Nair

Molecular alterations in central nervous system in mouse models of chickungunya virus neurovirulence

Mentor - Dr. E. Sreekumar
February 2019

RGCB EXTRA MURAL RESEARCH GRANTS

Principal Investigator	Name of Grant	Funding agency	Duration
Anantharaman Devasena	Role of Human Papillomavirus Infection and other co-factors in the aetiology of the Head and Neck Cancer in India.	Indian Council of Medical Research	2016 - 2019
	Biomarkers of oral cancer risk prediction.	Department of Biotechnology	2018 - 2023
	Human papillomavirus (HPV)-related oropharyngeal cancer burden and the natural history of oral HPV infections: an Indian perspective	Wellcome Trust DBT Alliance	2019 - 2024
Anto Ruby John	Mechanistic evaluation and in vivo validation of the anticancer principle isolated from Chromolaena odorata against cervical cancer(PI)	Kerala State Council for Science, Technology and Environment	2016 - 2019
	Isolation, identification and characterization of anticancer principle from the medicinal plant Corallocarpus epigaeus (Co-PI)	Kerala State Council for Science, Technology and Environment	2016 - 2019
	Investigating the mechanism behind the protective effect of the anticancer compounds isolated from Woodfordia fruticosa(L.)Kurz flowers against hepatocellular carcinoma (Co-PI)	Kerala State Council for Science, Technology and Environment	2016 - 2019
	'Mechanistic evaluation and in vivo validation of the anticancer potential of Uttroside B against hepatocellular carcinoma' (PI)	Department of Science and Technology - Science and Engineering Research Board	2017 - 2020

RGCB EXTRA MURAL RESEARCH GRANTS

Principal Investigator	Name of Grant	Funding agency	Duration
Dutta Debasree	Cellular transition-an epigenetic perspective in development and disease	Department of Biotechnology	2017 - 2020
	Role of PKC signaling in dictating naïve vs. primed pluripotency	Department of Biotechnology	2017 - 2019
	Histone chaperone HIRA as a novel modulator in dictating differentiation vs. proliferation	Department of Science and Technology	2017 - 2020
	Evaluation of Histone chaperone APLF as a novel biomarker in Triple Negative Breast Cancer (TNBC)	Department of Biotechnology National Women Bio-scientist Award	2018 - 2023
Das Ani V	Identification of and functional evaluation of Piwi-associated regulatory RNAs in the stem cell population of HPV-associated cervical cancer	Council of Scientific and Industrial Research	2017
	Epigenetic regulation of multidrug resistance genes in embryonic carcinoma stem cells: implications in targeting cancer stem cells in germ cell tumors	Department of Biotechnology	2018
George Sanil	Strategies for enhancing biological activity of novel peptides (brevinin-1 and 2) identified from the skin secretion of an endemic frog	Department of Science and Technology - Science and Engineering Research Board	2019 - 2022

RGCB EXTRA MURAL RESEARCH GRANTS

Principal Investigator	Name of Grant	Funding agency	Duration
Harikumar K B	An integrated network analysis to identify genomic alteration profiles of human pancreatic cancer	Department of Biotechnology	2017 - 2020
	Regulation of hepatic metastasis of colorectal cancer by exosomes	Science and Engineering Research Board	2018 - 2021
	A mechanistic evaluation of Chiravilvadi Kashayam in colitis associated colorectal cancer	Science and Engineering Research Board	2018 - 2021
	Mex3C: A novel tumor suppressor in colorectal cancer	Indian Council of Medical Research	2018 - 2021
	Understanding the role of Sphingosine kinase isoforms in Systemic lupus erythematosus (SLE)	Council of Scientific and Industrial Research	2018 - 2021
Jaleel Abdul K A	Identification of Metabolic Alterations in Sub-clinical Vitamin B12 Deficiency by Mass Spectrometry Based Metabolomics	Kerala State Council for Science, Technology and Environment	2016 - 2019
	Metabolomics Profiling of Normal Healthy People in Kerala: Impact of family History of Diabetes	Department of Biotechnology	2017 - 2020
Johnson John Bernet	Rhabdovirus components and complement factors in virus assembly, pathogenesis, neurovirulence and modified viral vectors.	Department of Biotechnology - Ramalingaswami fellowship	2013 - 2018

RGCB EXTRA MURAL RESEARCH GRANTS

Principal Investigator	Name of Grant	Funding agency	Duration
Johnson John Bernet	Mechanisms of complement activation and evasion strategies in Chandipura virus pathogenesis.in virus assembly, pathogenesis, neurovirulence and modified viral vectors.	Department of Science and Technology	2016 - 2019
James Jackson	Guiding retinal ganglion cell axons to brain visual centers: Is Pax6 the key molecule?	Department of Science and Technology	2017 - 2020
	Expression of Notch independent Hes-1 (NIHes-1) specifically in ES cell derived Organoids representing developing neocortex: Understanding its functional significance	Department of Biotechnology	2018 - 2020
	National Bioscience Award for Career Development	Department of Biotechnology	2018 - 2021
Joseph Iype	Prevalence survey of rodent ectoparasites. Democratising Science through a Major Twinning Programme of the North East with other parts of India. DBT-India. Funded by the Department of Biotechnology	Department of Biotechnology	2018 - 2019
Kumar Ajay R	Dissecting the physiological role of Rv3423.1, a novel histone acetyltransferase in Mycobacterium tuberculosis H37Rv, in the bacterium as well as in infected guinea pig.	Science and Engineering Research Board, Department of Science and Technology	2017 - 2020

RGCB EXTRA MURAL RESEARCH GRANTS

Principal Investigator	Name of Grant	Funding agency	Duration
Kurthkoti Krishna	Characterization of iron starvation induced dormancy in mycobacteria and its application in drug discovery	Department of Biotechnology, Ramalingaswami Re-entry fellowship	2017 - 2022
	Deciphering the role of mycobacterial error-prone polymerase DnaE2 in antibiotic persistence and conferring adaptation to stress during biofilm formation.	Science and Engineering Research Board Core Grant, Department of Science and Technology	2019 - 2022
Kumar Pradeep G	Interrelationship between polymorphism in four obesity genes, their expression and its correlation with infertility and obesity in subjects from Kerala	Kerala State Council for Science, Technology and Environment	2016 - 2019
	Transdifferentiation of Spermatogonial Stem Cells (SSC) into somatic cell lineages via Embryonic Stem Cell (ES) like intermediaries	Department of Biotechnology	2017 - 2010
	Evaluation of the role of AIRE in germ cell development and differentiation (CSIR, New Delhi), 2018-2021.	Council of Scientific and Industrial Research	2018 - 2021
Kumar Vinod G S	Development of a novel three dimensional self aggregating peptide fiber as an implant for brain tumors	Science and Engineering Research Board, Department of Science and Technology	2018 - 2021
	Development of cotton-like bioadhesive antimicrobial peptide based hydrogel patches for wound healing	Indian Council of Medical Research	2019 - 2022

RGCB EXTRA MURAL RESEARCH GRANTS

Principal Investigator	Name of Grant	Funding agency	Duration
Laishram Rakesh S	Role of RBM10 in gene expression and 3'-end processing and its cellular implications	Science and Engineering Research Board - Department of Science and Technology	2016 - 2019
	3'UTR processing in regulation of cardiac genes with roles in pressure overload cardiac hypertrophy	Department of Biotechnology	2017 - 2020
	Linking the two poly(A) tails: Eukaryotes vs Prokaryotes	Department of Biotechnology	2017 - 2020
Laloraya Malini	Deciphering the role of ER alpha in modulating the strength of STAT3 function.	Department of Science and Technology	2015 - 2018
	Delineating the DNA-binding function of DOCK180.	Department of Biotechnology	2017 - 2019
Mahendran K R	Antibiotic translocation through porins in Gram-positive bacteria at the single-molecule level	Department of Biotechnology, Ramalingaswami Re-entry fellowship	2016 - 2021
	Controlled assembly of transmembrane α-helix-barrel pores for single-molecule sensing	Department of Biotechnology, Innovative Young Biotechnologist award	2017 - 2020
	Single-molecule biosensing with hetero-oligomeric protein nanopores.	Science and Engineering Research Board	2018 - 2021

