



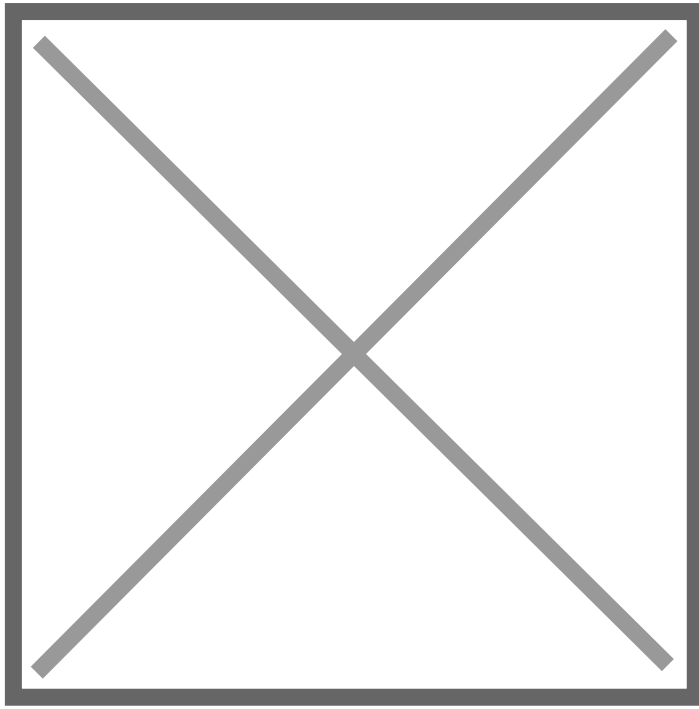
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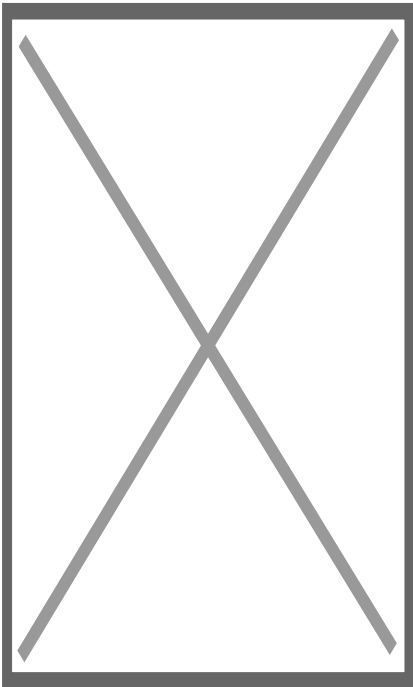
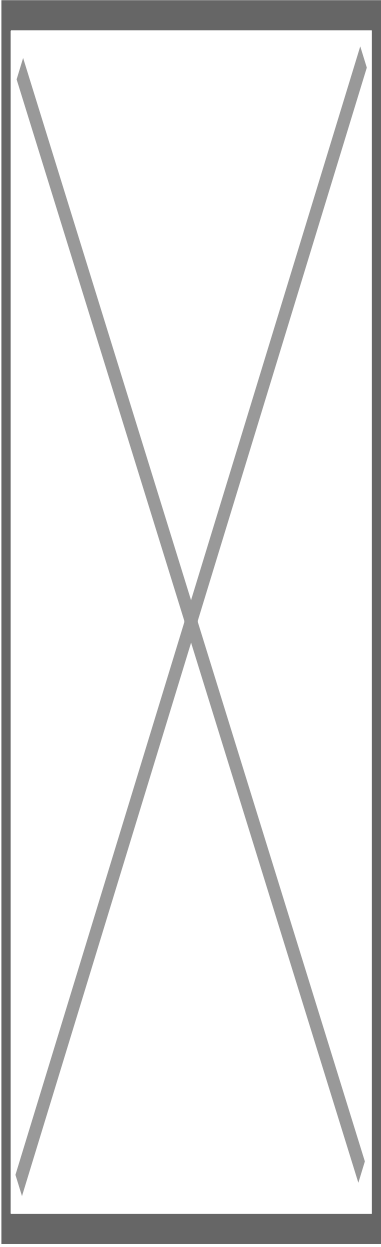
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A great scientist, teacher, and human being

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A great scientist, teacher, and human being



Govindarajan Padmanaban, born on March 20, 1938, is a renowned biochemist and a pioneer in Indian biotechnology. The former director of the Indian Institute of Science (IISc) still continues to do research as honorary professor in the department of biochemistry, IISc.

