RGCB
DISCOVERIES FOR A BETTER TOMORROW

30

ANNUAL REPORT 2019-20

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THREE DECADES OF BREAKTHROUGHS

ANNUAL REPORT 2019-20

Research doesn't just happen. Every discovery, large or small, occurs because somebody put their heart and soul into it. And that somebody - a scientist - didn't do it alone. Countless other people were part of each discovery, from technicians to lab assistants, engineers to students; everyone involved was part of the journey.

In these 30 years, scientists at RGCB were part of numerous breakthroughs. Those findings, we believe, have improved the lives of many people in many ways. In these pages, we feature some of the discoveries for which RGCB has received national and international recognition, since its inception in 1990. These and many other breakthroughs over the last 30 years in various disciplines have contributed to making RGCB one of the leading research centres in the country.

CONTENTS

सत्यमेव जयते

Government of India

Dr. Renu Swarup
Secretary
Department of Biotechnology
Government of India

Rajiv Gandhi Centre for Biotechnology was taken over by Govt. of India as a National Institute on 1st April 2007 as an Autonomous Institute of Department of Biotechnology, Ministry of Science & Technology.

RGCB as a state run institute had established great strength in biotechnology research and as a National institute during the last 13 years, RGCB has demonstrated its competence in wide ranging areas of Disease biology, and Cancer Research, Chemical Biology and Plant Disease Biology.

RGCB is a premier institute of DBT, unique in its mandate because it covers all aspects from basic to translational research and its focusses on local, regional, national and global problems.

The institute has over these years created a great impact in connecting academia – industry, promoting start-ups through the incubator and has also focussed on capacity building both for human resource and infrastructure.

From a Centre for Development, Education, Science and Technology, of the state to a premier National institute of the Govt. of India the RCGB has gone a long way in the last 30 years delivery high quality research out comes.

I am confident this institute will continue to play a pivotal role in the growth trajectory of Biotechnology.

REVISITING 15 YEARS OF LEADERSHIP AT RGCB

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

It is a proud privilege for RGCB to bring out this Annual Report celebrating 30 years of the institute. This time is all the more important and significant since this will be the last RGCB Annual Report published by our current Director, Professor M. Radhakrishna Pillai whose 15 year remarkable tenure ends in August of 2020. The Editorial Team (ET) therefore decided in place of the customary introductory Director's message, to have a personal interview with Professor Pillai and his reflections of the growth and success of RGCB in the past 15 years.

ET: We are celebrating the 30th anniversary of RGCB this year. You have been at the helm for the last 15 of the 30 years, which forms a major part of the Institute's existence. How do you feel about the journey?

MRP: The Rajiv Gandhi Centre for Biotechnology (RGCB) is a growing phenomenon. RGCB began in 1990 amongst humble surroundings as a small charitable society called the Centre for Development of Education, Science and Technology (C-DEST). On April 18, 1994 the Government of Kerala took a landmark decision to restructure the institute into a comprehensive biotechnology center and thus was created the Rajiv Gandhi Centre for Biotechnology under the Kerala State Council for Science, Technology and Environment. I must place on record the wonderful contributions of the two previous Directors, Dr. M.R. Das and Dr. Raghava V Thampan for their efforts in making RGCB one of the most active and vibrant state research institutes. I joined in 2005 and was given a mandate by the state government to take RGCB forward to a final goal of becoming a national institute. In December 2005 I was given an opportunity to present RGCB to the Honorable Prime Minister of India at his residence for a one to one meeting. Hardly 8 months into the job, this was a huge challenge for me and at the same time, a most important opportunity to place RGCB on the national scene. The meeting lasted 40 minutes. With divine blessings of god and results of hard work done by my colleagues, we could finally convince the central government of our commitment and capability. On February 28, 2006 while presenting the Union Budget to Parliament, The Honorable Union Finance Minister announced, *"If agriculture is an ancient Indian skill, biotechnology is the new frontier that India will conquer. In order to foster research and development in biotechnology, the Ministry of Science and Technology has decided to accord the status of an autonomous National Institute to the Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram, Kerala".*I firmly believe that this was the greatest honor RGCB has received. RGCB had clearly stood up to the trust, confidence and faith put in it by the Government and people of Kerala as well as the Department of Biotechnology that had unflinchingly supported the center through research grants for almost a decade. RGCB's long awaited tryst with destiny became a reality on August 2, 2007 when the Union Council of Ministers chaired by the Honorable Prime Minister approved the take over of RGCB from April 1, 2007. Addressing a press conference on the same day, the Honorable Union Minister for Science, Technology and Ocean Development thanked the Government of Kerala for allowing the union government to develop RGCB into an institute of international standards. He went on to outline future plans for the institute including state of the art programs in cancer research, emerging viral infections and disease biology. I was present at that press conference and it remains to date a most memorable event in my life. Fifteen years on and looking at where RGCB is placed now, I feel a sense of great pride, when I look back at these events. "It's good to have an end to the journey towards, but in the end, it's the journey that matters"

ET: What are your thoughts on the progress of RGCB over these years from a small institute in rented premises to the Internationally acclaimed autonomous Institution with three beautiful campuses as it stands now?

MRP: In 2005 and 2006 research objectives will RGCB were relatively diffuse with individual scientists working mostly in silos. We had no defined programs but only PI driven research

projects. Extra mural projects were dismally low. There was shortage of space and infrastructure. The reincarnation of RGCB as a national institute and its subsequent development has allowed a redefining of its research and development programs. All RGCB research domains can now designated as programs in the larger domain of Disease Biology including state of the art discovery and translationd research programs in Cancer Research, Cardiovascular & Diabetes Biology, Pathogen Biology, Neurobiology, Chemical Biology, Reproduction Biology and Plant Disease Biology all underlined with a strong interdisciplinary sciences denominator. RGCB could also successfully pilot a second phase development to create a unique Bio-Innovation Center (BIC). While emphasis in RGCB was hitherto primarily on Investigator driven science, the second phase concentrated on team driven science for accelerated discovery and early translation. This new innovation center has been conceptualized to interface very well with the present institute creating an excellent ecosystem for discovery science and translation. Another significant successful venture of RGCB has been BioNest. Established in association with the state government, BioNest, located in Kochi is a bio-incubator facility that serves to accelerate commercialization of new technologies, to nurture emerging ventures and to assist new enterprises to forge appropriate link with other biotech companies, academia and government. BioNest currently has 26 companies incubated that will eventually also be a creator of new jobs in technology development, scale-up and translational biotechnology.

ET: The growth of RGCB has not just been in terms of infrastructure or autonomy, but also reflected in the science that churns out of its laboratories. Whom do you credit this growth of scientific publications and discoveries?

MRP:Since 2007 RGCB's research has progressed at warp speed. Our scientists quickly lived up to new expectations that a national institute needed. Quality and quantity of research publications improved significantly. Extra mural funding rapidly increased. Studies with translational implications were implemented. Team science became evident. For all this I give full credit to our Scientific Advisory Council. This group of illustrious scientific personalities worked individually with our scientists sharpening their talent, sharing research strategies and demanding much higher standards. But perhaps the best thing that happened at RGCB to raise the standards of science was the induction of a new younger breed of exciting scientists. These highly accomplished, well-trained and highly dedicated scientists not only served as excellent catalyst to increase scientific output but also introduced a new work culture in the institute. The future of RGCB science is safe in these hands.

ET: Can you elaborate on the most exciting scientific breakthroughs, which has placed RGCB as a topnotch research Institution in India?

MRP: There are large number of very exciting science findings from RGCB, which have tremendous value addition to the management of human diseases and agriculture. The HPV vaccine trial set international standards for cervical cancer prevention. The discovery of Uttroside B as a candidate drug for liver cancer marks the first time that an RGCB discovery is entering clinical evaluation and bringing commercial benefit. The discovery of natural bioactive peptides also has potential for management of both human and animal viral diseases. RGCB established a standard preclinical model for molecular studies in cardiomyopathy and developed a possible biomarker for predicting atherosclerosis development in diabetic patients. We identified several metabolic alterations associated with insulin resistance in normoglycemic young adults who are overweight and also found that those metabolic alterations are profound in young adult men compared to young adult women, highlighting importance of gender as a factor to be considered in therapeutic interventions of prevention of type 2 diabetes. Models developed at RGCB for vascular damage in dengue could soon become an assay system for new drug development to take forward management of dengue associated vascular complications. RGCB data on delineating the pathogenesis of varicose veins will become crucial to develop non-invasive therapeutic approaches without post-treatment relapse. We isolated the first ever histone acetyl-transferase (HAT) from a human pathogen, Mycobacterium tuberculosis. Another significant finding was that Mycobacterium

tuberculosis infection enhances expression of histone deacetylase 1 (HDAC1) in macrophages and when HDAC1 is knocked down or inhibited, survival of intracellular M. tuberculosis is significantly reduced. We realized that Schizophrenia is influenced by both gene and environment and went on to demonstrate epigenetic changes seen in schizophrenia may not be a consequence of pathogenesis but could be a drug induced response. RGCB made significant contributions to stem cell biology including characterization of the role of signaling molecule Wnt5a and the transcription factor Tlx3 in the development of the cerebellum. Similar studies have also shown the existence of a Notch-independent Hes1 expressing neural stem cells that are slow dividing and precede the Notch-dependent Hes1 expressing radial glia. Perhaps these Notch-independent Hes1 stem cells mark a crucial step in the transition of neuroepithelial precursors into radial glia progenitors generating neurons. RGCB could show that downregulation of histone chaperone Aprataxin PNK-like factor (APLF) enhanced the kinetics and efficiency of generation of induced pluripotent stem cells (iPSCs) from differentiated, cells. We demonstrated the critical role of cancer stem cells in surgical management of colorectal cancer by proving that though distal margin seems to be tumor free in conventional histopathological analysis, it could harbor cancer stem cells.Another related study was design of a peptide that could able to detect lymph node metastasis in mouse models, even in the initial stages as well as for predicting tumor deposits in surgical margins. Such data emphasizes that modern pathology should include molecular tools to identify primordial or stem like cells in tumor niches Our data on nanopores in membrane biology have been outstanding. RGCB successfully fingerprinted the ancient medicinal rice Njavara that will play a major role in GI protection of this plant. We provided crucial evidence for developing anti fungal strategies for Kerala's major cash crop, Pepper. There are numerous other exciting research findings which are described elequently in the following pages.

ET: Molecular Diagnostic Laboratory Services came into existence a few years back at RGCB. What made you realize that diagnostic services would be a value addition for the Institution?

MRP: I have firmly believed in taking science from the laboratories to direct public benefit. It is not always groundbreaking scientific accomplishments that make an institute great but how even the most trivial achievements can be applied into effective means to serve humanity. During the period 2006 to 2011, Kerala was swamped with very serious outbreaks of viral fevers including chikungunya and dengue followed by the H1N1 flu pandemic. The state did not have a laboratory to do molecular viral diagnostics and turned to RGCB to provide expertise in assisting the public health service of Kerala. True to our institute's commitment and character, RGCB established a special purpose vehicle called Laboratory Medicine & Molecular Diagnostics (LMMD). LMMD which started off with 3 viral diagnostics, now performs over 40 viral and bacterial parameters and currently is arguably the only facility in India performing these many parameters under one roof. It was in recognition of these services that the Government of India's Department of Health Research designated this laboratory as a National Virology Network Grade 1 laboratory. Further recognition came as the facility was accredited by both NABL and NABH. With the advent of Covid 19 pandemic, it was only natural that RGCB became a leader for both Covid 19 diagnostics and an approved accredited validation center for new diagnostic kits. Further to cap these achievements, RGCB is now in collaboration with Mayo Clinic and Tetherex, a biotech company that is looking at a novel candidate vaccine trial in India, where all immunity parameters will be carried out at RGCB. Again this is a remarkable achievement for any research institute.

ET:Biotechnology has been a sought-after course for students at the Post Graduation level, with several Universities and Institutions offering two-year programs. What made you foray into this area and how do you think RGCB can excel as a teaching institute?

I had decided long back that RGCB would have a two-year post baccalaureate degree that would be a research based teaching program combining disciplines of biochemistry, cell biology, molecular biology, genomics, proteomics, microbiology and immunology as well as application of computer science to biology along with principles of design and engineering in biological systems. Several learned persons questioned this thought, pointing out that a research institute is not mandated to

do teaching postgraduate courses which is best left to universities. I disagreed with this opinion and went on to the Department of Biotechnology with three arguments. Firstly, institutes such as RGCB have huge investments done in terms of public money for building huge infrastructure that is grossly under utilized. Secondly, following the seventh pay commission the take home wages of such institute employees became huge compared to the total workload. Thirdly the Honorable Prime Minister's call for developing highly skilled work force required production of highly trained manpower ready to take up challenging PhD research problems and becoming the correct fuel for entrepreneurship. I therefore argued at the Governing Council that RGCB could do an excellent job in mentoring the best of students in India by placing them in the most of competitive and exciting teaching program in India. We were allowed to start a Masters Program in Biotechnology with three very significant specializations that reflected the ethos and character of RGCB – disease biology, genetic engineering and molecular diagnostics. We ensured the unique course structure was designed in consultation with clinical, agricultural and industrial experts to give students cutting-edge specialist knowledge and practical skills. Moreover students learn from real scientists; the program includes lectures, seminars and laboratory-based teaching by scientists who do exciting and high-end research. And finally we ensured students would be guided by the best of teachers from the medical and scientific education system as well as professionals from the biotechnology & pharmaceutical industry. Unlike any other Master program in the country RGCB's Masters program will introduce students to the concepts of "Enterprise and Entrepreneurship"- thus allowing students who wish for a career beyond the laboratory in an existing biotechnology industry or for those who dream of starting a new biotechnology enterprise. Students get trained in our own real business and technology development bio-incubator where 29 start up companies' now function. To ensure highest academic structure and affiliation, students get their degrees from the best: RGCB's MSc program is affiliated to the Regional Centre for Biotechnology, an 'Institution of National Importance' providing education, training and research established through an Act of Parliament under the auspices of the United Nations Educational, Scientific and Cultural Organization or UNESCO, a specialized agency of the United Nations (UN) based in Paris. I was surprised to see a lively debate on social media suggesting that RGCB scientists wanted to hide behind a teaching program to cover up apparent lack of performance in research. I can only sympathize on the lack of knowledge about RGCB by such commentators. Every faculty taking classes for MSc students have only further excelled in their research performance, published in top journals, obtained huge research funding and found themselves as dedicated teachers caring for these students as our own children. As a young colleague commented, "these students have brought a whiff of fresh air into RGCB".

ET: RGCB is venturing into several diverse programs, one of which is the Genome India Program and the other is Tribal Heritage Program. Can you elaborate on these programs and how they can be a value addition to the growth of RGCB?

MRP: It was a great honor for RGCB when it was chosen to be a key collaborator in the Genome India study. The primary criterion for selection was its experience, expertise and access to large population cohorts. In addition RGCB's unique experience in running large human DNA fingerprinting as parts of its Molecular Forensic Services also was significant factor in the selection of RGCB as a partner institute. Since India harbors more than one-sixth of the world population and because it has been a conglomerate of extremely diverse populations with long and varied demographic history, the rate of discovery of novel variants, both rare and common will be very high. This will help in teasing out rare debilitating mutations and researchers working in the field of monogenic disorders will find this catalogue helpful for screening out non-causal variations. This data will enable us to construct a much more reliable and comprehensive reference haplotype panel. That in turn will be used to design genome-chips andwill also act as are sourcer eference panelexpected to hugely improve the imputation accuracy in genome-wide studies involving different Indian populations. The genetic chips developed from this project will enable many researchers from India to undertake large scale genetic studies at the level of whole genome at a very affordable cost. For samples that has already been genotyped with arrays earlier, this deep

reference genetic variation panel for Indians will enable researchers to impute genetic variants with higher precision. This can be done only at the computing cost of performing the imputation, and thus help researchers get accurate genome-wide data even with existing genotyped samples. Therefore, identifying causal mutations for inherited disorders or tracing genetic variations in individuals associated with genetic diseases at a low cost will become more accurate and feasible for the country, thereby aiding the development of molecular diagnostics and predictive testing in the Indian context.

The second large program that was awarded to RGCB by the Department of Science & Technology was a center for excellence in inclusive technology interventions for tribal heritage resilience of Kerala. Again it was RGCB's track record in working on socially relevant application of science that led to the creation and sanction of this program. The first mandate given to RGCB in this program is correct and accurate traditional knowledge documentation including types of livestock, ethno-veterinary practices, traditional paddy varieties and cultivation practices as well as traditional art and craft. The second mandate is scientific validation of ethno veterinary preparations, genetic profiling and nutritional assessment of traditional varieties of paddy as well engineering & technology intervention for revamping of traditional art /craft through scientific interventions. The third mandate is product development based on tribal knowledge in ethno-veterinary medicine, value added products from herbal extracts/essential oils from spice and aromatic plants as well as nutraceutical products. The fourth mandate is capacity building for tribal development including ethno -veterinary service delivery centers in remote tribal regions, home herbal gardens, minor forest produce processing facilities, community owned enterprises for mini traditional paddy processing, essential oil extraction unit from spices & aromatic plants as well as community resource centers. These objectives ensure that RGCB delivers on the faith placed in it for standing with the community and country.

ET: Being the director of an institute for the last 15 years, what has been your biggest challenge, and how did you overcome it?

MRP: Keeping negative vibes and jabs out of daily duties and administration of the institute. That required huge effort. My terrific colleagues were a major source of support and inspiration.

ET:On a personal note how has the development of RGCB reflected on your achievements as a scientist and an administrator?

MRP: I am extremely satisfied with my research career. I believe I have done well and the science community has acknowledged this. More importantly than personal achievements, it was delight to see RGCB becoming a true translational science research center – be it in drug trials, vaccine trials, immune correlates of vaccine efficacy, biomarker applications in disease or diagnostic development. RGCB become synonymous with top class public health research and application of science for public service. A true reflection of the quality of our scientific capability at RGCB is easily reflected that cell and molecular biology research protocols and methodology was skillfully adapted to offer solutions for problems faced by the public, whether in clinical diagnostics, molecular forensics or solutions for better agriculture. I am also very satisfied with the 15-year tenure as an administrator. RGCB today has the best social welfare scemes in the country for its empoyees. It is the only institution of the Department of Biotechnology that has created a comprehensive pension scheme for its employees in service before January 1 2004 on par with the old pension plan of Government of India. This was done by getting LIC to manage the institute's self generated funds from clinical diagnostics, services & consultancies as well as EPF contributions, with no burden at all on Government of India. RGCB also boasts of one of the best medical care facilities for its empoyees including "cashless" access to the best of government and corporate hospitals. Looking back, I am reminded of a comment made in a post conference discussion, " Some leaders allow institutes to grow, while others use the institutes to grow" Today, I am delighted that I fullfulled both.

ET: As the Institute will enter a new phase later this year with a new leader, what would be your advice to your successor and the management of RGCB?

MRP: I am very sure that the new leader will do whatever is needed for best for the institute. I am also very confident that the new leader will have the total support and cooperation from the fantastic RGCB family.

ET: In your experience, what is the key to developing a good team?

MRP: Choose the best, place faith in them and leave them to do the job. "Maximum autonomy; Minimum governance"

ET: You recently won the prestigious Sun Pharma Award. What message does it send out to young scientists doing research in India?

MRP: Just follow your science passion and be consistently productive. Pick challenging problems and take great care not to slip into soft comfort zones. When this happens, one starts justifying mediocrity in the cover of academic freedom.

ET: Is there any aspect or any decision that you think you would have changed if given another chance?

MRP: I honestly do not want to go through all these endeavors once again in this lifetime. I have done my best and the record shows I have largely succeeded. Although I may be wrong, I do personally feel that based on the feedback received, I do have "a job well done" rating from at least 96% of my colleagues and even higher from the general public. When an institute rapidly grows there will minor murmurs of dissatisfaction, complaint and unhappiness.This is always part of any system. Yes - there are many lessons learnt that may make me take a different approach to some challenges. Perhaps the most important take home lesson is to not let profession become a personal mission. Identifying both as one is a sure recipe for total burnout. Believe me its true.

ET: We have been tuning into a conversation with a versatile and dynamic personality at RGCB in present times. It is said "You never really leave the place you love. You take part of it with you and leave part of you there." Professor Pillai is leaving an indelible mark on the lives of several people which includes not just the staff and students of RGCB but also a significant proportion of general public whose lives he has touched with his services, kindness and accomplishments. RGCB is truly indebted to this leader for having placed the institute as among the best in the country.

The Editorial Team (L-R) Mr. G. Harish, Ms. R. Lakshmi, Dr Surya Ramachandran and Dr. Debasree Dutta with Professor M. Radhakrishna Pillai

The Editorial Team also places on record the excellent creativity and design done by Mr. Roy V Mathew, Mr. Manjit Lal J and Mr. Gopakumar R S at Stark Communications

A PROUD HISTORY

1995

Campus site before construction

RGCB Foundation stone laying 18 November 1995

1999

Nobel laureate Dr. Watson visiting RGCB

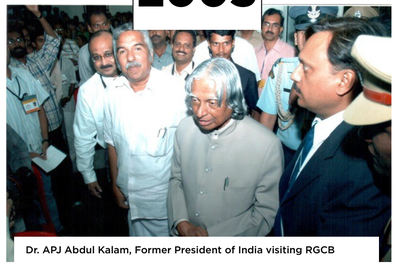
2003

Dr. Manju Sharma, Secretary, Department of Biotechnology visiting RGCB

Dr. Murli Manohar Joshi, Former Minister for Human Resources Development, Govt. of India visiting RGCB

Mr K C Pant, Former Deputy Chairman, Planning Commission visiting RGCB

2005



Dr. APJ Abdul Kalam, Former President of India visiting RGCB

International Symposium on Translational Research Apoptosis and Cancer

Unveiling the Portrait of RGCB Founding Director, Dr. M R Das

Mr. Kapil Sibal, Former Minister for Science, Technology and Earth Sciences, Govt. of India visiting RGCB

2007

RGCB became Central Government Autonomous Institute

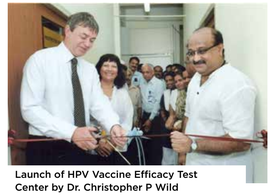
2008

First RGCB General Body Meeting

2010

Launch of New Animal Research Facility

Indo-US Workshop Translating Molecular Cardiology into Clinical Practice



Launch of HPV Vaccine Efficacy Test Center by Dr. Christopher P Wild

2011

Nobel Laureate Dr. Martin Chalfie visiting RGCB

2013

Foundation Stone laying for RGCB Bio Innovation Centre, Akkulam

International Symposium on Legacy of Nitric Oxide Discovery Impact on Disease Biology

2014

Prof. K Vijay Raghavan, Secretary, Department of Biotechnology and General Body of RGCB Society visiting RGCB

Arogya 2014 Expo

2015

Dr. Harsh Vardhan, Honorable Union Minister for Science & Technology launching the RGCB Bio Innovation Center

International Day of Yoga

2019

Global Bio-India

MSc Biotechnology Course Launch

India International Science Festival (IISF)

2020

Indian Association for Cancer Research (IACR): Annual Convention – 2020

THE EUREKA MOMENTS

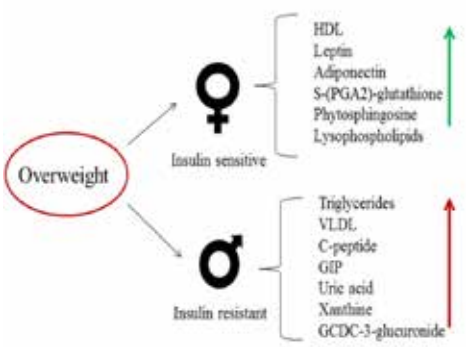
K A Abdul Jaleel, PhD
Cardiovascular Diseases & Diabetes Biology

METABOLIC ALTERATIONS DURING DEVELOPMENT OF DIABETES

My laboratory focuses on studying the metabolic adaptations towards onset of Type 2 Diabetes Mellitus (T2DM), specifically of the Kerala population. We completed a 10-year prospective cohort study in central Kerala and estimated that the cumulative incidence of T2DM and pre-diabetes were 21.9% and 36.7% respectively and the incidence rate of T2DM and pre-diabetes were 24.5 per 1000 person years and 45.01 per 1000 person years respectively. This is the first report from the State of Kerala, highlighting the epidemic trend of T2DM to solicit an immediate public health action (1). Further, to determine the early predictive markers of transition from normal to a prediabetes state, we studied the basal metabolism and metabolic response to a mixed-meal in normal healthy young adults (age 18 to 40 years, both men and women 1:1) from this population. We identified several metabolic alterations associated with insulin resistance in normoglycemic young adults which were profound in young adult men compared to young adult women (2). Our results highlight importance of gender as a factor to be considered in therapeutic interventions of prevention of T2DM.