RGCB EXTRA MURAL RESEARCH GRANTS

Principal Investigator	Name of Grant	Funding agency	Duration
Mahendran K R	Structure determination and targeting of ubiquitously expressed membrane integrated form of chloride intracellular channels (CLICs) for discovery of small molecular anti-cancer therapeutics	Science and Engineering Research Board	2019 - 2022
Manjula S	Transcriptome analysis and characterization of key metabolic and hormone signaling pathway genes in Piper nigrum in response to defense elicitors (in collaboration with NCBS)	Department of Biotechnology	2018 - 2021
	Identification and functional characterization of Phytophthora capsici effectors specific to 'quick wilt' disease in black pepper (Piper nigrum)	Department of Biotechnology	2018 - 2021
Mukherjee Ananda	Domain-specific role of tumor suppressor PTEN in genomic stability: A systematic approach.	Department of Science and Technology - Science and Engineering Research Board	2019 - 2022
	Studies on noncanonical role of tumor suppressor PTEN in endometrial adenocarcinoma.	Department of Biotechnology	2018 - 2023

RGCB EXTRA MURAL RESEARCH GRANTS

Principal Investigator	Name of Grant	Funding agency	Duration
Maliekal Tessy Thomas	Virtual National Oral Cancer Institute: Development of Animal Model Systems to study oral cancer progression.	Department of Biotechnology	2018 - 2021
	Evaluation of the role of TIF1γ in the regulation of self-renewal ability of OSCC stem cells	Department of Science and Technology	2016 - 2019
Mishra Rashmi	Identification of the Role of Redox Signaling Pathways in the Mechanobiology of Neural Stem Cells and its Implications on the Pathology of Glioblastoma multiforme	Department of Biotechnology	2018 - 2021
Nair Asha S	Development of Novel NIR absorbing sensitizers and their nano-conjugates for the multimodal cancer imaging and therapy.	Department of Biotechnology	2017 - 2020
Nair Radhika	Deciphering Breast Cancer Metastasis	Science and Engineering Research Board	2015 - 2020
	Deciphering the molecular circuitry of Cancer Stem Cells	Science and Engineering Research Board	2016 - 2019
Nayar Saraswati	Functional characterization of Chlorella hormone biosynthesis and signaling genes for phytoremediation and bio-diesel production	INSPIRE Faculty Award, Department of Science and Technology, Government of India	2015 - 2020
	Characterization of a MADS box transcription factor in a unicellular microalgae	EMR Grant, Science and Engineering Research Board, Department of Science and Technology, Government of India	2017 - 2020

RGCB EXTRA MURAL RESEARCH GRANTS

Principal Investigator	Name of Grant	Funding agency	Duration
Omkumar R V	Investigations on the role of the biochemical bistable switch in learning and memory in vivo	Science and Engineering Research Board	2019 - 2022
	Detailed state Model of CaMKII activation and autophosphorylation in the presence of NR2B and its behaviour in Epileptic conditions	Kerala State Council for Science, Technology and Environment	2015 - 2018
Pillai M Radhakrishna	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	Bill & Melinda Gates Foundation and International Agency for Research on Cancer of the World Health Organization	2009 - 2021
	Understanding Measles Vaccine Failure (and success) in Southern India	National Institutes of Health, USA	2017 - 2022
	National Facility for Drug Discovery and Developmental Therapeutics (NFDDDT) by Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram	Department of Biotechnology	2016 - 2019
	Program Support on Translational Research in Triple Negative Breast Cancer (Center of Excellence)	Department of Biotechnology	2016 - 2020
	Biomarkers of Oral Cancer Prediction	Department of Biotechnology	2018 - 2021

RGCB EXTRA MURAL RESEARCH GRANTS

Principal Investigator	Name of Grant	Funding agency	Duration
Rajavelu Arumugam	Functional studies on the lncRNAs of Plasmodium falciparum and its role in antigenic variation process	Science and Engineering Research Board, ECR program	2016 - 2019
	Molecular determinants of vascular differentiation in the pathogenesis of cerebral arteriovenous malformations	Kerala State Council for Science, Technology and Environment - KBC program	2016 - 2019
	Functions of N-6 adenine methylation (m6A) in mRNA plasticity of Plasmodium falciparum at various developmental stages in RBC: Exploring Novel drug targets	Department of Biotechnology, Infectious Disease Biology task force	2019 - 2021
Ramachandran Surya	How does Cyclophilin A, an Oxidative Stress Induced Secretory Protein Modulate Vascular Disease Progression in Type 2 Diabetes?	Indian Council of Medical Research	2015 - 2018
	Does Cyclophilin A, an Immunophilin under High Glucose Conditions Regulate Efferocytosis in Atherosclerotic Lesions?	Kerala State Council for Science, Technology and Environment	2018 - 2021
	Cyclophilin A and Efferocytosis in Vascular Disease Associated with Type 2 Diabetes	Madras Medical Mission, Chennai	2017 - 2020

RGCB EXTRA MURAL RESEARCH GRANTS

Principal Investigator	Name of Grant	Funding agency	Duration
Ramachandran Surya	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 (As Co-PI from RGCB)	Department of Biotechnology	2017 - 2020
Sathi Shijulal Nelson	Major Gene influxes in microbial genome evolution, INSPIRE Faculty Award, DST	Department of Science and Technology	2016 - 2021
	Towards an early warning system for infectious disease outbreaks – Geospatial scale mmetagenomic profiling of mass-transit systems in Kerala. Young Investigators programme in Biotechnology (YIPB), KBC	Kerala State Council for Science, Technology and Environment	2018 - 2020
	The Structure and Evolution of Environmental Resistomes, Early Career Research Award (ECR)	Science and Engineering Research Board - Department of Science and Technology	2019 - 2021
	International Collaboration with Institute of Molecular Evolution, Heinrich Heine University, Düsseldorf, Germany	Science and Engineering Research Board - Department of Science and Technology	2019 - 2021

RGCB EXTRA MURAL RESEARCH GRANTS

Principal Investigator	Name of Grant	Funding agency	Duration
Santhosh Kumar T R	Understanding the role of Hypoxia induced mitophagy in cancer cell survival and drug resistance :Implications on tumor stem cell like cells	Department of Science and Technology	2017 - 2020
	Understanding epigenetic changes and cell state transitions that contribute for recurrence in triple negative breast cancer	Department of Biotechnology	2017 - 2020
	Design and Characterization of peptide based cell targeting domains with live cell and animal imaging methods	Department of Biotechnology	2018 - 2021
Santhosh Kumar K	Bio-prospecting of Anti-Microbial Peptides from Hymenopteran (ants, bees and wasps) insects Collaborating institute: UAS, Bangalore.	Department of Biotechnology	2016 - 2019
	Identification and immmunosensor based detection of peptide biomarkers in mastitic milk and development of synthetic anti-microbial peptide hydrogels as alternative therapy for bovine mastitis	National Agricultural Science Fund (NASF)	2016 - 2020
	Development of a new and cost effective biosensor based on transparent conducting oxide thin films working in near IR frequency	Department of Science and Technology	2018 - 2020

RGCB EXTRA MURAL RESEARCH GRANTS

Principal Investigator	Name of Grant	Funding agency	Duration
Sengupta Suparna	Analysis of Fodrin Association with Gamma-Tubulin Complex, the Microtubule Organizer	Department of Science and Technology	2017 - 2020
	An approach towards Liquid Biopsy for Cancer	Department of Biotechnology	2017 - 2020
Soniya E V	DNA profiling of Asian Elephants (Elephas maximus) in Kerala and establishment of a DNA fingerprint database of captive elephants in Kerala.	Forest Department, Govt. of Kerala	2017 - 2018
	Characterization of key structural genes involved in flavonoid synthesis in Indian Gooseberry, (Emblica officinalis Gaertn.).	Kerala State Council for Science, Technology and Environment	2015 - 2019
Sreeja S	Screening and Pre-Clinical evaluation of compounds of Pomegranate in Antagonizing Endogenous SERM-27 Hydroxycholesterol in Breast cancer	Science and Engineering Research Board	2016 - 2019
	Development of probiotic therapy for enhancing urolithin production by using bacterial flora of human origin	Department of Science and Technology - Science and Engineering Research Board	2018 - 2021

