

Short Living Biography

Dr B K Thelma

Dr. Bittianda Kuttapa Thelma

Fellow- IASc, INSA, NASI

Professor, Department of Genetics, University of Delhi- South campus

by Piyush Kumar

Prof B K Thelma, known as Thelma among the BioScience community is a well recognized leader in Medical Genomics Scientific research and among the few scientists who translated her research into application. Dr Thelma is an excellent example to understand how Genomics is done and how it is applied for the welfare of general public. Thus we are trying to write as much as possible about her for our readers who search for new avenues and career prospects in Genomics.

Early Life

Dr Thelma came from a pretty little town called Madikeri, situated in the hills and valleys of a heavenly place called Coorg, some three hours away from Mysore. She was raised by a very loving, caring and progressive family - which included her parents, grandparents and several aunts - in a small house with a large backyard. Her parents were busy state government officials. Her grandfather was a highly disciplined, gentle yet firm man who had served in the British army and was an art teacher in a government school. Thelma's father, B G Kuttapa, had a transferable job but her mother, Muthamma, also a government employee, chose to stay with her elderly parents and look after them and the extended family.

One of her aunts, who was the first woman to serve in the government office in Coorg, took on the role of her mother and teacher. In her household, there was no discrimination done between boys and



RESEARCH INTERESTS:

- * Human molecular genetics and Medical genomics
- * Genetics of complex brain and inflammatory disorders in humans (Schizophrenia, Parkinson's disease, Rheumatoid arthritis, Inflammatory bowel disorders, Celiac Disease)
- * Pharmacogenetics of commonly used antipsychotic, anti-PD, anti rheumatoid drugs
- * Identification of new gene(s) for Mental retardation and Parkinson's disease
- * Population genomic architecture
- * DNA Diagnostics

Notable Honors and Awards

- * Dr Thelma received the Fogarty International Research Career Award in 1997.
- * Fellow, Indian National Science Academy
- * Fellow, Indian Academy of Sciences, India
- * Fellow, The National Academy of Sciences, India
- * J.C. Bose fellow
- * Ex-Member, Scientific Advisory Council to the Prime Minister
- * Ex-Member, Science and Engineering Research Board (SERB)
- * Ex-Member, Human Genetics Task Force, Dept. of Biotechnology;
- * Subject expert, Indian Council of Medical Research
- * Member, Guha Research Conference
- * Trustee, XV International Genetics Congress Trust
- * Ex-Vice President, Indian Society of Cell Biology
- * Member - KVPY Management Committee

girls. Everyone was held to the highest standard. She began primary school at the age of 3. She got the best education which middle-class parents could afford and, her parents repeatedly reminded her and her two siblings that education was the only thing which would stand by them.

Opting Science

Since there was a close relative who was a doctor, Thelma always wanted to be a doctor but her father wanted her to do either a Master's in Maths or join the IAS. Somewhere at the back of her mind the notion of serving people was always there maybe because she saw the way her mother and her aunts took care of her grandparents. She was told that if she wanted to do medicine the best option was to get into biology. In Class X, she was the only one in her school to get first class in all four parts. Thelma did not do badly in her pre-university exams but she was only 14 years old and one had to be 16 to get into medical school so there was no option but to do a BSc. and Thelma was very disappointed. She went back to Mount Carmel College, Bangalore and took biology during her BSc.

Upon completing B. Sc., she decided to pursue a Master's in Zoology. While doing Master's, the head of the department gave her cytology as the special paper, instead of physiology – which she wanted. She could not come to terms with their decision and resisted dedicating too much time to the course. She constantly interacted with another mentor and her students who were pursuing Ph.D in Animal physiology. This stint motivated her to pursue a Ph.D in biomedical research.



Doing Ph.D

Due to poor preparation, she says, she did not get to do Ph.D at any of her first choice schools but she joined Ph.D. in the Zoology department, at Delhi University. Her obsession to do biomedical research led her to her Ph.D. mentor Prof. S.R.V. Rao. The first two or three years in the lab she recalls were a breeze, for in the 1970s the pressure of doing research in science was not as much as it is today and things were more relaxed. There were no computers or the internet. The students had to go through journals to read articles to be aware of current state of research on a subject. Thelma says that she cannot claim to have done great science at that time but what she did, she did well.. The lab had a very relaxed environment and the passion and commitment to a research question that she saw in her teacher made a lasting impression. Prof. Rao used to spend long hours at work, discussing not just the project at hand, but all other contemporary findings. He nurtured a passion for scientific research and emphasized the research process, rather than just the results. Thelma could not work on a direct biomedical project then but used a wild rat as her animal model to understand some basic concepts in cytogenetics. She had the opportunity to do a lot of tissue culture work.

During her PhD, the fellowship was just four hundred rupees. But it did not seem to matter. It covered her hostel costs, was enough for occasional outings and even small trips outside Delhi. It even allowed for small but precious gifts for her family when she visited them annually.