FIGURE

Effect of Overweight and Sex on Insulin Sensitivity and Metabolome. The green color arrow indicates parameters positively correlated with insulin sensitivity, and red color arrow indicates parameters negatively associated with insulinsensitivity.



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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;19:140 DOI (https://doi.org/10.1186/s12889-019-6445-6).

Aneesh Kumar, GopikaSatheesh, GadadharanVijayakumar, Mahesh Chandran, Priya R. Prabhu, Leena Simon, Vellappillil Raman Kutty, Chandrasekharan C. Kartha&Abdul Jaleel. Postprandial Metabolism is Impaired in Overweight Normoglycemic Young Adults without Family History of Diabetes. Scientific Reports. Volume 10, Article number: 353 (2020) DOI (https://doi.org/10.1038/s41598-019-57257-2)

R Ajay Kumar, PhD
Pathogen Biology Program

BIOLOGY OF TUBERCULOSIS

The most important finding from my lab was the isolation of the first ever histone acetyltransferase (HAT) from a human pathogen. After successful entry into the macrophage, Mycobacterium tuberculosis secretes Rv3423.1 protein that was characterized to be a functional histone acetyltransferase, into the cytoplasm from where it moves into the nucleus, and is recruited to the chromatin at the promoter region of certain genes. There it acetylates histone H3 at K9/14 positions and the resulting repulsion between the nucleosome and DNA exposes the promoter to initiate transcription of these genes. Another significant finding was that M. tuberculosis infection enhances expression of histone deacetylase 1 (HDAC1) in macrophages. As opposed to the function of HATs, HDACs are suppressors of gene expression. Recruitment of HDAC1 to the promoter of IL-12B gene of the macrophage represses its expression leading to the reduction in the amount of interleukin IL-12 secreted. IL-12 plays a critical role in inducing Th1 responses to combat intracellular pathogens like M. tuberculosis. When HDAC1 is knocked down or inhibited, survival of intracellular M. tuberculosis is significantly reduced. Unlike in conventional anti-TB therapy in which the drugs target proteins of the pathogen, inhibition of host HDAC1 opens up a novel strategy for host-directed therapy to treat tuberculosis.

In our quest for anti-mycobacterial molecules from natural resources we isolated, characterized and identified two molecules. Ethyl p-methoxycinnamate from the rhizomes of Kaempferia galanga (used in the preparation of Ayurvedic medicines for chest infections), and chrysomycin A from a Streptomyces sp. isolated from Trivandrum. Both of them were shown to be inhibitory to multi-drug resistant clinical isolates of M. tuberculosis.

PUBLICATIONS

Jose L, Ramachandran R, Bhagavat R, Gomez RL, Chandran A, Raghunandanan S, Omkumar RV, Chandra N, Mundayoor S and Kumar RA (2016). Hypothetical protein Rv3423.1 of Mycobacterium tuberculosis is a histone acetyltransferase. FEBS J. 283(2): 265-81.

Chandran A, Antony C, Jose L, Mundayoor S, Natarajan K and Kumar RA (2015). Mycobacterium tuberculosis Infection Induces HDAC1-Mediated Suppression of IL-12B Gene Expression in Macrophages. Front. Cell. Infect. Microbiol, Dec 2; 5:90.

RGCB @30

RGCB is the only NABL, ILAC and NABH accredited Centre approved by ICMR for testing and validating test kits and devices used in COVID19 testing.

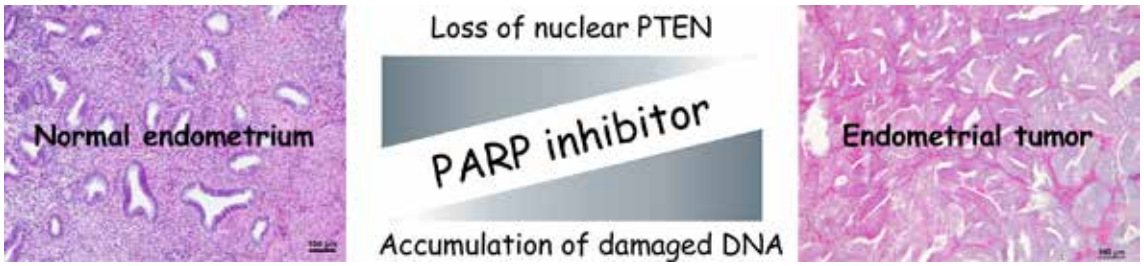
Ananda Mukherjee, PhD
Cancer Research Program

"PTEN" AND CANCER IN THE ENDOMETRIUM

Upon the damage, several checkpoints and repair pathways get activated and fix our genome. The failure of the processes either induces programmed cell death or accumulates mutation if the genome remains unrepaired during the cell division. The next can leads to cancer. Therefore, the precise DNA damage tolerance and repair mechanism is a tumor suppressor process and responsible for the maintenance of genomic integrity. PTEN is a dual protein and lipid phosphatase and plays an essential role in tumor suppression. The loss of PTEN stimulates cellular proliferation and promotes genomic instability, which are the hallmarks of cancer. Endometrial adenocarcinomas are a heterogeneous group of tumors derived from endometrial epithelial cells. The disease has a positive correlation with obesity, with an increasing incidence rate, where the PTEN is the most commonly mutated tumor suppressor. Recently, we have investigated the DNA repair functions of PTEN in endometrial cancer development, progression, and outcomes. We have seen nuclear PTEN expression in approximately half of endometrial cancer patient tumors, independent of grade and cytoplasmic PTEN expression. The results from functional and drug treatment assays suggest that nuclear PTEN subcellular localization in human endometrial tumors could be diagnostic when considering DNA damage repair therapeutic intervention (Mukherjee et al. 2018).

FIGURE

Human normal endometrial glands lose expression of nuclear PTEN and accumulate DNA damage as disease progress to endometrial tumors. The drug that intervenes in DNA repair functions such as PARP inhibitor, olaparib, could target these tumors.



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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.

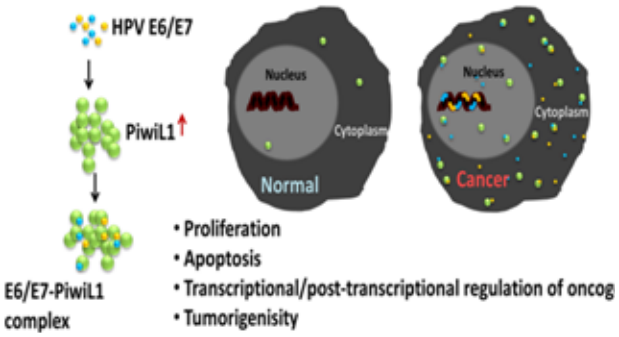
Ani V Das, PhD
Cancer Research Program

STEM CELLS: FROM EYE TO CANCER

Retinal degeneration that involves photoreceptors is the cause for diseases like Age Related Macular Degeneration (ARMD) and Retinitis Pigmentosa (RP). Finding the factors that are involved in the specific cell type generation in the retina could be useful in designing a better therapeutic approach for such diseases. During the quest of finding such regulatory factors, we found that microRNA cluster 143/145 targets Nrl, the major factor that regulates rod photoreceptor specification. Our study revealed a regulatory feedback loop in which Nrl positively regulates miR cluster 143/145 and this auto-regulation may be needed for maintaining the rate of photoreceptor generation or favoring the generation of other retinal cell types (Figure 1). These findings were published in Molecular Neurobiology (Sreekanth et al., 2017). The fact that many non-coding RNAs, including miRNAs play significant roles in cancer prompted us to investigate their involvement in tumorigenesis and also in maintaining cancer stem cells. My team has found that Piwi-interacting RNAs (piRNAs) and their associated Piwi proteins have roles in cervical cancer. PiwiL1, one of the four Piwi homologs, showed increased expression and a differential cellular localization pattern in response to HPV oncogenes. We found that PiwiL1 was co-expressed with HPV oncogenes and not only E6 and E7 physically interacted with PiwiL1, but also they accentuated its expression in cervical cells, suggesting a positive role for PiwiL1 in HPV-mediated tumorigenesis (Figure 1).

FIGURE

PiwiL1 is regulated by HPV oncogenes and also physically interacts with E6 and E7 in cervical cells: HPV oncogenes, E6 and E7 accentuate the expression PiwiL1 and bind with to form a complex which could later differentially translocated in different cellular compartments to impart various functions in cancer cells.



PUBLICATIONS

Sreekanth S, Rasheed VA, Soundararajan L, Antony J, Saikia M, Sivakumar KC and Das AV. miR Cluster 143/145 Directly Targets Nrl and Regulates Rod Photoreceptor Development. Molecular Neurobiology, (2017) 54(10): 8033-8049. doi: 10.1007/s12035-016-0237-0.

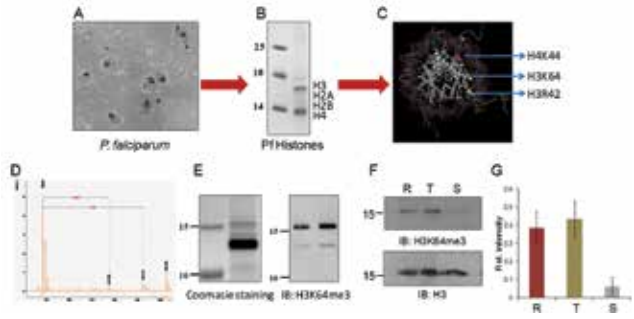
Arumugam Rajavelu, PhD
Pathogen Biology Program Group

UNDERSTANDING GENETICS OF MALARIA

Gene regulatory mechanisms are poorly studied about DNA methylation of malaria parasite. The malaria parasites encode DNMT2 homologue TRDMT1. We have carried out detailed biochemical analysis and found that the parasite TRDMT1 enzyme no longer methylates DNA substrates; however it strongly methylates tRNA substrates. This is first study to report on tRNA methylation in apicomplexan parasites. The tRNA methylation in malaria parasites may have critical role in translational regulation of important proteins and modulate the pathogenicity of parasite. Stage specific gene expression is also poorly characterized in P. falciparum and the regulators of chromatin stricture mediated gene expression in various developmental stages of parasite remain elusive. We have identified methylation marks at H3K64, on histone globular domains of P. falciparum. Further, we found that H3K64me3 mark is deposited in stage specific manner (Figure 1). This suggests a strong role of unconventional histone core methylation in regulation of dynamic chromatin structure in parasite.

FIGURE

P. Falciparum carries methyl marks at unique sites on histone core. The H3K64me3 methyl mark is validated with WB and found that the histone core methyl mark enriched only in ring and trophozoite stages but reduced in schizont stage.



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Govindaraju G, Jabeena CA, Sethumadhavan DV, Rajaram N, Rajavelu A. DNA methyltransferase homologue TRDMT1 in Plasmodium falciparum specifically methylates endogenous aspartic acid tRNA. BBA – Gene Regulatory Mechanisms. 2017 Oct; 1860(10): 1047-1057.

Jabeena CA, Rajavelu A; Epigenetic players of chromatin structure regulation in Plasmodium falciparum. ChemBioChem. 2019, 20(10): 1225-1230.

RGCB @30

Q LINE: Low cost Viral Transport Medium and RNA Extraction Kit jointly developed by RGCB & POCT Services, New Delhi.

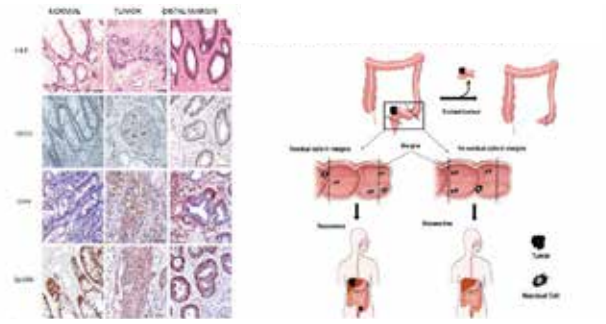
Asha S Nair, PhD
Cancer Research Program

SIGNATURES BEYOND BOUNDARIES

Colorectal Cancer (CRC) stands as the fifth cancer related mortality in India. A 2018 study from 12 cancer registries of India demonstrated that the risk of CRC in India has been rising slowly and by 2035 is expected to rise by 80 percent. In addition patients would present at a younger age and a later stage of the disease. Studies on identification of markers that could target residual cells happen to be critical in CRC prognosis and have been a heated topic of research. Considering that molecular assessment of margins could be more sensitive and informative than conventional histopathological analysis, we evaluated the distal surgical margins for expression of cancer stem cell markers. Our clinical study in collaboration in Regional Cancer Centre first looked at 150 CRC tissue samples that included normal, tumor and distal margin from the same patients. Flow cytometry assay revealed CD133 and CD44 enriched cells in distal margin and tumor compared to normal CR tissues, which was further confirmed by IHC. Most importantly IHC also revealed enrichment of CSC markers expression in pathologically negative distal margins. Patients with distal margin enriched for CD133 expression showed an increased recurrence rate and decreased disease free survival. This study revealed that though distal margin seems to be tumor free in conventional histopathological analysis, it could harbor cells enriched for CSC markers. CD133 could thus be a promising molecule to be used in molecular pathology for disease prognosis after surgery in CRC patients. We suggest that modern pathology should include molecular tools to identify CSCs in tumor niches and liquid biopsies for better disease management. Further, we believe that more analytical studies are needed to understand role of field effect in residual disease in CRC as well as other cancers as well.

FIGURE

Enriched CSC Markers expression in Pathologically negative distal margin in CRC and their possible role in disease recurrence.



PUBLICATIONS

Tapas Pradhan, Padmanabhan, K, Prasad. M, Chandramohan K, Nair AS(2019). Augmented CD133 expression in distal margin correlates with poor prognosis in colorectal cancer. J of Cellular Mol Med 23 (6): 3984-3994https://doi.org/10.1111/jcmm.14284

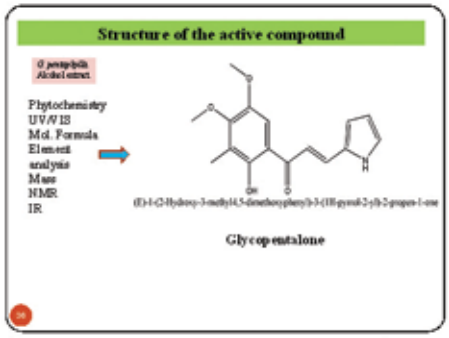
Asha V V, PhD

Plant Biotechnology & Disease Biology Program

PLANT DERIVED BIOACTIVE COMPOUND DISCOVERY

Glycosmis pentaphylla (Retz.) Correa, has been traditionally used by the tribal people of India besides being recognized in Ayurveda as one of the most important options for curing fever, cough, rheumatism, anaemia, cancer and liver disorders. From our phytopharmacological investigations, Glycopentalone, a novel chalcone compound was isolated and characterized from the active alcohol extract of Glycosmis pentaphylla. Glycopentalone was isolated in bulk by silica gel column chromatography, and structurally characterized by interpretations from various spectroscopic and chromatographic techniques including HPLC, TLC, IR, LC-MS and NMR. It has a molecular formula C16H17N1O4 with a molecular weight 286.2. The compound was unambiguously identified as (E)-1-(2-Hydroxy-3- methyl 4, 5-dimethoxyphenyl)-3-(1H-pyrrol-2-yl)-2-propen-1-one (Sreejith and Asha, 2015). We scientifically proved the anti-hepatocellular carcinoma property of G. pentaphylla in vitro and identified the anti B-RAF inhibitory effect of the compound and in addition confirmed that its efficacy is comparable with sorafenib, sorafenib being the most recent and the only FDA approved drug for HCC. Druggability and lead optimization of the compound were done by in silico methods. The in vivo toxicity studies showed that the alcohol extract and the active compound of G. pentaphylla had no any significant toxicity. Further studies for determination of efficacy of the compound in vivo utilizing xenograft tumour models of HCC in SCID mice are underway.

FIGURE



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P.S. Sreejith, V.V. Asha (2015). Glycopentalone, a novel compound from Glycosmis pentaphylla (Retz.) Correa with potent anti-hepatocellular carcinoma activity Journal of Ethnopharmacology, 172: 38-43

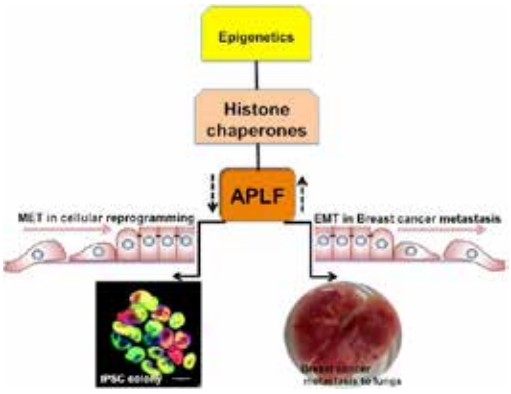
Sreejith P. S. and Asha V. V. (2017). In vitro pharmacological, in vivo toxicological and in silico molecular docking analysis of glycopentalone, a novel compound from Glycosmispentaphylla (Retz.) Correa. Medicinal Chemistry Research 26(8): 1697-1707

Debasree Dutta, PhD
Regenerative Biology Program

USING STEM CELLS TO UNDERSTAND DISEASE

Epigenetics of histone is a multi- layer regulatory process leading to the formation of open or closed chromatin state that regulates gene expression. Histone chaperones, one of the epigenetic layers, are responsible for histone metabolism and other physiological processes. Recently, we showed that downregulation of histone chaperone Aprataxin PNK-like factor (APLF) could enhance the kinetics and efficiency of generation of induced pluripotent stem cells (iPSCs) from differetiated cells (published in J Cell Sci).The outcome has a significant implication in improving the quality of iPSCs for their use in regenerative medicine or disease modelling. This work contributed to the receipt of DBT National Women Bioscientist Award, 2016. Mechanistically, downregulation of APLF in embryonic fibroblasts could induce the expression of E-cadherin (CDH1), associated with Mesenchymal-to-epithelial transition (MET) thereby enhancing the efficient generation of iPSCs. This cellular transition has been widely involved in dieases especially in cancer metastasis. Upon investigation of invasive ductal breast carcinoma patient samples, the expression of APLF was found to be significantly enhanced (published in Mol Cancer). Here also, APLF regulated the genes associated with EMT/MET by incorporation of repressive histone variant macroH2A.1 at the EMT-specific gene, and recruitment of the master regulator FOXA1 at the MET-specific CDH1 locus. So, APLF could be targeted for further therapeutic approaches and can be explored to be used as breast cancer biomarker. Conclusively, an histone chaperone could dictate cellular transition associated with both development and disease.

FIGURE



PUBLICATIONS

Syed et al. (2016). Histone chaperone APLF regulates induction of pluripotency in murine fibroblasts.J Cell Sci. 129(24):4576-4591

Majumder et al. .(2018).Enhanced expression of histone chaperone APLF associate with breast cancer. Mol Cancer. 17(1):76.

Devasena Anantharaman, PhD
Cancer Research Program

A VIRUS AND A CANCER

The laboratory has its major focus in developing studies of cancer prevention, cancer screening and molecular characterization of human papiloomavirus (HPV) - related tumors. Using the tumor tissues collected from central India (Sevagram) as a part of the European Union framework program (FP7) that was ongoing in the lab, we estimated the prevalence of type-specific HPV in cancers of the head and neck region. We demonstrated that the proportion of HPV-positive oral cancer in the Indian population differs from the western world. Further, we showed that HPV types other than HPV16 (HPV18, 35 and 56) could play an important role in the aetiology of HPV-related oral cancers in India (Gheit T et al, Int J of Cancer 2017). In the context of the Indian HPV vaccination trial examining the efficacy of two dose versus three dose vaccination, data generated in her group has demonstrated that the seven month HPV major capsid (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. Further, none of the girls receiving two had persistent infection from vaccine-targeted types (Basu P et al, Papillomavirus Res. 2019). These findings indicate that two-vaccination schedule can be extended to 15 to 18 year old girls.

PUBLICATIONS

Role of mucosal high-risk human papillomavirus types in head and neck cancers in central India. Gheit T, Anantharaman D, Holzinger D, Alemany L, Tous S, Lucas E, Prabhu PR, Pawlita M, Ridder R, Rehm S, Bogers J, Maffini F, Chiocca S, Lloveras B, Kumar RV, Somanathan T, de Sanjosé S, Castellsagué X, Arbyn M, Brennan P, Sankaranarayanan R, Pillai MR, Gangane N, Tommasino M; HPV-AHEAD study group. International Journal of Cancer. 2017 Jul 1;141(1):143-151. doi: 10.1002/ijc.30712. PMID: 28369859

Two-dose recommendation for Human Papillomavirus vaccine can be extended up to 18 years - updated evidence from Indian follow up cohort study. 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, S2405-8521(18)30133-2. PMID: 30711698

George Thomas, PhD
Plant Biotechnology & Disease Biology Program

BIOTECHNOLOGY TO PROTECT GINGER AND DEFINE ANCIENT RICE

The long-term goal of one of the research topics in my laboratory is to develop soft-rot protection methods in ginger. As ginger is an obligate asexual and all ginger cultivars are susceptible to Pythium soft-rot, our strategy is to identify a resistant congener, dissect the resistance trait and try to translate this knowledge to develop soft-rot protection methods in ginger. Major findings include: (i) located soft-rot resistance in Z. zerumbet; (ii) pattern of transcriptional reprogramming in ginger and Z. zerumbet against Pythium infection; (iii) a dominant role for cell wall signaling in governing soft-rot resistance in Z. zerumbet; (iv) chemical elicitors to induce soft-rot tolerance in ginger.

