Joseph Devassy Padayatty (1928–2014)

Joseph Devassy Padayatty, a teacher, who by dint of sheer hard work and application of mind, became a doyen of molecular biology in India, passed away on 26 August 2014. Born on 10 July 1928 in Puthanpally, Varapuzha (Kerala) he was the only child to the farming family of Devassy Ouseph Padayatty and Mariam Devassy (*nee* Vithayathil). He had one of the sharpest minds in life sciences, whose trade-mark character was to question conventional ideas and always play the devil's advocate to bring out the best in his students. He began his career as a teacher, but soon he felt that his intellect needed challenges, and went to the US to work towards a Ph D on bacteria and phages at a time when 'phage' was a term discussed only in Cold Spring Harbor and CalTech. Enrolling at the St Louis University, Missouri, in the Department of Biochemistry, then headed by the Nobel Laureate Edward Adelbert Doisy (who discovered vitamin K), he did Ph D (1961–65) followed by postdoctoral research (1965–68). In 1968, he joined Indian Institute of Science (IISc) Bangalore as a pool officer and was eventually offered a faculty position at the Department of Biochemistry where he worked until his retirement in 1988. At IISc he elucidated the molecular mechanisms involved early in the germination of rice and was the first to clone a gene in India. He, along with his colleagues at IISc, introduced molecular biology in India, eventually establishing it as a distinct field within biochemistry.

His decision to go to the US in 1961, travelling in a cargo ship (he would explain later that the cabins were quite comfortable) to do advanced research, leaving behind his wife Mary and his young children Sebastian and Jasmine, for what turned out to be seven long years, demonstrates his single-minded pursuit of his scientific goals. He was working on T4D bacteriophage (D stands for Delbruck who identified the phage) during his postdoctoral work as well as during his stint at IISc as a pool officer, from where he continued the work on phages in his independent laboratory. During one of his visits to IISc, Max Delbruck was very pleased to see that his strain was being worked on in Padayatty's lab! Not satisfied with working on T4 phage, as it had no direct relevance to India, Padayatty started working on a locally isolated phage, the colitis phage. Additionally, he wanted to take up relevant, albeit challenging, work on the molecular biology of rice germination in his laboratory. This decision, which was far ahead of his time, was ignited by his zest for challenges combined with an intense desire to make a useful contribution to the largely agricultural economy of India. He made remarkable contributions in both the fields, molecular biology of phages and rice, establishing himself as a pioneer.

Working as a faculty member in the Department of Biochemistry, IISc, for 20 years (1968–1988), he initiated recombinant DNA research in India. He prepared himself for this by spending one year as a visiting scientist at the UCLA laboratory of Winston Salser, working on the chicken globin gene. It may be recalled that Salser went on to establish Amgen, one of the first and most successful biotech companies. This time he went with his wife and younger daughter Maylin to UCLA, leaving behind Sebastian and Jasmine in hostels. He performed the Maxam and Gilbert method of sequencing at UCLA, much before it was published. On returning to the IISc lab, at a time when DNA sequencing was unknown to most Indian labs, he urged his research students to use the Maxam and Gilbert method of sequencing to study genes at the sequence level. It took some time to procure all the chemicals required for sequencing and to standardize pouring a sequencing gel. But the major challenge was to procure gamma-32P nucleotides for the sequencing reactions. Much of the library screening, restriction mapping and partial sequencing work in the early days were performed using the wash of an empty vial of labelled nucleotide. This material was brought under special permission for a DST-sponsored sequencing workshop conducted by one of his students, Sushil Devare, who was at NIH in the US. After using all the contents for the workshop, the empty vial was 'gifted' to the Padayatty lab! In contrast, protein work was a lot easier to do, as BARC was supplying ^{14}C-labelled chlorella protein hydrolysate. For higher specific activity in labelling, 35S-methionine used to be prepared by growing bacteria in 35S-sulphuric acid, isolating and purifying 35S-methionine by paper chromatography from protein hydrolysate. It was Krishna Kesari, a research student in the Microbiology and Cell Biology Laboratory at IISc, who had mastered this technique and used to supply 35S-methionine in large quantities!

Trained by his questioning nature, students in his laboratory were encouraged to ask fundamental questions in biology. The moment water is given to the dormant rice seed, its embryo bursts forth with life! Many rounds of cell division and expression of a large number of genes occur. What is the design in the seed to achieve such rapid growth? It was discovered that the embryo contains translation-ready conserved mRNAs, which get instantly translated the moment water is given to the dormant seed. These were the mRNAs for histones, but strangely lacking the poly(A) tail, a hallmark of typical mRNAs that are rather short-lived. Conserved mRNAs have to be fairly stable and the translation machinery needs to be on a 'ready-to-go' mode for instantaneous translation, the moment water is given. Conserved histone proteins were also found in the rice embryo. Thus, all the ingredients for the initial transcription and translation required to trigger germination-related gene expression, are already present in the dormant embryo! These original findings from Padayatty's lab answered, to an extent, the question on the special design in the dormant embryo on the readiness for instantaneous germination.