International Exposure

Once a person completes a Ph.D the obvious choice is to go for a Post-doc. Thelma now wanted to work in the area of genetic disease and engage in bio-medical research. She was fortunate enough to get a post-doctoral fellowship in 1984 at the Department of Research, University Hospital, Human Genetics Laboratory at Zentrum fur Lehre and Forschung (ZLF) at Basel, Switzerland. The renowned Dr Hans Jakob Muller took her on as a Post-doc student.

Because she was finally in a hospital setting, the experience was very satisfying for her. Thelma was supposed to work on the genetics of human male infertility. It interested her because she knew it would give her the opportunity to work in a clinical setting. Maybe it was an indirect way of looking for what she had missed by not being a doctor. But she felt that she was finally on the road to doing something she had always wanted to do. There she began work on assessing chromosome anomalies in male

Academic Achievements:

- * Team Leader, Centre For Excellence In Genome Sciences And Predictive Medicine - Funded by Department of Biotechnology, Govt. of India
- * Member, International consortia on Genetics of Celiac disease & Inflammatory bowel disorders
- * Member, Task Force, Dept. Biotechnology & Indian Council of Medical Research
- * Mentored several Ph.D. students, Published several research papers
- * Recipient of several national and international research funding.
- * Visiting scientist, Max Planck Institute for Molecular Genetics, Berlin, Germany
- * Visiting Scientist, Dept. of Psychiatry, Hadassah Medical Centre, Jerusalem, Israel
- * Visiting scientist, Dept. of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh, Pittsburgh, USA
- * Fogarty International Research Career Award- Univ. Pittsburgh, USA
- * Visiting Scientist- Dept. of Human Genetics, Memorial Sloan Kettering Cancer Centre, New York, USA
- * Biotechnology Associateship- Institute of Human Genetics, Berlin, Max-Planck Institute, Munich, and Physical Chemistry Institute, Heidelberg, Germany
- * Biotechnology Associateship- Centre for Cellular and Molecular Biology, Hyderabad

Member- Scientific and advisory committee
The Fragile X Society is based in Mumbai, India, and has successfully created a network all over the country with parents and eminent doctors. The society promotes public and professional awareness. We extend help to families with affected children in terms of literature (translated versions available on request), guidance and a deep understanding of how Fragile X Society can impact families.

Scientific Achievements:

Dr Thelma contributed significantly to the teaching of cytogenetics and developed a very strong teaching and research programme in human genetics. She pursued intensive research on the understanding of functional significance of repetitive sequences on the X and Y chromosomes using a rodent model.

Her later researches focused on: genetics of complex traits, particularly brain disorders including schizophrenia (SCZ), Parkinson's disease (PD), mental retardation (MR); and inflammatory diseases such as Rheumatoid arthritis and inflammatory bowel disorders. Role of genes from the dopaminergic pathway in SCZ, PD and tardive dyskinesia are her major findings. Her studies on disease genomics of the genetically distinct Indian population provided major insights into the population specific genetic susceptibility patterns.

Pharmacogenetics, the science of inter-individual variation in drug response, is another area where her group made significant contributions. She has mentored 21 PhD students and has over 100 publications to her credit.

Other Research based Contributions:

Dr Thelma established the DNA-based diagnosis facilities for fragile X syndrome, the most common form of inherited mental retardation, with financial support from Department of Biotechnology. Her Lab is one of the few which offers this national level diagnostic service.

infertility and trained in in vitro fertilization method.

The Basel institution where she did Post-doc wanted her to stay on and offered her a job, but Thelma knew she had to come back to her country.

Returning to India

She returned to India and decided to become a teacher - scientist so that she could inspire others the way Prof. Rao did. When Thelma returned, Professor and Mrs Rao were not in the country. Thelma could return to her parent lab, but finding accommodation on the university campus for post-doctoral workers, especially women, was very difficult at that time.

She took over Professor Rao's teaching responsibilities to the students doing their Master's in Zoology for the six months when he was out of the country and also stayed with their three children. Meanwhile she applied for a Pool Officer's post and got the position. She joined as a Pool Officer, continued her research and fulfilled her assignment of teaching students doing their Master's. She was subsequently selected as a University Research Associate in the same department.

People often asked her why she did not opt for a permanent position as a college lecturer but Thelma enjoyed doing research in her parent lab and within there she nurtured the desire to have a university job where she could teach and also have a research lab of her own.

Thus she had several years of research experience, and knew her cytogenetics well. She worked with animal models but along the way she also had a chance to look at humans who wanted to get their chromosomes tested in the laboratory, so she also had experience working with human material. All this was in her bag while she waited for a job of her liking.

Getting a Job

She applied for the posts of lecturer and Reader in the Genetics Department in the South Delhi University Campus. When the interview letters came, she prepared very well. After performing well for the interview for the lecturer's post, she went in the afternoon for the interview for the Reader's post. The Vice-Chancellor of the University who was in both the interview panels jokingly remarked, 'Oh Thelma, you have returned like a bad coin'. Thelma said, 'No, I have returned as a prodigal daughter'.

