Better Health through Scientific Research

MIMS RF

MIMS RESEARCH FOUNDATION

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E-mail:mimsrf@mimsindia.com Website: www.mimsindia.com

Vision

- To leverage Scientific Research to find solutions for common causes of morbidity and mortality from diseases

Mission

- To reduce the incidence and morbidity of Diabetes Mellitus in the community
- To understand and find solutions for the cure and arrest of cancer through new modality
- To find innovative solutions for bacterial resistance to antibiotics
- To find new plant derived molecules for curing various chronic diseases

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ABOUT US

MIMS Research Foundation (MIMS RF) was established in 2008. It is a SIRO recognized by The Department of Scientific and Industrial Research, Ministry of Science and Technology, Government of India. MIMS RF is a subsidiary of MIMS Academy Trust.

The trustees are

1. Dr. M. Azad Moopen
2. Er. M. Salahuddin
3. Dr. Abdulla Cherayakkat
4. Dr. M. Ali
5. Mr. S. M. Syed Khalil

PERSONNEL

Director- Dr. K. Karthikeya Varma, M.S., FRACS.

We have the following personnel working for the MIMS RF

1. Prof. M. Lilly, Pathologist, MIMS and retd. Principal, Medical college Calicut. Chairperson of Scientific Research Committee of MIMS RF
2. Dr. Raghava Varman Thampan, Ph.D. Senior Scientist, MIMS RF and former Director of RGCB
3. Dr. P.J. Wills, Ph.D, Scientist
4. Mrs. Radha Malattiri. M.A, MLIS, M.Phil. Assistant Registrar.
5. Mr. Varun Raghuveeran, Junior Research Fellow
6. Ms. Ramya, Research Assistant
7. Ms.Praseetha.S, Senior Research Fellow
8. Mr.Finose.A, Senior Research Fellow

MIMS RF undertakes projects in Cell Biology, Molecular Biology and New Molecules Research. All activities are related to the field of medicine and health care.

MIMS IN THE RESEARCH FIELD

With the decision to develop MIMS RF, what has been achieved in a creative sense is the entry of MIMS into the field of fundamental research. Clinical research, clinical trials and short term research projects were all components of its function right from the beginning. MIMS RF added two more categories into this list by introducing Medical Biology and Basic Science and Small molecules research as areas of interest.

AIMS AND OBJECTIVES

- To conduct state of the art research programmes in areas of special interest to MIMS hospital. Here the emphasis will be on areas that have direct relevance to healthcare and clinical medicine.
- To conduct advanced research in areas of fundamental science, the immediate beneficiary of which will be the patient community.
- To undertake contract research programmes.
- To conduct training programmes and short-term courses in selected areas of fundamental and clinical science for the benefit of postgraduate students in biology.
- To instil an element of intellectual curiosity into the minds of young medical graduates.

CURRENT RESEARCH FOCUS

MIMS RF has recognized 3 areas as THRUST AREAS for research.

1. Diabetes Mellitus, because of its prevalence and the deleterious effect on the person, family and the community.
2. Cancer, because of the several grey areas present even today.
3. Chronic obstructive pulmonary disease (COPD).

DIABETES MELLITUS

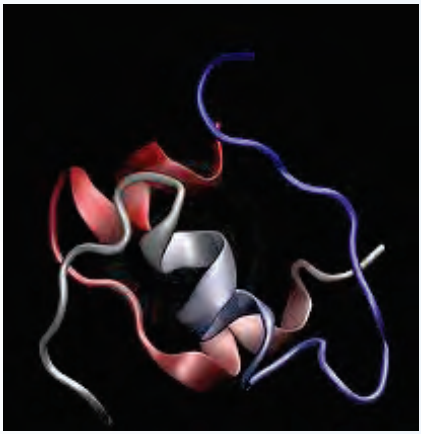
1. WHO estimated that over 275 million persons would be affected by Diabetes with or without its complications world wide and 75 millions will be in India.
2. In MIMS, 49% of patients undergoing Coronary Artery By-pass surgery or stenting are diabetics.45% of patients on chronic dialysis are diabetics. 25% of patients admitted to ICU are victims of complications of Diabetes.
3. On an average, a diabetic spends 60% more on hospital bills for any admission than a non-diabetic.
4. One person with diabetes adds on an average Rs.1500.00 to the monthly household expenditure.

Mortality and Morbidity due to Diabetes are enormous.

At MIMS-RF we are looking at the molecular mechanism of Insulin Resistance and we are optimistic about the result. From there ways and means will be designed to wash the cells off its Insulin Resistance for further application in people. It is a long road but early signs are encouraging.

