

Special Feature

DNA Profiling and
Establishment of a DNA
Fingerprint Database of
Captive Elephants in Kerala

Flash from the Past

Anand Krishnan
Former PhD student in
Dr. Asha Nair's laboratory and
presently pursuing postdoctoral
studies at Alberta, Canada

Science Spotlight

A high-throughput real-time
in vitro assay using
mitochondrial targeted
roGFP for screening of drugs
targeting mitochondria



Dedicated to Lord Vishnu, the Sree Padmanabhaswamy Temple in Thiruvananthapuram is believed to be the world's richest temple.

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FOREWORD

We are now fully into 2019 and with it comes the promise of continued success. RGCB is proud today to be an institute deeply embedded in Indian and international science enterprise with significant contributions to basic science, translational & applied research, public health intervention, education, society outreach and a large platform of services to the community. RGCB is proud to be a unique and privileged ecosystem. As part of this expansion and growth, we are excited to launch our inaugural newsletter, RGCB PULSE, that is specifically designed to provide latest information and news updates to help the Indian public and other stakeholders better understand the institute, its people, its contribution to society as well as its research performance.

We have designed RGCB PULSE to bring you, in each of the quarterly issues, latest science spotlights on research from the institute, a column on “know your scientist”, RGCB news, profiles of people who make RGCB tick continuously, RGCB bazaar on patents and technologies, RGCB outreach activities and a host of other interesting news & features.

We have put you on our mailing list of the newsletter in the hope that you will find value in its content and that it will be informative to you. If you ever find that what we offer is not for you, simply send an email to pulse@rgcb.res.in (for those receiving print versions) or click 'unsubscribe' at the bottom of the email in case you are getting a PDF version.

Please do send us your feedback and comments so that we can keep improving.

Jai Hind

Professor M. Radhakrishna Pillai
FRCPATH, PhD, FAMS, FNA, FASc, FNAsc
Director

EDITORIAL TEAM

Debasree Dutta, Devasena Anantharaman & Surya Ramachandran
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RGCB NEWS



RGCB Director handing over the DNA based genetic ID for the captive jumbos to the Chief Wildlife Warden, Mr. P K Kesavan

Special Feature

DNA Profiling and Establishment of a DNA Fingerprint Database of Captive Elephants in Kerala

Asian Elephant (*Elephas maximus*), the largest terrestrial mammal of India belongs to the endangered category as per International Union for Conservation of Nature (IUCN) Red list. Considering the importance of conservation of elephants, the Government of India launched Project Elephant in the year 1992, to protect elephants, their habitat and corridors; to address issues of man-animal conflict; and for the welfare of captive elephants.

Molecular genetic studies are modern tools for management of endangered populations. With regard to captive elephants, apart from ownership certificates and microchip implants, the owners are to maintain data book for elephants as prescribed in the rules. There are strong restrictions on trading captive elephants. However, there have been instances where complaints regarding the identity of the elephants were raised. On such occasions and in cases where the competent authority wants to ensure cross verification, DNA fingerprinting would be the most scientific method to establish the identity of an elephant.

The task to develop a microsatellite marker based DNA fingerprint of Asian elephants and to create a reference database of captive elephants in Kerala was given to RGCB, an autonomous institution under Department of Biotechnology,



Times of India
Dated 19.12.2018

Government of India which hosts a facility for Molecular Forensics. This advanced laboratory routinely performs person identification tests, paternity disputes, crime scene genetic analysis and identification of samples associated with poaching of protected wildlife and biodiversity conservation.

Blood and dung samples from captive elephants provided by Kerala Forest Department officials were analyzed and a DNA database was developed. This database is open to the Kerala Forest Department for use in identification. An identification card with details of elephant with DNA database ID and QR code will be issued to the owner. This is the first time in India that DNA data has been included in ownership details of captive elephants.

In addition to the development of the DNA database, a protocol was also developed to determine DNA fingerprint of elephants from their dung and tusk/ivory samples, which will be useful in cases of poaching and illegal trade.

awards

RGCB Merit Awardees 2018



Nimmy Fathima Francis, PhD student in Cardiovascular Disease Biology Lab was awarded the RGCB Student Merit Award 2018 by Dr. Shekhar C. Mande, Director General, Council for Scientific & Industrial Research on the RGCB Foundation Day.



Tapas Pradhan and Riya Ann Mary Paul shared the second prize of the Student Merit Award 2018



Dr. Debasree Dutta receiving the second best poster award from Dr. Renu Swaroop and Dr. Chandrima Shaha at the women conclave in the recently held India International Science Festival 2018 at Lucknow, India.



Haritha H Nair, PhD student receiving the budding scientist award for best oral presentation at the 3rd International conference on Nutraceuticals and Chronic Diseases held at Rishikesh, Dehradun, on September 14th-16th 2018.