In the other project, we determined the genetic characteristics and the phylogenetic position of the local Njavara (Shashtika in Sanskrit) rice, whose medicinal properties are referred in Sanskrit literature in India for last 3000 years. Major findings include: (i) Njavara is not a single type as previously thought, but is a composite of at least five genotypes under four morphotypes; (ii) it is not an indica, but is genetically distinct and closest to aus; (iii) domesticated in North India and likely reached Kerala concomitant with Ayurveda in late BC or early AD.

PUBLICATIONS

Vishnu Sukumari Nath, Sayuj Koyyappurath, Teena Elizabeth Alex, Kiran Ayyanperumal Geetha, Lesly Augustine, Alka Nasser and George Thomas (2019). Transcriptome-based mining and expression profiling of Pythium responsive transcription factors in Zingiber sp. Functional & Integrative Genomics 19: 249-264.

Kiran Ayyanperumal Geetha, Sayuj Koyyappurath, Lesly Augustine, GeorgeThomas. 2019. Transcriptional analysis and histochemistry reveal a dominant role for cell wall signaling in mediating Pythium myriotylum resistance in Zingiber zerumbet. Physiological and Molecular Plant Pathology 106 7–15.

Jose, M., Dinesh Raj, R, Vinitha, M. R., Madhu, R., Varghese, G., Jan Bocianowski, Yadav, R., Patra B.C, Singh O.N., Rana J.C., Leena Kurmari, S., and George Thomas. 2018. The prehistoric Indian Ayurvedic rice Shashtika is an extant early domesticate with a distinct selection history. Frontiers in Plant Science. 9:1203. doi: 10.3389/fpls.2018.01203

RGCB @30

Uttroside B in liver cancer patients - transferred the technology to the multi-national company, Q Biomed.

K Harikrishnan, PhD
Transdisciplinary Biology Program

SEARCHING THE ENVIRONMENT FOR SOLUTIONS

Metagenomics is the direct analysis of community DNA isolated from environmental samples for elucidating the hidden genetic and functional diversity of uncultivable bacteria. Soil metagenomic libraries of 0.72 Giga base pairs size, equivalent to 360 bacterial genomes was constructed with plasmids and bacterial artificial chromosome (BAC) vectors. The clones in libraries when screened were found to be harboring genes for industrially and therapeutically important enzymes. L-asparaginase, an enzyme used as an antineoplastic agent in acute lymphoblastic leukemia (ALL) therapy was further studied in detail. L-asparaginase derived from the metagenomic library had a novel origin showing only 84% amino acid sequence similarity with other reported bacterial L-asparaginases. The purified protein exhibited a specific activity of 696 IU/mg that was higher than the commercially available native E. coli L-asparaginase (200 IU/mg). The antitumor activity of the enzyme was measured in various human leukemia cell lines and the IC50 values ranged between 0.23-0.47 IU/mL, which is much better than the commercial therapeutic asparaginases available from Erwiniasp. and E. coli (0.5 to 10 IU/mL). The enzyme characteristics indicate that the metagenome derived novel L-asparaginase is a potential candidate to be developed as an efficient drug against ALL.

Polyhydroxyalkanoates (PHAs) are a group of polyesters accumulated in microorganisms in response to unbalanced growth conditions and are regarded as a green-substitute for synthetic plastics due to their biodegradability. A recombinant E. coli strain was engineered using the PHA biosynthesis genes from Bacillus aryabhattai, a potential PHB producer isolated from the environment. The recombinant cells accumulated maximum level of biopolymer (6.22 g/L) utilizing crude glycerol, a cheap carbon source. Recovery of polymer from bacterial cell mass is the major factor contributing more than 50% of the PHA production cost and majority of the industrial processes are not ecofriendly. Hence, an EDTA-microwave cell lysis method was developed for an easier and eco-friendly polymer extraction, which yielded a polymer recovery rate of 93.75%, purity 97.21% with 2.9 fold improvement in molecular weight and better poly dispersity index than the conventional chemical lysis method. The procedure is simple, with minimum polymer damage and more eco-friendly than the conventional methods. The findings are published in the journal AMB Express

PUBLICATIONS

Kumar, A. J., Pillai, A. B., Thulasi, K. &Kumarapillai, H. (2018) Characterization of a novel asparaginase from soil metagenomic libraries generated from forest soil. Biotechnology Letters; 40: 343-348.

Pillai, A. B., Kumar, A. J. &Kumarapillai, H. (2018) Enhanced production of poly(3-hydroxybutyrate) in recombinant Escherichia coli and EDTA-microwave-assisted cell lysis for polymer recovery. AMB Express 8:142.https://doi.org/10.1186/s13568-018-0672-6

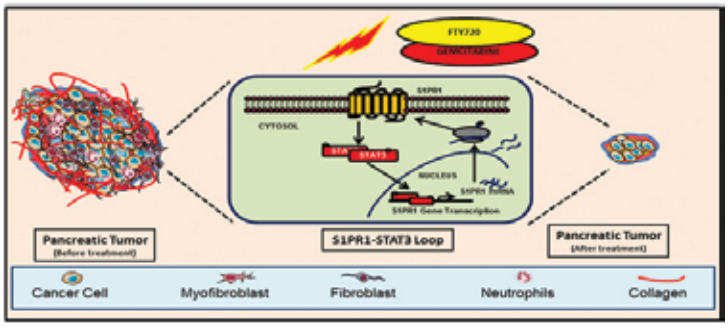
K B Harikumar, PhD
Cancer Research Program

LOOKING AT CANCER THROUGH LIPIDOMICS

Pancreatic cancer is currently the seventh leading cause of cancer-related deaths worldwide. The pancreatic tumor microenvironment consists of pancreatic stellate cells, extra cellular matrix and cancer-associated fibroblasts. Sphingosine 1-Phosphate (S1P) is a pleiotropic lipid molecule present inside the cells. S1P acts either intracellularly or through the cell surface G protein-coupled receptors (S1P receptor, S1PR 1-5). S1PR1 has been reported as one of the key factors responsible for persistent STAT3 activation in different tumor types. However, the precise role of S1PR1 in pancreatic cancer is not clear. We identified that S1PR1/STAT3 pathway regulates the desmoplasia and subsequently the increased pancreatic cancer progression and drug resistance. Fingolimod (FTY720) is the first FDA-approved oral drug for the treatment of the relapsing form of multiple sclerosis and acts as a functional antagonist to S1PR1.Collectively, our findings suggested that inhibition of S1PR1/STAT3 loop resulted in inhibition of desmoplasia, reduced resistance to gemcitabine, and improved the delivery of gemcitabine to tumor sites which eventually lead to decrease in the progression of pancreatic cancer.

FIGURE

Graphic illustration showing that by targeting S1PR1/STAT3 loop in pancreatic cancer lead reduction in desmoplastic content and decrease in the growth of pancreatic cancer



PUBLICATIONS

Lankadasari M B, Aparna J S, Mohammed S, James S, Aoki K, Binu V S, Nair S, Harikumar K B). Targeting S1PR1/STAT3 loop abrogates desmoplasia and chemosensitizes pancreatic cancer to gemcitabine. Theranostics. 2018 8(14): 3824-3840

Iype Joseph MB.BS, MPhil
Pathogen Biology Program

ZOONOTIC DISEASES FROM RODENTS

Lakshadweep islands have a serious problem with rodent infestation, the most prominent carrier of Leptospira (through urine) and transmitter of Typhus (through ectoparasites). But, neither of these diseases has been recorded in any of the nine inhabited islands. In contrast, these are significant medical issues in Andaman & Nicobar Islands and islands near the African shore like Reunion and Seychelles.

A case-record review of all Medical cases admitted to the main government hospital in Kavaratti Island during the year 2017 was done. 11 persons with symptoms and signs overlapping with that of Leptospirosis were identified. 5 patients could not be traced and one person refused to cooperate. The remaining five persons provided blood samples. All are permanent residents of Kavaratti Island. They were tested for presence of IgG anti-leptospira antibodies by Novatec Immunediagnostica kit as per the manufactures instructions.nOne person was identified to have IgG anti-leptospira antibodies. This is the first report of Leptospirosis from Lakshadweep islands. In addition, two persons with Typhus (one with pathognomonic eschar) from Kadamath and Kavaratti islands were discovered from the record review.

RGCB @30

Unique genetic IDs for elephants were generated by a joint effort of RGCB and Forest Department, Govt. of Kerala.

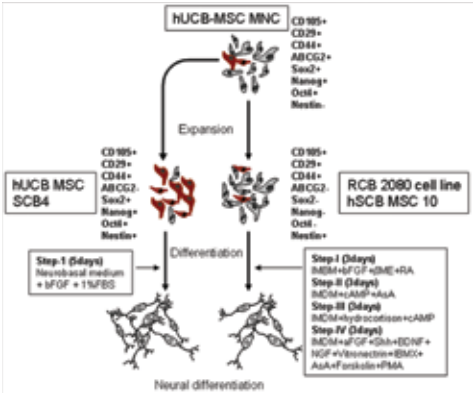
Jackson James, PhD
Regenerative Biology Program

NETWORKS IN STEM CELL BIOLOGY

In 2012 we discovered the presence of a unique small population of mesenchymal stem cells (MSCs) in Umbilical cord blood that express pluripotent stem cell markers (Oct4, Nanog and Sox2) along with MSC markers (CD105, CD29 and CD44) and possess an inherent neurogenic potential (Figure -1). Our findings therefore form the basis for developing better neuronal differentiation protocols from MSCs, which can be used for therapeutic applications.

In 2017 we showed for the first time that non-canonical NIHes-1 is essential for maintenance of the neural stem cells during neocortical development and these cells latter transit to the canonical Notch-dependent Hes-1 (NDHes-1) expressing state that is required for maintaining neural progenitors/Radial Glial cells. This basically gave an insight to the significant differences between two very closely related populations. Though Hes-1 expression is maintained in neural progenitors, a transition from Notch-independent to dependent state makes it pleotropic 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.

FIGURE



PUBLICATIONS

Divya MS, George RE, Divya TS, Rasheed VA, Santhoshkumar TR, Elizabeth KE, James J& Pillai MR. Umbilical Cord blood derived mesenchymal stem cells consist of a unique population of progenitors co-expressing MSC and neuronal markers capable of instantaneous neuronal differentiation; Stem Cell Research & Therapy, (2012) 3:57

Dhanesh SB, Subashini C, Riya PA, Rasheed VA &Jackson James; Pleiotropic Hes-1 concomitant with its differential activation mediates neural stem cell maintenance and radial glial propensity in developing neocortex: Cerebral Cortex 27(2017) 3943–3961.

Jackson James selected for National Bioscience Award - 2016, Department of Biotechnology, Government of India

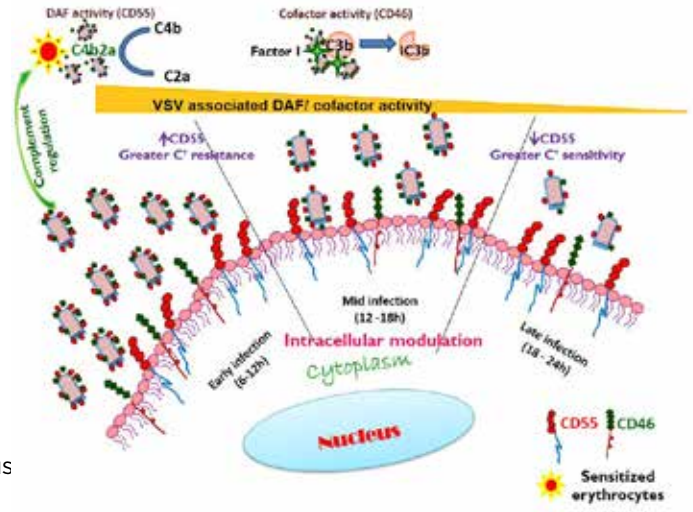
John B Johnson, PhD
Pathogen Biology Program

COMPLEMENT FOR A VIRUS

The susceptibility or resistance of the host to viruses or vice versa is a delicate balance determining the overall fate of the pathogen or the host. Using rhabdovirus family of viruses as model pathogens and the human complement system we propose to derive valuable insights into rhabdovirus-immune interactions. While the rhabdoviruses are potent pathogens such as rabies virus, vesicular stomatitis virus (VSV), Chandipura virus (CHPV), the complement system is an important and integral component of the innate immune system. Our investigations revealed that CHPV is sensitive to human complement and preferentially activated the immune complex dependent classical pathway of complement, interestingly in an antibody independent manner. Despite the close relationship, VSV neutralization was by lysis while complement mediated CHPV aggregation. Mortality associated with these viruses painted a different picture of resistance to complement. We have unraveled that these viruses hijack our own membrane associated complement regulators to thwart complement. Our laboratory is also exploiting the cytopathic properties of CHPV in targeting cancers. Besides unravelling rhabdovirus-complement interactions our findings have opened up endless avenues to not only target CHPV but to exploit its potential to develop novel vectors.

FIGURE

Infection of permissive cells by members of rhabdovirus family results in virus replication. Both virus and infected cells activate complement resulting in complement dependent neutralization and clearance. However modulation of host genes results in maintenance of certain complement regulators like CD55 facilitating enhanced incorporation in virus envelope. This phenomenon is strictly time dependent and the incorporated host regulators thus protect the virus and limit complement dependent neutralization.



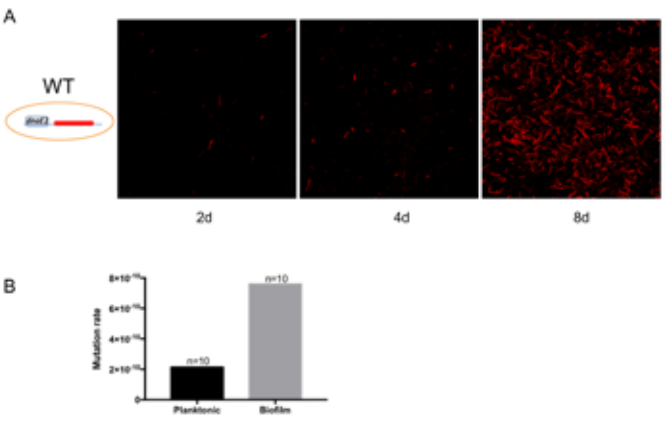
Krishna Kurthkoti, PhD
Pathogen Biology Program

GENETIC ERRORS AND SURVIVAL OF M. TUBERCULOSIS

Biofilms are multicellular communities held together by an extracellular polysaccharide matrix. Due to the complex cellular organization of bacteria in the biofilm, the availability of nutrients will not be uniform among the bacterial population resulting in heterogeneity among the bacterial cells. In this study, we have used Mycobacterium smegmatis as a model organism to understand the causes for nutritional and genetic heterogeneity arising within the biofilm. Using a dual iron reporter and a GFP reversion reporter, we observed both nutritional and genetic heterogeneous population in the biofilm. We reasoned that the source of genetic heterogeneity could be arising due to the expression of DnaE2, a Pol III family DNA polymerase associated with error-prone DNA synthesis in mycobacteria. Using a fluorescent reporter, we observed a temporal increase in the expression of dnaE2 as the biofilm matured. The expression of dnaE2 resulted in an increase in mutation within the biofilm compared to planktonic culture. The deletion of dnaE2 resulted in reduced mutagenesis in biofilm, and the mutant strain displayed fitness defect when competing with the parental strain in the biofilm culture. Our results suggest that the expression of dnaE2 generates genetic variation within the population and facilitates bacterial adaptation within the biofilm.

FIGURE

Expression of DnaE2 in biofilm results in increased mutagenesis: Up-regulationof the expression of the mCherry fused to dnaE2 promoterduring biofilm formation detected by confocal microscopy (panel a). Comparison of mutation rate of wild-type strain in the planktonic and the biofilm culture determined by spontaneous rifampicin resistance assay (panel b).



RGCB @30

RGCB started 9 Molecular Laboratory Services with NABH accreditation across Thiruvananthapuram district, which provides diagnostic support to the people of the state.

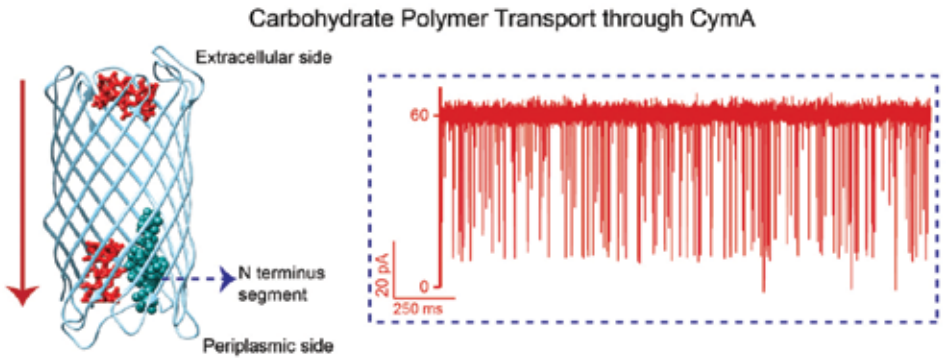
K R Mahendran, PhD
Transdisciplinary Biology Program

TINY PORES IN MEMBRANE BIOLOGY

We assembled a transmembrane peptide pore from 40 amino acid α-helical synthetic peptides based on the membrane protein of the bacterium, Corynebacterium jeikeium. By chemical and biophysical techniques, we defined the structural composition of the pore and elucidated its assembly mechanism in the membrane. The peptide pore is ion-selective, functional and capable of binding blockers. Such designed synthetic transmembrane pores are useful for applications in biotechnology and synthetic biology.

Proteins in the membranes allow nutrients across the barriers. We define an innovative, naturally evolved mechanism for regulating the selective uptake of the nutrients effectively through membrane pores. We present a specialized substrate selective bacterial nanopore CymA, which has the 15-residue segment inside the pore barrel, restricting its diameter, generating a sophisticated architecture. We elucidate the dynamics of carbohydrate polymers transport through CymA and provide quantitative kinetics of translocation.

FIGURE



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Krishnan R S, Satheesan R, Puthumadathil N, Kumar KS, Jayasree P, Mahendran KR. Journal of the American Chemical Society. 2019. 141(7): 2949-2959.

Vikraman D, Satheesan R, Kumar KS, Mahendran KR. ACS Nano. 2020 (In press).

Awards for K.R. Mahendran:

- DBT-Innovative Young Biotechnologist Award (2017)
- DST SERB-Early Career Research Award (2018)
- Merck Young Scientist Award (2019) in Biological Science

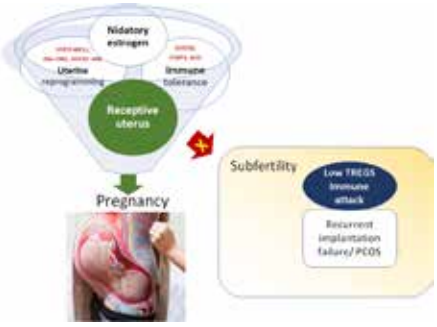
Malini Laloraya, PhD, FNASc
Reproduction Biology Program

PREGNANCY AND DISEASE

My laboratory's first theme on understanding the impact of 'nidatory estrogen' in creating a conducing environment leading to successful embryo implantation has led to the identification of estrogen mediated STAT3-MCl1 interaction to be involved in regulating epithelial mesenchymal transition. We have identified ERα-CrkL interaction during embryo implantation and this association is also seen in human endometrial cancers which led to an exacerbated ER transactivation establishing CrkL, an oncogene, as a co-activator of ER alpha thereby resulting in enhanced tumorigenesis. Our recent work has found an indispensable role of DOCK180 in pregnancy via a consolidated impact on decidualization and angiogenesis by regulating AIRE nuclear entry, which is critical for implantation sites formation and uterine reprogramming for decidualization.

As part of my second theme of my laboratory, we have identified lowered Tregs in polycystic ovarian syndrome (PCOS) due to diminished STAT5B phosphorylation leading to defective IL2 signaling loop and reduced NO. We have shown that STAT5B can bind to NOS promoter and modulate NO levels. Thus, transcriptional regulation of Nos2 by STAT5B in addition to its control of FOXP3 places STAT5B as a central figure responsible for Treg homeostasis. Thus our lab's findings have added new dimensions for understanding implantation and PCOS

FIGURE



PUBLICATIONS

Mohan, J. J., Narayan, P., Padmanabhan, R. A., Joseph, S., Kumar, P. G., and Laloraya, M. (2018) Am. J. Reprod. Immunol.80, e12844

Soumya, V., Padmanabhan, R. A., Titus, S., and Laloraya, M. (2016) Am. J. Reprod. Immunol.76, 224-234

Krishna, M. B., Joseph, A., Subramaniam, A. G., Gupta, A., Pillai, S. M., and Laloraya, M. (2015) J. Clin. Endocrinol. Metab100, 282-292

Krishna, M. B., Joseph, A., Thomas, P. L., Dsilva, B., Pillai, S. M., and Laloraya, M. (2017) Cell Physiol Biochem.43, 1880-1892

Joseph, A., Nair, L. C. R., Johnson, B. S., Thomas, P. L., Padmanabhan, R. A., Puthumadathil, N., and Laloraya, M. (2019) Cell Physiol Biochem.52, 141-155

S Manjula, PhD
Plant Biotechnology & Disease Biology Program

DISEASE RESISTANCE IN PEPPER

The indigenous spice crop Piper nigrum or black pepper has been under domestication for thousands of years and as with many crop plants, continuous selection for yield traits have resulted in permanent loss of valuable attributes including disease resistance. Wild species of crop plants are valuable genetic resources that can be utilized for the genetic improvement of their cultivated counterparts. For the past many years, we have been studying the mechanism of defense in wild (resistant) and cultivated (susceptible) pepper (Piper sp) to the oomycete pathogen Phytophthora capsici. The presence of a rich repertoire of defense genes and their high inducibility by defense signalling compounds established the intrinsic capacity of wild pepper to resist the infection of Phytophthora capsici. (Current Science, 2005), and our ensuing efforts corroborated the functional roles of these genes in host defense (Mol. Biotechnology (2011), Plant Cell Tiss. Organ Cult. (2015). These findings led to further studies for elucidation of critical components of defense signalling in susceptible pepper (cultivated black pepper). It was an interesting observation that despite being highly susceptible, cultivated pepper do possess a robust and highly inducible innate immune system These results have led to our conclusion that 'defense priming' or induction of innate immunity is the only possible crop protection strategy in black pepper.

FIGURE

Phytophthora capsici with sporangia (X100)

PUBLICATIONS

Krishnan, A., Mahadevan, C., Mani, T., & Sakuntala, M. (2015). Virus-induced gene silencing (VIGS) for elucidation of pathogen defense role of serine/threonine protein kinase in the non-model plant Piper colubrinum Link. Plant Cell, Tissue and Organ Culture (PCTOC), 122(2), 269-283.