Science is everything for Prof. G Padmanaban, NASI-Platinum Jubilee Chair and Honorary Professor, Department of Biochemistry, Indian Institute of Science (IISc), Bangalore. A home grown and a genuine scientist, Prof. Padmanaban, popularly known as GP, has never been to a bank or a shop for the last 30 years. Thanks to his wife, who managed everything for him outside his lab. At 70, he still drives his own car, goes to his lab at IISc, just like he used to do before his retirement, champions the cause of development of biotech in the country, and is a motivation to young researchers.

Prof. Padmanaban is understood to be the person, who got cloning and recombinant technology to India as early as in 1980-81.

He was destined to be a scientist, though he was equally popular and good at cricket and music. He was an all rounder in cricket and played for prestigious clubs and has also won prizes for both classical and light music.

"I wanted to do PhD in biochemistry and was advised by the head of the biochemistry laboratory at Indian Agricultural Research Institute (IARI), New Delhi, to go to IISc as it was the Mecca for biochemistry," said Prof. Padmanaban. In the late 1960s, he was denied admission to do PhD at IARI.

He saw a newspaper advertisement for the position of JRF fellow at IISc to work on trace element metabolism in fungi, a subject that was to his liking. He applied for the same and was interviewed by a committee that comprised the director of the institute, the registrar, and the head of the department of biochemistry (Prof. PS Sarma). He was selected. Prof. Padmanaban later came to know from his seniors that he was called for the interview because a girl, who was shortlisted as the most favored candidate, did not appear for the interview. He believes it was destiny that led him to a life-long association with IISc.

Prof. Padmanaban was fully engaged in research and did not even think about a career or a job. It was sheer coincidence that he applied for a faculty position and got selected as an assistant professor in 1969. Till then IISc was not appointing anyone without postdoctoral experience abroad. Dr Satish Dhawan, professor in aerospace department, who had taken over as director of IISc, lifted the embargo on faculty appointment and so Prof. Padmanaban was selected. Later, he inherited the lab after the untimely death of Prof. Sarma.

Fascination with heme molecule

Prof. Padmanaban's PhD project was on trace element metabolism in fungi. But he was not getting satisfactory results and observed that an iron-binding compound (siderophore) was being generated in the medium. He was excited and worked on the structure of the siderophore compound and was able to establish that it had high-binding properties for the iron. And the fungus was able to release the iron and use it for metabolic purposes when he was adding iron complexes.

He went to show that the siderophore can be iron source to make heme (part of the protein) in the fungus. He was fascinated with the heme molecule and examined the pathway of biosynthesis of heme in the fungus. He observed that one of the enzymes in the pathway was regulated by iron and it was getting repressed in iron-deficiency condition and re-repressed when iron was added. The summary of the experiment was that a concerned gene was getting modulated. That was how his tryst began with molecular biology.

As he was fascinated with the heme molecule, he took the next step of examining the regulatory role of heme molecule in the cell and chose the rat liver system where a group of proteins known as cytochrome P-450 were induced by drug molecules. These proteins are both drug metabolizing enzymes as well as hemoproteins. "I felt this was an ideal system to study the regulatory role of heme on cytochrome P-450 gene expression induced in response to drugs (phenobarbitone) and determining the drug metabolizing potential of individuals," said Prof. Padmanaban. This is how he entered the field of pharmacogenomics, without realizing that he was entering an exciting area.