Principal Investigator	Name of Grant	Funding agency	Duration
Sreekumar E	Elucidation of the role of endothelial cell signaling pathways in vascular permeability modulation in Dengue virus infection	Indian Council of Medical Research	2017 - 2020
	Identification of cellular pathways differentially modulated in Human microvascular endothelial cells upon Dengue virus infection	Kerala State Council for Science, Technology and Environment	2016 - 2019
	Characterization of the role of Nucleophosmin and other selected host proteins identified from differential proteomics in Chikungunya virus infection	Department of Biotechnology	2016 - 2019
	Antivirals from medicinal plants of Western Ghats selected based on traditional knowledge (TK) / Ethnomedical information	Department of Biotechnology	2015 - 2020
Srinivas Priya	Assessment of Cell Growth and Microbial Contamination in Mammalian Cell Culture using Foldscope in the Laminar Flow Hood	Department of Biotechnology-Foldscope	2015 - 2018
	Targeting Cancer associated fibroblasts for Metastasis Inhibition in BRCA1 defective cancer	Department of Science and Technology - Science and Engineering Research Board	2017 - 2020

RGCB EXTRA MURAL RESEARCH GRANTS

Principal Investigator	Name of Grant	Funding agency	Duration
Sumi S	Role of hemodynamic shear stress in the pathogenesis of varicose veins	Kerala State Council for Science, Technology and Environment	2018 - 2021
	Molecular pathogenesis of varicose veins	Dr. N Radhakrishnan Venous Research Fund	2018 - 2020
	Molecular determinants of vascular differentiation in the pathogenesis of arteriovenous malformations	Kerala State Council for Science, Technology and Environment	2016 - 2019
Thomas George	Development of rice varieties for Kerala with pyramided genes for resistance to BLB by marker assisted selection	Department of Biotechnology	2013 - 2019
	Delineation and characterization of defense signaling pathways and genetic regulation of induced systemic resistance in Zingiber¬-Pythium pathosystems.	Department of Biotechnology	2018 - 2021
Thomas Sabu	Analysis of polymicrobial biofilms in chronic wound infections and development of anti-biofilm therapeutic to promote wound healing	Department of Biotechnology	2016 - 2019
	A study on the antimicrobial resistance pattern in Kerala	Department of Health and Family Welfare, Government of Kerala	2018
	Health promoting properties of potential probiotic strains isolated from infant gut microflora	Indian Council of Medical Research	2018 - 2020

RGCB EXTRA MURAL RESEARCH GRANTS

Principal Investigator	Name of Grant	Funding agency	Duration
Thomas Sabu	Development of probiotic therapy for enhancing urolithin production by using bacterial flora of human origin	Science and Engineering Research Board - Department of Science and Technology	2018 - 2021
Umasankar P K	Endocytic modulation of BMP signaling: deciphering mechanistic insights into health and disease	Department of Biotechnology	2016 - 2021
	Uncovering mechanisms to remodel cholesterol landscape in cancer cells (SERB-DST-Extramural Research grant)	Department of Science and Technology	2018 - 2021
BIONEST	Fabrication of lateral flow device to detect plant viruses such as Banana Bunchy Top Virus BBTV, Banana Bract Mosaic Virus BBMV and Cardamom Mosaic Virus CdMV	Incubatee: Phytocom Pharmaceutical (P) Ltd	
	Microbial Photo Voltaic cells: Clean Fuels through photosynthetic and electrochemically active micro algae	Incubatee: Scire lifesciences (P) Ltd	
	Cost Effective and large scale production of high quality ginger planting material	Incubatee: Green Clones (P) Ltd	
	Development of a poly microbial multifunctional bio-fertilizer from slurry produced from rubber processing unit	Incubatee: Biomount Nutrients LLP	
	Accessible and affordable non-cytotoxic melanin in sunscreen formulation for skin cancer prevention.	Incubatee: Greenle life sciences (P) Ltd	
	Development of rapid test kit for assessment of CRP and Procalcitonin levels to prevent Antibiotic misuse	Incubatee: Sushruta Innovation And Wellness (P) Ltd	

RGCB LIST OF PUBLICATIONS

Anantharaman Devasena	Du E, Mazul AL, Farquhar D, Brennan P, **Anantharaman D**, Abedi-Ardekani B, Weissler MC, Hayes DN, Olshan AF, Zevallos JP. Long-term Survival in Head and Neck Cancer: Impact of Site, Stage, Smoking, and Human Papillomavirus Status. Laryngoscope. 2019 Jan 13 Abrahão R, **Anantharaman D**, Gaborieau V, Abedi-Ardekani B, Lagiou P, Lagiou A, Ahrens W, Holcatova I, Betka J, Merletti F, Richiardi L, Kjaerheim K, Serraino D, Polesel J, Simonato L, Alemany L, Agudo Trigueros A, Macfarlane TV, Macfarlane GJ, Znaor A, Robinson M, Canova C, Conway DI, Wright S, Healy CM, Toner M, Cadoni G, Boccia S, Gheit T, Tommasino M, Scelo G, Brennan P. The influence of smoking, age and stage at diagnosis on the survival after larynx, hypopharynx and oral cavity cancers in Europe: The ARCAGE study. Int J Cancer. 2018 Jul 1;143(1):32-44 Basu P, Muwonge R, Bhatla N, Nene BM, Joshi S, Esmy PO, Poli URR, Joshi G, Verma Y, Zomawia E, Shastri SS, Pimple S, **Anantharaman D**, Prabhu PR, Hingmire S, Sauvaget C, Lucas E, Pawlita M, Gheit T, Jayant K, Malvi SG, Siddiqi M, Michel A, Butt J, Sankaran S, Rameshwari Ammal Kannan TP, Varghese R, Divate U, Willhauck-Fleckenstein M, Waterboer T, Müller M, Sehr P, Vashist S, Mishra G, Jadhav R, Thorat R, Tommasino M, Pillai MR, Sankaranarayanan R; Papillomavirus Res. 2019 Jun; 7: 75-81
Anto Ruby John	Vinod Vijayakurup, Arunkumar T.Thulasidasan, Mohan Shankar G, Archana P. Retnakumari, C. Devika Nandan, Jannet Somaraj, Jayesh Antony, Vijai V. Alex, Balachandran S.Vinod,Vijayasteltar Belsamma Liju, Sankar Sundaram, G. S.Vinod Kumar, and Ruby John Anto*. Chitosan encapsulation enhances the bio-availability and tissue retention of curcumin and improves its efficacy in preventing B[a]P-induced lung carcinogenesis. **Cancer Prevention Research**, 2019; DOI: 10.1158/1940-6207.CAPR-18-0437. Amrutha Nisthul A., Archana P. Retnakumari, Shabna A., Ruby John Anto & C. Sadasivan. In silico screening for identification of fatty acid synthase inhibitors and evaluation of their antiproliferative activity using human cancer cell lines. **Journal of Receptors and Signal Transduction**, 2018, Sep 26:1-7. doi: 10.1080/10799893.2018.1511730. Minakshi Saikia, Archana P.R, Shabna A, NP Anto, Rashmi Mittal, Shabna S, Kavya S Pillai, B S.Vinod, Vidya Peter, Reeba Thomas and Ruby John Anto*, Heteronemin, a marine natural product, sensitizes acute myeloid leukemia cells towards cytarabine chemotherapy by regulating farnesylation of Ras, **Oncotarget**, 2018, 9, 18115-18127