PhDs AWARDED IN THE LAST QUARTER

Syed Khaja Mohieddin

Title of thesis: Role of histone chaperones in cellular reprogramming

Name of Mentor: Dr. Debasree Dutta

Lesly Augustine

Title of thesis: Expression profiling of phenylpropanoid biosynthetic pathway genes in Zingiber spp. with contrasting response to soft-rot pathogen Pythium

Name of mentor: Dr. George Thomas

Aneesh B

Title of thesis: Cloning and expression of polyhydroxybutyric acid biosynthesis genes from bacteria isolated from the environment and the optimized production of the biopolymer'

Name of mentor: Dr. K. Harikrishnan

Arjun JK

Title of thesis: Generation of metagenomic libraries and screening for potential biomolecules

Name of mentor: Dr. K. Harikrishnan

Subashini C

Title of thesis: Wnt5a signaling and its implications in cerebellar neurogenesis

Name of mentor: Dr. Jackson James

Sneha Singh

Title of thesis: The role of endothelial cell Angiopoietin-1 (Ang-1) signaling in vascular leakage induced by Dengue virus

Name of mentor: Dr. E Sreekumar

Anu Priya MG

Title of thesis: Elucidation of endothelial cell signaling mechanisms and vascular permeability in dengue

Name of mentor: Dr. E. Sreekumar

REGIONAL CHILDREN'S SCIENCE CONGRESS @RGCB



The Navodaya Vidyalaya Samithi conducted the Regional Children's Science Congress at RGCB in November 2018

FLASH *from the* PAST



I am Anand Krishnan, a former PhD student in Dr. Asha Nair's laboratory and presently pursuing postdoctoral studies at Alberta, Canada.

I was fortunate to be a part of the highly talented pool of PhD trainees in RGCB during 2006-2011. Now I wear the hat of a Postdoctoral Neuroscientist in Alberta. Adorned by Glacier filled Rocky Mountains, turquoise lakes and awesome national parks, this place has a lot to offer for active living, from backcountry hiking, white water rafting, road-trip to the ice field parkways, summer barbecues and camping, despite the -20°C winters.

After 8 years of leaving RGCB, today I may want to close my eyes for flashes of memory - Of course, I see myself in extra large white lab coat and my supervisor Dr. Asha Nair laughing loud besides me at some silly jokes- friendly working atmosphere; Regular tea-breaks with friends in the cafeteria - time for harmless gossip; those colourful Onam celebrations when we get our turn to perform some amateur acts - team work and fun; the meetings and conferences - light and HEAVY moments in the socials; The Director's office - admirable administration; scientists who excelled and are now nationally and internationally known - fighting spirit and persistence; training undergraduate and more enthusiastic school students cancer biology lessons - teaching skills.

In addition to picking few life lessons mentioned above, my

learning curve in the five-year period was incredible. I never had to complain on my technical and theoretical knowledge I gained from RGCB. Indeed, my transition from a Cancer biologist to Neuroscientist was quite smooth, like playing different songs using same musical notes. I believe that anything could stay strong when built upon a strong base. So, I sincerely thank all RGCB scientists, staff and fellow trainees for my successful ongoing research tenures and in qualifying prestigious independent funding schemes like DST Fast Track Scheme for Young Scientists and DST-Ramanujan and DBT-Ramalingaswami Early Career Fellowships and achieving a long-dreamt nature publication. Every interaction and advice counts.

My two cents advice to the new trainees: being a scientist is a mindset and when combined with the right soft skills you can be a true scientist or Entrepreneur of today's world. Soft skills - communication and personality eats a big chunk of it - will help you grab the right opportunity. If you don't know how to sell yourself, you can't sell your product. So, consider developing your soft skills seriously along with the lab research.

I must stop here. Here is a woman yelling at me for staring at the computer screen for long time - my life partner I also got from RGCB.

Where am I going to, next? Moving forward with applied research and gearing towards Entrepreneurship.

18
NOVEMBER
RGCB
FOUNDATION
DAY

RGCB FOUNDATION DAY



Dr. Shekhar C Mande, Director General, Council for Scientific & Industrial Research delivered the RGCB Foundation Day lecture on November 18, 2018 that was followed by a sumptuous “Kerala Sadya” served on plantain leaves with 28 mouth-watering dishes!

know me better: i am rakesh laishram

Scientist E-II and Wellcome Trust-India Alliance Fellow
Rajiv Gandhi Centre for Biotechnology, Trivandrum-India

I was born in Imphal, Manipur and studied at the Churachand Higher Secondary School for my undergraduate, and Dhanamanjuri College of Sciences for graduate courses. I then moved to New Delhi for post-graduate studies at the Jamia Millia Islamia University. During that time, I got my first laboratory research experience from the Indian Institute of Sciences, Bangalore with a JNCASR summer research fellowship for three months which inspired me to pursue research as a career. I did my Ph.D. in Molecular Biology from the Centre for DNA Fingerprinting and Diagnostics, Hyderabad working with Dr J Gowrishankar, where I identified a novel mechanism of transcription in bacteria wherein RNA polymerase is inactively trapped at the promoter that controls bacterial amino acid transport. I then switched to eukaryotic post-transcriptional RNA processing when I joined University of Wisconsin-Madison, USA for my post-doctoral training. I worked on a unique nuclear phosphoinositide-signaling pathway that modulates mRNA polyadenylation. In 2012, I started my own laboratory at the Rajiv Gandhi Centre for Biotechnology, Trivandrum. My work focuses on processing of mRNAs and long non-coding RNAs (LncRNA), and its implications in human diseases with particular emphasis in the heart.

In one of the salient discoveries from my laboratory, we have identified an RNA binding protein, RBM10 as a central regulator of cardiac hypertrophy and myocyte apoptosis in the heart, the two integral components in the pathogenesis of heart failure.

My work on poly(A) polymerase Star-PAP has defined a new mechanism of 3'-end processing that changed the previously believed canonical concept in the field. I have publications in high impact journals such as Genes Dev, Mol. Cell, Nature, EMBO, Trends in Cell Biol, Nucleic Acid Res., Cell Reports, Mol. Cell. Biol., FEBS Letters, and J. Bacteriol.