At present, by the time diabetes is recognized with the increased presence of glucose in blood and urine, the complications of Diabetes which are mainly vascular have already set in. The vascular injury can happen in large blood vessels such as coronary arteries and peripheral arteries as well as in small vessels such as seen in retina and kidneys.

Therefore we started looking at children at the second decade of life for evidence of Insulin Resistance which is considered as the root cause of Type 2 Diabetes. Studies done in one school showed that we can predict incidence of Insulin Resistance in children at 10 years of age with 95% confidence. This, if effectively done will give us almost 40 years to formulate strategies to either prevent or at least delay the onset of complications. This is being validated by a much larger study in a less opulent school.



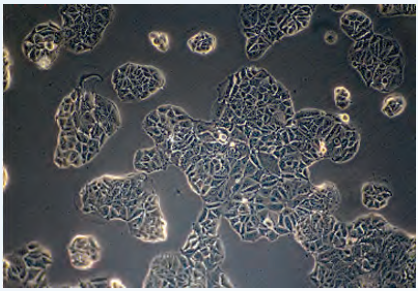
Insulin - ribbon structure

At the same time, studies are afoot to see whether Insulin Resistance can be reduced or made normal by strategies that can be effectively deployed in children, thereby preventing or delaying the onset of diabetes. Although enough hard evidence is lacking at present, indications are that we are on the right track.

On a community level, screening of school children for Insulin Resistance and trying to reduce the same by simple interventions may be taken up by the State of Kerala as part of a Diabetes Prevention Plan of the Government.

CANCER

The often asked question is “Why are cancer cells immortal?”. Huge amount of knowledge is available on this subject and what we are doing will only add to the confusion. But this is one road we must travel along with our projected NEW MOLECULE Research.

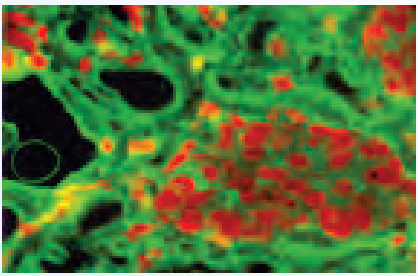


MCF-7 breast cancer cells

Breast cancer and estrogen action– The emphasis here is on identifying the correlation, if any between the diagnostic stage of the breast cancer and the presence of gene regulatory proteins that could control cell proliferation. A modest beginning has been made.

Estrogen Receptor Activation Factors (E-RAF) in health and disease-

E-RAF(s) are highly fascinating proteins that regulate totally independent



E-RAF in human breast cancer cells

biochemical responses at the cellular and molecular levels. There are E-RAF species which function as transcription factors and an E-RAF form which regulates mitochondrial steroidogenesis. There is no doubt that deeper knowledge into the biology of these proteins will open up a whole new era in clinical medicine.

Anticancer agents from natural products-

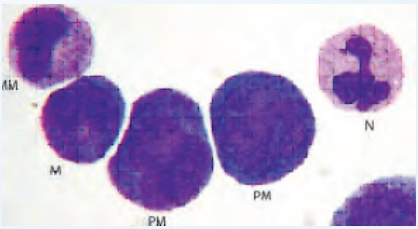
Understanding the mechanism of action of natural compounds will provide useful information on their application in cancer therapy and also in cancer prevention. Our aim is to develop

Medicinal plant

effective compounds or fractions from rare or threatened medicinal plants before their extinction. We are planning to screen anticancer agents from marine sources as well.

Novel stem cell therapy-

Neutropenia is a common complication of High Dose Chemotherapy in cancer patients leading to death due to any of the numerous opportunistic infections. MIMS RF aims to find out an effective defense to this condition. The feasibility of using invitro cultured neutrophil precursor cells obtained through Hematopoetic Stem Cell Culture, for this purpose, is being examined.



Neutrophil cells

COPD

According to the WHO estimates COPD is the 4th largest killer disease among the ailments that affect humanity. Considerable focus has been made in projecting smoking as the major cause that leads to COPD particularly in men. However, the possibility exists that other factors such as absence of certain key hormones may play a major role in precipitating COPD in post menopausal women. This possibility is being addressed in our recent approach towards deciphering the fundamental reasons that underlie post menopausal COPD. The hormone under consideration is the estrogen itself and the molecular targets for estrogen action are two genes: alpha-1 antitrypsin (AAT) in the liver and collagenase in the lungs.