Mahadevan, C., Krishnan, A., Saraswathy, G. G., Surendran, A., Jaleel, A., & Sakuntala, M. (2016). Transcriptome-assisted label-free quantitative proteomics analysis reveals novel insights into Piper nigrum - Phytophthora capsici Phytopathosystem. Frontiers in Plant Science, 7, 785.

Moinak Banerjee, PhD
Neurobiology Program

MENTAL DISEASE AND GENE METHYLATION

Schizophrenia is known to be influenced by both gene and environment. DNA methylation is one of the most common signatures of the environmental impact on the host epigenome. Several reports suggest differences in the pattern of DNA methylation both at global and gene specific level in Schizophrenia. However, many of these observations could not be replicated unanimously. Most of the studies have considered that genetic and epigenetic events as two independent events. None of these studies have implied the role of genomics of methylome in Schizophrenia. We for first time demonstrated that the DNMTs which are responsible for maintaining the methylations, are themselves associated with Schizophrenia that might possibly explain the discrepancies in global or gene specific methylations. Genes involved in methylation pathway can influence the urea cycle, neurotransmitter cycle, folate cycle, methionine cycle and transulfuration cycle. Therefore, in continuation to our previous observation on methyltransferases, we have extended this work on genetics of methylome to cover the genes that could intrinsically or extrinsically modulate the methylome, and identify their role in Schizophrenia pathogenesis and therapeutic response. Till date most of the studies have investigated on the role of epigenetics from the perspective of Schizophrenia pathogenesis but none of them have investigated whether the drugs could also induce these epigenetic changes itself. We have recently demonstrated that this epigenetics response in schizophrenia may not be of pathogenesis but could be drug induced epigenomic response.

PUBLICATIONS

B Swathy, KR Saradalekshmi, Indu V Nair, Chandrasekharan Nair and Moinak Banerjee Pharmacoepigenomic response of antipsychotic drugs on pharmacogenes is mediated by microRNAs. Epigenomics 9(6): b811-821.

B Swathy, Moinak Banerjee Haloperidol induces pharmacoepigenetic response by modulating miRNA expression, global DNA methylation and expression profiles of methylation maintenance genes and genes involved in neurotransmission in neuronal cells. PLoS ONE 12(9): e0184209

B Swathy, KR Saradalekshmi, Indu V Nair, Chandrasekharan 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.

RGCB @30

RGCB's services were hailed during the identification of human remains from the devastating Puttingal temple fire tragedy.

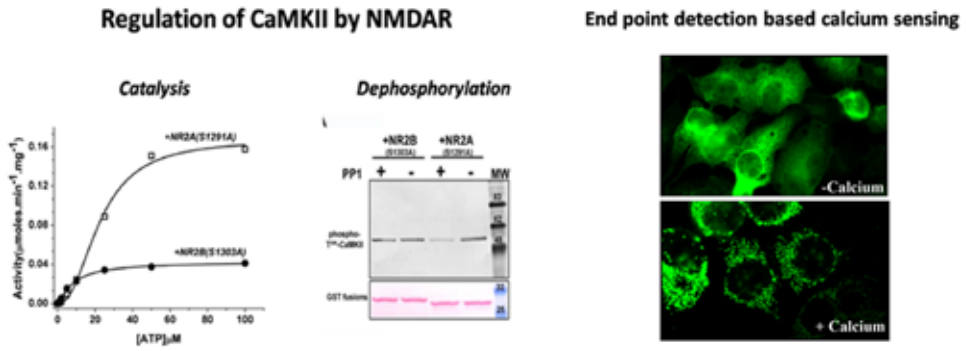
R V Omkumar, PhD
Neurobiology Program

THE CONTINUING CALCIUM SAGA

Learning and memory are brain functions that are being extensively studied world over. Calcium/ calmodulin dependent protein kinase II (CaMKII) and NMDA type glutamate receptor (NMDAR) have emerged as key players in these functions. A bistable switch model has been proposed to explain how neuronal activity seen as calcium signaling events lead to stable molecular states of CaMKII. Our experiments have shown that the complex of CaMKII and the NMDAR subunit GluN2B is suited to function as the switch. We discovered that the catalytic activity of CaMKII is regulated allosterically by binding of GluN2B. As a consequence, CaMKII activity is reduced and stabilised against variations in ATP concentrations. Dephosphorylation of CaMKII by phosphatises is also reduced in the complex. Thus our data helps in substantiating and refining the bistable switch model of learning and memory (Pradeep et al, 2009, Biochem J. Vol. 419, p123; Cheriyan et al, 2011, PLoS One, Vol. 6, e16495)

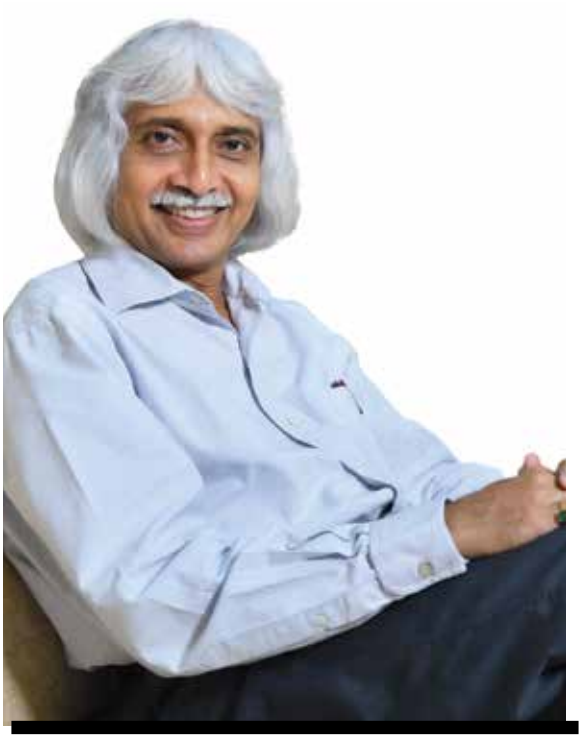
Our second major achievement is the development of a novel technique for calcium sensing. This is the first endpoint detection based method for intracellular calcium sensing. This technique is simple to perform and less expensive and thus facilitates discovery of calcum channel inhibitors (Chandrika et al, 2019, Cell Calcium. 2018,Vol. 74, p73). We have been able to identify several NMDAR inhibitors using this technique. Many of these inhibitors are currently undergoing validation in preclinical models.

FIGURE



AWARD

The calcium channel assay method was selected among the Top 50 innovations for the year 2012-13 in the "DST- Lockheed-Martin India Innovation Growth Programme" conducted by DST, Lockheed-Martin, FICCI, etc.



G Pradeep Kumar, PhD
Reproduction Biology Program

UNDERSTANDING SPERM ARCHITECTURE

My primary focus is on the identification of differentially expressed proteins in the spermatozoa of fertile and infertile human males and to elucidate their functional roles in the context of spermatogenesis, sperm-oocyte fusion and oocyte-embryo transition. Extensive sperm proteome profiling led to the identification of several proteins missing out in the spermatozoa from infertile men. These included NOX2 and its components, TRLP, AIRE, DYNLT1, CNNM1, NPHP1, TDP43, etc. To gain functional insights, we manipulated their expression in a spermatogonial cell line and evaluated the responses. Thus, overexpression of DYNLT1 in GC1-spg cell line resulted in the upregulation of several cytoskeletal proteins and molecular chaperones involved in cell cycle regulation. Proteome level changes in GC1-spg cells overexpressing DYNLT1 were suggestive of its possible involvement in protein trafficking, membrane vesiculation, cell cycle regulation and stem cell differentiation.

AIRE was detected in the testis of neonatal, adolescent and adult mice. GFRα+ (spermatogonia), GFRα-/SCP3+ (meiotic) and GFRα-/PGK2+ (post-meiotic) germ cells expressed AIRE. GC1-spg cells did not express AIRE. Retinoic acid induced AIRE expression in GC1-spg cells. Ectopic expression of AIRE in GC1-spg cells redefined the proteomic landscape of these cells, increasing the levels of various nucleic acid binding proteins and transcription factors and a decreased level of various cytoskeletal and structural proteins. Molecular function network analysis indicated that AIRE influenced gene expression in GC1-spg cells by acting at multiple levels including transcription, translation, RNA processing, protein transport, protein localization and protein degradation.

PUBLICATIONS

Radhakrishnan K, Bhagya KP, Anilumar TR, Devi AN, Sengottaiyan J and Kumar PG (2016) Autoimmune regulator (AIRE) is expressed in spermatogenic cells and it altered the expression of several nucleic acid binding and cytoskeletal proteins in GC1-spg spermatogonial cells. Mol Cell Proteomics 15(8), 2686-2698. doi:10.1074/mcp.M115.052951.

Anilkumar TR, Devi AN, Pillai SM, Jayakrishnan K, Oommen OV and Kumar PG (2017) Expression levels of Protocadherin 11Yb (PCDH11Y) in the germ cells in the semen correlate with fertility status in men. Reprod. Fertil. Dev. 29(11): 2100-2111. doi: 10.1071/RD16478.

Bhagya KP, Aswathy JR, Radhakrishnan K, Jeeva SE and Kumar PG (2020) Autoimmune regulator enhanced the expression of caspase-3 and did not induce massive germ cell apoptosis in GC1-spg cells. Cell PhysiolBiochem. 54, 40-52.

Awards Received for the Work Described

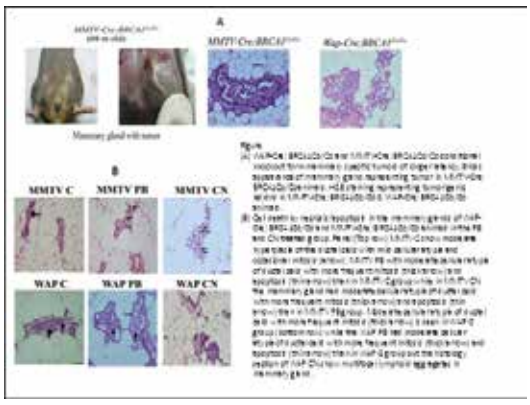
- National Bioscience Award for Career Development 2006-2007 from Department of Biotechnology, Govt. of India.
- Labhsetwar Foundation (USA) Award of Indian Society for the Study of Reproduction and Fertility, 2015.
- Dr. TC Anand Kumar Memorial Gold Medal and Oration Award of Indian Society for the Study of Reproduction and Fertility, India, 2016.
- Dr. Subhas Mukherjee Memorial Oration Award of Association of Clinical Embryologists, India, 2016
- 19th Royan International Research Award, 2018
- Prof. P. Govindarajulu Oration and Gold Medal of Society for Reproductive Biology and Comparative Endocrinology, 2018.

A PLANT DERIVED QUENCHER OF FREE RADICALS

Priya Srinivas, PhD
Cancer Research Program

Breast cancer is the leading cause of cancer mortality, 80% of hereditary breast ovarian cancers (HBOCs) have been associated with BRCA1 mutation. Also, 30-40% of sporadic breast cancers are associated with decreased BRCA1 expression owing to its promoter hypermethylation. BRCA1 defects would cause cancers at a very young age and are highly drug resistant. Our research mainly focuses on BRCA1 associated cancers, in almost all the realms including molecular, therapeutic and diagnostic aspects of these cancers, focusing on analyzing the genetic causes and unleashing the possibilities of attenuation and implication of BRCA defects in tumorigenesis.
We identified that a plant-derived naphthoquinone, Plumbagin, isolated from the roots of Plumbago zeylanica has targeted anti-cancer activity against BRCA1 defective breast and ovarian cancers. We have published our research on plumbagin in international journals, including International Journal of Cancer, Molecular Carcinogenesis, BMC Cancer, Scientific Reports and Pharmacological Research during the years 2004-2016. Along with ROS mediated DNA damage inducing ability, plumbagin inhibits multiple tumourigenic pathways in DNA repair defective, BRCA1 deficient cells. We also showed that plumbagin can inhibit cancer stem cells specifically in BRCA1 mutated cancers. Extensive anti-cancer activity in BRCA1 conditional knockout transgenic mouse models proved that plumbagin has a better anticancer activity at about 16 fold lower concentration than standard chemotherapeutic drug, carboplatin. These studies led the way to several national and International accolades, including the ICMR Prem Nath Wahi Award (2013), and the American Association of Cancer Research (AACR)-National Cancer Institute (NCI) International Investigator Opportunity Grants, USA (2008) for her research on identifying potential ways to kill BRCA1 defective cancer cells in a targeted manner using this naphthaquinone.

FIGURE



Radhika Nair, PhD
Cancer Research Program

DEFINING TUMOR SPREAD

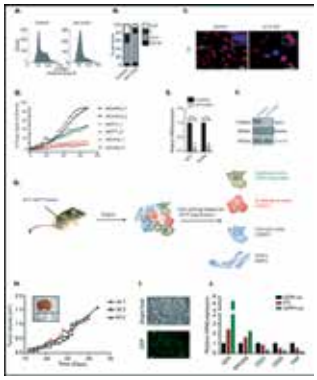
Metastasis or the spread of cancer from the primary site to other parts of the body is a silent killer in breast cancer, with 90% mortality rate for women with metastatic disease. Therapeutic targeting requires a deeper understanding of this complex cascade of events eventually leading to metastasis. 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 have completed two projects aimed at understanding the mechanism by which Id proteins control the cancer stem cell phenotype in the Triple negative breast cancer molecular subtype. We have successfully used combination therapy to target the bulk cancer more effectively by using small molecule inhibitors and chemotherapy in a TNBC model.

In an effort to understand the role of the stroma in tumor progression, we have discovered two phenotypically distinct tumor cell populations that respond diversely to the microenvironment. We have established complex in vivo and ex vivo models and have isolated the subpopulation of cells from the heterogenous primary tumor and matched lung metastasis. We are exploring the transcriptome of the cells using RNA Sequencing to comprehend the genomic basis for the tumor heterogeneity in the metastatic microenvironment.

FIGURE

Modelling the intrinsic and extrinsic factors affecting metastasis (A) Ex vivo culture of stromal subpopulations from primary tumor and metastases where primary fibroblasts were found to be associated with tumor cells. (B) Two distinct cell populations were obtained from primary tumor based on GFP expression. (C) Proliferation capacity of the GFPHi cells is significantly less than GFPInt population. (D) The self-renewal capacity on the other hand of the GFPHi tumor cells is higher than the GFPInt. (E) GFPHi and GFPInt are phenotypically distinct subpopulations in the primary tumor.



PUBLICATIONS

Aurélie Cazet*, Mun Hui*, Ben Elsworth, Sunny Wu, Caroline Cooper, Michael Samuel, Jessica Yang, Niantao Deng, Nicola Foreman, Andrea McFarland, Radhika Nair, Sandra O'Toole, Rosalía Caballero, Miguel Martín and Alexander Swarbrick.

Stromal Smoothened inhibition depletes triple negative breast cancer stem cells and sensitizes to chemotherapy. Nature Communications.2018 Jul 24;9(1):2897. doi: 10.1038/s41467-018-05220-6.

IN SERVICE FOR THE NATION

Radhakrishnan R Nair, PhD
Laboratory Medicine & Molecular Diagnostics

The most significant accomplishment by the Laboratory Medicine and Molecular Diagnostics (LMMD), facility, which reflects the social commitment of RGCB by performing over 220 diverse nucleic acid-based testings is, getting itself accredited by NABL, ILAC (with recognition across the globe) and certified by NABH, for the 5th successive year. This at present is the only facility in India both in the Government sector and the private sector likewise, to have these many certificates of acceptance. This facility assists diagnostics by timely reporting of infectious and non-infectious diseases, at the lowest cost in the country. The guidelines for successful accreditation were published and are now a standard reference document for the country.

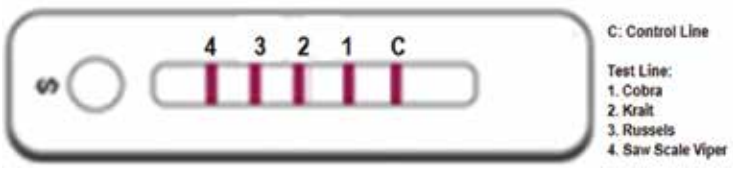
Seetha Dayakar, Heera R. Pillai, Sanughosh Kalpathodi, Ganesan Jeya Chandran, Radhakrishnan R. Nair, A Guide to Total Quality Management System (TQMS) in Molecular Diagnostics from Experiences in Seeking Accreditation and Implementation, SN Comprehensive Clinical Medicine (2019) 1:123–133. https://doi.org/10.1007/s42399-018-0018-3

The research and development group of LMMD drew national attention through the development of a rapid, economical, straightforward to manufacture, and operate, a lateral flow detection device for the assessment of snake envenomation. This kit is tested by impartial evaluators across the State and certified to be outclassing in accuracy and precision in the discovery of snake venom utilizing a single drop of the victim's blood. A lateral flow device with this ability and a two year shelf life, covering all the deadly snake venom detection, is a single strip, is conceptualized, developed, and verified for the first time in the world, attaining widespread media coverage.

FIGURE

Snake Venom Antigen Rapid Test Kit

Qualitative Immuno-chromatographic assay for rapid detection of Snake Venom antigen in human blood within10-15minutes.



VACCINATING WOMEN AGAINST CANCER

Professor
M Radhakrishna Pillai
FRCPath, PhD, FNA, FAMS, FNASc, FASc
Pathogen Biology Program

We investigate human immune response to natural infection and vaccines of three clinically important viruses. The HPV vaccination study evaluates the clinical and biological effectiveness of one, two and three doses of quadrivalent HPV vaccine in preventing cervical neoplasia. The second program does a comparative evaluation of natural versus vaccine induced immune response to the H1N1 influenza virus. The third study examines cellular and molecular immune responses in understanding reasons for measles vaccine failure (and success).

The initiation of the Indian HPV vaccine trial examining the efficacy of two-dose versus three-dose regimen in 2009 led to the establishment of a comprehensive HPV vaccine efficacy testing facility in my laboratory. The evidence generated on immune responses and infection outcomes following quadrivalent HPV vaccination has pioneered the evidence base for policy decisions by the World Health Organization (WHO) in implementation of these vaccines in low and medium income countries. We demonstrated that two doses of quadrivalent HPV vaccine, administered with an interval of 180 days or more, is non-inferior to the three-dose schedule and affords protection against incident and persistent infections by HPV 16, 18, 6,and 11 (Sankaranarayanan R et al, Lancet Oncol 2016). Subsequently, we showed that L1-binding antibody titres and neutralizing antibody titres against HPV types targeted by the vaccine in 15-18 year old two-dose recipients were non-inferior to 15-18 year old and 10-14 year old three-dose recipients until the 48 month time point (Bhatla N et al, Papillomavirus Res. 2018). We further demonstrated that, at a median follow-up of 7 years, no persistent HPV 16 infection and only one (0.2%) persistent HPV 18 infection was noted in the 3-dose and 2-dose cohorts compared to 1.7% HPV 16/18 persistent infections in unvaccinated women (Basu P et al, Papillomavirus Res. 2019).

We have been the first to demonstrate the efficacy of 2 dose HPV vaccination in older girls up to 18 years of age. This finding has led to HPV vaccination policy recommendation change by the WHO. In addition we could also demonstrate a robust and sustained immune response against HPV 16 and 18 over a 4-year period following single dose HPV vaccination. 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 (Sankaranarayanan R et al, Vaccine 2018). These results are promising towards the value of single dose HPV vaccination, particularly in low and medium resource settings.

RGCB @30

The well-known multi-centric cancer vaccine clinical trial, conducted by Professor M Radhakrishna Pillai and his team is a land mark study in vaccine efficacy testing.

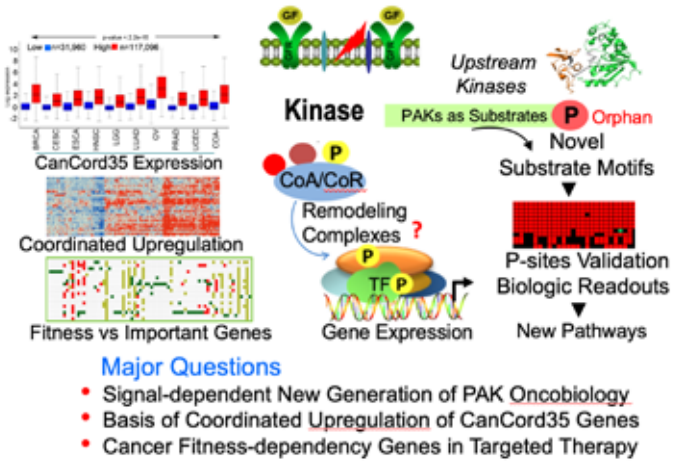
THE CANCER SIGNAL NETWORK

Rakesh Kumar, PhD

Distinguished Professor & National Chair in Cancer Research

The laboratory has been long interested in understanding the mechanisms utilized by growth factors to regulate distinct cancer phenotypes with a particular focus on cytoskeleton and chromatin remodeling and coordinated bifurcation and integration of nodular signals. The work has put the p21-activated kinase (PAK) family and NuRD coregulators on the cancer scientific map, including the discovery of the role and nuclear functions of PAK in human cancer for the first time. I have had the distinct privilege to associate and contribute to the academic and educational fabrics of RGCB for almost a decade of its 30- year transformed journey, first as a visiting distinguished professor starting mid-2010 and then as a faculty in mid-2017. During this time, while collaborating with Professor Pillai and co-directing doctoral research, the laboratory has published 6 original papers and 7 invited reviews from RGCB, and 3 papers and 5 invited articles with external collaborators in mainstream journals. These research topics have also allowed four of our PhD students to graduate, while the work of two current graduate students is progressing well. More recently, I along with Prof. Pillai postulated that cancer is a polygenic disease that is best tackled by pursuing a polygenic hypothesis. We discovered the co-upregulation of a set of 35 continuously organized protein-coding genes at a single locus in human cancer. We also developed a new, data-driven approach to potentially repurpose approved drugs for cancer-types for which these drugs have previously not been approved. The overarching goal of the laboratory continues to be to unearth the inner working of nodular molecules

FIGURE



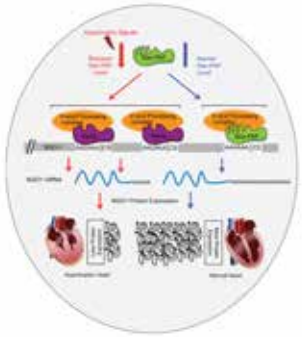
Rakesh S Laishram, PhD
Cardiovascular Diseases & Diabetes Biology Program

A PAP IN THE HEART

My laboratory focuses on the processing of coding and long non-coding RNAs and implications in human diseases with a particular emphasis in the heart. In a recent publication in Cell Reports (2018), we discovered a master regulator, RNA binding motif protein 10 (RBM10) of cardiac hypertrophy, a key heart condition involved in most heart pathologies including heart failure. RBM10 functions with poly(A) polymerase Star-PAP to regulate myocyte hypertrophy and apoptosis, the two integral components in the pathogenesis of heart failure. We demonstrated that Star-PAP-RBM10 controls an anti-hypertrophy gene program through alternative polyadenylation that generates multiple transcripts from a single gene of different UTR length. We have reported in another publication in Nucleic Acid Res., 2019 that the UTR length variation determines protein expressions of anti-hypertrophy regulators in the heart. Using physiologically relevant in vitro myocyte and in vivo rat heart model, we showed that reduction in RBM10 and Star-PAP expression causes myocyte hypertrophy in the heart. Re-expression of RBM10 and/or anti-hypertrophy regulator (NQO1) specifically with longer UTR rescues hypertrophy in the cardiomyocytes. Our results establish a central anti-hypertrophy mechanism involving RBM10-Star-PAP interaction that can be targeted for future heart failure preventive strategy.