I have received several international and national awards including the DBT Ramalingaswami fellowship and the Innovative Young Biotechnologist Award, the American Heart Association Post Doctoral Fellowship, and the prestigious Wellcome Trust-India Alliance Fellowship. I am also a recipient of University Gold Medal in Chemistry from Manipur University.



ADIEU..



Saying goodbye on retirement day, coincided with birthday as well.

Professor C Chandrasekharan Kartha

Distinguished Professor at RGCB
Thiruvananthapuram (January 2009-2018)

“Not every light is a true light; to the wise the light of truth is light itself.”

- Thiruvalluvar, Tirukkural

There are plenty of mentors who impart knowledge but very few who help in gaining wisdom. Such a mentor is a critical requirement for any young research investigator, however competent, getting ready to tackle the world of science, but unsure on which path to tread. It is at this point of time that an effective and inspirational mentor is vital to lead the way and motivate others to follow.

RGCB was fortunate to have Cheranalloor Chandrasekharan Kartha fill this void as he joined the institute in December 2009 as a Professor of Eminence after vacating his position of

Professor and Head, Cellular & Molecular Cardiology at Sree Chitra Tirunal Institute for Medical Sciences and Technology. Professor Kartha's primary mandate at RGCB was to provide mentoring and leadership to young investigators to understand the biology of cardiovascular and diabetes associated diseases. It is truly remarkable to see the transformation of four of our young scientists from excellent naïve molecular biologists to competent investigators addressing critical questions in disease biology.

Professor Kartha in his benevolent and unassuming yet candid way, initiated setting up the Cardiovascular Disease Biology Program in RGCB. Each research project was developed as an individual program having far reaching basic and clinical implications and included development of congenital heart diseases to pathogenesis of varicose veins, discovering biomarkers of vascular disease in diabetes to cardiac remodeling in heart failure; pulmonary hypertension to metabolic switch in the heart as well as pathogenesis of cerebral arterio-venous malformations and traditional ayurvedic formulations in reversing age associated cardiac

dysfunction. Amongst his 177 publications, 42 were published in the last nine years from RGCB. He also received several grants from government funding agencies such as ICMR, DBT, DST and KSCSTE. The cardiovascular laboratory set up under the guidance of Professor Kartha has excellent infrastructure for physiological measurements such as Echocardiography, Rat Telemetry, Non Invasive blood pressure measurement apparatus, organ bath, semi autoanalyser, rat treadmill, trinocular and stereo microscopes, Ibidi flow chambers and langendorff apparatus to name a few apart from regular molecular biology equipments and tissue culture facilities. Another very significant input of Professor Kartha was his immense span of knowledge in disease pathogenesis. His very high level of academic training in pathology and voracious reading qualities ensured that many RGCB scientists could refine the research questions asked in many disease biology investigations.

Professor Kartha is an elected Fellow of Royal College of Physicians (London), International Academy of Cardiovascular Sciences (Canada), National Academy of Medical Sciences (India), Indian Academy of Sciences, National Academy of Sciences (India) and Indian College of Pathology. He is the current President of India Section of International Academy of Cardiovascular Sciences and a former Vice President of India Section of International Society for Heart Research and Kerala Academy of Sciences. During his tenure at RGCB, he was awarded the Makoto Nagano Award for Distinguished Achievements in Cardiovascular Education, International Academy of Cardiovascular Sciences (2018), Prof RK Goyal Oration Award, International Academy of Cardiovascular Sciences (2016), Distinguished Leadership Award, International Academy of Cardiovascular Sciences (2015) and Prof Manjeet Singh Oration Award, International Society for Heart Research, India Section (2014).



The fortunate young PIs mentored by Professor Kartha.



Dr. Kartha with an idol of Lord Krishna as a parting gift

Together with academic excellence, Professor Kartha also organized two international conferences in his tenure at RGCB. The first in 2010, an Indo-US Symposium on “Translating Molecular Cardiology into Clinical Practice” was a huge step forward for RGCB’s continuing research collaborations with Oklahoma Medical Research Foundation in Oklahoma City, USA. The Indo Canadian Symposium on Heart Failure in 2015 was conducted under the aegis of the International Academy of Cardiovascular Sciences. This symposium was different in several aspects. There was a pre-conference workshop for learning techniques used in cardiovascular biology research, wherein participants got a taste of research using the high-end equipment available in his laboratory and RGCB. Secondly, a public forum was initiated with cardiologists from Sree Chitra Thirunal Institute for Medical Sciences and Technology educating the general public about heart failure and prevention of heart diseases. The response and feedback from these events led to several outreach programs in schools, and which Dr. Kartha named as PRO♥C (Promotion of heart health among children) and Matters of the Heart, a newsletter designed to provide public health education for cardiovascular health protection.

Professor Kartha retired from RGCB on 17th of December 2018 to rekindle his first love - music and playing violin, arts that he has been doing for the past 30 years and sharing the same guru with the late violin legend Balabhaskar. We at Rajiv Gandhi Centre for Biotechnology will forever cherish his contributions to the growth of the institution and his efforts in placing it one among the top most in cardiovascular research in the country. You will be missed Kartha Sir!