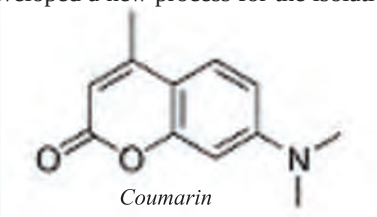
Plans are underway to probe into the molecular details underlying COPD.

ONGOING RESEARCH

Phytoestrogens – There is a general thinking among the modern day clinicians that estrogens of plant origin (phytoestrogens) could function as powerful tools in the treatment of postmenopausal osteoporosis. MIMS RF has already made advancement in the isolation of a phytoestrogen from a plant source used for human consumption. Two additional plants are also being investigated. With this discovery MIMS RF could take the first concrete step forward in bridging fundamental research and clinical medicine.

Plants-derived bioactive agents of commercial interest.

MIMS RF has just completed a collaborative project with a major pharmaceutical industrial unit and has developed a new process for the isolation and development of certain specified bioactive agents of pharmaceutical interest from plant sources. It is anticipated that additional ventures will be forthcoming.



Coumarin

Seasonal fevers


Cocoons

It is a common finding that in certain months there is a large-scale admission of patients with fever at the hospital. These fevers resemble viral fevers and are classified as such. **But Are They?**

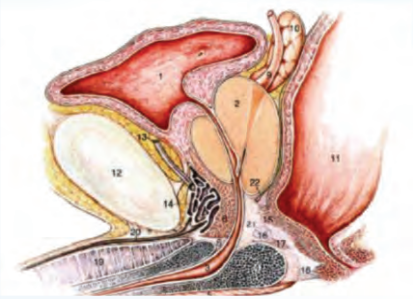
It was found that even in a major hospital like MIMS, less than 20% of these fevers can really be said to have even the weakest evidences of a viral fever. Dr.Wills during his research found that certain volatile toxins excreted by tiger moths could induce fevers that mimic viral fevers. The incidence of such fever corresponds seasonally with the maturation of these moths.


Host plant

Existence of Lepidopterism during fever epidemics - The work is based on the observation on outbreak of the population of a particular moth species and its correlation with the high incidence of fever epidemics in Kerala. The analysis revealed that they cause severe complications in humans, who inhale certain toxic compounds released into the air by these moths. We are now concentrating on identifying the presence of moth toxins in fever-affected patients.

OTHER AREAS

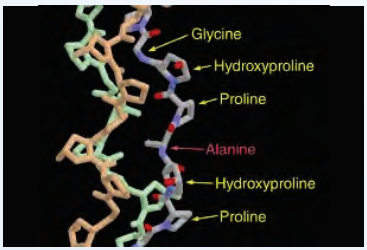
- **Student's Research:** MIMS Academy conducts post-graduate training towards DNB in 10 specialties. As part of their training, each candidate must engage in some research projects and MIMS RF oversees these projects.
- Students of M.Sc. biological sciences come to work at MIMS RF to conduct short-term research as part of their curriculum.
- Short Projects are done in other areas such as Quality, Human resource management, Laboratory Medicine, Relations etc. These are done in MIMS Hospital.



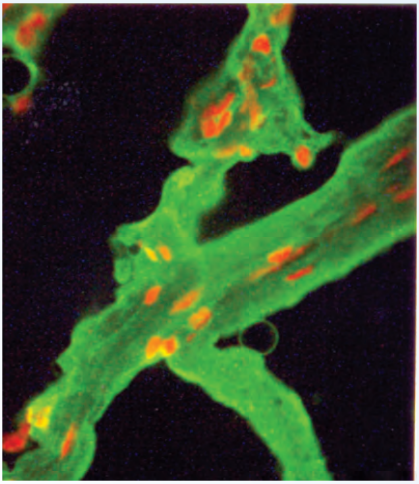
Benign Prostatic Hyperplasia

RESEARCH WORK PROJECTED FOR THE NEXT 5 YEARS

- **Anti BPH agents of plant origin**– It is known to traditional medicine that some plant sources have the potential to reduce and inhibit the growth of prostate during Benign Prostatic Hyperplasia (BPH) in men of age 50 and above. The drugs that are currently available in the market for treating BPH are prone to heavy side effects. It is in this context that MIMS RF plans to explore the bioactive agents derived from medicinal plants known to traditional medicine (or tribal medicine) with potential for use in BPH therapy.