RGCB LIST OF PUBLICATIONS

Ali Jamshaid	Kumar A, Ghosh DK, Ali J, Ranjan A. Characterization of Lipid Binding Properties of Plasmodium falciparum Acyl-Coenzyme A Binding Proteins and Their Competitive Inhibition by Mefloquine. ACS Chem Biol. 2019;14:901–15.
Asha V V	Tom G, Philip S, Isaac R, Praseetha PK, Jiji SG, Asha VV.Preparation of an efficient and safe polymeric-magnetic nanoparticle delivery system for sorafenib in hepatocellular carcinoma.**Life Sci**. 2018 Aug 1;206:10-21.
Banerjee Moinak	B Swathy, KR Saradalekshmi, IV Nair, CM Nair, Moinak Banerjee Understanding the influence of antipsychotic drugs on global methylation events and its relevance in treatment response. **Epigenomics**, 10(3):233-247,2018. D Venugopal, V Shivakumar, M Subbanna, SV Kalmady, AC Amaresha, M Agarwal, JC Narayanaswamy, Moinak Banerjee, Monojit Debnath, G Venkatasubramanian. Impact of antipsychotic treatment on methylation status of Interleukin-6 [IL-6] gene in Schizophrenia. **Journal of Psychiatric Research**, 104, 88–95, 2018 Ann Mary Alex, Moinak Banerjee.: Melatonin disruption in autism and their regulation by natural supplements. Book titled "Serotonin and Melatonin: Their Functional Role in Plants, Food, Phytomedicine and Human Health."Taylor and Francis CRC Press Chapter 32 499–512, 2016. Swathy B, Moinak Banerjee. Serotonin Transporters in Theranostics of neuropsychiatric disorders. Book titled "Serotonin and Melatonin: Their Functional Role in Plants, Food, Phytomedicine, and Human Health." Taylor and Francis CRC Press, Chapter 35, 539–550 2016. Swathy Babu, Binithamol K Polakkattil, Moinak Banerjee. Pharmacoepigenetics of antipsychotic drugs. Book Titled "Pharmacoepigenetics". Ed. Ramón Cacabelos and Oscar Teijido. Academic Press Chapter 22.442-450. 2019 Alex AM, Saradalekshmi KR, Shilen N, Suresh PA, Banerjee M. Genetic association of DNMT variants can play a critical role in defining the methylation patterns in autism. **IUBMB** Life. 2019 Feb 20. doi: 10.1002/iub.2021.
Das Ani V	Sumitra Shankar, Ahalya Sreekumar, Deepti Prasad, Ani V. Das, M.R Pillai. Genome editing of oncogenes with ZFNs and TALENs: caveats in nuclease design. **Cancer Cell International**, 2018, 18:169. doi.10.1186/s12935-018-0666-0 Shankar S, Prasad D, Sanawar R, Das AV and Pillai MR. TALEN based HPV-E7 editing triggers necrotic cell death in cervical cancer cells. **Scientific Reports**, 2017, 7: 5500. doi:10.1038/s41598-017-05696-0

RGCB LIST OF PUBLICATIONS

Dutta Debasree	Majumder A, Syed KM, Mukherjee A, Lankadasari MB, Azeez JM, Sreeja S, Harikumar KB, Pillai MR, Dutta D.**Mol Cancer**. 2018 ;17(1):76.
George Sanil	Vineeth kumar,T.V, Shyla Gopal and Sanil George. 2018. Smallest lectin-like peptide identified from the skin secretion of an endemic frog Hydrophylax bahuvistara. **Acta Biologica Hungarica** 69(1), 110–113. Vineethkumar T.V, Asha R, Shyla Gopal and Sanil George 2018. Studies on the mode of membrane interaction of C-terminally amidated Brevinin1 HYba1& 2 peptides against bacteria. **Int J Pept Res Ther** 24:117–129.
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Harikumar K B	Lankadasari MB, Mukhopadhyay P, Mohammed S, Harikumar KB. TAMing pancreatic cancer: combat with a double edged sword. **Mol Cancer**. 2019; 18(1):48 Vijayan Y, Lankadasari MB, Harikumar KB. Acid Ceramidase; A novel therapeutic target in cancer. **Curr Top Med Chem**. 2019 Feb 27. [Epub ahead of print] Mohammed S, Vineetha NS, James S, Aparna JS, Lankadasari MB, Allegood JC, LiQZ, Spiegel S, Harikumar KB. Examination of the role of sphingosine kinase 2 in amurine model of systemic lupus erythematosus. **FASEB J**. 2019 Mar 6:fj201802535R. [Epub ahead of print]
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RGCB LABORATORY MEDICINE AND MOLECULAR DIAGNOSTICS

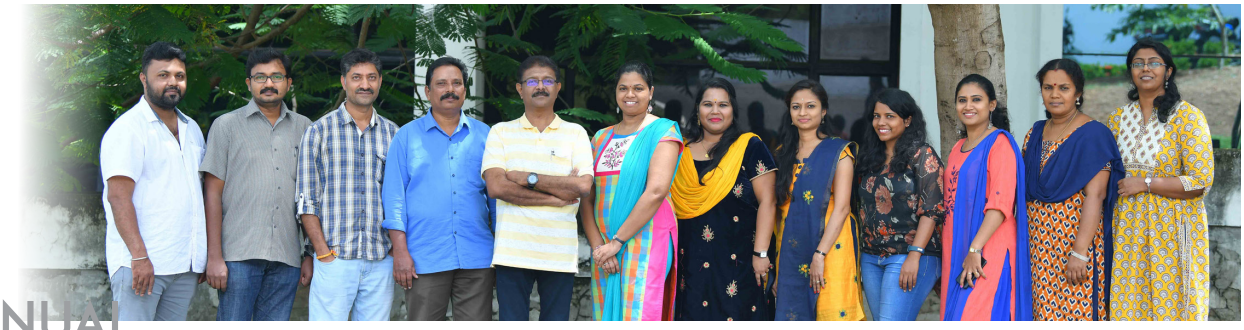
Radhakrishnan R, PhD

Laboratory Medicine and Molecular Diagnostics (LMMD) is the molecular diagnostic hub of Rajiv Gandhi Centre for Biotechnology, Dept of Biotechnology, Government of India. The facility was initiated in 2011 under the ICMR Virology Network program and currently, it serves as a stand alone laboratory. The facility adheres to the quality control and quality management protocols laid down by NABL (ISO 15189-2012) and NABH. The facility was recently accredited with ILAC (International Laboratory Accreditation Corporation), gaining acceptance for its results worldwide. The facility introduced BCR-ABL quantitative assay in August 2018 for the diagnosis and treatment response assessment of chronic myelogenous leukemia (CML) and Acute lymphoblastic leukemia (AML). A total of 725 samples were screened within a span of 8 months. The facility has introduced Brucella virus, Crimean Congo Virus and HLAB 27 mutation analysis during the current year.

A total of 9072 samples were diagnosed last year . A total of 702 samples were subjected for different mutation analysis such as BCR-ABL, BRCA 1& 2, HLA B 27, etc. In addition to diagnostic services, the facility also has a research and development arm. The facility mainly focuses on development of point of care testing technology and to develop new diagnostics tools. The facility has trained 53 MD students and 20 science and engineering graduates during 2018 - 2019.

India is estimated to have the highest snakebite mortality in the world. In most of the snakebite cases, victims and clinicians failed to identify the snake and take time to calculate the venom payload amount. We have developed a lateral flow immunoassay with a smartphone-based reading which helps to detect snake species and quantify payload in the sample within minutes, hence making diagnosis easier.

We are investigating the role of polymorphisms in CYP3A5 and CYP3A4 genes and their interactions on tacrolimus response, dosing strategies and adverse drug reactions (ADRs) in renal transplant recipients. We have demonstrated that, CYP3A5*3 GG and CYP3A4 *1G GG presented a significant association with higher Tac C0/D on a postoperative day 6. ABCB1 C3435T showed a trend towards association with higher Tac C0/D. We have also identified genotypes which are associated with adverse effects like NODAT.