Farewell party for Dr. Maya Devi at RGCB

M. Maya Devi

Scientist E1 at RGCB Thiruvananthapuram
(1993-2018)

We shall never know all the good that a simple smile can do

- Mother Teresa

In addition to being an excellent researcher Dr. M. Mayadevi is a wonderful human being, always with a charming smile on her face that endears her to all. Anative of Thiruvananthapuram and part of Rajiv Gandhi Centre for Biotechnology for the past 25 years, she was one of the few people to join RGCB in its very early days. Dr. Mayadevi obtained her Masters in Chemistry from the University of Kerala in 1981. After a brief stint as Junior Research Fellow at CSIR Regional Research Laboratory, Thiruvananthapuram, she moved to the United States where

she worked as Research Assistant in the Biochemistry Division of Case Western Reserve University, Cleveland for three years and then at Baylor Research Foundation, Dallas, for another one year. Later she returned to India and joined RGCB as a Research Assistant in 1992. In 1993, she became regular staff member at RGCB and started her career as a Research Officer. After a few years of service as Research Officer, she became Scientist B and obtained PhD working with Dr. RV Omkumar. Maya exemplifies commitment being a “true bench worker” doing experiments by herself and it is a common sight to see her walking in and out of the radioactive isotope laboratory. Maya completed her tenure at RGCB and superannuated in October 2018.

During her tenure at RGCB, she worked on the regulatory interactions of CaMKII with different proteins that are involved in learning and memory. She found that the interactions of CaMKII α , a natural inhibitor of CaMKII and NMDAR subunit of GluN2B along with CaMKII, mediated through its T-site, inhibits the dephosphorylation of CaMKII. These interactions may have a role in maintaining the persistent activity of CaMKII which is known to be important for learning and memory. In addition to these, she also discovered that curcumin and its analogs inhibited the calcium-dependent and independent activity of CaMKII. This finding demonstrated the potential of curcumin to be used as a neuroprotective agent by inhibiting CaMKII activity under excitotoxic conditions.

Her beautiful family includes her husband, Dr. K.N. Rajasekharan, a renowned professor in chemistry, Department of Chemistry, University of Kerala and a lovely daughter Parvathi R. Nair, a computer engineer settled in the UK. RGCB wishes Maya a wonderful stress free retired life ahead.



PEOPLE WHO MAKE RGCB A BETTER PLACE



Jayanandan J - Gardener

The man behind the ‘green revolution’ in RGCB seldom smiles. But his face lights up when he starts talking about his lilies, bougainvillea and bamboo that remains his

favorite plants. Serving RGCB since 1998, Jayanandan aka Francis, the RGCB gardener, has been instrumental in landscaping the lawns, tending to the potted plants placed in each floor of the institute and also the organic farms on top of our animal research facility. His terrace garden grown organic ladyfingers, long beans and tomatoes are used to serve lunch to our staff in the cafeteria along with the “skygreen” products. Based in Peyad, Trivandrum, he has two children who though share his passion for plants and trees have chosen information technology and engineering as their vocation



Sreejith S - Office Assistant
(Stores and Purchase)

Sitting hidden amongst huge stock registers, sub stock files and issue slips in the purchase department of RGCB is a

pleasing young man, Sreejith. He is the one person to go to when the intercom rings from the stores calling for stock delivery. Item verification, receiving stores items, maintaining registers, payment updates and customs clearance is part of his duties since 2009. Sreejith lives with his mother, wife and one-year old child in Pothencodu. His wife is a student of B.Pharm. He belongs to the generation which worships Tendulkar and plays in his home turf (read nukkad/playground) along with his friends. When he is not playing cricket, he enjoys watching Malayalam, Tamil and Hindi movies.

Sanjai D - Chief Manager
(Technical Services)



One of our senior most technical personnel, Sanjai, joined RGCB 20 years ago with Dr. M. R. Das. An alumnus of Post Graduate Institute for Medical Education & Research (PGIMER), Chandigarh, he worked on Hepatitis C testing and provided electron microscopy services at RGCB. He was a key resource person in managing the influenza virus testing laboratory which provided support to the state of Kerala in 2010 during the epidemics. After a brief stint at Laboratory Medicine and Molecular Diagnostics as technical services manager, Sanjai has now taken up the challenge of studying the human virome in the Pathogen Biology group. He believes “virome research has translational implications such as developing fecal microbiome transplantation which can change our lives”. Married to Leena, a higher secondary school teacher, Sanjai lives in Mananbure, Kallamballam and has two school going children. A drama artist during his college days, is now a avid reader.

