

## Janakiraman Ramachandran (1935–2020)

Prof. J. Ramachandran straddled the areas of bioorganic chemistry and molecular biology. He made outstanding contributions to hormone biochemistry, particularly hormone receptor biology and mechanisms of signal transduction, during a university career of more than two decades. Later, while continuing his association with the university, he entered the then nascent modern biotechnology industry and was involved in significant developments in biotechnology research that led to revolutionary drugs and other pharmaceuticals. He went on to head a biotechnology research centre set up in India by a Swedish pharmaceutical company, and then to found his own company to develop new ways of treating infections.

Janakiraman Ramachandran was born in Bombay (now, Mumbai) on 12 June 1935 to Sri Janakirama Iyer and Smt. Ganga Bhagirathi. After his early education in Bombay, he moved to Madras (now Chennai) where he studied with T. R. Govindachari, a renowned natural products chemist at the Department of Chemistry, Madras University. He received M.A. degree in chemistry in 1956. Subsequently, after a short stint in the Department of Chemistry of the Indian Institute of Science, with B. H. Iyer, he moved to the Department of Chemistry at De Paul University, Chicago, USA, where he received an M.S. in physical organic chemistry in 1959. He received the Ph.D. degree in biochemistry in 1962 at the University of California, Berkeley, where he was a graduate student with C. H. Li. His doctoral thesis pertained to structure–activity relationship of adrenocorticotrophic hormone (ACTH). While he was a graduate student, he collaborated with C. N. R. Rao and synthesized a number of organic compounds to designate infrared frequencies of various functional groups. After obtaining his doctoral degree at the University of California, Berkeley, he spent a year in 1965–66 as Weizmann Memorial Fellow at the Weizmann Institute in Israel with Ephraim Katchalsky. He returned to the US in 1968 to the University of California, San Francisco, to join its faculty, and carried out extensive studies on ACTH and other tropic hormones. Later, in 1984, he was invited to the position of

Director of Protein Chemistry at the world's first modern biotechnology company, Genentech, in San Francisco, where he was responsible for solving the problem of expression of recombinant insulin receptor. This seminal work led to the production of a number of recombinant muscarinic receptors. His interest in calcium channel blockers led him to form a new company, Neurex. At Neurex he continued work on the structure of conotoxin (SNX-111), which was associated with its analgesic property. Synthesis of the toxin with the correct disulphide bridges led him to develop the toxin into a very effective pain control



for the treatment of pain in cancer patients. Ziconotide (SNX-111; Prialt), an atypical analgesic agent for the amelioration of severe and chronic pain, derived from *Conus magus*, a cone snail, is the synthetic form of an  $\omega$ -conotoxin peptide, and is 1000 times as powerful as morphine and considered to be the best compound for the treatment of pain.

From 1987 Ramachandran began his association with the Swedish pharmaceutical company Astra AB as Director of Astra Research Centre India (ARCI) in Bengaluru and was responsible for Astra's R&D activities in India. During his tenure with Astra, he established state-of-the-art R&D programmes for discovering and developing novel therapies for the treatment of drug-resistant tuberculosis and other antibiotic-resistant infections. After retiring from ARCI, he founded a new company in Bengaluru, GangaGen, in the year 2000 for discovery and development of novel bacteriophage-derived therapies, including lysis-deficient phages and tail-associated

muraltic enzymes, for prevention and treatment of antibiotic-resistant infection. P128, GangaGen's first product for the control of *Staphylococcus aureus*, including methicillin-resistant *S. aureus* (MRSA), completed phase II clinical trials. P128 has shown very promising therapeutic effects in the control of bacteraemia due to *S. aureus*.

Ramachandran (JR, or Ram as he was known to his close associates) was a fine individual, generous, and a great host. He was also a good cook, and knew many Asian and European recipes which he would cook by himself. He enjoyed inviting his numerous friends to his home, both in Bengaluru (India) and in Palo Alto (USA) for lunch or dinner. He was a great conversationalist, well read in many subjects, including history, culture, music and politics. He loved the Tamil language. He often mentioned that if he had not continued with chemistry, he would have pursued Tamil literature. He lived both in Bengaluru and in Palo Alto and spent 5–6 months in each place every year. His house in a two-acre land in Yelahanka (Bengaluru) is a mansion designed by the architect (late) Prabhakar Kulkarni. Ram was deeply interested in Carnatic music and he had a large collection of recorded Carnatic music of famous musicians, both past and present. He often mentioned that he was envious, because he grew up in a house with girls (his sisters) who were learning Carnatic music while he was excluded because he was a boy. However, he knew the intricacies of Carnatic *ragas* and their rendering. He preferred male singers because he claimed that rendering of the nuances of *gamakas* was better in male voices.

Ramachandran passed away on 23 September 2020 in Palo Alto (USA). He is survived by his wife Denise Foley and a son, Janak, from a previous marriage. Ramachandran's demise is a great loss to the field of biochemical sciences.

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