TEAM: Sanughosh K, Mohammed Ashiq, Dayakar S, Vinod Kumar S, Heera Pillai R, Jayalekshmi D, Vineetha P T, Sruthi Shankar, Karthika V, Sumaja V, Lakshmy Sreenivas

GENOMICS SERVICE FACILITY

DNA Sequencing Facility (Sanger sequencing & Genotyping)

The facility equipped with Multicapillarry systems 3730 & 3730 XL DNA analyzers, are fully functional and analysed bacterial, viral, plant and animal samples from both in-house as well as external clients. The jobs from research labs, such as neurobiology (Aneurism, Deafness, Autism, Alzheimer's, Dimentia patient samples), Plant Disease Biology (microsatellite screening, marker screening), Pathogen Biology lab, Cholera lab, Cardio vascular disease lab, Mycobacterium lab, Molecular Virology lab, and Laboratory Medicine and Molecular Diagnostics (HBv, HCv, HIV, Dengue, Chikuguinea samples) were sequenced. Approximate 40,000 samples were handled in the facility during the period. For genescan analysis, 3000 samples of plants / animals were processed for SNP genotyping and microsatellite analysis of various research laboratories. They were subsequently analyzed using genemapper software.

Q-PCR analysis

Gene expression studies with Real Time PCR 7500, 7900 HT systems, helped in SNP analysis, absolute quantitation, relative quantitation, Allelic discrimination (for Autism spectrum disorder) & Taqman low Density (TLDA) array applications using Sybr green /Taqman chemistry,for various research labs of both internal and external investigators.

Next generation sequencing and microarray facility:

The facility handled exome sequencing & Transcriptome sequencing, using ionproton platform, small genome sequencing and metagenomics, using ionpgm platform for various investigators. Microarray platform using the affymetrix genechip technology has been fully utilized with human and mouse arrays. Few Peer reviewed publications generated with direct help from the facility this year include:

1 Genetic association of DNMT variants can play a critical role in defining the methylation patterns in autism, Ann Mary Alex, Korammannil R. Saradalekshmi, Neena Shilen Poovathinal A. Suresh, Moinak Banerjee: 20 February 2019, IUBMB Life (using ABI7500 RTPCR)

2 Genomic Insights into Biofilm-Forming Enterococcus faecalis SK460 Isolated from a Chronic Diabetic Ulcer Patient, Suryaletha K, Narendrakumar L, John J, Reghunathan D, Manoj P, Thomas S, 'Genome announcements" Genome Announc.;6(2), 2018. (using ionPGM)

3 Characterization of a novel asparaginase from soil metagenomic libraries generated from forest soil. Biotechnology letters, 2018, 40(2):343-348. Arjun JK, Aneesh BP, Kavitha T, Harikrishnan K.Biotechnol Lett.; 40(2):343-348. (16S rDNA sequences-using ion PGM)

4 Efficient methanol-degrading aerobic bacteria isolated from a wetland ecosystem, Article in Archives of Microbiology 200(5) • April 2018, Kavitha Thulasi, Arjun Jayakumar, Aneesh Balakrishna Pillai, Vinod Kumar Gopalakrishnapillai Sankaramangalam, Harikrishnan Kumarapilla (using ABI 3730)

5 Sphingolipid signaling modulates trans-endothelial cell permeability in dengue virus infected HMEC-1 cells. Anupriya MG, Singh S, Hulyalkar NV, Sreekumar E (2018), Prostaglandins & other lipid mediators, (2018) May; 136:44-54 (using Affimetrix microarray)

Apart from this there were number of genebank submissions (NCBI) generated from ABI 3730 / ABI3730XL systems, few patents, and many publications in pipeline with direct help from facility.

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 last year (April 2018- March 2019) around 900 samples of various types and forms have been analysed by the facility.

ANIMAL RESEARCH FACILITY

The main focus of the Animal Research Facility is to provide services and resources for researchers to achieve their animal research objectives. The facility is registered with the "Committee for the Purpose of Control and Supervision of Experiments on Animals" (CPCSEA) for breeding animals for in-house use & trade and for conducting experiments of small laboratory animals. The institute has established an Institutional Animal Ethics Committee for approving and monitoring the animal experiments to ensure the conduct of research prescribed by the norms of CPCSEA and maintains the welfare of animals in its fullest standards.

The Animal Research Facility currently maintains 26 strains of mice, 3 strains of rat and one strain of rabbit in separate designated rooms. The animal rooms are maintained in controlled environment with 14:10 light and dark cycle and other parameters like temperature, humidity and air changes based on the specific requirement for each species. At present, ARF houses general purpose, transgenic and immune-compromised strains of mice in individual ventilated caging system having a separate air handling unit and animal change station. The rats and rabbits are maintained in conventional system. All species of animals are provided with autoclaved commercially procured pellet feed and drinking water according to their specific physiological requirements. In addition to pellet feed, rabbits are also provided with green forages.

The animal research facility is actively involved in the various in vivo studies. We have successfully developed different animal models for research like orthotopic mammarytumour, oral tumour and hepatic tumourxenograft mouse models, wound excision mouse models, ovariohysterectomised mouse models and rabbit ileal loop model. The in-vivo studies currently conducted in the Animal Research Facility include efficacy and toxicity evaluation of drug formulations, staging of gestation and collection of embryos at different stages of gestation, atherosclerosis studies in rabbits,generation of polyclonal /monoclonal antibodies in rabbits and mice ,development of different xenograftmice models for cancer research, wound healing studies and stereotaxic surgeries to evaluate the biocompatibility of drugs administered in brain.

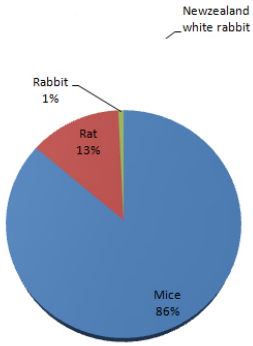
MANAGEMENT TEAM: Archana S, Arya Aravind, E Sreekumar, Vishnu Sunil Jaikumar

ANIMAL RESEARCH FACILITY

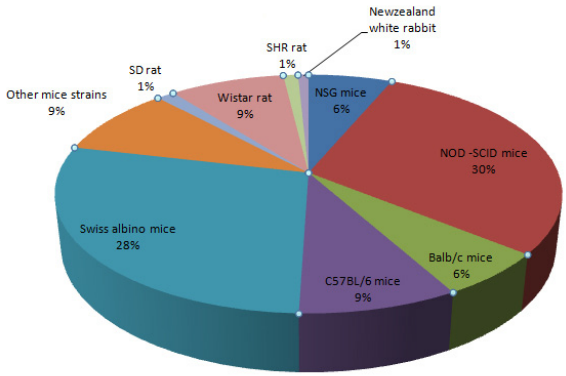
Services provided:

- Supply of Specific Pathogen Free animals.
- Non -Invasive and invasive animal procedures including live animal surgeries.
- Development of different animal models for research.
- Gross and histopathological evaluation of tissues.
- Custom breeding and maintenance of transgenic strains.
- Conduct contract studies based on the requirement of clients from other institutions.

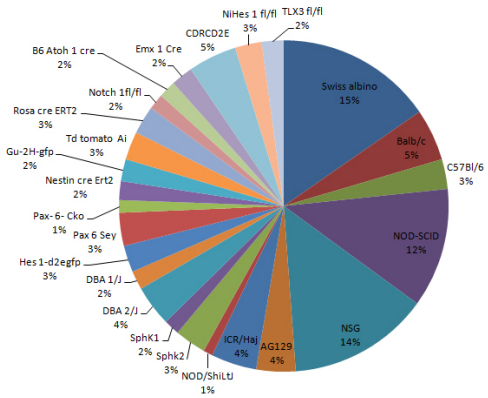
Animal Species maintained at ARF



Data on animal usage during the year 2018-2019



Strains of mice purchased and maintained at ARF



SUPPORT TEAM: Dileep R K, Vinod V M, G Vinod, Rajeev R V, Anvar

RGCB RESEARCH ENGINEERING AND TECHNICAL SUPPORT TEAM

Research Engineering Service Department has been playing an important role since inception of the Institute. Having operations in both the 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 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 both Main Campus and Bio Innovation Centre.