FIGURE

Mechanism of hypertrophic signal mediated alternative polyadenylation operated through Star-PAP at the NQO1 UTR



PUBLICATIONS

Mohan, N., Kumar, V., Kandala, D., Kartha, C.C. and Rakesh S. Laishram. 2018. A new splicing independent function of RBM10 controls specific 3'-UTR processing to regulate cardiac hypertrophy in the heart. Cell Reports. 24:3539-3553 (https://doi.org/10.1016/j.celrep.2018.08.077).

Sudheesh, A.P., Mohan, N., Nimmy, F., Rakesh S. Laishram, and Richard Anderson. 2019. Star-PAP controlled alternative polyadenylation coupled poly(A) tail length regulates expression in hypertrophic heart. Nucleic Acid Res. gkz875 (https://doi.org/1 0.1093/nar/gkz875)

Rashmi Mishra, PhD
Neurobiology Program

TRADITIONAL MEDICINE INSPIRED EFFICACY FOR BRAIN TUMORS

Glioblastoma multiforme (GBM) is the most aggressive and deadliest brain tumor, noted for low survival rates due to ineffective chemotherapies and multiple relapses. Macropinocytosis is a crucial constitutive mechano-adaptive process through which both normal and tumor cells uptake excess nutrients in a fluid phase. Intriguingly, in contrast to constitutive macropinocytosis which is a 'calcium dependent' process, tumor cells were observed to predominantly rely on 'non-calcium dependent' macropinocytosis to acquire excess nutrients. We found that this switch is mainly because tumor cells, contrary to normal cells, are not efficient in handling excess calcium, which is required for constitutive macropinocytosis, and this can lead to uncontrolled fluid uptake. This knowledge clearly hinted that forcefully triggering calcium-burst in GBM cells could lead to excessive macropinocytotic uptake of extracellular fluid that may transform into irreversible hydraulic stress and cellular damage, enabling tumor eradication. In order to test this possibility, we scored Indian traditional medicinal plant Bacopa monnieri (BM) and its bioactive component Bacoside A as a potential drug candidate to disturb the delicate calcium mechano-homeostasis of tumor cells. BM has been previously shown to activate an intracellular calcium release kinase CaMK2A, thereby can modulate calcium levels. BM and Bacoside A could indeed generate dosage associated tumor specific disturbances in the hydrostatic pressure balance of the cell via a mechanism involving excessive phosphorylation of calcium/calmodulin-dependent protein kinase IIA (CaMKIIA/CaMK2A) enzyme that was further involved in the release of calcium from intracellular reserves. High intracellular calcium stimulated massive macropinocytotic extracellular fluid intake causing cell hypertrophy in the initial stages, excessive macropinosome enlargement and fluid accumulation associated organellar congestion, cell swelling, cell rounding and membrane rupture of glioblastoma cells. All these events finally culminated into a non-apoptotic, physical non-homeostasis associated glioblastoma tumor cell death, demonstrating Bacopa monnieri aqueous extract and its bioactive components as promising drug candidates for the deadly brain cancer-the Glioblastoma multiforme:

FIGURE

This work was published in the Frontiers in Molecular Neuroscience in 2017 (doi: 10.3389/fnmol.2017.00171).

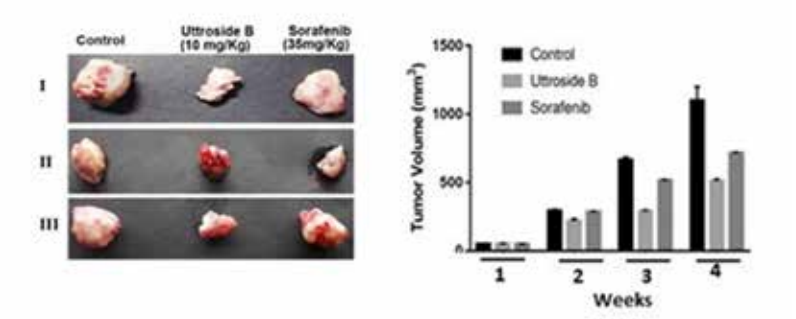
Ruby John Anto, PhD, FNASc
Cancer Research Program

LONG AWAITED HOPE FOR LIVER CANCER

My research focuses on bio prospecting for compounds having chemotherapeutic, chemopreventive or chemosensitizing potential. We demonstrated that curcumin sensitizes cervical cancer cells towards paclitaxel chemotherapy (Bavaet al., 2005; Bavaet al., 2011, Sreekanth et al., 2011, Thulasidasan et al., 2017) and breast cancer cells towards 5-FU chemotherapy (Vinod et al., 2013). We proved that curcumin is an excellent chemopreventive against nicotine induced proliferative signals (Puliyappadamba et al., 2010) and B[a]P-induced lung carcinogenesis (Vijayakurup et al., 2019). We also evaluated the chemosensitizing efficacy of resveratrol against docetaxel chemotherapy for breast cancer (Vinod et al., 2015) and Heteronemin against cytarabine chemotherapy for acute leukemia (Saikia et al., 2018). We also identified another compound, tryptanthrin, which exhibits excellent anticancer potential against melanoma (Antony et al., 2015) and non-melanoma skin cancer (Shankar et al., 2019). For these studies, I was awarded National Woman Bio-Scientist Award, by Department of Biotechnology and subsequently elected as Fellow of National Academy of Sciences and Kerala Academy of Sciences.

My laboratory identified a compound, Uttroside B, which exhibits exceptional cytotoxicity towards liver cancer cells (Nath et al., 2016) and is more potent than sorafenib, the only FDA-approved drug against liver cancer. Both national and international patents have been filed on this finding (Application No. 201641018401 dated 28 May 2016; PCT/ IN20 17/050204 dated 27th May 2017). The technology has been transferred to a multinational company. A MoU has been signed between RGCB and Oklahoma Medical Research Foundation (OMRF), USA, for further clinical evaluation of the compound. I received 'Keystone Symposia Global Health Travel Award' by Bill and Melinda Gates Foundation to present this work in the Keystone Symposia meeting-2019, held at Brazil.

FIGURE



Anticancer efficacy of uttroside B against hepatocellular carcinoma

UNDRESSING CHOLERA BACTERIA

Sabu Thomas, PhD
Pathogen Biology Program

Bacteria exist in two forms- planktonic and biofilm. Bacteria that reside within mature biofilms are highly resistant to antibiotics and host immune response due to the complex architecture and composition of the extracellular matrix. Recent studies showed the role of biofilm mode of life in the emergence of resistant strains, pathogenicity, host colonization and survival in the natural as well as human niches. So biofilm inhibition is considered as a potential anti-virulent strategy to treat infections caused by bacterial pathogens. The major finding from the laboratory included decoding the proteomic changes involved in the biofilmformation of Enterococcus faecalis, astrong biofilm forming chronic wound pathogenand elucidated potential biofilm determinants. The study unraveled LuxS quorum sensing and pheromone associated proteins in biofilm development of E. faecalis that can act as potential inhibiting targets in Enterococcal infections (Karthika et al., 2019). Also, tryptanthrin, a phytochemical was identified to possess strong anti-biofilm activity at sub-MIC (2 g ml-1) against Vibriocholerae, causative agent of cholera. LuxO was identified to be the putative target of tryptanthrin by molecular docking and real time analysis. The phytochemical was identified safe and possessed synergistic action with ciprofloxacin, a commonly used quinolone antibiotic to treat cholera (Narendrakumar et al., 2019).

PUBLICATIONS

Karthika.S, Lekshmi N, Joby John, Megha P.R, Sanil Gand, SabuThomas, (2019). Decoding the proteomic changes involved in the biofilm formation of Enterococcus faecalisSK460 to elucidate potential biofilm determinants. BMC Microbiology, 19:146.doi: 10.1186/s12866-019-1527-2

Narendrakumar L, Theresa M, Krishnankutty Chandrika S and SabuThomas (2019). Tryptanthrin, a potential biofilm inhibitor against toxigenic Vibrio cholerae, modulating the global quorum-sensing regulator, LuxO. Biofouling, 35(10): 1093-1103doi: 10.1080/08927014.2019.1696315

Sanil George, PhD
Transdisciplinary Biology Program

FROGS TO THE RESCUE

The endemic amphibian fauna of the Western Ghats offers a unique model system to explore the hitherto unexplored novel molecules present in their skin secretions. Studies conducted on the skin secretion of an endemic frog (Hydrophylax bahuvistara) yielded novel anti-microbial peptides belonging to Brevinin and Esculentin families. The peptides showed antibacterial activity against both Gram-positive and Gram-negative bacteria. They exhibited low hemolysis and potent cytotoxic activity against cancer cell lines. Upon amidation, the peptides showed increased activity against the microbes without altering their hemolytic and cytotoxic properties. The peptides initially induce membrane depolarization, followed by pore formation in a concentration-dependent manner. A microscopic examination revealed the fact that the peptides are capable of destroying bacterial cells physically. The activity of these peptides against Gram-negative bacteria was dependent on the presence of divalent cations (Ca2+ and Mg2+) but not in Gram-positive bacteria. It was found that the sub-MIC of both peptides induced transient pores on the bacterial membrane. The study emphasizes to utilize the ability of these peptides to produce transient pores at sub-MICs in combinatorial therapy.

PUBLICATIONS

The research was published in the International Journal of Peptide Research and Therapeutics (2017; DOI 10.1007/s10989-017-9598-0); Chemical Biology and Drug Design (2018: DOI: 10.1111/cbdd.12937); Animal Biotechnology (2019; DOI: 10.1080/10495398.2019.1668402.) and Natural Product Research (2019; DOI: 10.1080/14786419.2019.1644636)

RGCB @30

Laboratory Medicine and Molecular Diagnostics (LMMD), the molecular diagnostics arm of RGCB, provides the services of molecular diagnostics to the society, and have been awarded the NABL accreditation and NABH certification.

T R Santhosh Kumar, PhD
Cancer Research Program

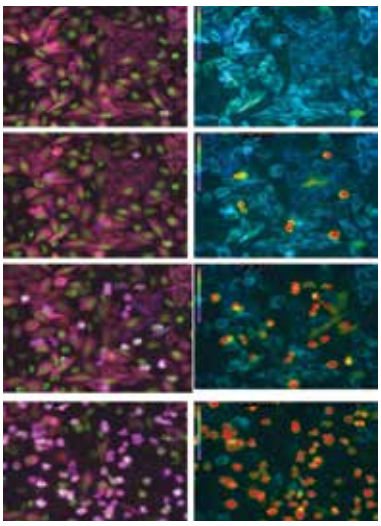
DEFINING TREATMENT RESISTANT CANCER

Secondary emergence of aggressive therapy-resistant phenotype after chemotherapy is a serious clinical problem. To understand the molecular and cellular events, we have developed a real time model of cell death and cell cycle that reveled rare escape of cells that generate stable colonies with an aggressive tumor stem cell-like phenotype. These cells displayed higher CD133 and Oct-4 expression. Notably, the drug-selected cells that contained low levels of reactive oxygen species (ROS) also showed an increase in antioxidant enzymes. Consistent with this in vitro experimental data, we observed lower levels of ROS in breast tumors obtained after neoadjuvant chemotherapy compared with samples that did not receive preoperative chemotherapy. These latter tissues also expressed enhanced levels of ROS defenses with enhanced expression of superoxide dismutase. Higher levels of Oct-4 and CD133 were also observed in tumors obtained after neoadjuvant chemotherapy. Further studies provided evidence for the stabilization of Nrf2 due to reduced 26 S proteasome activity and increased p21 association as the driving signaling event that contributes to the transition from a high ROS quiescent state to a low ROS proliferating stage in drug-induced tumor stem cell enrichment.

FIGURE

The real time sensor cell for cell death and cell cycle: The nuclear green is a marker for G2 phase of cell cycle. The cytoplasm represents the FRET sensor of cell death that changes ratio upon caspase activation. The left panel is the time-lapse sequence of dying cells in ratio mode.

Merged channels FRET Ratio image



Sara Jones, PhD
Pathogen Biology Program

PROTECTING CHILDREN AGAINST MEASLES

Measles is a global public health problem and a leading cause of death in children worldwide. One infected person can infect up to 18 others, making it the most transmissible human virus. Measles vaccination began in India in the 1980s and in 2010 the country adopted the two-dose schedule to further reduce measles mortality. Despite high levels of two-dose vaccine coverage, outbreaks continue to occur, accounting for nearly half of all global measles mortality. While most of the cases are unvaccinated individuals, measles vaccine failure does play a role in these outbreaks. In fact, 10-50% of the cases in recent outbreaks have occurred in recipients of two doses of measles vaccine (MV). In order to eradicate measles from India, in 2017, a phased supplementary immunization scheme using measles-rubella (MR) vaccine targeting children aged 9 months–14 years was initiated. The universal measles vaccination program has brought down the measles transmission significantly, but vaccine failure is not uncommon. It was in this background that the National Institutes for Health waraded a RO1 grant to RGCB, Mayo Clinic and Emory University to investigate the biological factors involved in measles vaccine success and failure.

The primary focus of our group is to understand why vaccines fail to protect a subset of the vaccinated cohort. The possibilities include inefficient vaccination due to malnutrition, vitamin deficiencies in children that could diminish immune response to measles vaccine and the presence of measles-specific maternal antibodies in infants. Antibodies passed from the mother to foetus during pregnancy interfere with the immune response tovaccine and hence the first vaccination age for measles has been fixed at nine months of age after the maternal antibodies have dissipated. In our earlier study we observed that children under the recommended vaccination age of nine months are highly susceptible to measles and more importantly, waning of measles specific antibodies, occurs with time in those vaccinated with a single dose of vaccine. We also observed rare cases of measles in those who have had multiple doses of vaccine. To understand the sero-conversion rate in children (4-16 years) who had received 2-3 doses of measles vaccine, we screened for measles specific IgG antibodies. IgG titers in the children ranged between2.8 to 58.2 NTU (Novatech Unit). A total of 388 individuals (92.02%) were found to be seropositive, 12 (3.09%) were equivocal, and 19 (4.89%) were sero-negative. Significant variations in IgG titres were not noticed between female and male subjects ($p \leq 0.058$). Similarly, there was no significant difference in measles IgG specific antibody levels between age groups 4-16. Serum retinol levels were also assessed and the data suggested that the serum vitamin A levels in children were inversely related to age with Vitamin A levels decreasing with increase in age ($p=0.002331$). We further identified a core set of 36 genes playing a role in vitamin storage, transport, metabolism, and signalling. Single Nucleotide Polymorphism (SNPs) from these genes will be identified and selected for genotyping to understand its association with variations in immune responses.

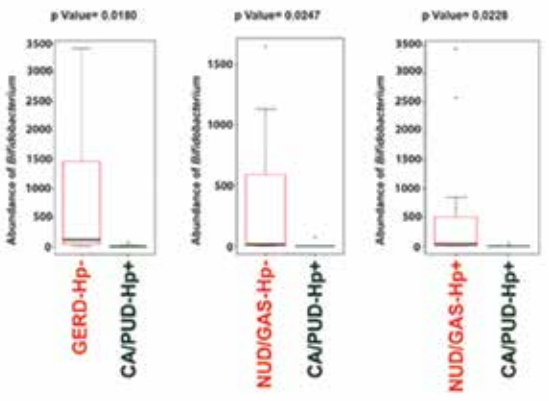
Santanu Chattopadhyay, PhD
Pathogen Biology Program

A BUG IN THE STOMACH

Low Bifidobacterium abundance in intestinal microbiome is related to Helicobacter pylori infection and severe gastroduodenal diseases like peptic ulcer and gastric cancer. Why most Helicobacter pylori infected individuals remain asymptomatic while a certain proportion develops peptic ulcer and gastric cancer has remained enigmatic. Since only a fraction of the H. pylori infected population gets affected the influences of other factors in the development these diseases are undeniable. Here, we studied the associations among H. pylori infection and its virulence genes, intestinal microbiome and clinical status of Trivandrum residents (N=375) in Southwest India. Our results show that gastric colonization by virulent H. pylori strains is necessary but not sufficient for developing these severe gastroduodenal diseases. We found that distinct gut microbial pools exist for H. pylori infected vs non-infected individuals. Notably, those who carried H. pylori in stomach and had developed aggressive gastroduodenal diseases also had lower relative abundance of Bifidobacterium in intestine (Figure 1). This is valuable information for developing effective probiotic as well as early prognosis of gastric cancer and peptic ulcer. The results also show the link between lower gastrointestinal microbes and upper gastrointestinal diseases.

FIGURE

Box plot analysis showing the abundance of Bifidobacterium in intestinal microbiome for the H. pylori infected patients with gastric cancer or peptic ulcer (CA/PUD-Hp+) as compared to the individuals with milder diseases like gastroesophageal reflux disease without H. pylori infection (GERD-Hp-), non-ulcer dyspepsia or gastritis without H. pylori infection (NUD/GAS-Hp-) and non-ulcer dyspepsia or gastritis with H. pylori infection (NUD/GAS-Hp+). The analysis shows that the abundance of Bifidobacterium is significantly lower for the CA/PUD-Hp+ group than other groups.



Saraswati Nayar, PhD

Plant Biotechnology & Disease Biology Program

INCREASING ALGAL BIOMASS

Overexpression of HRG in Chlorella led to a longer log phase and stationary phase compared to the wild type. The stationary phase of wild type was reached around 19 days post inoculation (dpi) and for HRG overexpressor it was around 28 dpi as the growth of its cells was initially slower than the wild type. The HRG overexpressor survived for almost two weeks more than the wildtype. The biomass of the HRG overexpressor was more than the wildtype in terms of dry cell weight in their respective stationary phases. The HRG overexpressor had almost 46% increase in biomass compared to the wild type strain during their respective stationary phases without any extra effort such as changes in medium composition or any external input. There was also approximately 30% increase in total carbohydrates and approximately 20% increase in total lipids. It was interesting to note that the size of the cell in the overexpressor had also increased by almost 15-20% at the same dpi. The cell number in the overexpressed strain was 11% more than the wild type during their respective stationary phases. This seems to be a very good way to increase biomass without much effort just by elongating the life of the algae.

RGCB @30

BioNest, Kochi, the business incubator in association with Kerala Startup Mission, caters to translational biotechnology and nurtures entrepreneurship among young scientific and inquisitive minds.

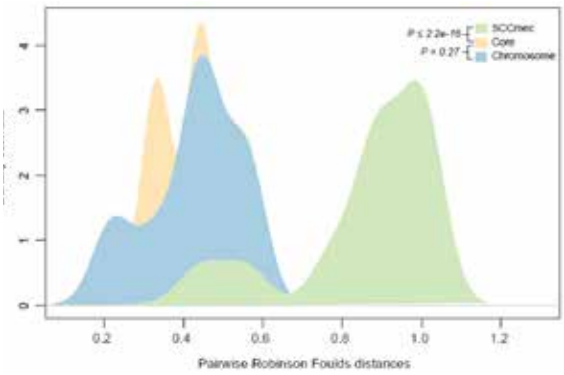
Shijulal Nelson Sathi, PhD
Transdisciplinary Biology Program

EVOLUTION OF ANTIBIOTIC RESISTANCE

Antibiotic resistance in S. aureus is a global health problem. However, the origin and evolutionary route of resistant genes in S. aureus are stillremaining unclear. Phylogenomic methods developed to analyze largescale genomic data were applied to 152 completely sequenced S. aureus strains in comparison with 7,529 non-S. aureus reference bacterial genomes. Our results reveals that S. aureus has a large open pan-genome where 97 (55%) of its known resistant related genes belonging to its accessory genome. The physically linked mec-box genes (MecA-MecR-MecI) that are responsible for the maintenance of SCCmec elements is not unique to S. aureus, instead it is widely distributed within Staphylococcaceae family. The phyletic patterns of SCCmec encoded resistant genes in Staphylococcus species are significantly different from that of its core genes indicating frequent exchange of these genes between Staphylococcus species. Our in-depth analysis of SCCmec resistant gene phylogenies reveals that genes such as blaZ, ble, kmA and tetK that are responsible for beta-lactam, bleomycin, kanamycin and tetracycline resistance in S. aureus were laterally transferred from non-Staphylococcus sources. In addition, at least 11 non-SCCmec-encoded resistant genes in S. aureus were laterally acquired from distantly related species. Our study evidently shows that gene transfers played a crucial role in shaping the evolution of antibiotic resistance in S. aureus.

FIGURE

Distribution of pairwise tree distances of core and resistant genes.



PUBLICATIONS

John J, George S, Nori SRC, Nelson-Sathi S. Phylogenomic Analysis Reveals the Evolutionary Route of Resistant Genes in Staphylococcus aureus. Genome Biol Evol. 2019 Oct 1; 11(10): 2917-2926. doi: 10.1093/gbe/evz213. PubMed PMID: 31589296;

Award: Kerala Sate Young Investigator Award 2019

E V Soniya PhD, FNASc

Plant Biotechnology & Disease Biology Program

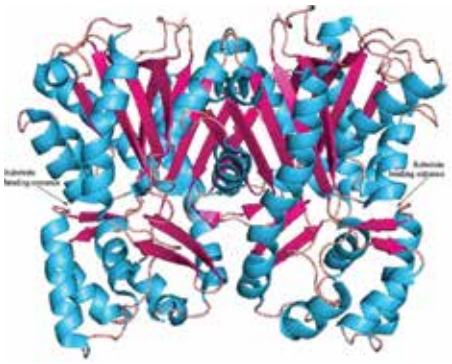
PLANT SCIENCE TO UNDERSTAND METABOLITES AND DISEASE

Ala-133, at the putative QNS active site, was identified using homology-based structural modelling. Site-directed mutagenesis and kinetic analysis indicated that the catalytic efficiency of the protein to accept larger acyl-CoA substrate is several fold higher than that for smaller substrates. This work also shed light on the evolution of QNS from a structurally homologous chalcone synthase type III protein by the substitution mutation of active site residues.

Our laboratory reported first time the presence of the least explored small RNAs, derived from ribosomal RNAs (srRNAs) and transfer RNAs (tRFs) in black pepper. The sRNAs profile and analysis of Piper nigrum, a unique magnoliid plant have unveiled the candidature role these novel sRNAs during Phytophthora capsici infection. A high-throughput systematic analysis of the small RNAome (sRNAome) by our group has revealed the predominance of 5 tRFs in the infected leaf and root. The differential expression and cleavage of 5 5.8S srRNAs in Phytophthora infected P. nigrum tissues indicated the critical biological functions of these srRNAs during stress response. We have also documented the association of these novel sRNAs with Argonaute proteins, and the insilico target prediction and the cleavage validation studies have reinforced the regulatory role of srRNAs and tRFs is stress response.