Gene cloning

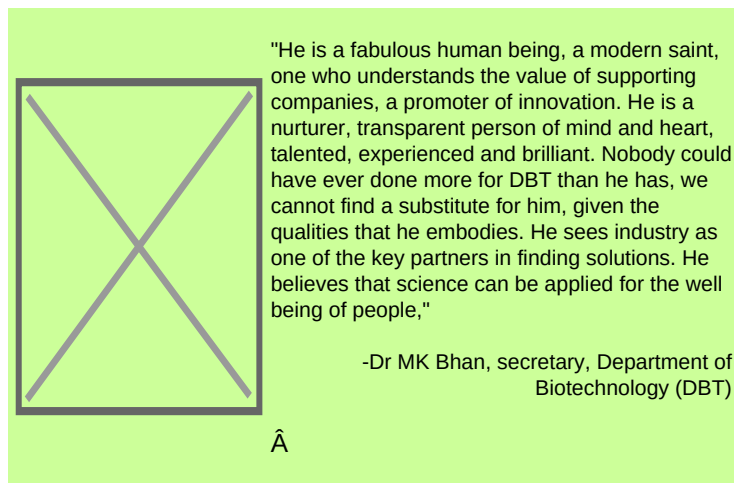
Prof. Padmanaban took up molecular biology in a big way in 1973 and he wanted to study eukaryotic systems (higher organisms) rather than bacteria. Molecular biology (DNA-RNA-protein) was mostly done with bacteria (*E. coli*) those days and eukaryotic systems were sidelined.

He was working with rat liver cytochrome P-450 and had showed that sedatives like phenobarbitone can augment the P-450 content by increasing its synthesis. This was most likely due to increase in RNA content. And he was very keen to study the P-450 gene structure. But gene cloning (recombinant DNA) and other molecular biology techniques were not practiced in India and to be conversant with those techniques, Prof. Padmanaban went to the lab of Murray Rabinowitz at the University of

Chicago.

Doing science in India in the 1970s wasn't easy. For instance he needed radioactive compounds like S-Methionine and it was impossible to import them. Importing biochemicals and radio labeled compounds was a herculean task and Prof. Padmanaban used to make some of these on his own. He made S-Methionine from SO_4 grown E.coli and even transferred the technologies to BARC, which was a major source for radio labeled compounds.

"Our efforts to undertake challenges to modernize science were mostly spent on trying to source biochemicals, radiochemicals, and appropriate gadgets. Simple things like an electrophoresis set up for DNA sequencing was not available and the easy way out was to perform the sophisticated experiments in the West and bring back the data and the slides," said Padmanaban. Though such an effort would have helped in getting a good publication, he was in favor of helping to improve the infrastructure in India and therefore indigenized the techniques that he learnt at the University of Chicago. Things today are different, he said.



Biotech entry

The National Biotechnology Board (NBTB) was set up in 1982 with the mandate to promote biotechnology and it became an independent Department of Biotechnology (DBT) in 1986. He believes that biotechnology can be a powerful tool to improve the quality of life and that India should not miss the biotech revolution. So he concentrated on developing a broader vision on biotechnology and expand his knowledge base.

That was also the time when Astra, now AstraZeneca, decided to come to India to start a research center [AstraZeneca Research Center (ARC)] in Prof. Padmanaban's lab and he convinced the IISc director to permit the unit. "We got additional space, hired fresh PhDs, mostly our own students, and started four research projects," recounted Prof. Padmanaban. The research projects included investigations on the pathogens causing diarrheal diseases, tuberculosis, malaria, and cysticercosis.

There was a lot of opposition to IISc-ARC arrangement, but Padmanaban stood by his conviction and he even declined the offer to be the head of ARC. The center has now moved out from the IISc premises. But Prof. Padmanaban gained a lot from that relationship. The most significant benefit was that he was able to fully study the malaria parasite with the aim to identify new drug targets and new anti-malarials. A lot of progress has been made in the malaria research further.