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 equipment. On top of the above, the Division also undertakes customisation by designing, fabrication & modification of components of research automations.

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. 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 maintenance 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, 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.

TEAM: Manoj P, Sanjai D, George Varghese, Rajasekharan K, Jiji V, Jamshaid Ali

RGCB RESEARCH ENGINEERING AND TECHNICAL SUPPORT TEAMS

RGCB Technical Support team includes highly skilled and dedicated personnel providing essential support for biological, chemical, physical, computational and life science research. These personnel manage core research facilities and equipment ensuring effective functioning, adhering to correct procedures and safety guidelines. Major facilities supported by the technical team include Mass Spectrometry & Proteomic Core, Animal Imagers, Confocal Laser Scanning Microscopes, High Speed Flow cytometer sorter systems, Super Resolution Microscope, Next generation genetic sequencing systems and Animal Research Facility.

TEAM: Bindu Asokan, Indu Ramachandran, Sudha B Nair, Ciji Varghese, Laiza Paul, Rahul C S Nair, Ajithkumar S, Sajan I X, Sivakumar K C, Saravana kumar M

TEAM: Saptarshi Biswas, Mahesh Chandran, Deepa Mathew P, Viji S, Arya Anoop, Surabhi S V, Vishnu T S, Tilak Prasad, Amal V, Gopikrishnan K, Suresh Kumar U

TEAM: Rajeev S, Antony K P, Sheela G, Velthai G, Rintu T Varghese, Edwin S, Biju S Nair, Unnikrishnan V R, Santhosh S, Johny G

TEAM: Preetha V Rajan, Remya R C, Devika M Nair, Renju Krishnan R V, Abhilash M K, Ratheesh R V, Anandhu A

TEAM: Shaji V, Soumya S P, Lekshmi C, Arunima B, Sreelekshmi A S, Aswathy G Raj, Dinesh D M, Renadeep C S Nair, Sidharth A, Anoop M L, ManojKumar K, Shibin J, Ullas Chandran C D, Mohan Nallatt, Ajithkumar R, Akhil Kumar T, Unniraj S, Ancy Prince T S, Vijaya Kumar, Premkumar V

RGCB GENERAL ADMINISTRATION

The main responsibility of general administration is to ensure the efficient performance of all departments at GCB serving as the connecting link between the senior management and the employees. The major mandates of general administration include good coordination among all the departments ensuring attainment of organisational goals, optimum utilization of resources, minimization of cost, human resources and payroll, vigilance and security, transportation, fulfilment of social and economic needs of the employees and organization as well as development and growth of the institute.

TEAM: Abilal G O, Sujitha S, Vinod Lal K A, Reena Prasad, Sutha Kumari, Asha R Nair, Aryasri P, Wilson T, Vinod Kumar S R

RGCB TRANSPORT GROUP: Anil kumar B, Hari kumar S, Ashok kumar S, Ratheesh, Praveen B, Suresh kumar S K, Vijayakumar S, Manu kumar V M, Pradeep kumar V S

RGCB FINANCE, ACCOUNTS AND PROJECT MANAGEMENT

The Finance & Accounts group 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 acclimatise the available resources' utilisation in achievement of its mandated science, thereby paving the way for productive application of all available resources. The dedicated Project Management Division of the Institute supports the Finance & Accounts Department in all Financial as well as Administrative works related to extra-mural funded projects of the Institute, all matters related to PhD, M.Sc. & Summer Training programmes, Post-Doctoral Fellows etc. Accounting in respect of all service facilities of the Institute are exclusively done by this Division.

Prompt generation and submission of Internal Management Information by the Finance & Accounts Department always facilitates the Institute in taking accurate and apt financial decisions. Matters related to RGCB's Finance Committee, Audit, Processing of Payments, TDS/GST, Accounting of Receipts & Disbursements, Revenue Refunds, Reconciliation of Bank Accounts and Rendition of Utilisation Certificates/ Statements of Expenditure are always promptly attended by the Finance and Accounts Department of RGCB. 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 & Accounts Department has always resulted in building organisational strength, enthusiastic and motivated personnel & robust Institution.

ACCOUNTS TEAM: Meena H, Vishnu Priya, Jyothisree V T, Vineetha V, S Sathichandran, Kumar R, Sreejith S, Priya R

PMD TEAM: Dileep Kumar R, Preetha J, Asha V S, Smitha L

RGCB LEGAL AND ESTATE AFFAIRS

This group is entrusted with works related to Estate Affairs, House Keeping & Welfare, Legal matters under various Acts (including RTI), Building Engineering & Construction, Security & Surveillance, Vigilance & Disciplinary matters and Official Language. The following major activities are reported from this Department.

1 33 applications seeking information under RTI Act were received during the year 2018-19, and information sought was provided to all the applicants within the prescribed time limit. These replies were all self-contained that only 2 appeals were received, which were also disposed within the authorized time-frame. No further appeals to the CIC were made by any such applicants.

2 All Reports and Returns pertaining to Official Language were submitted promptly to the Department of Biotechnology and to the TOLIC, Thiruvananthapuram. A Team from Rajbhasha Vibhag, Department of Biotechnology, Government of India came for inspection at Rajiv Gandhi Centre for Biotechnology and appreciated the overall performance of this Institute.

3 Various work requirements at RGCB (in all campuses) were promptly attended to,adhering to all laid down Rules, and upkeep of all premises of the Institute were ensured at all times.

4 Swatch Bharat Abhiyan, Hindi Pakhwara, Vigilance Awareness Week etc. were conducted and Anti-Terrorism Day, Martyrs' Day, Sadbhawana Divas etc. were observed with guidelines of the Government of India.

5 Numerous visits to RGCB Laboratories by the students from various parts of the country were effectively coordinated by this Department.

6 This Department also coordinated and made all arrangements for various meetings, seminars and conferences organized by RGCB.

TEAM: Usha B, Thankamany R, Chitra G S, Mohanan C, R Jayachandran Nair, V K Raghu Kumar, Ravindran V, Subash K, Dinesh Kumar S, Jayanandan J, Santhosh S, R Anil Kumar, Vishnu P, Sarath S N

RGCB STORES AND PURCHASE

The Purchase Division occupies a vital and unique position in RGCB. This department ensures procurement of the right material in right quantities and of correct quality. The section ensures procurement from right and reliable sources or vendors, procurement of the material economically and ensuring total compliance with GPR i.e., at right or reasonable price. The RGCB Central Stores serves all three 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.

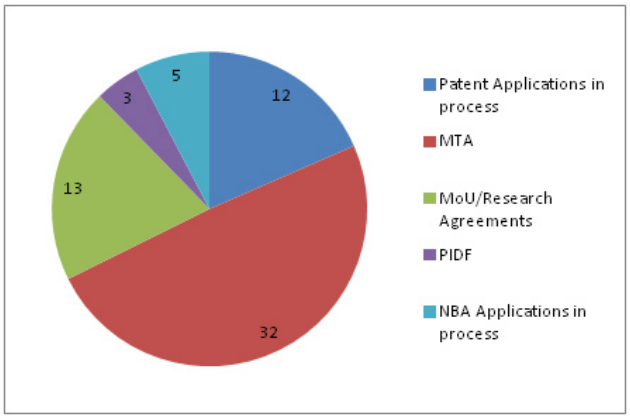
TEAM: Renjit Kurup, Pradeep Kumar T M, Sreevidya R C, Kumari Geetha T R, Sandhya S J, Anitha Kumari O, Jeevan Chacko, Jayakrishnan N, Vishnu S, Thapasi Muthu, Briji S

RGCB OFFICE OF TECNOLOGY VENTURES

The administration and execution of the Intellectual Property and know-how (IP) developed out of RGCB research activities are managed by Office of Technology Ventures. OTV is administered by a Chief Scientific Officer supported by a Research Assistant and is currently in its fifth year. It has taken keen interest in making the in-house research community acquainted with the institutional IPR policy, IP assignment execution as well as by interfacing itself as a single point of correspondence for all IP related matters.