Tyagarajan (Tyaagu)
Canteen Assistant



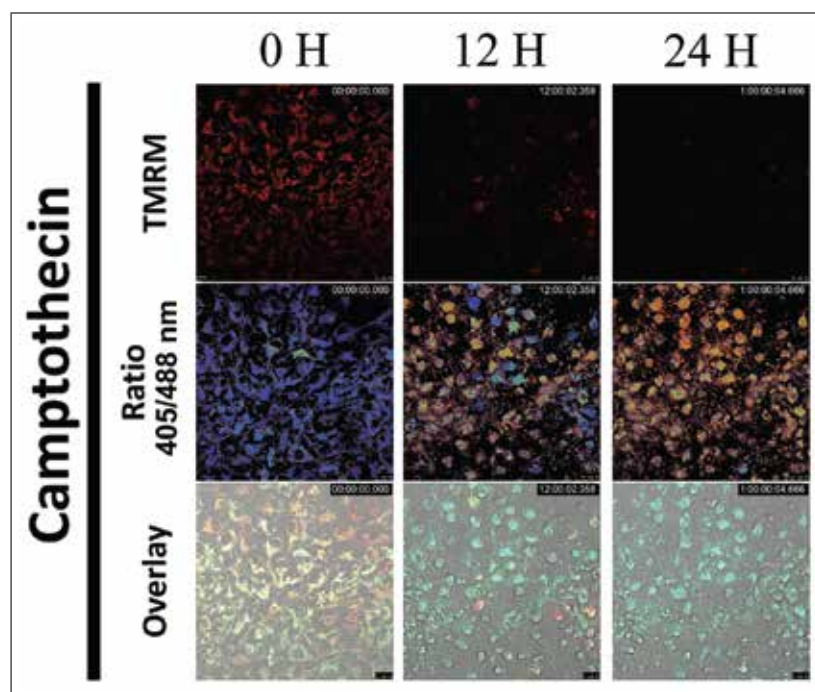
Tyagarajan hails from the land of Nataraja – Chidambaram in Tamil Nadu over 600 km away from Trivandrum. He left behind his large joint family and came to RGCB in 2006 as a young lad. Armed with politeness and a face full of smiles, bringing along the regional tradition of never turning anyone away without something to eat, he stitched in seamlessly to serve at the RGCB cafeteria. It was no surprise when he was called back into service after the kitchen management changed. He enjoys playing badminton and was a regular in the shuttles court of RGCB. An avid movie watcher, Tyagu loves films starring Mohanlal (surprisingly leaving out the Tamil superstars). Over time, RGCB has become his home away from home, he fondly recalls. While the Institute remains visible for its science, here is someone who quite literally, provides us all with “food” for thought! As with many other RGCB stories, this one too tugs along happily with his family back home enjoying the privileges of a comfortable life, supported by the hardworking son!

RGCB SCIENCE SPOTLIGHT

A High-throughput Real-time *in Vitro* Assay Using Mitochondrial Targeted Rogfp for Screening of Drugs Targeting Mitochondria

Most toxic compounds including cancer drugs target mitochondria culminating in its permeabilization. Cost effective and reliable methods to detect mitochondrial damage is important in cancer drug screening and toxicology testing. Redox sensitive Green Fluorescent protein (roGFP) is a redox sensitive fluorescent protein that changes its

excitation based on its redox status. This protein has been stably expressed at the mitochondria of diverse cancer cells using genetically encoded probe. Ratiometric imaging in highthroughput mode was developed to screen large number of compounds that damage mitochondria. Mitochondrial oxidation is a reliable



indicator of mitochondrial damage that can be readily determined in live cells using roGFP targeted at mitochondria using diverse imaging techniques and flow cytometry. The image-based assay using mt-roGFP outperformed other quantitative methods of apoptosis detection or mitochondrial damage sensors. The cell system is a valuable resource for identifying cytotoxic agents that target mitochondria and also for dissecting cell singling relevant to redox biology.

Figure: U2OS cells expressing mt-roGFP stained with TMRM and treated with camptothecin (10µg/ml). The confocal imaging for ratio and TMRM is shown at indicated times. Change in ratio indicates mitochondrial oxidation and loss of TMRM red indicates mitochondrial membrane potential loss.

Reference: Chandrasekharan A, Varadarajan SN, Lekshmi A, et al. A high-throughput real-time *in vitro* assay using mitochondrial targeted roGFP for screening of drugs targeting mitochondria. *Redox Biol.* 2018;20:379-389.

BRCA1 Defective Breast Cancer Cells Induce *in Vitro* Transformation of Cancer Associated Fibroblasts (CAFs) to Metastasis Associated Fibroblasts (MAF)

During metastasis, Cancer Associated Fibroblast (CAFs) of tumor stroma, accompany cancer cells to colonize at the secondary site. As cancer cells keep on accumulating novel mutations due to genomic instability, we speculated that, as and when cancer cells accumulate mutations in key genes like BRCA1 that control motility, it will induce transformation of CAFs to Metastasis Associated Fibroblasts (MAF), aiding metastasis. BRCA1 mutation enhances metastasis by altering

cellular motility through Ezrin that controls actin filaments. Our study demonstrated for the first time that CAFs, when co-cultured with BRCA1 mutated cells, transform CAFs to MAF *in vitro*, which augmented proliferation, migration and invasion along with high over-expression of Ezrin and CCL5, promoting metastasis (Figure). Therefore, we inhibited Ezrin and CCL5 *in vitro* in MAF, which attenuated their migration and invasion

abilities. Thus, combination therapy implying MAF inhibitors as anti-metastatic agents along with anti-cancer drugs might control the metastatic spread more efficiently.