FIGURE

Identification and characterization of a Type III Polyketide Synthase involved in Quinolone Alkaloid Biosynthesis from Aegle marmelos Correa.



PUBLICATIONS

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Asha Srinivasan and E.V Soniya (2017). The sRNAome mining revealed existence of unique signature small RNAs derived from 5.8SrRNA from Piper nigrum and other plant lineages. Scientific Reports. 7:41052.

A FRUITY SOLUTION TO BREAST DISEASE

Sreeja S, PhD
Cancer Research Program

Pomegranate, from very ancient times, has been used to treat various ailments in Ayurveda. The vast literature of its medicinal properties prompted us to investigate its Selective Estrogen Receptor Modulatory (SERM) activity. Along this line, we found that the methanolic extract of pomegranate pericarp displays a SERM profile and may have potential for prevention of estrogen-dependent breast cancers with beneficial effects in other hormone-dependent tissues. Also, it could reduce the LDL levels induced upon ovariectomy and prevent the cell proliferation induced by 27 hydroxycholesterol, an endogenous SERM. This cholesterol metabolite has also been found to act via estrogen receptor and result in breast cancer proliferation. Pomegranate has abundant amount of ellagitannins that are broken down to ellagic acid within the body, which further is metabolized to urolithins by colon microflora. The past decade has witnessed extensive research on metabolites of ellagic acid from pomegranate and they have been found highly beneficial for human health. We are now in the journey of finding whether urolithins can act as an ideal SERM.

FIGURE

PUBLICATIONS

Sreeja, S., Kumar, T. R. S., Lakshmi, B. S., & Sreeja, S. (2012). Pomegranate extract demonstrate a selective estrogen receptor modulator profile in human tumor cell lines and in vivo models of estrogen deprivation. The Journal of Nutritional Biochemistry, 23(7), 725-732.

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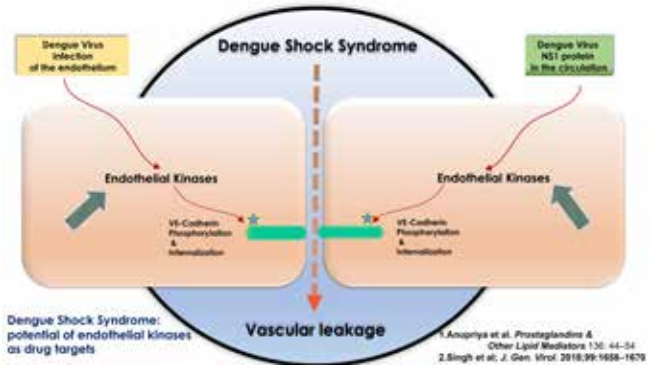
TACKLING DENGUE

E Sreekumar, MVSc, PhD
Pathogen Biology Program

Dengue is a mosquito-borne viral disease of major concern. Most dengue patients recover without complications after a short- period of febrile illness. However, a small percentage of them proceed to develop shock syndrome, a potentially fatal condition.

Our understanding on the mechanisms of shock syndrome development in dengue is limited. So much so, there are no specific drugs available to treat such patients; and current management is only symptomatic and empirical. We identified this as a critical need that demanded urgent attention while establishing the dengue virus research program in RGCB in the last decade. Our concerted efforts using dengue infection models have identified a few endothelial cell kinases as critical players. Kinases involved in Sphingosine signaling pathway (Anupriya et al, 2018) and Angiopoeitin/ Tie-2 signaling pathway (Singh et al, 2018) were found to contribute to endothelial dysfunction in dengue (Fig.1). Since many FDA approved kinase inhibitors are available, we explored the possibility of using them to alleviate the enhanced permeability. Dasatinib, an Src-family kinase (SFK) inhibitor that prevents Src phosphorylation, was found to be very effective. Also, initial results of targeting ROCK Kinase, SRC-family kinases and Sphingosine Kinases seem to be highly promising. We are steadily moving towards our goal to evolve a drug-repurposing approach for therapeutic use of these kinase inhibitors in clinical cases of dengue shock syndrome.

FIGURE



PUBLICATIONS

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Singh S, Anupriya MG, Modak A, Sreekumar E (2018). Dengue virus 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. 99:1658–1670

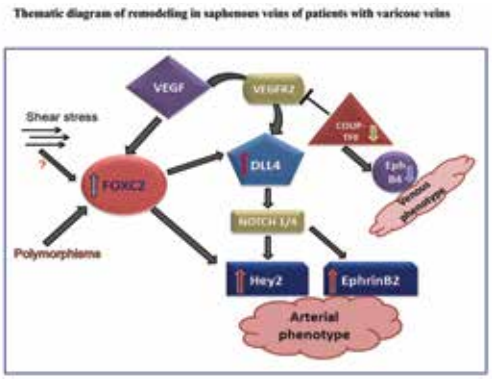
Sumi S, PhD

Cardiovascular Diseases and Diabetes Biology Program

UNDERSTANDING TWISTED VEINS

Varicose veins are the earliest manifestation of incompetence in saphenous and deep venous system. Pathogenesis of this common venous condition is still not elucidated which leads to several ineffective management strategies. Delineating the pathogenesis of varicose veins is crucial to develop non-invasive therapeutic approaches without post-treatment relapse. Blood reflux in larger veins was hitherto considered the key factor for varicose veins. Based on our studies in 6350 patients with venous disease, we found that reflux and varicosity in smaller reticular veins and tributaries is associated with severe disease manifestations, rather than the involvement of large truncal saphenous veins (Int J Angiol 2018). Of note is the fact that a positive family history is a strong risk factor for varicose veins. We demonstrated that polymorphism in FoxC2 gene promoter is a predisposing factor for varicose vein development (PLoS ONE 2014). We went on to study how FoxC2 initiate the venous wall remodelling that is characteristic of varicose vein pathology. We found that the molecular alterations in FoxC2-Dll4-Hey2 signalling are associated with non-physiological arterialization of saphenous veins in varicosities (Lab Invest 2016). Current focus of our lab is to delineate regulators of venous remodelling and identify compounds that can ameliorate abnormal arterialization

FIGURE



PUBLICATIONS

N Radhakrishnan, Deepu George, R Jayakrishnan, Sumi S*, CC Kartha*. Vein size and disease severity in chronic venous diseases. International Journal of Angiology2018; 27(4):185-189.* Co-corresponding author.

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Suparna Sengupta, PhD
Cancer Research Program

CANCER CYTOSKELETON

Our laboratory deals with proteins and external agents that alter mitosis. Since cell division and apoptosis are inherently related to cancer, antimitotic drugs that cause apoptosis are widely used in the treatment of cancer. However, their use is limited by drug resistance phenotype, high cost of treatment and several other drug specific limitations. We have developed a class of compounds that show high preclinical efficacy in tested models of colon and breast cancer. Through a series of papers published in British Journal of Pharmacology, Apoptosis, JPET, Mol Cancer Therapeutics, Carcinogenesis and Molecular Cancer, we have shown that 2,4-diaminothiazoles are highly effective in killing cancer cells targeting microtubule dynamics and tubulin in its colchicine binding site. The compounds can also escape multidrug resistance in human xenograft models as is shown by highly used anticancer agents. Further these compounds could inhibit angiogenesis and were effective in a p53 independent way even in Ras/Raf mutated colon cancer models. The team has one Indian and one US patent patent for preparation of 2,4-diaminothiazoles. Suparna Sengupta received the National Young Woman Bioscientist award from DBT in 2005 and Indian Association of Cancer Research Award 2003 for this work. Currently, the laboratory is also looking for the mechanisms of involvement of the protein fodrin in cancer. They have showed for the first time that fodrin is a component of γ-Tubulin ring complex and is involved in the regulation of microtubule nucleation, chromosome alignment and organization of functional microtubules during mitosis. These studies have been published in journals including J Cell Biochem, PLoS One, FEBS Lett and Cell Cycle.

FIGURE

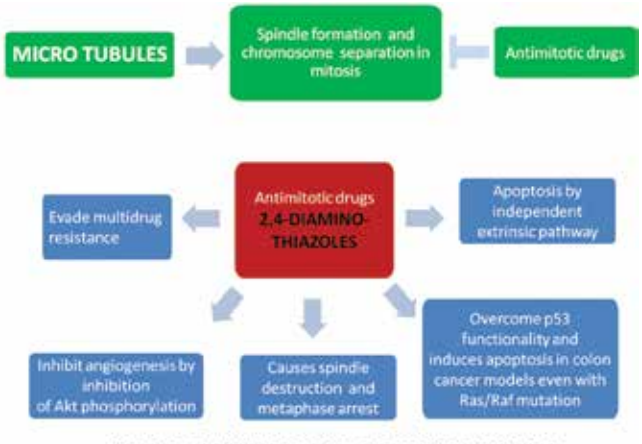


FIGURE 1. ANTIMITOTIC DRUGS: 2,4-DIAMINO-THIAZOLES

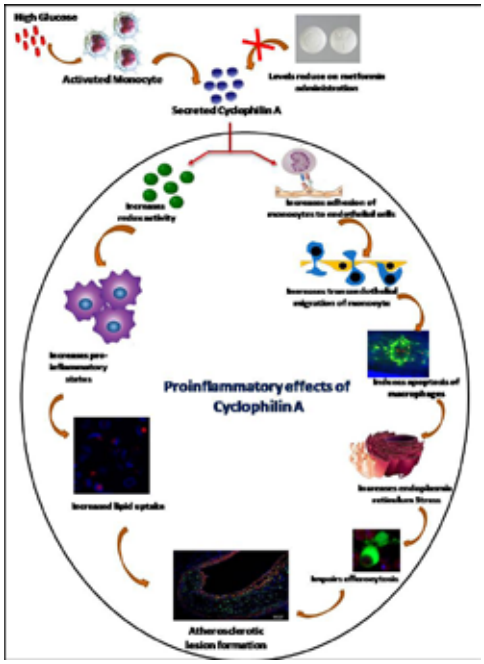
Surya Ramachandran, PhD

Cardiovascular Diseases and Diabetes Biology Program

PREVENTING HEART DISEASE IN DIABETES PATIENTS

Our studies on secretory monocyte proteins using in vitro cellular systems and clinical patients of diabetes mellitus associated coronary artery disease have led to the identification of cyclophilin A as an important marker for detecting coronary artery disease early in patients with type 2 diabetes (Proteomics, 2012; Cardiovascular Diabetology, 2014). We have described a possible cellular basis by which cyclophilin A accelerates atherogenesis in diabetes mellitus (Cardiovascular Diabetology, 2016). Recently, we also identified Metformin as a suppressor of proatherogenic effects of cyclophilin A in high glucose conditions by attenuating expression of the cytokine and repressing the cytokine induced decrease in AMPK-1α activity in macrophages (Clinical Science, 2018). We are in the process of identifying suitable receptors/ agents, which can inhibit its action thus preventing progression of atherosclerosis in diabetes mellitus. In a collaborative study with Madras Medical Mission, Chennai, we are conducting a prospective observational study to assess the levels of Cyclophilin A as a predictor of vascular risk in patients with Type 2 Diabetes Mellitus. Surya Ramachandran received the Torrent Young Investigator Award (2017) and the ICMR Chaturvedi Kalawati Jagmohan Das Memorial Award (2018) for these research findings.

FIGURE



Tessy Thomas Maliekal, PhD
Cancer Research Program

PEPTIDES TO DEFINE TUMORS

Since cancer is a leading killer worldwide, further research and development is the need of the hour. Our laboratory focuses on methods for early detection and improvement of treatment efficacy. We address these issues by using peptides as a tool and showed that peptides can be designed which can go into live cells and bind to defined targets (Kochurani et al, 2015, Sci Rep) and its possible use in live sorting in different areas of biology (Abraham et al, 2017, Cellular and Molecular Life Sciences). Another peptide that was designed was able to detect oral cancer and its lymph node metastasis in mouse models, even in the initial stages. We demonstrated (Suganya et al, 2016, Scientific Reports), that it could be used for predicting surgical margins. Another discovery from the laboratory was the identification of the target of a host defense peptide from frog, which is the active receptor complex of IL6 pathway, involved in immune response. Surprisingly, the signaling is twisted when this peptide binds to an already active receptor complex, and results in apoptosis. This discovery could be exploited for treatment of disorders involving aberrant activation of IL6 pathway, including arthritis and cancers.

PUBLICATIONS

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Suganya SA, Kochurani KJ, Nair MG, Louis JM, Sankaran S, Rajagopal R, Kumar KS, Abraham P, P GB, Sebastian P et al (2016) TM1-IR680 peptide for assessment of surgical margin and lymph node metastasis in murine orthotopic model of oral cancer. Sci Rep 6: 36726

RGCB @30

RGCB pavilions at consecutive India International Science Festival (IISF) starting from 2016 showcased its high quality research in a supremely innovative approach that fetched the best pavilion award in 2019.

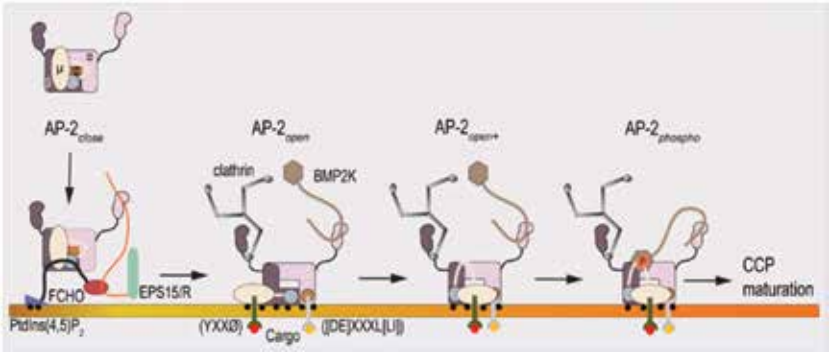
P K Umasankar, PhD
Transdisciplinary Biology Program

HOW CELLS SWALLOW?

The overarching theme of my laboratory is to understand the regulatory mechanisms of clathrin-mediated endocytosis (CME), a process vital for the internalization of most transmembrane proteins (cargo) in eukaryotes. Aberrations in this process are hallmarks of cancer, metabolic and neurological diseases. Furthermore, viruses and intracellular pathogens hijack CME for cellular entry and dissemination. Despite its clinical relevance, the regulatory mechanisms of CME are poorly understood. In 2017, we identified a novel kinase (BMP2K) that promotes CME by reversibly phosphorylating clathrin adaptor protein complex AP-2, the core organizer of CME. By integrating reverse genetic, pharmacological and biochemical approaches in genome-edited mammalian cells, we demonstrated that BMP2K functions in an allosteric feed-forward axis along with FCHO-EPS15/R protein complex to activate AP-2 on plasma membrane. In collaboration with Institute of Life Sciences, Bhubaneswar, we used D. rerio (zebrafish) model and showed that the FCHO-AP-2-BMP2K axis is vital for spine formation in vertebrates. These findings are currently under consideration in the journal eLife. Our findings propose new working model for CME (Figure) that may help identify novel inhibitors and activators of CME for various clinical uses including iron and cholesterol treatment, anti-viral therapy, nanodrug delivery to tumor cells, spine related disorders etc.

FIGURE

Our proposed model for clathrin-mediated endocytosis

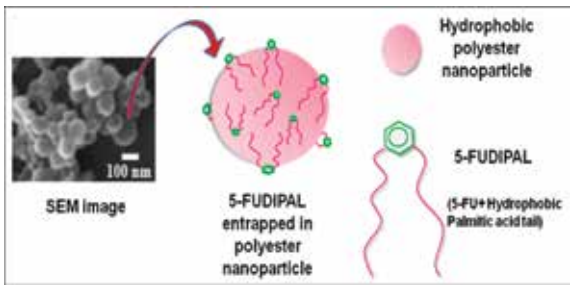


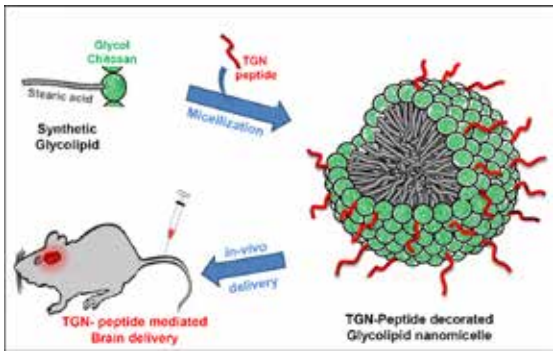
G S Vinod Kumar PhD
Cancer Research Program

TAKING DRUGS INTO THE TUMOR

We focus on designing and development of peptide synthesis and multifunctional nanostructures for programmed drug delivery targeting systems in cancer. Our results have been published in leading scientific journals. In addition we have Indian and US patents. One such system developed is a prodrug with 5-fluorouracil (5-FU), a lipid drug conjugate. The study revealed that drug could conjugate to lipid without losing its activity. The structural-based approach to facilitate enhanced drug loading in nanoparticle can improve efficacy by increasing half-life of the drug (N.Ashwanikumar et al. Acta Biomaterialia 2014; Fig.1). The second system developed is self-assembling glycolipid nanomicelles decorated with a targeting peptide (TGN) as a drug delivery system (DDS) for crossing the blood–brain barrier (BBB). The green synthesis of the glycolipid polymer followed by TGN peptide conjugation produced nanomicelles with desired physicochemical properties. In vitro and in vivo analysis of the nanomicelles demonstrated the TGN peptide-mediated entry into the rat brain within one hour post injection; support the efficacy of this new DDS as a potential therapeutic cargo for crossing the BBB (S.Meenu Vasudevan et al, Biomaterials Science 2019; Fig.2). The ongoing work focus to develop injectable post surgical gel based implant systems for brain tumor.

FIGURE





RGCB @30

In 2005, during his first year at RGCB, the then President of India, Late His Excellency Dr. A P J Abdul Kalam, visited the institute to inaugurate the International Symposium on Translational Research, Apoptosis and Cancer.

SAVOURING THE MOMENTS

1999

All India Cell Biology Conference

2005

INSA-Dr.M R DAS Memorial Lecture

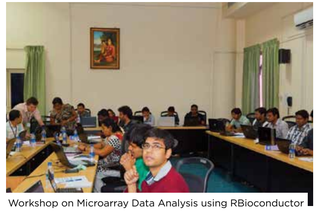
Role of Media in Promoting New Research in Biotechnology

2008

International Symposium on HPV

2013

Second Ramalingaswami Re-entry Fellowship Conclave



Workshop on Microarray Data Analysis using RBioconductor

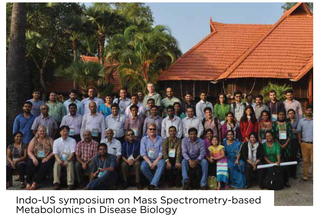
2014

Swachh Bharat Mission, Gandhi Jayanti

IACR 2014

General Body of RGCB

Next Generation Sequencing Data Analysis Workshop



Indo-US symposium on Mass Spectrometry-based Metabolomics in Disease Biology

2015

Arogya Expo

National Technology Day

Science Day Celebration

Embo Conference

2018

India International Science Festival (IISF)

Largest innovation hub opened in Kochi

Arumugam Award

Science expo

RGCB Foundation Day

2018

Flag hoisting at at RGCB-BioNest Campus

Outreach program as part of IISF

Regional Children's Science Congress

National Science Day

National Women Bioscience Award

2019

Onam

Young Scientist Award from the Indian Society for Parasitology

2019

International Womens Day

Independence Day celebrations

TMA Management Leadership Award

Showcasing RGCB Woman Science Power

2019

National Science Day

IISF Outreach Programme

ICMR Chaturvedi Kalawati Jagmohan Das Memorial Award

Swachh Bharat Abhiyan

Elephants Get Own Genetic IDs

Launching PULSE, the quarterly official RGCB newsletter

Anti terrorism Day

Best Women Scientist Award, National Academy of Biological Sciences

2019

Dr. Shijulal Nelson Sathi receiving Young Scientist Award from the Govt of Kerala

Hon. Governor of Mizoram, Shri Kummanam Rajasekharan's visit to RGCB

2020

Honorable Justice K.T. Thomas, Former Supreme Court Judge and outgoing chairman, RGCB Human Ethics Committee visiting RGCB

Dr. K R Mahendran receiving Merck Young Scientist Award

ICMR - Dr. Prem Nath Wahi Award

Prof. M Radhakrishna Pillai receiving Sun Pharma Award

The RGCB MSc Biotechnology 1st year students along with Dr. Renu Swarup, Secretary, Dept. of Biotechnology

FUELING DISCOVERIES

AWARDS AND HONOURS

	NAME & DESIGNATION	YEAR
1	**ASHA S NAIR,** Scientist F	
	ICMR International Fellowship for Young Biomedical Scientists	2011-2012
2	**ARUMUGAM RAJAVELU,** Program Scientist	
	Young Scientist Medal Award, from Indian Society for Parasitology, JNU, New Delhi	2019
	Recipient of the Kerala State Young Scientist Award, from KSCSTE, Govt of Kerala	2019
	Recipient of the SERB Early Career Research award with research grant, Department of Science and Technology, Government of India	2016
	Recipient of the Innovative Young Biotechnologist Award (IYBA), Department of Biotechnology, Government of India	2015
	Recipient of the DST INSPIRE Faculty award, Department of Science and Technology, Government of India	2013
3	**DEBASREE DUTTA,** Scientist EII	
	DST Fast Track fellowship	2013
	DST International Travel Grant	2013
	DBT International Travel Grant	2014
	DBT National Women Bioscientist Award	2016
	Best talk at World Congress on Cancer	2018
	Second best poster award in Women conclave at ISSF	2018
	EMBO Travel award	2019
4	**K.B.HARIKUMAR,** Scientist E1	
	Ramalingaswami re-entry fellowship from Department of Biotechnology, Government of India	2012-2017
	Fast track fellowship from Department of Science and Technology, Government of India	(2013-2016)
	Travel award from Centre for International Co-operation in Science (CICS), Chennai	2014
	International Brain Research Organization (IBRO)'s North American Laboratory activity program at UT. M. D. Anderson Cancer Center, Houston, TX	2015