In the early 1970s and 1980s, there were no initiatives by the industry to exploit the research in the academics. "I had no clue as to how to convert my leads into products. In the early 1990s, I wanted to translate the findings on the phenobarbitone-inducible promoter-growth hormone fusion gene to rat liver. We could only show that the injection of phenobarbitone to the animal led to production of growth hormone. These could not be translated into human for want of expertise in translational research," pointed out Prof. Padmanaban. Prof. Padmanaban and his team focused on gene therapy and his students have been able to develop DNA vaccines and have also transferred some of them to the industry.

Prof. Padmanaban wanted to be a scientist and he is one of the most respected scientists in India. And he wants to continue to do his research as long as he can. His wish is to see India become a global leader at least in areas like vaccines, biopharmaceuticals, and traditional holistic medicine.

GP, the "musician" speaks

"I come from a simple middle class family. My parents were god fearing and valued education, music and good behavior as the wealth they could bestow on us.

When I started my research at IISc, my father had retired from service at Burmah Shell and decided to buy a small house in Bangalore. Raising loans, etc seemed to be a complicated affair for me and I never had time to seriously think on such matters.

I have two daughters and a son, who after years of stints in the US returned back to India.

If not scientist I would have been a musician. I do sing in small groups but never mastered the art of public performances since there was no motivation.

During my tenure as a director, we kept our own house locked and we would go back to the house to spend the weekend as I did not want to get used to the luxury of a big house, security, servants, etc.

In a way science has shielded me from several family commitments for which I want to thank my wife for letting me spend all my time in science and related matters.

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Who are your role models?

There are two people who have left an indelible mark in my professional life. One is Prof. PS Sharma who taught me that doing science is important but it should always be useful. Science doesn't fructify unless it gives useful results.

The other person is Prof. Murray Rabinowitz at the University of Chicago. I went to his laboratory in 1973 for a year as an Argonne Cancer Research Fellow. He was a remarkable person. Prof. Rabinowitz was on the wheelchair suffering with muscular dystrophy and his condition was deteriorating every day. I was allowed to visit his lab any time and I visited his lab about 10 times between 1975 and 1986. Even though he was sick, he came to the lab five-days a week, conducted lab meetings, wrote grant proposals, published papers, and was elected to the US National Academy of Sciences. He was an actual scientist. I still keep his photograph in my lab. He died in 1985.

How do you see the progress of biotechnology in the next few years?

In India, we don't see innovative products. Most of the products in India are from reverse engineering. Biotechnology will definitely grow in the coming years. I have seen some good ideas from some of the companies. We made the hepatitis B vaccine here (indigenously), while it was already available in the US for over 20 years. The difference we made was developing the vaccine which could be sold for Rs 50 instead of Rs 400. Indigenization is a justification to do, but I feel innovation is lacking here.

Are our research institutions doing innovative research?

There certainly is a lot of research work happening at the institutes, but to take it to the level of developing products needs a different kind of attitude and expertise. Many people publish a paper and just leave it. They should rather follow the idea and develop a product out of it. But they are happy publishing papers, getting promotions and getting awards. We will keep making insulin, interleukin and similar products, if we do not innovate.

How important is industry-academia interaction?

We really push our students towards industry interaction at IISc. We have the Society for Innovation and Development (SID) where all types of companies come. We have a new innovation center built out of the money earned from the society.

What is your vision for Indian biotechnology?

We should exploit biotechnology to the extreme level. For e.g., we should have a transgenic rice which can provide minerals, carbohydrate, vitamin A and everything and most importantly should be affordable so that a mid-day meal can provide all kinds of nutrition to the children. The second thing is all the children should be immunized. There are some 8-10 vaccines needed for the children. I have been talking to the government and the planning commission pursuing them to introduce the vaccines in the immunization program. What we need now is an active participation from the government, NGOs, institutes and industry. A child's nutrition and immunization according to me are the most important concerns.