In 2018-19, OTV conducted a "One day Awareness Program on Importance of IPR" for the scientists and students with the support of PHD Chamber of Commerce and Industry, Delhi on January 15, 2019. OTV also coordinated in arranging an interactive session with Faculty in charge of BIRAC Bio-Incubator at Kanpur for our fellow faculty and students on the grant applications for the Research Project Proposals from BIRAC (Biotechnology Industry Research Assistance Council), Government of India under the BIG (Biotechnology Ignition Grant) scheme. OTV has also been helping RGCB researchers/ scientists in preparing; managing and administering agreements related to Material Transfer, Confidential disclosures, collaborations (MoUs), sponsored research/consultancy services and Technology licensing. RGCB has filed 28 patent applications so far and among these, 14 patents were granted with jurisdictions of grant in various countries including India, USA, Europe, Japan and China. OTV manage the correspondences with patent attorneys and patent offices for the rest of the applications and are presently under process in various Patent Offices including India, China, Republic of Korea and USPTO.OTV also assisted in accomplishing thirty two Material Transfer Agreements (MTA) and thirteen MoUs for research collaborations. This year three Preliminary Invention Disclosure Forms (PIDF) were submitted by scientists of RGCB and appropriate actions were taken after a prior art analysis. OTV also manage applications of RGCB scientist's with National Biodiversity Authority (NBA) for attaining approval for research involving materials from biodiversity origins. This year we processed five applications pertaining to the approval of NBA for transfer of research results to foreign collaborators and prior approval for IPR in India. We have received approval for transfer of research results for two applications and the approval for applying Indian IPR for another two applications. A pie chart depicting the statistics of the work associated with OTV is shown below:

A pie chart depicting the statistics of the work associated with OTV is shown below:



TEAM: Hima Sithul, E Sreekumar

RGCB LIBRARY AND INFORMATION SERVICES

RGCB Library in keeping with its place of distinction as a repository of well – informed resource materials catered to the emerging needs of the scientific community in their research and academic pursuits. The library showed justice to the expectations of one and all in their hour of need with a positive response and a sense of contentment in fulfilling its onerous responsibility in an institute of this stature and magnitude. This was made possible by its special care in updating all the available facilities to deliver the maximum output for the service of the various divisions.

During the year 137 new books on life science and 42 books on general reading were added to our collection, PhD theses, back volumes of journals, protocols, standards, manuals, reports, reprints, CDROMs, DVDs etc. were also included. Major e-resources materials were obtained through Department of Biotechnology's e- Library Consortium (DeLCON). More than thousand e-journals and e- books, database etc. were thus obtained regularly. Resource sharing from other DBT,DST institutes and Developing Library Network (Delnet) enabled to make available hundreds of articles to the information seekers, thereby fulfilling their need for additional information.

The database of documents were updated by adding new additions of books, Phd theses, reports protocols, manuals, standards etc in the Online Public Access Catalogue (OPAC/Web OPAC). Institutional repository of RGCB functioning as part of the Science Central updated by uploading 694 research articles of RGCB for the period 2010 – 2019. Library also extended all assistance in the maintenance and updating of our website. Bibliographic analysis, citation analysis of RGCB publications for the year under review were carried out.

Library also gave assistance to the scientific community in the publication of their research papers in high quality journals by subjecting them before hand for plagiarism check and prior art search using relevant software. Provision was also made available in the library for the application of writing support tool for ensuring error free manuscripts. RGCB continued to be a member of Biomed Central and this enabled the publication of four articles during the period.

The subscription was renewed for the Journal of Visualized Experiments (JoVE) a peer-reviewed scientific journal that publishes experimental methods in video format. Biology, and four more journals JoVE Bioengineering, Cancer Research, Immunology & Infection, Neuroscience were also added to our collection.

In addition to the traditional collection, the library also continued to maintain a systematic in house digital resources offering facilities of easy retrieval of paid resources and open access resources.

TEAM: K Lathika, Suma, Meera N V, Gopakumar G

RGCB ACADEMIC AFFAIRS MANAGEMENT

Academic Affairs management at RGCB includes the Academic Council, Academic Committee and the Office of Academic Affairs.

Academic Council is the highest academic body of the RGCB and is responsible for the policies used in maintenance of standards of instruction, education, examination and awards within the institute and also advises the RGCB management on all academic matters.

CONSTITUTION OF THE ACADEMIC COUNCIL

Name	Position	Designation
Professor M. Radhakrishna Pillai	Director	Chairman
Dr. K. Santosh Kumar (Research Administration)	Scientist G & Dean	Vice Chairman
Dr. T.R. Santosh Kumar (Academic Affairs)	Scientist G & Dean	Member
Dr. E.V. Soniya	Scientist G & Associate Dean	Member
Dr. R Ajay Kumar	Scientist F	Member
Dr. Jackson James	Scientist F & Associate Dean	Member
Dr. E. Sreekumar	Scientist E-II & Associate Dean	Member
Dr. Debasree Dutta	Scientist E - I	Member Secretary
Dr. Surya Ramachandran	Program Scientist	Special Invitee
Professor G. Jagadeesh Chandran	Senior Manager (Academic Administration)	Special Invitee

RGCB ACADEMIC COUNCIL: Jackson James, T R Santhosh Kumar, K Santhosh Kumar, Professor M Radhakrishna Pillai, Soniya E V, Debasree Dutta, Surya Ramachandran, Ajay kumar R, E Sreekumar

RGCB ACADEMIC AFFAIRS MANAGEMENT

Office of Academic Affairs (OAA)

Office of Academic Affairs (OAA) supports the management of academic programs at RGCB including PhD program, MSc program, short term and long term training programs, Post-doctoral training, other specialized training programs and biotechnology skill development programs. The OAA also provides leadership in development of a strong academic program, policy formulation, program planning and student research progress evaluation. OAA keeps abreast of trends and changes in higher education; works for institutional vision, growth, and excellence; provides a connection between administration and faculty; serves as catalyst to create a climate conducive to academic activities in an atmosphere committed to the mandates of the institute and the Department of Biotechnology. In addition OAA conducts screening tests and examinations for selection of various positions in the research projects handled by RGCB. This year along with the IT section, the online leave submission was implemented. The OAA ensures coordination and collaboration to ensure quality learning for students and excellence in academic administration.

OFFICE OF ACADEMIC AFFAIRS: Beena Nair L, Professor Jagadeesh Chandran, Ajith Gopal

RGCB INFORMATION TECHNOLOGY COMPUTATIONAL BIOLOGY AND DATA MANAGEMENT GROUP

The IT infrastructure of RGCB main campus provides technical support to Local Area Network, more than 400 Desktops, Laptops, and Network Printers, etc. and houses of one of the best computing network with constant up-gradation in a bid to provide the students and staff with state-of-the-art facilities. The Institute has connected through to National Knowledge Network which provides 1Gbps leased line with multiple redundant backups. The highly distributed computing environment at RGCB uses sophisticated computer simulation to solve problems for Staff and Research Scholars. It is managed and actively supported by the experienced engineers in the IT Department. IT department develops, maintains and host online exam portal, leave management system for Ph.D. students, online Internship portal and conference website for maintaining and administrating the RGCB Website and Mail Servers. IT Department provides technical support to staff and students within the Institute on LINUX, WINDOWS platforms and also provides software development for research groups. Internet facilities provided throughout the campus through 1 Gbps and 10 Mbps leased lines from NKN and BSNL respectively. RGCB has invested in a high-speed Fibre Optic Backbone with high-end security for networking across the campus. Controller-based Wireless connectivity provided with multiple authentications provides Internet access to the RGCB faculty anywhere in the campus. The Information Technology Division also supports Electrical and networking of all MLS divisions in Thiruvananthapuram District. The Information Technology Division of Bioinnovation Centre at KINFRA, Kazhakuttom uses cutting-edge technology to provide high-quality services and capabilities to different research groups. It includes two servers with active directory domain infrastructure, secured network with state of the art firewall system, 10Mbps leased line and 100Mbps broadband line with failover backup connection, secured wifi connectivity, meeting room with video conferencing and wireless projection facilities, etc.