5	**JACKSON JAMES,** Scientist F	
	National Bioscience Award -2016, Dept. of Biotechnology, Govt. of India.	
	DST Young Scientist Award (2004, Fast Track Scheme)	
6	**MAHENDRAN KR,** Scientist E1	
	DBT Innovative Young Biotechnologist Award	2017
	DST SERB Early Career Award	2018
	Merck Young Scientist Award (Winner in Biological Science)	2019
7	**MALINI LALORAYA**	
	Prof. G. P. Talwar Gold Medal Award of Indian Society for Study of Reproduction & Fertility	2020
	Conferred Fellowship in Reproduction and Endocrinology	2019
	Elected Fellow of The National Academy of Sciences, India (NASI)	2018
	Elected Overseas Fellow of the Royal Society of Medicine	2018
	Labshetwar Award of Indian Society for Study of Reproduction & Fertility	2014
	Raine Visiting Professorship University of Western Australia by Raine Medical Research Foundation	2008
	Raine Visiting Professorship University of Western Australia by Raine Medical Research Foundation	2006
8	**S. MANJULA,** Scientist EII	
	DBT overseas training fellowship	2007
9	**M RADHAKRISHNA PILLAI,** Professor	
	Sun Pharma Research Award in Medical Sciences	2019
	Management Leadership Award of the Trivandrum Management	2019
10	**DR. R. V. OMKUMAR,** Scientist-G	
	Visiting Scientist Fellowship of National Institute of Advanced Industrial Science and Technology (AIST), Japan	2009
	DST- Lockheed-Martin India Innovation Growth Programme	2012-13
11	**DR. PRADEEP KUMAR G,** Scientist G	
	National Bioscience Award for Career Development from Department of Biotechnology, Govt. of India	2006-2007
	Biotechnology Overseas Associateship (BTOA), Department of Biotechnology	2008
	Labhsetwar Foundation (USA) Award of Indian Society for the Study of Reproduction and Fertility	2015
	Dr. TC Anand Kumar Memorial Gold Medal and Oration Award of Indian Society for the Study of Reproduction and Fertility, India	2016

	Dr. Subhas Mukherjee Memorial Oration Award of Association of Clinical Embryologists, India	2016
	19th Royan International Research Award	2018
	Prof. P. Govindarajulu Oration and Gold Medal of Society for Reproductive Biology and Comparative Endocrinology	2018
12	**PRIYA SRINIVAS,** Scientist F	
	NCI's Cancer Prevention Fellowship, National Cancer Institute, National Institutes of Health, USA.	2016
	Indian Council of Medical Research (ICMR) Prem Nath Wahi Award	2013
	DBT overseas Associateship (Visiting Scientist, Mayo Clinic, Rochester, Minnesota, USA)	2009
	AACR-NCI International Investigator Opportunity Award in recognition of the need to globalize cancer research and to equalize the exchange of scientific knowledge - presented at AACR meeting at Washington DC	2008
	DST Young Scientist Project (Fast Track Scheme)	2004
13	**RADHIKA NAIR,** Program Scientist	
	Ramanujan Fellowship	2015-2020
	Early Career Research Grant	2016-2019
14	**RAKESH LAISHRAM,** Scientist E-II	
	Swarnajayanti Fellowship – Department of Science and technology	2019
	Innovative Young Biotechnologist Award (IYBA), DBT, India	2013
	Wellcome Trust (UK) - India Alliance Intermediate Fellowship	2012
	Ramalingaswami Fellowship, Department of Biotechnology, India	2012
15	**RASHMI MISHRA,** Scientist EI	
	DBT-Ramalingaswami Fellowship	2012
	DBT-Rapid Grant for Young Investigator Award	2013
16	**SANIL GEORGE,** Scientist-EII	
	Travel Bursary Award, Consortium of Barcode of Life, Washington, USA	2009
17	**SHIJULAL NELSON-SATHI,** Scientist C	
	Kerala State Young Scientist Award	2019
18	**DR. E. SREEKUMAR,** Scientist F	
	Fulbright Nehru Academic & Professional Excellence Fellowship (FNAPE)	2015

19	**SUMI S,** Progam Scientist	
	DST Women Scientist fellowship	2014
	N K Ganguly award for young scientists in cardiovascular clinical research	2012
20	**SUPARNA SENGUPTA,** Scientist F	
	DR. V.B. Kamat Memorial Award from Indian Association of Cancer Research	2003
	National Woman Bioscientist Award (Young) from Department of Biotechnology	2005
	International Union Against Cancer (UICC) International Study Award	2007
21	**SURYA RAMACHANDRAN,** Program Scientist	
	Indian Council of Medical Research, Chaturvedi Kalawati Jagmohan Das Memorial Award for Research in Cardiovascular Diseases	2018
	Third prize at Women Scientists & Entrepreneurs Conclave, India International Science Festival-2017, Chennai	2017
	ISHR-Torrent Young Investigator Award 2017 at Cardiovascular Research Convergence, Translational Health Science & Technology Institute, Faridabad, India	2017
	Distinguished Service Award in Cardiovascular Science Medicine and Surgery; International Academy of Cardiovascular Sciences, Canada	2015
	DBT International Travel Fellowship	2015
	Visiting Scientist fellowship, Oklahoma Medical Research foundation, Oklahoma, USA	2012
22	**P.K. UMASANKAR,** DBT-Ramalingaswami Faculty Fellow	
	Ramalingaswami Fellowship	2016

RGCB received quite a number of international grants including Bill & Melinda Foundation Grant, UK-DBT Welcome Trust, IARC.

EXTRAMURAL RESEARCH GRANTS

ONGOING AND FROM APRIL 2019 ONWARDS

Principal Investigator and Name of Grant	Funding Agency	Year
Abdul Jaleel K A		
Identification of Metabolic Alterations in Sub-clinical Vitamin B12 Deficiency by Mass Spectrometry Based Metabolomics	KSCSTE	2016-2019
Metabolic Profiling of Normal Healthy people in Kerala: Impact of Family History of Diabetes	DBT	2017-2020
R Ajay Kumar		
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.	DST-SERB	2017-2020
Ananda Mukherjee		
Domain-specific role of tumor suppressor PTEN in genomic stability: A systematic approach.	DST-SERB	2016-2019
Studies on noncanonical role of tumor suppressor PTEN in endometrial adenocarcinoma	DBT	2017-2020
Ani V Das		
Identification of and functional evaluation of Piwi-associated regulatory RNAs in the stem cell population of HPV-associated cervical cancer	CSIR	2017-2020
Epigenetic regulation of multidrug resistance genes in embryonic carcinoma stem cells: implications in targeting cancer stem cells in germ cell tumors Funding agency	DBT	2018-2020
Arumugam Rajavelu		
Study the aberrant functions of altered metabolic pathway enzymes in artemisinin drug resistant Plasmodium falciparum	ICMR	2020-2023

ABBREVIATIONS: **KSCSTE:** Kerala State Council for Science, Technology and Environment
DBT: Department of Biotechnology, Govt. of India | **SERB:** Science and Engineering Research Board
DST: Department of Science and Technology, Govt. of India | **CSIR:** Council for Scientific and Industrial Research | **ICMR:** Indian Council of Medical Research

Functions of N-6 adenine methylation (m6A) in mRNA plasticity of Plasmodium falciparum at various developmental stages in RBC: Exploring Novel drug targets	DBT	2019-2022
S Asha Nair		
Development of Novel NIR absorbing sensitizers and their nano-conjugates for the multimodal cancer imaging and therapy	DBT	
Debasree Dutta		
Cellular transitions in development and disease- an epigenetic perspective	DBT	2017-2020
Role of PKC signaling in dictating naïve vs primed pluripotency	DBT	2017-2019
Histone chaperone HIRA as a novel modulator in dictating proliferation vs differentiation	SERB	2017-2020
Evaluation of Histone chaperone APLF as a novel biomarker in Triple Negative Breast Cancer (TNBC)	DBT	2018-2023
Devasena A		
Biomarkers of oral cancer risk prediction.	DBT	April 2018,5 years
Human papillomavirus (HPV)-related oropharyngeal cancer burden and the natural history of oral HPV infections: an Indian perspective	Wellcome Trust DBT Alliance	Jan 2019, 5 Years
George Thomas		
Development of rice varieties for Kerala with pyramided genes for resistance to BLB by marker assisted selection	DBT	2013-2020
Delineation and characterization of defensesignaling pathways and genetic regulation of induced systemic resistance in Zingiber-Pythiumpathosystems	DBT	2018-2021
K B Harikumar		
An integrated network analysis to identify genomic alteration profiles of human pancreatic cancer	DBT	2017-2020
Regulation of hepatic metastasis of colorectal cancer by exosomes	DST-SERB	2018-2021
A mechanistic evaluation of an Ayurvedic formulation in colitis associated colorectal cancer	DST-SERB	2018-2021
Understanding the role of sphingosine kinase isoforms in systemic lupus erythematosus (SLE)	CSIR	2018-2021
Mex3C: a novel tumor suppressor in colorectal cancer	ICMR	

Iype Joseph		
Studies in Lakshadweep islands on Leptospirosis and Asthma	CSIR – NISCAIR	
Jackson James		
Guiding retinal ganglion cell axons to brain visual centers: Is Pax6 the key molecule?	DBT-SERB	2017-2020
Expression of Notch independent Hes-1 (NIHes-1) specifically in ES cell derived Organoids representing developing neocortex: Understanding its functional significance	DBT	2018-2020
Regulation of stemness by Pleiotropic Hes-1 expression in neuroblastoma	National Bioscience Career Award, DBT	2018-2021
Krishna Kurthkoti		
Characterization of iron starvation induced dormancy in mycobacteria and its application in drug discovery	DBT	2017-2022
Deciphering the role of mycobacterial error-prone polymerase DnaE2 in antibiotic persistence and conferring adaptation to stress during biofilm formation	SERB, DBT	2019-2022
Mahendran KR		
Antibiotic translocation through porins in Gram-positive bacteria at the single-molecule level	Ramalingaswamy fellowship, DBT	2016-2021
Controlled assembly of transmembrane α-helix-barrel pores for single-molecule sensing	Innovative Young Biotechnologist Award, DBT	2017-2020
Single-molecule biosensing with hetero-oligomeric protein nanopores.	Early career research award, Department of Science and Technology (SERB)	2018-2021
Structure determination and targeting of ubiquitously expressed membrane integrated form of chloride intracellular channels (CLICs) for discovery of small molecular anti-cancer therapeutics	Department of Biotechnology, Multi-institutional grant, Centre for excellence in membrane biology	2019-2021
Merck award travel grant	Merck	2020-2021

Malini Laloraya		
Delineating the DNA binding function of Dock180	DBT	2017-2020
Investigating the role of superoxide in regulating the major events during embryo implantation	SERB, DBT	2020-2023
S Manjula		
'Transcriptome analysis and characterization of key metabolic and hormone signaling pathway genes in Piper nigrum in response to defense elicitors' (Collaborative project with NCBS, Bangalore)	DBT	2019-2021
'Identification and functional characterization of Phytophthoracapsici effectors specific to 'quick wilt' disease in black pepper (Piper nigrum).	DBT	2019-2021
Moinak Banerjee		
Evaluating pharmaco-epigenomic response of antipsychotic drugs	SERB	2017-2020
Genomic and epigenomic characterization of 9p21 in Intracranial aneurysm patients from two distinct ethnic population of the world	DST-JSPS	2017-2019
Association of RNF213 gene polymorphism in Moya moya disease susceptibility	Welcome Trust Clinical research fellowship (Dr.Arun K)	2018-2020
Role of genetic variations in genes associated with autophagy, inflammation and oxidative stress as risk for Alzheimer's Disease and Frontotemporal Dementia	DST- NPDF (Dr.Aswathy PM)	2017-2019
Genetics of complex pediatric epilepsy syndromes: electro-clinico-imaging based genotype-phenotype correlations in an Indian cohort	ICMR	2019-22
R V Omkumar		
Investigations on the role of thebiochemical bistable switch in learning and memory in vivo	DST-SERB	2019-2022
Novel derivatives of Tacrine, acholinesterase inhibitor, withadded pharmacological actions - A preclinical experimental study	ICMR	2020-2023
Pradeep Kumar G		
Inter-relationship between polymorphisms in four obesity genes, their expression and its correlation with infertility and obesity in subjects from Kerala	KSCSTE	2016-2019

RGCB @30

RGCB Outreach Programme included the DBT-Foldscope Project for the popularisation of the foldscope as an educational, training or research tool at the primary level of education.

Transdifferentiation of Spermatogonial Stem Cells (SSC) into somatic cell lineages via Embryonic Stem Cell (ES) like intermediaries	DBT	2017-2020
Evaluation of the role of AIRE in germ cell development and differentiation	CSIR	2018-2021
PriyaSrinivas		
Assessment of cell growth and microbial contamination in mammalian cell culture using foldscope in the laminar flow hood	DBT	2017-2019 (completed)
Targeting Cancer associated fibroblasts for Metastasis Inhibition in BRCA1 defective cancer	DST-SERB	2018-2021
Radhika Nair		
Deciphering Breast Cancer Metastasis	DST-SERB	2015-2020
Professor Radhakrishna Pillai M		
Role of Human Papillomavirus Infection and other co-factors in the etiology of the Head and Neck Cancer in India.	ICMR	2016-2019
National Facility for Drug Discovery and Developmental Therapeutics (NFDDDT)	DST	2016-2019
Translational Research in Triple Negative Breast Cancer (Center of Excellence). .	DBG	2017-2020
Glue Grant: Biomarkers of Oral Cancer Prediction.	DBG	2018 -2021.
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.	NIH, USA	2017-2022
Rakesh S Laishram		
Alternative Polyadenylation in gene expression – implications in cardiovascular diseases	Swarnajayanti Fellowship, SERB, DST	2020-2024
Star-PAP control of 3-end processing and alternative polyadenylation in cancer progression	SERB	2020-2022
3'UTR processing in regulation of cardiac genes with roles in pressure overload cardiac hypertrophy	DBT	2017-2020
Linking the two poly(A) tails: Eukaryotes vs Prokaryotes	DBT	2017-2020

Role of RBM10 in gene expression and 3'-end processing and its cellular implications	SERB	2016-2019
Rashmi Mishra		
Identification of the Role of Redox Signaling Pathways in the Mechanobiology of Neural Stem Cells and its Implications on the Pathology of Glioblastomamultiforme	DBT	2018-2021
Identification of the Role of Redox Signaling Pathways in the Mechanobiology of Neural Stem Cells and its Implications on the Pathology of Glioblastomamultiforme	DBT	2018-2021
Ruby John Anto		
Mechanistic evaluation and in vivo validation of the anticancer principle isolated from Chromolaenaodorata against cervical cancer(PI)	KSCSTE	2016-2019
Isolation, identification and characterization of anticancer principle from the medicinal plant Corallocarpusepigaeus (Co-PI)	KSCSTE	2016-2019
Investigating the mechanism behind the protective effect of the anticancer compounds isolated from Woodfordiafruticosa(L.)Kurz flowers against hepatocellular carcinoma (Co-PI)	KSCSTE	2016-2019
'Mechanistic evaluation and in vivo validation of the anticancer potential of Uttroside B against hepatocellular carcinoma'	DST-SERB	2017-2020
Sabu Thomas		
A study on the antimicrobial resistance pattern in Kerala	Dept. of Health and Family Welfare, Govt. of Kerala	-
Analysis of polymicrobial biofilms in chronic wound infections and development of anti-biofilm therapeutic to promote wound healing	DBT	-
Health promoting properties of potential probiotic strains isolated from infant gut microflora	ICMR	
Development of probiotic therapy for enhancing urolithin production by using bacterial flora of human origin	SERB, DST	
Sanil George		
Strategies for enhancing the antimicrobial activity of frog skin peptides	DST, SERB	2019-2021
Santanu Chattopadhyay		
Helicobacter pylori infection and modulation of gastrointestinal microbiome in the context of peptic ulcer and gastric cancer	SERB-DST	2017-2020

Helicobacter pylori infection in Sikkim and possible use of probiotics isolated from ethnic fermented foods of Sikkim against H. pylori	DBT	2018-2021
T R Santhosh Kumar		
Understanding the role of Hypoxia induced mitophagy in cancer cell survival and drug resistance: Implications on tumor stem cell like cells	DST	2017-2020
Understanding epigenetic changes and cell state transitions that contribute for recurrence in triple negative breast cancer	DBT	2017-2020
Design and Characterization of peptide based cell targeting domains with live cell and animal imaging methods	DBT	2018-2021
Saraswati Nayar		
Functional characterization of Chlorella hormone biosynthesis and signaling genes for phyto-remediation and bio-diesel production	DST-INSPIRE Faculty Award	2015-2020
ShijulaL N S		
Major gene influxes in microbial genome evolution	DST-INSPIRE Faculty Award	2016-2021
Structure and Evolution of Environment Resistomes	Early Career Award , SERB, DST	2018-2021
Microbial Pathogen Pangenome Evolution (PANPATH)	Heinrich Heine University, Düsseldorf	2018-2021
Soniya E V		
Characterization of key structural genes involved in flavonoid synthesis in Indian Gooseberry, (EmblicaofficinalisGaertn.)	KSCSTE	2015-2019
Development of a disease management strategy against Phytophthoracapsici utilizing an effective biocontrol agent and green synthesized silver nanoparticles from black pepper	DST	2020-2023
GenomeIndia: Cataloguing the Genetic Variation in Indians	DBT	2020-2022
S Sreeja		
Study of progesterone receptor foci and progesterone signalling in the breast cancer cells	DBT	2019-2022

RGCB @30

Work on encapsulation of Curcumin in chitosan nanoparticles improves cell uptake and prolongs tissue retention of Curcumin, thereby increasing the compound's chemo preventive activity by Ruby John Anto and her team make it to the cover page of Cancer Research Prevention, 2019, vol. 12, issue 4

Screening and Pre-Clinical evaluation of compounds of Pomegranate in Antagonizing Endogenous SERM-27 Hydroxycholesterol in Breast cancer	DST-SERB	2016-2020
S Sreeja (Co PI)		
Development of probiotic therapy for enhancing urolithin production by using bacterial flora of human origin	DST-SERB	2017-2021
E Sreekumar		
Elucidation of the role of endothelial cell signaling pathways in vascular permeability modulation in Dengue virus infection	ICMR	2017- 2020
Identification of cellular pathways differentially modulated in Human microvascular endothelial cells upon Dengue virus infection	KSCSTE	2016-2019
Characterization of the role of Nucleophosmin and other selected host proteins identified from differential proteomics inChikungunya virus infection	DBT	2016-2019
Antivirals from medicinal plants of Western Ghats selected based on traditional knowledge (TK) / Ethnomedical information	DBT	2015-2020
Therapeutic targeting endothelial kinases to abrogate Dengue virus-induced vascular permeability	ICMR	2019-2022
Sumi S		
Role of hemodynamic shear stress in the pathogenesis of varicose veins	KSCSTE	2018-2021
Molecular Pathogenesis of varicose veins	Dr N Radhakrishnan Charity fund	2018-2020
Do epigenetic alterations in shear stress regulatory genes induce endothelial mesenchymal transition in patients with cerebral arteriovenous malformations?	ICMR	2019-2022
Suparna Sengupta		
Analysis of Fodrin Association with Gamma-Tubulin Complex, the Microtubule Organizer	DST	2017-2020

Investigating the Nanomaterial Based Exosome Sensor for Cancer Prognostic: An approach towards Liquid Biopsy for Cancer	DBT	2017-2020
Surya Ramachandran		
Does maternal hypercholesterolemia influence cholesterol transport mechanisms across the placenta during gestation?	ICMR	2019-2022
Does Cyclophilin A, an Immunophilin under High Glucose Conditions Regulate Efferocytosis in Atherosclerotic Lesions?	KSCSTE	2018-2021
Screening lead molecules identified by structure-based rational drug design methods against cytochrome b5 reductase 3 and dopamine beta hydroxylase in spontaneously hypertensive rat models for antihypertensive effects.	DBT	2017-2020
Cyclophilin A and Efferocytosis in Vascular Disease associated with Type 2 Diabetes	Madras Medical Mission, Chennai	2017-2020
How does cyclophilin A an oxidative stress induced secretory protein modulate vascular disease progression in type 2 diabetes?	ICMR	2015-2018 (Completed)
Tessy Thomas Maliekal		
Virtual National Oral Cancer Institute: Development of Animal Model Systems to study oral cancer progression	DBT	2018-2021
P K Umasankar		
Endocytic modulation of BMP signaling: deciphering mechanistic insights into health and disease.	DBT	2016-2021
P K Umasankar		
Uncovering mechanisms to remodel cholesterol landscape in cancer cells	DST	2018-2021
G S Vinod Kumar		
Development of a novel three dimensional self aggregating peptide fiber as an implant for brain tumors	DST-SERB	2018-2021
Development of cotton-like bioadhesiveantimicrobial peptide based hydrogel patches for wound healing	ICMR, Government of India	2019-2022

RGCB @30

RGCB offers exclusive health benefits to its employees.

LIST OF PUBLICATIONS

April 2019 to March 2020

Abdul Jaleel K

- Vineetha, R. C., Sreedharan, H., Jaleel, A., Chandran, M., Nair, R. H. (2020). L-Ascorbic acid and-Tocopherol synergistically triggers apoptosis inducing antileukemic effects of arsenic trioxide via oxidative stress in human acute promyelocytic leukemia cells. *Frontiers in Oncology, section Molecular and Cellular Oncology, 10:65 doi: 10.3389/fonc.2020.00065*

- Kumar, A. A., Satheesh, G., Vijayakumar, G., Chandran, M., Prabhu, P. R., Simon, L., Kutty, V. R., Kartha, C. C., Jaleel, A. (2020). Postprandial Metabolism is Impaired in Overweight Normoglycemic Young Adults without Family History of Diabetes. *Scientific Reports 10(1):353. doi: 10.1038/s41598-019-57257-2.*

- Satheesh, G., Ramachandran, S., Jaleel, A. (2020). Metabolomics-Based Prospective Studies and Prediction of Type 2 Diabetes Mellitus Risks. *Metabolic Syndrome and Related Disorders, 18(1):1-9. doi: 10.1089/met.2019.0047.*

- Kumar, V., Kumar, A. A., Joseph, V., Dan, V. M., Jaleel, A., Kumar, T. R. S., Kartha, C. C. (2020). Untargeted metabolomics reveals alterations in metabolites of lipid metabolism and immune pathways in the serum of rats after long-term oral administration of Amalakirasayana. *Molecular and Cellular Biochemistry, 463(1-2):147-160. doi: 10.1007/s11010-019-03637-1.*

- Kumar V, Kumar, A. A., Sanawar, R., Jaleel, A., Kumar, T. R. S., Kartha, C. C. (2019). Chronic Pressure Overload Results in Deficiency of Mitochondrial Membrane Transporter ABCB7 Which Contributes to Iron Overload, Mitochondrial Dysfunction, Metabolic Shift and Worsens Cardiac Function. *Scientific Reports, 9(1):13170. doi: 10.1038/s41598-019-49666-0.*

- Krishna, M. S., Revathy, V.M., Jaleel, A. (2020). Adipocytes utilize sucrose as an energy source-Effect of different carbohydrates on adipocyte differentiation. *Journal of Cellular Physiology. 235(2):891-899. doi: 10.1002/jcp.29003.*

R Ajay Kumar

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

Ananda Mukherjee

- Majumder A, Dharan AT, Baral I, Varghese PC, Mukherjee A, Subhadradevi L, Narayanan G, Dutta D. *FASEB BioAdvances. 2019; 1:525-537.*

Arumugam Rajavelu

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RGCB @30

Kiranam, a non-profitable organisation of RGCB students, help the poor underprivileged kids in their study and getting access to study materials.

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RGCB @30

RGCB scientists won significant number of International, national and state level awards including Sun Pharma Award, Swarnajayanti Fellowship among others.

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G S Vinod Kumar

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CATALYSING THE FUTURE

RGCB Support Systems

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.