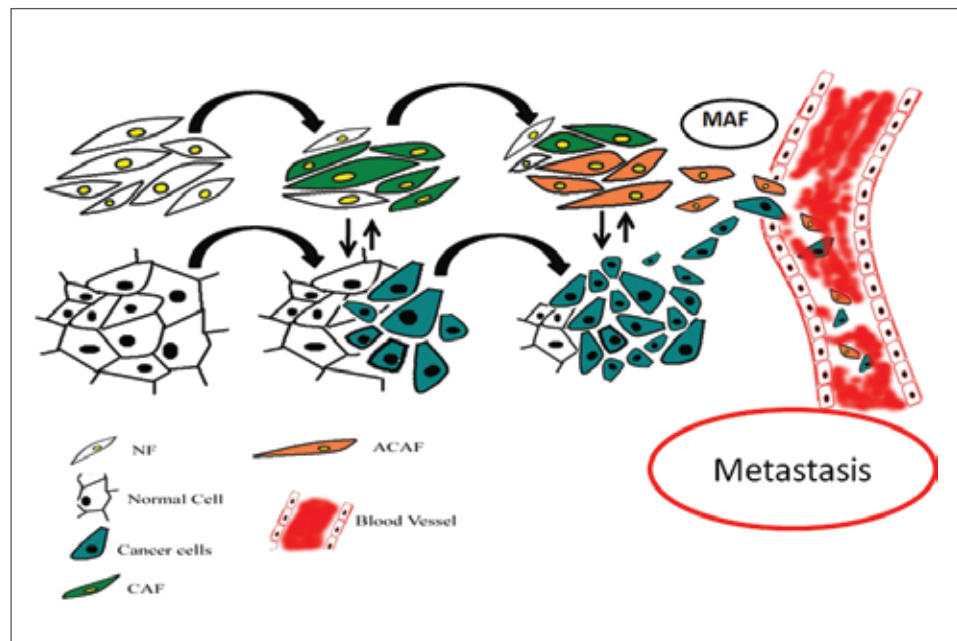


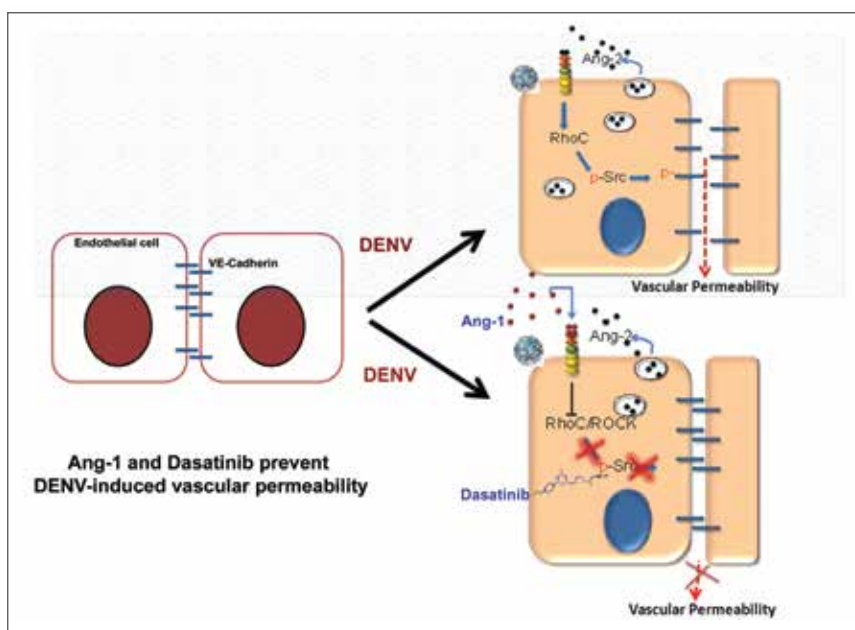
Figure: BRCA1 deficient cancer cells and transformation of Cancer Associated Fibroblasts to Metastasis Associated Fibroblasts: An analysis with human breast fibroblast cells

Reference: Sreelatha K Hemalatha, sathesh kumar Sengodan, Revathy Nadhan, Jithin Dev, Reshma R, Sushama, Veena Somasundaram, Ratheesh kumarThankappan, Arathi Rajan, Neetha Rajan Latha, Geetu Rose Varghese, Arun Peter Mathew, Thara Somanathan, and Priya Srinivas. BRCA1 defective breast cancer cells induce in vitro transformation of cancer associated fibroblasts (CAFs) to metastasis associated fibroblasts (MAF). Scientific reports, 2018 Sep 7;8(1):13903. doi: 10.1038/s41598-018-32370-w.

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

Dengue is a major public health problem. Death in severe dengue occurs because of shock caused by increased vascular permeability. Currently specific drugs are not available to prevent this shock and death in dengue. Our research focus is to elucidate the molecular mechanisms behind the fluid leakage and to develop the use of specific pharmacological inhibitors to prevent shock in dengue patients. We used a monolayer culture of microvascular endothelial cells for studying permeability changes. An assay to measure changes in monolayer permeability, that would reflect the fluid leakage potential, was standardized in our lab using the molecule FITC-dextran, and used in these experiments. Intracellular molecular level changes were evaluated using immunofluorescence and western blot techniques. We found that dengue virus infection by itself or by a virus-specific protein NS1 that is found in high level in the blood of dengue patients increase endothelial cell permeability. This

can be effectively prevented by treatment with a recombinant protein Angiopoietin-1. During the permeability increase, intracellular proteins such as Rho and Src are activated that leads to opening of endothelial cell junctions by removing VE-Cadherin protein. Specific pharmacological inhibitors such as Dasatinib can prevent activation of these proteins and abolish the leakage. Our study identified two key intracellular proteins that can be therapeutically targeted, as well as the use of a



Reference: Singh S, Anupriya MG, Modak A, Sreekumar E. J Gen Virol. 2018 Oct 24. doi: 10.1099/jgv.0.001163

recombinant protein Angiopoietin-1 for preventing enhanced endothelial cell permeability in dengue. Dasatinib, that was found effective in this study, is an SFK-family inhibitor and an FDA approved drug available in the market. Also, Angiopoietin-1 is an upcoming biological extensively studied for its pharmacological effects. Thus, our results open up new approaches in drug repurposing and therapeutic targeting of Dengue shock syndrome.