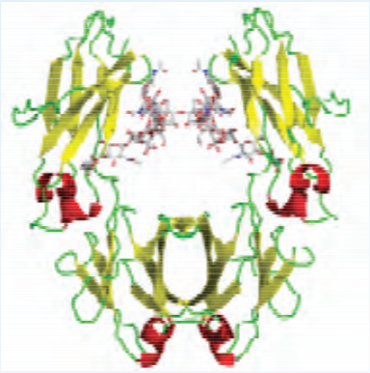


Collagen



E-RAF in human breast cancer cells

- **Collagen Synthesis Stimulating Factor**– There are bioactive agents in certain plants employed in human consumption with specific positive effects as on the synthesis of collagen. Isolation of this agent is in MIMS RF's interest particularly in view of its potential use in enhancing wound healing.
- **Factors regulating Estrogen Receptor Activation factor (E-RAF) gene expression**- There is a clear possibility that the therapeutic potential of E-RAF analysis will be identified not just in analyzing breast cancer progression but also in detecting abnormalities in human pregnancy. A wide range of fundamental studies are being planned in order to approach this research field from hitherto unimagined quarters. The discovery of a new hormone with potential for the correction of abnormalities in pregnancy is also a clear possibility.



Immunoglobulin G

Major Work In Offing:

1. Molecular basis of Antibody formation- This is going to be a high voltage research field in the years to come. The underlying belief is that the therapeutic procedures of tomorrow will rely more on antibodies than on antibiotics. Existence and induction of multi-drug resistant bacteria is threatening to push our fight against microorganisms into a tailspin with failure looming large on the horizon. Pharmaceutical industry and medical fraternity are making newer and newer antibiotics but as soon as they are introduced, the bacteria attain resistance. We seem to be losing the fight against bacteria by the antibiotic route. MIMS RF is taking a different route by trying to produce antibodies against microbes. Work is already going on.

2. Eraftrophin-This is a newly discovered hormonal factor of as yet unknown tissue origin. The PI believes that Eraftrophin is the key hormone that regulates the expression of E-RAF (estrogen receptor activation factor) gene in the uterus and other estrogen target tissues. It is anticipated that eraftrophin will be the key hormonal agent needed for preventing premature termination of human pregnancy. The possibility also exists that detection of E-RAF in human breast cancer biopsies and of eraftrophin in circulation could provide vital clues towards detecting the true functional status of human breast cancer.

3. Nuclear Estrogen receptor that regulates post transcriptional events in gene expression

Nuclear estrogen receptor II (nERII) is a RNA binding (non-DNA binding)nuclear estrogen receptor that has its major functional role in the regulation of post transcriptional events like splicing, nucleocytoplasmic transport of RNA and finally the translation process itself. Considerable amount of work has already been made by the PI in this direction. With this project the PI anticipates that new molecular targets for estrogen action will be identified following which it should become possible to regulate estrogen action by influencing these molecular targets.

4. Collagen synthesis stimulatory factor (CSSF)

The PI has recently identified certain plants- derived factors which stimulate collagen synthesis in human/animal cells in culture. These bioactive agents are currently being isolated for further use in structural and functional studies. The plan is to create collagen membranes containing CSSF, which should find application in the repair of bone and cartilage, healing of deep wounds and burn injuries and even in plastic /reconstruction surgery.

FUNDING

MIMS RF has following main sources of funds.

1. **MIMS.** Hospital allocates a certain amount from its income towards research activities. This is the main source of funds.
2. **Project funding from Central Govt. funding agencies.** We have three projects funded by CSIR, ICMR & DST and have applied for funding from others as well
3. **Short-term project fees.** Nominal amounts are collected from project students towards cost of reagents and materials.
4. **Collaboration with industry.** Industry collaboration will be allowed according to the ethical principles of the institution

COMMITTEES

1. **Research Advisory Board**- Consists of experts in the field from in- house and various institutions.
2. **Scientific Research Committee (SRC)**- Discussion on scientific aspects and approval of the projects.
3. **Institutional Ethics Committee (IEC)**- Critically evaluates the ethical issues and approval of the projects.
4. **Institutional Animal Ethics Committee (IAEC) –**Approval of projects involving animals and procurement of animals.
5. **Executive Committee**- Managing day today affairs of the Foundation.