TEAM: Sivakumar KC, Manoj P

RGCB @30

RGCB Regional Facility for DNA Fingerprinting (RFDF) has been granted certification under the Medical Laboratory Certification Programme by NABH and NABL.

MASS SPECTROMETRY 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 MALDITOF-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.

TEAM: Mahesh Chandran, Abdul Jaleel K A

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 mammary tumour, oral tumour and hepatic tumour xenograft 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 xenograft mice 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

RGCB @30

RGCB is serving as the center for excellence in inclusive technology interventions for tribal heritage resilience of Kerala.

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

Services provided:

Supply of Specific Pathogen Free animals.

Non -Invasive and invasive animal procedures including live animal surgeries.

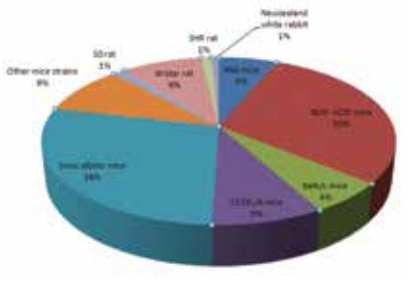
Development of different animal models for research

Gross and histopathological evaluation of tissues.

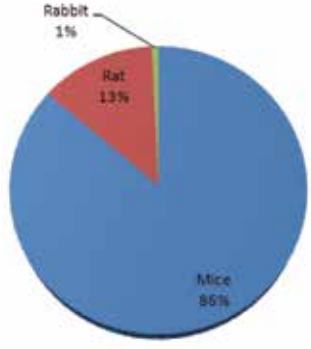
Custom breeding and maintenance of transgenic strains.

Conduct contract studies based on the requirement of clients from other institutions.

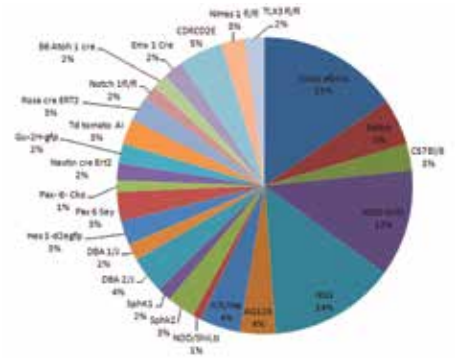
Data on animal usage during the year 2018-2019



Animal Species maintained at ARF



Strains of mice purchased and maintained at ARF



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.

Professor M Radhakrishna Pillai FRCPath, PhD, FNA, FAMS, FNASc, FASc,	Director
Mr. Mohanan Nair	Chief General Manager
Ms. Jayalakshmi U S	Senior Manager
Ms. Priya R	Senior Manager
Mr. Venugopalan J	Senior Helper

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

RGCB @30

RGCB Medical Laboratory Services (MLS) has been given accreditation and certification by National Accreditation Board for Hospitals & Healthcare Providers (NABH) and NABL.

RESEARCH ENGINEERING AND TECHNICAL SERVICES

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.

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

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.

TECHNICAL II: 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

TECHNICAL III: 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

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

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

TECHNICAL SUPPORT: 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

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.

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

RGCB @30

RGCB MSc Programme, initiated in the year 2019, boasts of a unique way of teaching, one-to-one faculty to student, especially in the laboratory courses.

LABORATORY MEDICINE AND MOLECULAR DIAGNOSTICS

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, Radhakrishnan R, Heera Pillai R, Jayalekshmi D, Vineetha P T, Sruthi Shankar, Karthika V, Sumaja V, Lakshmy Sreenivas

GENERAL ADMINISTRATION

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

CONTROLLER OF ADMINISTRATION

The controller of administration directs and coordinates the administrative, finance and business service functions & procedures of the institute and ensures compliance with all applicable regulations & policies of the Department of Biotechnology & Government of India. The Controller of Adminstration is the primary link between the general administration groups and the Office of the Director. The Controller also provides leadership & supervision of business services, administrative duties, all recruitment & promotions of non scientist personnel, compilation and monitoring of revenue and expenditures.

Mohanan Nair S

RGCB @30

RGCB launched its own Newsletter, 'PULSE', specifically designed to provide latest information, news update, memories to Indian public and other stakeholders to better understand the institute, its people, their contribution to the society as well as the research performance.

GENERAL ADMINISTRATION GROUP

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

GENERAL ADMINISTRATION I: TOP ROW: L-R: Usha B, Subash K, Jayanandan J, Vinod Lal K A, Wilson T, Vinod Kumar S R, Thankamany R BOTTOM ROW: L-R: Santhosh S, Vishnu P, Anil Kumar R, Jayachandran R Nair, Asha R Nair, Reena Prasad, Sujitha S

GENERAL ADMINISTRATION II: TOP ROW: L-R: Abilal G O, Sarath S N, Anandu Ashok, Dinesh Kumar S, BOTTOM ROW: L-R: Chitra G S, Mohanan C, V K Raghu Kumar, Ravindran V, Aryasri P

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

PURCHASE AND STORES

The Purchase & Stores Group occupies a vital and unique position in RGCB. This unit ensures procurement of the right material in right quantities and of correct quality. The section ensures procurement from right and reliable source or vendor as well as procurement of the material economically, i.e., at right or reasonable price. The RGCB Central Stores serves all 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

FINANCE & ACCOUNTS

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 acclimatize the available resources' utilization in achievement of its mandated science, thereby paving the way for productive application of all available resources. A dedicated Project Management Division 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, MSc, Summer training programs, Post-Doctoral Fellows etc. Accounting in respect of all service facilities of the Institute are exclusively done by this Group. Prompt generation and submission of internal management information by the Finance & Accounts Group always facilitates RGCB 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 utilization certificates and statements of expenditure are always promptly implemented by the Finance and Accounts Group. 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 Group have always resulted in building organizational strength, enthusiastic and motivated personnel and hence a robust institution.

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

RGCB @30

RGCB received Rs. 100 Crore grant to constitute a Bio-Innovation Center, supported by the Government of Kerala.

PROJECT MANAGEMENT DIVISION

This specialized unit of the Finance & Accounts group plays an extremely important management role of all extramural and institute generated funds. It is the connecting link between all funding agencies and RGCB. The vital duties of the group includes implementation of procedures related to recruitment of project personnel, salary Bill Preparation, Utilization Certificate (UC) and Statement of Expenditure (SE) preparation for Extra Mural Projects, PhD Fellowships, Post Doctoral Fellowships, Program Scientist Fellowships, sending of joining, yearly and assessment reports to the corresponding funding agencies, uploading the UC & SE in the RGCB portal under PFMS Website, activation of Fellowships and preparation of Claim Bill, maintaining online portal for UGC fellows, and fund management of Extra Mural Projects.

TEAM: Dileep Kumar R, Preetha J, Santhosh Kumar T R, S Sathichandran, Asha V S, Smitha L

OFFICE OF TECHNOLOGY VENTURES (OTV)

E. Sreekumar, MVSc., PhD
Chief Scientific Officer
Hima Sithul, M.Sc,
Technology Transfer Associate,

General course of work in OTV deals with preparing; managing and administering agreements related to Material Transfer, Confidential disclosures, collaborations (MoUs), sponsored research/consultancy services and Technology licensing Agreements to the in-house scientists/ researchers and accomplish its primary portfolio in effective administration, execution and Technology Licensing of the Intellectual Property and know-how (IP) developed out of RGCB research activities. A Chief Scientific Officer supported by a Research Assistant manages the OTV and it act as a single point of correspondence for all IP related matters including IP assignment and execution, acquainted with the institutional IPR policy etc.

Currently RGCB is processing twelve patent applications, both National and International. RGCB has been granted fifteen patent applications 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 all these applications and are presently under process in various Patent Offices including India, China, Republic of Korea and USPTO. This year OTV received six Preliminary Invention Disclosure Forms (PIDF) from the scientists of RGCB and is currently in the process of filing them as Patent applications. OTV executed twenty one Material Transfer Agreements (MTA) and ten MoUs for research collaborations. 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 three applications pertaining to the approval of NBA for transfer of research results to foreign collaborators and prior approval for IPR in India.

In order to support the efforts on managing COVID Pandemic, RGCB was able to license out technologies relating to the diagnosis of SARS CoV- virus which include Viral Transport Media, Viral RNA Extraction Kit and Rapid Antibody Test kit. Also, RGCB have licensed out technologies titled "Uttroside B and derivatives thereof as therapeutics for hepatocellular carcinoma" and "A mouthwash composition for managing oral mucositis, process and methods thereof" during this period.

TEAM: Hima Sithul, E Sreekumar

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

ACADEMIC AFFAIRS AND MANAGEMENT

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

This committee is also respobsible for setting of syllabus, timetables and examinations for the PhD course work and MSc programs. This committee also recommends suitable persons as faculty and adjunct faculty for these programs, decides on times and duration of specialty training and internships and ensures coordination between academic affairs management and all other administrative sections of the institute.

CONSTITUTION OF THE ACADEMIC COUNCIL

NAME	POSITION	DESIGNATION
Professor M. Radhakrishna Pillai	Director	Chairman
Dr. K. Santhosh Kumar	Scientist G & Dean (Research Administration)	Vice Chairman
Dr. T.R. Santhosh Kumar	Scientist G & Dean (Academic Affairs)	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
Prof. Jagadeesh Chandran	Senior Manager, Academic Administration	Special Invitee
Dr. Surya Ramachandran	Program Scientist	Special Invitee

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

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, and program planning and student research progress evaluation. OAA keeps abreast of trends and changes in higher education; works for institutional vision, survival, stability, growth, and excellence; provides a connection between administration and faculty; serves as catalyst to create a climate conducive to scholarly research in an atmosphere committed to the mandates of the institute and the 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 OAA the online leave submission was implemented. The OAA's ensures coordination and collaboration to ensure quality learning for students and excellence in academic administration.

TEAM: Beena Nair L, Ajith Gopal

RGCB @30

The Genome India project by RGCB is aimed at cataloguing the genetic variation in Indians, to build a grid of the Indian reference genome to fully understand the type and nature of diseases.

INFORMATION TECHNOLOGY, COMPUTATIONAL BIOLOGY AND DATA MANAGEMENT GROUP

INFORMATION TECHNOLOGY

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-theart 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. Controllerbased 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.

COMPUTATIONAL BIOLOGY AND DATA MANAGEMENT GROUP

Major highlights of the work done

The activities of the 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.

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

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.

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”.

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

RGCB @30

RGCB outreach programme opens the door to school and college students to visit the different labs at RGCB.

GENERAL BODY OF RGCB

The General Body of RGCB shall comprise of all members referred to in Clause 11 of the Memorandum of Association of the Rajiv Gandhi Centre for Biotechnology. The General Body lays down general policy directions consistent with the mandates of the institute, considers and approves proposals placed before it and also approves any modifications to the rules and regulations of the institute. The General Body also approves the Annual Report and audited accounts of the institute for placing before the parliament.

President of RGCB General Body

Dr. Harsh Vardhan
Honorable Union Minister for Science & Technology and Health, Government of India

Members of RGCB General Body

Dr. Shashi Tharoor
Honorable Member of Parliament, Thiruvananthapuram

Dr. Renu Swarup
Secretary, Department of Biotechnology, Government of India

Dr. Nirmal Kumar Ganguly
Chairman, Scientific Advisory Council, Rajiv Gandhi Centre for Biotechnology

Mr. Chandra Prakash Goyal
The Joint Secretary to Government of India, Department of Biotechnology

Mr. B. Anand
The Financial Adviser Department of Biotechnology, Government of India

Dr. G. Padmanabhan
Distinguished Biotechnologist, Indian Institute of Science, Bangalore

The Secretary to Government of Kerala, Department of Health,

The Secretary to Government of Kerala, Department of Science & Technology

The Secretary to Government of Kerala
Department of Industries,

The Director
National Brain Research Centre, Manesar, Haryana

The Director
National Centre for Cell Sciences, Pune, Maharashtra

The Director
Institute for Cytology & Preventive Oncology, Noida, Uttar Pradesh

The Director
Institute of Life Sciences, Bhubaneswar, Orissa

The Director
Institute of Bioresources & Sustainable Development, Imphal, Manipur

Dr. Paul Sebastian
Director, Cancer Prevention & Training, Tata Memorial Trust, Mumbai

Dr. M. Vijayan
Eminent Scientist in Medical Biotechnology/ Biomedicine: Indian Institute of Science, Bangalore

Dr. Arun Balakrishnan
Representative from Biotech. Industry, Vice President (Biotechnology), Piramal Life Sciences Ltd., Mumbai

Dr. A.E. Muthunayagom
Former Secretary to Government of India, Ocean Development & Former Executive Vice President, Kerala State Council for Science, Technology & Environment

Dr. Sundeep Sarin
Adviser, Department of Biotechnology, (Nominee of the Department of Biotechnology and Nodal Officer for RGCB)

Mr. S. Mohanan Nair
RGCB Staff Representative

Professor M. Radhakrishna Pillai
Director Rajiv Gandhi Centre for Biotechnology

GOVERNING COUNCIL OF RGCB

The Governing Council is the principal executive body of the institute. The Governing Council shall generally carry out and pursue the objectives of the Society, as set forth in the Memorandum of its Association. The management of all the affairs and funds of the Society shall, for this purpose, vest in the Governing Council. The Governing Council shall exercise all the powers of the Society, subject, nevertheless, to such limitations as the Government of India may from time to time, impose in respect of the expenditure from the funds of the Society and of grants made by the Government of India.

Chairperson

Dr. Renu Swarup
Secretary, Department of Biotechnology, Government of India

Members

Professor N.K. Ganguly
Chairman, RGCB-Scientific Advisory Council

Mr. B. Anand
Additional Secretary & Financial Adviser Department of Biotechnology, Government of India

Mr. C.P Goyal
Joint Secretary (Administration) Dept. of Biotechnology, Government of India

The Secretary to Government of Kerala
Department of Science & Technology

Professor G. Padmanaban
Distinguished Biotechnologist, Indian Institute of Science, Bangalore

Dr. Amulya Panda
Director, National Institute of Immunology, New Delhi

Dr. Paul Sebastian
Director, Cancer Research & Training, Tata Memorial Trust, Mumbai

Dr. B. Ravindran
Professor of Eminence & Former Director, Institute of Life Sciences, Bhubaneswar

Professor Umesh Varshney
Indian Institute of Science, Bangalore

Professor Vijayalakshmi Ravindranath
Chairperson, Centre for Neurosciences Indian Institute of Science, Bangalore

Professor Apurva Sarin
Director, Institute for Stem Cell Biology & Regenerative Medicine (inStem), Bangalore

Dr. Sundeep Sarin
Adviser, Department of Biotechnology, (Nominee of the Department of Biotechnology and Nodal Officer for RGCB)

Professor M. Radhakrishna Pillai
Director, Rajiv Gandhi Centre for Biotechnology (Member Secretary)

RGCB @30

RGCB MSc Biotechnology students within the completion of first semester received fellowship ranging from INSA, CSIR NET to Khorana.

THE RGCB SCIENTIFIC ADVISORY COUNCIL (SAC)

The Scientific Advisory Council shall evolve the scientific and technical programs of institute, review them periodically and shall take further course of action as would be deemed fit for furthering scientific and technological research at the institute. The recommendations of the Council would be submitted to the Director.

Chairman

Professor Nirmal Kumar Ganguly
Former Director General, Indian Council of Medical Research

Members

Professor K.P. Gopinathan
Emeritus Professor, Indian Institute of Science, Bangalore

Professor Vijayalakshmi Ravindranath
Chairperson, Brain Research Center, Indian Institute of Science, Bangalore

Professor P. N. Rangarajan
Department of Biochemistry, Indian Institute of Science, Bangalore

Professor Grant N.
Pierce, Executive Director, St. Boniface Hospital & Professor of Pharmacy, Physiology and Pathophysiology, College of Medicine, Faculty of Health Sciences, University of Manitoba, Canada

Professor Joshy Jacob
Vaccine Center, Emory University, Georgia, USA

Professor Rakesh Kumar
Distinguished Professor & National Chair in Cancer Research, Rajiv Gandhi Centre for Biotechnology

Professor Subrata Sinha
Department of Biochemistry, All India Institute for Medical Sciences, New Delhi

Dr. Chandrima Shaha
President, Indian National Scence Academy & Former Director, National Institute of Immunology, New Delhi

Professor L.S. Shashidhara
Ashoka University, Sonipat, Haryana

Professor T. Rajkumar
Head, Molecular Oncology, Cancer Institute, Chennai

Dr. Robin Mukhopadhyaya
Former Head, Virology
Advanced Centre for Treatment Research & Education in Cancer (ACTREC)
Tata Memorial Center, Mumbai

Dr. Satyajit Rath
Agarkar Research Institute, Pune

Dr. Saji George
Distinguished Scientist and National Chair in Translational Biotechnology
Rajiv Gandhi Centre for Biotechnology

Dr. Sundeep Sarin
Adviser, Department of Biotechnology New Delhi and Nodal Officer for RGCB

Professor M. Radhakrishna Pillai
Director, Rajiv Gandhi Centre for Biotechnology (Member Secretary)

INSTITUTIONAL HUMAN ETHICS COMMITTEE (RGCB IHEC)

Registration No: (DCGI - ECR/484/Inst/KL/2013) & (DHR- EC/NEW/INST/2020/477)

RGCB IHEC is constituted under the authority of Drugs Controller of India, Central Drugs Standard Control Organization, Drugs and cosmetics (Third Amendment) Rule, 2013, Ministry of Health and Family Welfare, Department of Health, Government of India

The Terms of Reference of the Committee

IHEC will review and approve all types of research proposals involving human participants with a view to safeguard the dignity, rights, safety and wellbeing of all actual and potential research participants. The goals of research, however important, should never be permitted to override the health and wellbeing of the research subjects/participants. The IHEC will take care that all the cardinal principles of research ethics viz Autonomy, Beneficence, Non - malfeasance and Justice are taken care of in planning, conduct and reporting of the proposed research. For this purpose, it will look into the aspects of informed consent process, risk benefit ratio, distribution of burden and benefit and provisions for appropriate compensations wherever required. It will review the proposals before start of the study as well as monitor the research throughout the study until and after completion of the study through appropriate well documented procedures, such as annual reports, final reports and site visits etc. The committee will also examine compliance with all regulatory requirements, applicable guidelines and laws. The mandate of the IHECs will be to review all research projects involving human subjects including human biological materials and human biological data to be conducted at the Institute, irrespective of the funding agency.

RGCB @30

RGCB has published more than 800 publications in the last 30 years with 14695 citations and an h-index of 61.

Composition of RGCB-IHEC

Chairperson

Dr. M.Narendranathan, MBBS, MD (Gastroenterology), DM, MPH (USA)
Former Professor & Head, Department of Gastroenterology,
Government Medical College, Trivandrum.

Senior Consultant in Gastroenterology,

GG Hospital & Cosmopolitan Hospital, Thiruvananthapuram

Members

Vice Chairman
Professor. V. Ramankutty
MBBS, DCH, MD Pediatrics,
M.Phil, MPH, FIACS

Former Professor Achutha Menon
Center, Sree Chitra Thirunal Institute for Medical Sciences & Technology & Research
Director, Amala Cancer Centre, Thrissur

Professor H.V. Easwer
MBBS, MS (General Surgery), MCH (Neurosurgery) Sree Chitra Thirunal Institute of Medical Sciences & Technology (SCTIMST), Thiruvananthapuram.

Professor. S. Sankar
MBBS, MD (Pathology)
Head, Department of Pathology, Government Medical College, Kottayam

Dr. Bushera Beegom
MA, M. Phil, Ph.D (Sociology)|
Assistant Professor, Department of Sociology, University of Kerala.

Ms. Tigi Philip
MBA, Proprietor, Sarwaa Café,
Opposite All India Radio, Vazhuthacaud,
Thiruvananthapuram

Adv. Benoy T George
BA, LLB Nizar & George; Lawyers & Solicitors, Thiruvananthapuram.

Dr. Devasena Anantharaman
PhD, Scientist EII,
Cancer Research, RGCB

Affiliated Members

Dr. Priya Srinivas PhD
Scientist F, Cancer Research, RGCB

Dr. Rakesh Laishram PhD
Scientist E-II, Cardiovascular Disease & Diabetes Biology, RGCB

Dr. Abdul Jaleel PhD
Scientist F, Cardiovascular Disease & Diabetes Biology, RGCB

Coordinator
Ms. Divya Jayalekshmy MSc

INSTITUTIONAL ANIMAL ETHICS COMMITTEE (IAEC)

As per the "Breeding of and Experiments on Animals (Control and Supervision) Rules, 1998" RGCB has formed an Institutional Animal Ethics Committee for control and supervision of experiments on animals performed in the Institute. The IAEC is registered with the CPCSEA (Reg. No. 326/GO/ReBiBt/S/2001/CPCSEA) and its primary duty is to review and approve all types of research proposals involving small animal experimentation before the start of the study. The Committee also monitors research throughout the study and after completion of the study through periodic reports besides regular visits to the research faculty animal house and laboratories where the experiments are conducted. It also ensures compliance with all regulatory requirements, rules, guidelines and laws related to animal experiments. IAEC includes eight members of which three are nominated by CPCSEA and remaining five members by the institute. The chairperson and member secretary of the committee are nominated by the institute from the existing members. The term of appointment of the committee is for a period of 3 years. The committee meets at regular intervals to review new proposals, requests and existing policies. The committee also regularly monitors the procedures and practices related to animal experiments to ensure that animal welfare and ethics are strictly followed at every point of research.

Composition of RGCB-IAEC

Dr. T. R Santoshkumar
Biological Scientist & Chairperson,
IAEC Scientist G & Dean (Research Administration), Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram

EXTERNAL MEMBERS

Dr. K. R. Chandramohan Nair
Main Nominee of CPCEA
Senior Scientific Officer & Office In-charge of Animal House
Department of Anatomy,
Government Medical College
Thiruvananthapuram - 695 011, Kerala

Professor Lincy Joseph
Scientist from outside of the Institute
Pharmaceutical Chemistry
Pushpagiri College of Pharmacy, Medicity, Tiruvalla - 7, Kerala

Dr. Guruvayoorappan C
Link Nominee of CPCEA,
Assistant Professor
Division of Cancer Research
Regional Cancer Centre
Medical College Campus
Thiruvananthapuram - 695 011, Kerala

Dr. G. Christopher
Socially aware Nominee Research
Coordinator ACESSD Mahatma Gandhi University Priyadarsini Hills P O, Kottayam 686 560, Kerala

INTERNAL MEMBERS

Priya Srinivas PhD
Member Secretary, RGCB IAEC
Scientist F , Rajiv Gandhi Centre for Biotechnology

E. Sreekumar MVSc PhD
Chief Scientific Officer Animal Research Facility, Scientist E-II, Rajiv Gandhi Centre for Biotechnology

Jackson James PhD
Scientist F & Associate Dean, Rajiv Gandhi Centre for Biotechnology

Archana. S MVSc
Veterinarian, Rajiv Gandhi Centre for Biotechnology

RGCB
DISCOVERIES FOR A
BETTER TOMORROW

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