Thelma was chosen for the lecturer's post. The Reader's post was not filled. This was 1987 and for the next eleven years, Thelma remained a lecturer and enjoyed teaching in the Genetics Department. But in the afternoon, she had to take an auto or board the Univer-

Summary of scientific contributions of Dr B K Thelma

Dr Thelma is well recognized for her consistent and original contributions in the field of medical genomics in the country. Working together with clinicians to utilize the valuable patient resource available in the ethnically distinct Indian population and using contemporary genome analysis technologies, her contributions to discovery genomics both in single gene and complex disorders have been consistent and seminal.

Some of the major findings of global relevance in the last five years include:

- Discovery of
 - (a) ARL15, a susceptibility gene for rheumatoid arthritis (Negi et al., 2013) &
 - (b) seven non-HLA genes/loci for ulcerative colitis (Juyal et al., 2014) based on the first ever Genome-wide association studies in the country;
 - (c) several risk loci for celiac disease (Senapati et al., 2014) &

Based on next generation sequencing

- (d) MID2 for X-linked intellectual disability (Geetha et al., 2014);
- (e) PODXL for autosomal recessive juvenile parkinsonism (Sumedha et al., 2016a) &
- (f) RIC3 for autosomal dominant Parkinson's disease (Sumedha et al., 2016b) &
- (g) TAAR1 (John et al., 2017); TIMP2 (John et al., 2018) & a few more conferring susceptibility to schizophrenia

-Pharmacogenomics of methotrexate in rheumatoid arthritis (Senapati et al., 2014) &

Functional characterisation of pharmacologically relevant dopaminergic gene variants (Michealraj et al., 2014; Punchaichira et al., 2017)

- To address the biggest global challenge of phenotypic heterogeneity limiting the understanding of genetic basis of common complex disorders, her group is pursuing an innovative approach of combining the doctrines of Ayurveda for deep phenotyping of individuals with modern genome analysis tools (Ayurgenomics) which is breaking new ground for predictive and personalized medicine.
- Disease diagnostics: Besides high quality basic research, in an unparalleled contribution for translational medicine/science for society, her persistent efforts using a public-private partnership mode for screening ~200,000 newborns (NBS) in Delhi State for 46 inborn genetic diseases, has generated the first ever systematic epidemiological data and mutation spectrum. This undoubtedly is of immense value for facilitating national policy decision(s) on making NBS mandatory in India.

Taking discovery to lead molecule development under the Center of Excellence in Genome Sciences and Predictive Medicine is the current pursuit of her group.



●● B K THELMA AT HER PH.D. CONVOCATION IN 1983

city bus and return to the North Campus to her parent lab because the science departments at the South Campus were rather new and did not have any research labs yet.

As a lecturer Thelma taught cytogenetics, a subject she thoroughly enjoyed teaching. Alongside, she started writing research grant proposals. Her projects were still on the animal

model but all along she knew that she had to do human genetics. She kept telling herself that once she got sufficient lab space she would begin work in human genetics. And that was where the turning point lay.

The animal model they were working on had something called as a Fragile-X chromosome. Just around that time the gene responsible for the Fragile-X Syndrome, the biggest cause of inherited mental retardation in humans, was identified by scientists abroad. She started work on that gene and that marked the beginning of Thelma's human genetics work in her own lab. A series of lucky breaks had brought her to this point of research. She soon knew that she had got a much needed foothold to switch over to human genetics research 'to do what her heart was really longing for', to put it in her words. At that time human genetics research was being done in a small way and only in a few labs in the country and human molecular genetics

was almost not there.

1995 was the time when the Department of Genetics was getting a facelift. A new science building Bachawat Block with reasonable lab space was allotted for the Genetics Department. It was also the time when Thelma got her first Human Genetics Project from the Department of Biotechnology, Government of India to work on the molecular diagnosis of Fragile-X Syndrome together with Professor Meena Gupta, a paediatric neurologist at G B Pant Hospital, as a clinical collaborator. Together with her, Thelma started screening mentally retarded kids from several special schools across Delhi to detect if they had the Fragile-X mutation. Since it is an inherited condition one has to not only screen the affected child but also the extended family. Identifying one mutation positive child could help the entire family as expectant mothers can then be offered a prenatal diagnostic test to identify if there is a mutation in the growing foetus and thus prevent the birth of yet another affected child in the family. It is indeed a piece of work of immense applied value and a service which Thelma's lab continues to offer even today to clinical collaborators seeking diagnosis for hundreds of their young patients and their anxious parents from all over the country.

Thelma has been the Head of the Department of Genetics in the University of Delhi South Campus. Thelma tends to dismiss her struggle to reach this stage of her career and says that science is all that matters.

Current Status

Dr Thelma currently is a Professor at the Department of Genetics and Team leader, Centre of Excellence for Genome Sciences and Predictive Medicine funded by the Dept of Biotechnology, Govt. of India. She is a Science Advocate who is involved with many governmental and non-governmental organizations. Backed by a large body of data from a SERB, Govt. of India funded novel feasibility study on newborn screening for inborn errors of metabolism, that she recently completed along with a large team of clinical collaborators from 20 hospitals across Delhi state, she is advocating for newborn screening program to be made mandatory in the country. It will reduce the burden of this preventable group of disorders in the country and is an excellent example of translational medicine and a technology for the masses.

