

T. M. Jacob (1927–2014)

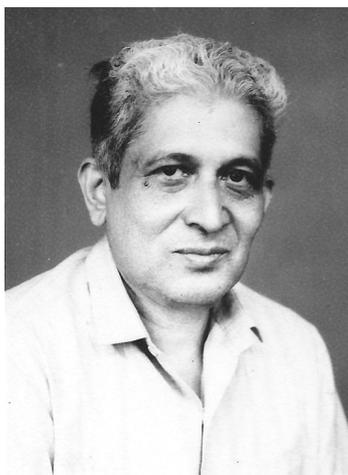
T. M. Jacob passed away on 6 June 2014, on his 87th birthday, after living a full life, as one of the remarkable mentors of research students at the Indian Institute of Science (IISc), Bangalore, and as one of the finest human beings one would have ever come across.

Thazhuthaveetil Mathai Jacob was born in Kaloor village (Thodupuzha taluk), in Kerala on 6 June 1927. He completed B Sc in Chemistry in 1949 and B Sc (Hons) in Chemistry in 1951 from Loyola College, Madras, under the University of Madras. Subsequently, he worked for a year as lecturer in St Joseph's College, Bangalore. During 1952–1957, he completed Ph D in Organic Chemistry from IISc, under the supervision of Sukh Dev. From 1957 to 1959, he worked as the National Research Fellow at the Institute and subsequently, one year each as Research Associate at the University of Toronto, Canada, and at Steven's Institute of Technology, New Jersey, USA.

The turning point in his academic career came in 1961, when he joined the research group of Har Gobind Khorana (at the Enzyme Research Institute, University of Wisconsin, USA), who later went on to win the Nobel Prize, along with Marshall W. Nirenberg and Robert W. Holley, in Physiology or Medicine, in 1968, for the cracking of the genetic code. Jacob worked there for three years as a Project Associate and later as an Assistant Professor from 1964 to 1966. The strong foundation in synthetic organic chemistry that Jacob built up through his academics in chemistry and then in organic chemistry in Sukh Dev's laboratory, helped him to become a significant contributor to the research projects of Khorana. In the sixties, Khorana published a series of about 60 papers under the main title, 'Studies on polynucleotides', on the chemical synthesis of polynucleotides of specific sequences and their ability to support homopeptide synthesis, in the *Journal of American Chemical Society* and the *Journal of Molecular Biology*. Jacob was a co-author in many of these publications. He was involved in the chemical synthesis of polynucleotides of different permutations and combinations of the bases, which were used for the *in vitro* decoding experiments by Nirenberg at the

National Institutes of Health, USA, which fetched the Nobel Prize.

Jacob returned to India in 1966 to join as a Senior Research Fellow at the Department of Biochemistry in IISc. He became Assistant Professor in 1968, went on to become Professor in 1975, and superannuated in 1987. Subsequently, he continued as INSA Senior Scientist till 1991 in the Department. Jacob initiated a new area of research – immunology of



nucleic acids, in the Department of Biochemistry, probably for the first time in the country. During the two decades of his stint as a faculty member, Jacob carried out a systematic investigation on the production, purification, and determination of the specificities of anti-nucleic acids antibodies, with a view to obtaining antibodies of well-defined narrow specificities for the use as tools to study genetic material both *in vivo* and *in vitro*. He also wanted to use such antibodies to study the specificity of nucleic acid–protein interactions occurring at different steps of gene expression.

During these investigations, it was demonstrated that the specificities of the antibodies could be directly and accurately assayed using radioactive haptens and a membrane filter binding method. Affinity columns were developed for the purification of the anti-nucleic acid antibodies. A novel and mild elution procedure was developed for these antibodies from affinity columns, based on the observation that antigen–antibody interaction is reversibly inhibited by low concentrations of pyridine. Anti-dpA antibodies were found to be highly

specific to the whole molecule of dpA, with the sugar, the adenine base, and the phosphate playing important roles in antibody recognition. The cross-reactivity of these antibodies with other nucleotides was found to be of a very low order. Jacob and his research students succeeded in generating antibodies that were specific for deoxyribo-dinucleotide sequences as well. This work was further extended to generate antibodies specific to tri, tetra, penta, hexa, and hepta deoxyribonucleotides of defined sequences. The distinct trait of hailing from a research tradition, where synthetic organic chemistry was used to understand biological processes, can be seen throughout the research contributions of Jacob.