A Splicing-independent Function Of Rbm10 Controls Specific 3'-UTR Processing To Regulate Cardiac Hypertrophy

Regulation at the mRNA 3'-UTR is a critical mechanism in the heart, but how it is accomplished during cardiac hypertrophy (CH) or heart failure (HF) is poorly understood. We report an anti-hypertrophy gene program mediated via RBM10, an established splicing factor that regulates HF. We identified RBM10 as a unique Star-PAP co-regulator that controls CH. We investigated RBM10-Star-PAP nexus in CH/HF using in vitro, cellular and in vivo approaches. We discovered a splicing-independent function of RBM10 that operates with Star-PAP in the heart. The RBM10 RRM2 domain binds the Star-PAP catalytic domain, which directs Star-PAP activity toward polyadenylation, and assembles the Star-PAP complex specifically on target mRNAs. Accordingly, we tested cellular hypertrophy in rat cardiomyoblasts and CH and the subsequent progression to HF in Wistar rat hearts. Ectopic re-expression of RBM10 rescued

cardiomyocyte hypertrophy. RBM10 depletion evoked a hypertrophic response in H9c2 cells. Our results establish an anti-hypertrophy gene program mediated by RBM10 in the heart that is directly linked to HF.

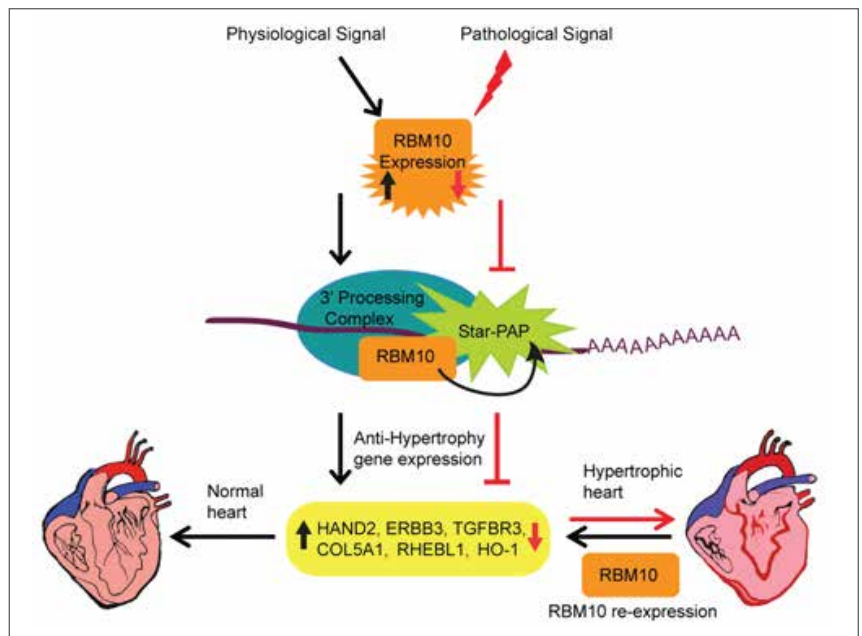


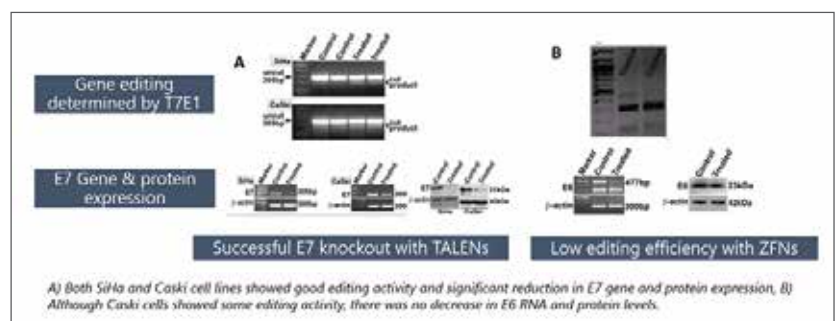
Figure: Model of RBM10-Star-PAP complex mediated regulation of Cardiac hypertrophy and heart failure

Reference: N Mohan, V Kumar, DT Kandala, CC Kartha, RS Laishram Cell reports 24 (13), 3539-3553

Genome Editing of E7 and E6 Genes Using Talens And ZFNs

Genome Editing tools offer tremendous possibilities in knocking out/in any gene of interest in vivo. Since the success of HIV pro-viral DNA excision using ZFNs, researchers have explored application of synthetic nucleases in HBV and HCV genomes as well. Our study compared the downstream effects of E7 and E6 genes of HPV 16 targeted by TALENs and ZFNs. These designer nucleases were transfected into the cells and editing was studied using T7E1 assay and gene expression using RT-PCR and blots. TALENs successfully edited E7 gene (~12%) with significant reduction at RNA and protein levels however, E6 (~6%) editing by both TALENs and ZFNs turned out to be ineffective at RNA and protein levels. Our results highlight that nucleases intended for therapeutic effect should have reasonably good

editing activity which is reflected phenotypically also; whereas low editing nucleases which do not show bulk reduction at protein level could be isolated by dilutional cloning for further applications like knockout cell lines.



Reference: Shankar S, Sreekumar A, Prasad D, Das AV, Pillai, MR. Genome editing of oncogenes with ZFNs and TALENs: caveats in nuclease design. Cancer Cell Int. 2018;18:169. Published 2018 Oct 22. doi:10.1186/s12935-018-0666-0

RGCB BAZAAR

Products from Kerala Remedies, BIONEST, Kochi



Antifats contains the fat fighting Garcinia fruit rind (Garciniacambogia HCA 50%) and Antioxidative Guggulu (Commiphorawightill), Detoxifying and Cleansing Emblic, Belleric and chebulicmyrobalan fruits (Embllicaofficialis, Terminaliabellerica, Terminaliachebula) as purified, standardized extracts in suitable serving size.