The colitis phage was a marvellous virus to work with. It was small and easy to culture, and gave huge yield of DNA from a litre of the lysate. I would just add SDS to a phage pellet and lo and behold, a solid gel comprising nothing but pure genomic DNA appeared! The DNA would easily transfect *E. coli* cells. One of the applications of this phage, using the transfection capabilities of its DNA, was to develop a sensitive biological assay for DNAses as well as a sensitive screen for mutagens. Padayatty was convinced that the colitis phage could be developed as an excellent vector system for expression studies. DNA of this phage was characterized, some of its genes expressed and the packaging of the genome was elucidated.

Asking important questions in biology and the relentless, uncompromising pursuit to find answers to those questions fostered an excellent academic ambience in his laboratory, which in turn led to notable achievements. At a time when it was rare for Ph D work to be accepted for publication in *Nature*, two papers in the 'letters' format got published in *Nature* from Padayatty's lab. The first one was on the transcriptional events that occur in rice embryo during germination. The second one was the discovery that the histone genes in rice were not restricted to one strand, but were distributed over both the strands of DNA, thereby establishing the bidirectional transcription of the histones gene cluster in rice. This was one of the many first findings to the credit of Padayatty's lab, which was the first to clone genes (including making a genomic library, screening for genes of interest, isolating and characterizing the genes and performing partial sequencing) and to report on the organization of histones genes in a plant system. In recognition of his pioneering work in these areas, he was elected to the fellowship of the Indian Academy of Sciences (1986) and the Indian National Science Academy (1987).

Padayatty was publicity shy and would present his work only in scientific fora. He was not one to hold back his thoughts and would express his opinions rather strongly and bluntly. After retirement, he went back to his ancestral home and spent his spare time advising various institutions in Kerala on Biotechnology, one of the main beneficiaries being the Cochin University of Science and Technology. His main passion, post-retirement, was farming and he tried to use his scientific knowledge and temper to do modern agriculture. This brought him rewards not only in good yields, but also an award for high productivity of coconuts.

It was unfortunate that several potential products, which were developed from the research work in his lab, did not see the light of commercialization. The *in vitro* translation system from rice embryos could have rivalled the commercially available wheat germ or rabbit reticulocyte systems. The lysozyme from colitis phage could have been a good reagent for molecular biology laboratories. The emphasis was not to patent or commercialize such products, but to do some good science with them. The IPR regime was not very conducive those days and commercialization of a Ph D scholar's work was fraught with lots of difficulties.

He had a zest for life and once confessed to me that death is not something that he looked forward to. He would learn new things all the time and would always question conventional ideas. His first student Suraj Bhat says – 'We never agreed on anything'. Most students would feel aggrieved and disappointed that he tears their ideas apart. It was only later they realized that by questioning their ideas, Padayatty was trying to bring out the best in them. In fact, he confessed to Bhat towards the end of his career that students 'these days' are not what they used to be, his major grouse being that they agreed with whatever he said! He wanted them to argue with him and come out with novel ideas.

He was very proud of his students and always stood by them. Once, the Department Chairman wanted to suspend one of his students for protesting on some student matter. Padayatty strongly stood by his student, protecting his right to dissent against whatever he found disagreeable. Another time, a complaint arose that his student's work could not be reproduced. He retorted that if it was done by that particular student, it was unquestionable. The complainant later confessed that he made a mistake and after correcting it he got exactly the same results as obtained by the earlier student. It might have been hard to convince him of new findings in the lab; but once he was convinced, no one could shake his belief in his students.

Towards the end of his career, he worked on application-oriented projects and one of the students, Suryanarayana, cloned and expressed an antigen from FMDV as a potential vaccine. Much before marker-assisted-selection became popular, he felt that non-conventional breeding can be achieved by simply transferring donor genomic DNA into an embryo!

His students are all in good positions in the US and elsewhere in the world. Nothing gave him more pleasure than a visit by his former students to his ancestral home in Karukutty, Kerala. Even in his eighties, he was talking eloquently about science. For instance, he was greatly fascinated by the genographic project and got his and his family's mitochondrial DNA analysed. He was not internet savy and even without googling, he gathered enough information and gave lectures on human migratory routes out of Africa. He was always willing to learn.

It was also his dream to see therapeutic proteins being produced in rubber latex. His idea was to produce these proteins at affordable cost and at the same time provide better returns to the rubber farmer for whom fluctuating rubber prices has been a major risk factor. He was never shy of ideas, some of them fancy, most of them, realistic. For me, his death is an immeasurable loss. From a strict disciplinarian Ph D guide, he slowly turned into an affectionate friend. I am proud to say, he was my guide, philosopher and friend!

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