In a parallel study with Joseph D. Cherayil, who was working on the modified bases on transfer RNAs (tRNAs) in an adjacent laboratory in the Department of Biochemistry at IISc, Jacob demonstrated that the antibody to the modified base, isopentenyl adenine, could specifically inhibit aminoacylation of tRNAs containing isopentenyl adenine, but not of other tRNAs. This observation opened up the possibility of using antibodies specific to rare modified bases in the study of the structure–function relationship of tRNAs. Jacob later attempted the use of anti-nucleic acid antibodies to recognize specific sequence of bases on chromosomes. He was also involved in collaborative studies with M. A. Viswamitra (Department of Physics, IISc), who studied the crystal structure of B-DNA sequences, which were synthesized by Jacob. The collaborative research project between Jacob and Viswamitra was one of the projects that supported the DST Unit on Genetic Engineering, which was established at IISc in 1982, with the efforts of T. Ramakrishnan, who was the then Chairman of the Microbiology and Cell Biology Laboratory (MCBL) at IISc, and others. Jacob was also a key member of the ICMR Centre for Advanced Research in Genetics and Cell Biology (1974–1991), an interdepartmental research group funded by the Indian Council of Medical Research. The other members of the group were H. Sharat Chandra, M. A. Viswamitra, and T. Ramakrishnan.

The origin of molecular biology in IISc took place in the 1970s, with the encouragement and support of the then

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Director, Satish Dhawan. Jacob, along with Joseph D. Cherayil (who was earlier in the research group of Robert W. Holley and who purified alanine tRNA for its structural determination that won the Nobel Prize), and Joseph D. Padayatty, initiated research on molecular biology based themes in the Department of Biochemistry. Jacob and Cherayil, who were colleagues and close friends, had the aura of having worked in the research groups that won the Nobel Prize in Physiology or Medicine. Hence their research groups at IISc were highly sought after by Ph D students every year. T. Ramakrishnan, who initiated molecular biology research in MCBL, and Jacob jointly launched an interdisciplinary Ph D programme in molecular biology at IISc. Jacob started the 'Lunch Time Molecular Biology Seminar', which used to be held on Thursdays between 1 PM and 2 PM, at the Department of Biochemistry. A large number of students from the laboratories across the Division of Biology used to present papers on molecular biology based themes in the seminar. Even after Jacob's leaving the Institute in 1991, the seminar was continued by G. Padmanaban, and it ran for almost 40 years since its inception.

Jacob was a mentor not only to the students of his research group (now

occupying high positions in both academia and industry all over the world) but also to a large number of students in the Department of Biochemistry and in IISc at large. He was always approachable to students with any problem, be it academic or personal, and many students have benefited from their interaction with him. Jacob was a dignified, contented individual. He was so soft spoken that one had to stand close to him to listen to him. We had never seen him getting angry at anyone, and he had never scolded any student, even on occasions of unrest among students. With a smile, he used to give gentle advice to students on such occasions. This remarkable personal composure and gentleness was an adorable character, rare to be seen in academicians – much rarer indeed these days.

In 1952, Jacob married Rosamma, who was the younger daughter of P. J. Thomas (a doctorate from Oxford, who was the noted economist at the Madras University, later nominated to Rajya Sabha, to become economic advisor to the Government of India). They are now survived by a large family, consisting of his son (Mathew Jacob at the Supercomputer Education and Research Centre and the Department of Computer Science and Automation, IISc), four daughters, all well placed in society, and their children.

Jacob was a life member of the Society of Biological Chemists (India) and the Association of Microbiologists (India). He was a Fellow of the Indian Academy of Sciences and the Indian National Science Academy. Looking at T. M. Jacob's rich experience and expertise in synthetic organic chemistry research, high academic calibre, and the breadth of scientific contributions spreading across chemistry and biology, one tends to feel that he did not get the recognition that he deserved in his professional life. The nation could have immensely benefited from his expertise, experience, and knowledge. These thoughts remind one of the following lines in Thomas Gray's poem, *Elegy Written in a Country Churchyard*:

'Full many a gem of purest ray serene,
The dark unfathom'd caves of ocean bear:
Full many a flow'r is born to blush unseen,
And waste its sweetness on the desert air.'

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