THE KEY PLAYERS

- **Dr. K. Karthikeya Varma**. M.S., FRACS, Former Professor of Pediatric Surgery and Principal, Emeritus Professor of Pediatric Surgery, Medical College, Calicut. Now Director, Quality, Academy and Research Foundation, MIMS Hospital. 4 time Research Fellow under ICMR, Research fellow at Royal Children's Hospital Research Foundation, Melbourne, Australia. Original work on physiology of continence for urine and feces, necrotizing enteritis in children, alternate methods of management of Hirschsprung's disease. Research guide of University of Calicut for Ph.D. Guided two Ph.D students.
- **Dr. Abdulla Cherayakkat.** MRCP. Managing Director, MIMS and Senior Physician, deeply interested in medical research.
- **Dr. Raghava Varman Thampan.** Ph.D., in the field of hormone Biochemistry, Delhi University; Post-doctoral research supported by W.H.O. at Baylor College of Medicine, Houston, Texas, USA and Indian Institute of Science, Bangalore; Senior faculty in Life Sciences at Hyderabad Central University (HCU) and Senior Scientist and former Director, Rajiv Gandhi Centre for Biotechnology (RGCB), Trivandrum; Pursued research for nearly 3 decades on estrogen receptors with credit of discovering new receptors and receptor associated proteins. Guided 17 Ph.D students at HCU and University of Kerala put together. Current focus on research at MIMS RF:- (1) estrogen receptor activation factors in breast cancer and pregnancy, (2) collagen synthesis stimulating factors, (3) phytoestrogens, (4) molecular basis of insulin resistance, (5) molecular basis of antibody formation.
- **Dr. P J Wills.** Ph.D. in the field of Molecular Pharmacology, University of Kerala and Rajiv Gandhi Centre for Biotechnology, Trivandrum. Postdoctoral Research Associate at School of Biosciences, Mahatma Gandhi University, Kottayam. Special interest in lepidopteran biology, dynamics and lepidopterism. Major research focused in identifying new anticancer molecules from plants as well as from marine sources.
- **Dr. A. P. Vijayan.** DCH., DNB., M.D. (Paediatrics), M.D.(Community Medicine), Consultant Paediatrician. In Charge of Safe School Initiative of MIMS. Published a recent paper on insulin resistance in School children.
- **Ms. Radha Malattiri.** M.A, MLIS, M.Phil. Coordinates all research activities.
- **Mr. Varun Raghuveeran.** M. Sc, Junior Research Fellow (MIMS-RF).

PUBLICATIONS

1. Vijayan.A.P, Varma.K.K, Meera Bhagyanathan, Dinesh.K.B, Divyanath.K.R and Bijayraj.R. Three Physical markers of Insulin resistance (body mass index, waist circumference and acanthosis nigricans): A cross-sectional study among children in south India. Medical Practice and Review Vol.2(4) p.37-43 June 2011.
2. Dr.RV.Thampan. Third chapter, 'Evolving Trends in Estrogen Receptor Biology' of the book, "Steroids-Basic Science" edited by Hassan Abduljabbar

INFRASTRUCTURE DEVELOPED

1. **Laboratories** - There are two major laboratories and one minor laboratory with essential instrumentation facility needed for conducting biological studies in depth.
2. **Cell culture facility** -A facility for developing and maintaining human and animal cell culture has been developed, with a clear understanding that cells in culture are unavoidable tools in modern biological research.
3. **Facility for extraction of bioactive agents from plants** - The basic tools employed for the extraction and concentration of plant-derived bioactive agents have been installed in this unit.
4. **Washing and Sterilization (W&S) facility** - Cleanliness of glass and plastic ware is critical with reference to their employment in biochemical and cell culture studies. The W&S facility has been created based on this perspective.
5. **Small animal facility**- A facility for maintenance of small animals has been designed and developed, ready to be used for experimental studies involving laboratory mice, rats and rabbits. CPCSEA registration has been obtained for the facility.

INFRASTRUCTURE AWAITING GOVT. OF INDIA APPROVAL

Radioisotope laboratory- Awaiting Govt. of India approval is the set up for handling radioactive isotopes. Modern biological research is crucially dependent on the use of radioactive chemicals. It is anticipated that this facility will become functional soon.

Research Laboratory - 1

Research Laboratory - 2

Small Animal Facility

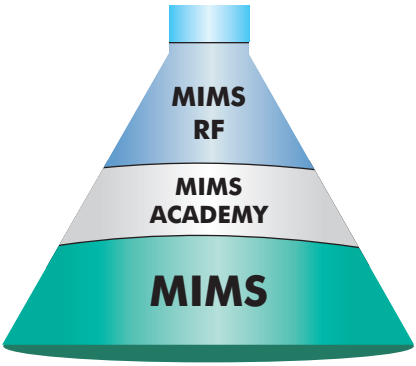
Cell Culture Room

Three Levels of Wisdom

1. **Malabar Institute of Medical Sciences (MIMS)**
   Parent Institution. 600 bedded first NABH accredited multispecialty hospital in India.

2. **MIMS Academy.**
   Education wing of MIMS, runs national and international Academic Programmes.

3. **MIMS Research Foundation**
   Better Health through Scientific Research



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a caring mission a global vision