TEAM: Amal V, Harish G, Jashaid Ali, Professor M Radhakrishna Pillai, Rajasekhara Kurup, Meena Vinay, Lekshmi R, Remya Rajan, Durga Prasad Chodisety, Muraleedhara Kurup

RGCB INFORMATION TECHNOLOGY COMPUTATIONAL BIOLOGY AND DATA MANAGEMENT GROUP

COMPUTATIONAL BIOLOGY AND DATA MANAGEMENT GROUP

Major highlights of the work done

The activities of our group can be divided in four categories

- Ongoing Research
- Collaborative Research Projects
- Teaching
- Management

Ongoing Research

Identification of new virus-cancer associations using next generation sequencing data sets (Jamshaid Ali and Soumya Daniel)

The virus-cancer associations can be detected in an unbiased and comprehensive way because of the advent of next generation sequencing (NGS). The most recently discovered human tumour virus, Merkel cell polyomavirus (MCV), was identified using a bioinformatics method namely digital transcriptome subtraction of NGS data sets. Our approach starts with extraction of non-human reads by mapping the quality filtered reads against human genome and then search for novel viruses in these non-human reads.

About 294 NGS data sets of seven cancers (cervical, ovarian, breast, glioblastoma, thyroid, bladder & colon cancer) were downloaded from NCBI SRA database and are being used to identify any new virus-cancer association.

Collaborative Research Projects

TempathncodR: Temporal Pathway Signature non coding RNAs
(Jamshaid Ali and Meena Vinaykumar)

BETEB: Breast epithelial tumor expression biology project
(Dr. Vinitha Richard and Meena Vijayakumar)

Prediction of piRNAs and their targets in HPV positive cervical cancers (Jamshaid Ali)

Teaching

For One Year Internship program in Bioinformatics, Jamshaid Ali & Meena Vinaykumar taught 80% of the total syllabus (10 out of 12 modules) for the session 2018-19.

Management

The group manages day to day activities of bioinformatics facility at BIC campus.

121 RGCB OFFICE OF THE DIRECTOR

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 Council; 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 Council to secure adequate funding for the operation of the organization.

TEAM: Priya R, Mohanan Nair, Professor M Radhakrishna Pillai, Jayalakshmi U S, Venugopalan J

RGCB CAFETERIA

Scientific Dining at RGCB: The Catering Services and Cafeteria

The RGCB Catering Services is committed to providing a sustainable choice for staff, students and visitors. The RGCB Cafeteria feeds hundreds of hungry staff, students, and scientists every day and is as good as any other class cafe. The cafeteria is a study in cleanliness. Walk in the door and there, immediately, is a most appetizing aroma. The cafeteria is impressive for its bright colors giving a mood of relaxation as well as for the menu it offers, including beverages, breakfast, lunch, snacks and dinner. Unique forethought is taken to give hygienic nourishment for the students. The menu is also sensitive to the requirements of staff and students coming from diverse parts of India. Food quality and hygiene are the two most important factors in cafeteria. There is regular quality control and quality checks at the cafeteria ensure highest standards of hygiene. Be assured, 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. A Management Committee comprising of senior staff members has been constituted to daily manage the cafeteria services.

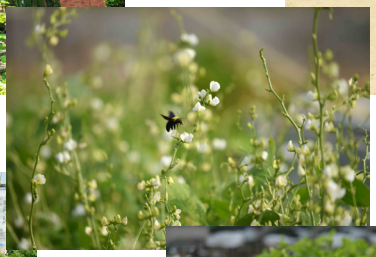
CAFETERIA MANAGEMENT TEAM: Edwin S, Sreeja S, Jayakrishnan N, Manoj P

RGCB CAFETERIA

CAFETERIA SUPPORT TEAM: Sivankutty Nair, Sajukumar, Tilbahadur Bakshey, Sajith C, Thyagarajan S, Manojkumar R, Deepu R V Nair, Manoj S, Najeem M, Suresh Kumar R, Gopakumar M S, Rakesh

Our friendly team also provides an efficient and reliable catering service to many of the large scientific and social events in the institute. The “onam” feast with 26 different dishes is just one example of the culinary skills of the cafeteria chefs. The cafeteria supports local farming and regional production efforts and give such suppliers first priority in all purchasing decisions. We aim to minimize the impact of catering operations on the environment and promote sustainable practices and consumption. The RGCB Sky Green organic vegetable garden provides its entire produce to the cafeteria. The RGCB cafeteria runs on a “no profit no loss basis”.

RGCB GARDEN AND SKY GREEN



RGCB MEDICAL LABORATORY SERVICES

Medical laboratory testing plays a crucial role in the detection, diagnosis and treatment of disease in patients. Laboratory tests help determine the presence, extent or absence of disease as well as monitor effectiveness of treatment. Approximately 60 to 70 percent of all decisions regarding a patient's diagnosis, treatment, hospital admission and discharge are based on laboratory test results. Hence it is critical that clinical laboratory services are not only cost effective, but provide highly accurate information to be used in clinical decision-making.

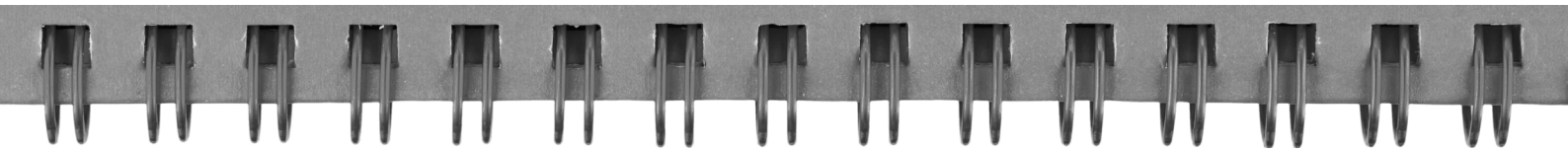
While technology continues to improve the productivity of today's laboratories, new technologies, new diseases and disease epidemics continue to drive the need for more innovative tests and testing methods. Changes in the world, such as bio-terrorism and the speed with which diseases spread globally drive the need for rapid diagnosis.
It is here that RGCB comes into the forefront with its unique translational capability in advanced laboratory and theoretical skills in disease biology as well as having highly trained manpower. RGCB Medical Laboratory Services (MLS) is an indispensable clinical laboratory professional partner that provides clinical laboratory information and services by use of optimal but advanced levels of health care resources. This permits maximizing effective delivery of care in today's complex healthcare system by accurate test results that enable providers to make the right diagnostic and therapeutic decisions.

RGCB has state of the art fully operational laboratories at Government Medical College, Trivandrum, Government Secretariat Trivandrum, General Hospital, Trivandrum, General Hospital, Neyyattinkara, Nedumangadu Hospital,Trivandrum and Techno Park Trivandrum.

RGCB-MLS provides all standard hematological, microbiological, immunological, biochemical and molecular investigations performed on latest and completely automated platforms. Complete list of investigations are described at www.rgcb.res.in All investigations are costed at Government of India approved (CCL) rates with special concessions to BPL patients.

MANAGEMENT TEAM: Ambili S Nair, Padmavathy Amma, Babu Mathai, Dr. R Ashok, Vishnu T S, Bobby R G

Vivekananda Rock Memorial is a popular tourist monument in Vavathurai, Kanyakumari, India. It was built in 1970 in honour of Swami Vivekananda who is said to have attained enlightenment on the rock.
Photographed by Dr. Ananda Mukherjee, PhD
DBT-Ramalingaswami Faculty Fellow



RGCB
DISCOVERIES FOR A BETTER TOMORROW

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