Grapelina capsules are a popular dietary supplement that has been shown to have a wide variety of beneficial actions. One of the key active components of red wine, proanthocyanidins are bioavailable in plasma and have potent antioxidant activity. Their free radical scavenging properties are greater than popular antioxidants such as vitamins C and

E. Grape seed extract shows a superior ability to protect cells against lipid peroxidation and DNA fragmentation.

Blacumin soft gels contain essential fatty acids from black cumin seed oil and flax seed oil to provide the much needed parent fatty acids of type Omega 3, Omega 6, Omega 9, alpha Linolenic acid, Linoleic acid and Oleic acid for good health.

GTCAPS: Purified standardized organic green tea extract.

Vegflax contains Omega-3 fatty acids from flaxseed oil which has the highest percentage of Omega-3 acids. Hence Kerala Nutraceuticals brings you Vegflax as Dietary Supplement Soft gels.

RGCB Patents

A mouthwash composition for managing oral mucositis, process and methods thereof

Inventors: Divya Ravindran, Ravikumar R K, K Ramadas, MR Pillai

Indian Patent Appl No: 3310/CHE/2010

A poly herbal cleansing composition that is used as an oral wash for delaying the onset of oral mucositis in cancer patients undergoing radiotherapy treatment.

Present status: Licensed out

Therapeutic Compositions From TheBrevinin-1 Family Of Peptides And Uses Thereof

Inventors: Sanil George

PCT Application No: PCT/IN2017/050239

A series of host defensive peptides from endemic amphibian fauna of Western Ghats (Hydrophylaxbahuvistara) were isolated and characterized. Two novel peptides viz. brevinin I (HYba1) and brevinin2 (HYba2) were found to have wide spectrum antimicrobial activity against microorganism of both Gram positive and negative categories with a MIC range of 1,5µM to 100 µM without any haemolytic activity. They also exhibited a pronounced cytotoxic activity against Hep 3B cancer cell line. The invention also covers amidated forms of peptides showing increased biological property in antimicrobial and cytotoxicity. The mechanism of antimicrobial activity is by nonspecific pore formation on the bacterial cell wall by interacting with cation binding site.

Present status: Under licensing agreement and negotiation

RGCB OUTREACH

THE FOLDSCOPE

The Foldscope is an origami-based, highly cost effective, optical microscope that can be assembled from a flat sheet of paper in less than 10 minutes. As a part of the Foldscope project, an initiative of the Dept. of Biotechnology, Ministry of Science & Technology, Government of India, in partnership with Foldscope Inc. and Prakash Lab (Stanford), Dr. Priya Srinivas conducted Outreach Programs in schools across four districts in Kerala, involving students especially those within the resource constrained environments, with the aim of inspiring them to love and cultivate science via experimenting through the foldscope. We also gave lectures on the research activities being conducted at RGCB aiming at generating curiosity and excitement involved in scientific exploration. We look forward for creating a social impact towards sharing the knowledge and igniting the scientific inquisitiveness in these young minds. Foldscope demonstration was also carried out at the Indian International Science Festival (IISF) Outreach Program 2018, conducted at RGCB, Thiruvananthapuram, where over 200 students from different schools and colleges participated.



Foldscope team at Holy Mass Central School, Edamon, Punalur, Kollam District

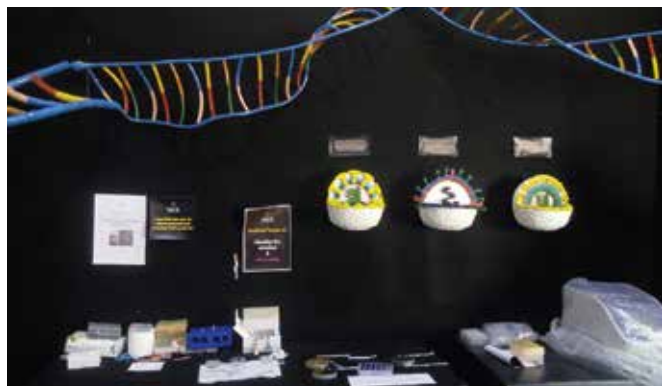


GHSS, Achankovil, Kollam District



Amrita Girls Higher Secondary School, Paracode, Adoor, Pathanamthitta District

INDIA INTERNATIONAL SCIENCE FESTIVAL, LUCKNOW 2018



The RGCB Pavilion at IISF 2018



Dr. Renu Swaroop, DBT secretary, at RGCB pavilion, IISF Lucknow accompanied Dr. Priya Srinivas and Mr. Saptarshi Biswas, RGCB.



RGCB pavilion at IISF Lucknow.



Award winner of the quiz with director of RGCB, IISF Lucknow.

IISF OUTREACH AT RGCB, OCTOBER 2018



RGCB conducted an outreach program as part of the IISF2018 on 19th September. 220 school and college students visited laboratories of RGCB.



Dr. E. Sreekumar, Senior Scientist RGCB delivered a lecture to the participants on "Emerging viral infections in India" for the outreach program as part of IISF 2018



**CULTURAL
PROGRAMS BY
STAFF AND
STUDENTS OF RGCB
ON INSTITUTE
FOUNDATION DAY**



Photographed by Dr. Ananda Mukherjee, Faculty Fellow, RGCB