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Mini-Review

Venki Ramakrishnan: Decoding the Machinery of Life and Transforming Molecular Biology

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ABSTRACT

Venki Ramakrishnan, a Nobel laureate in Chemistry, is a pivotal figure in molecular biology, best known for his pioneering work on the structure and function of the ribosome. His research, which employed X-ray crystallography to reveal the ribosome's atomic structure, has significantly advanced our understanding of how genetic information is translated into proteins-an essential process for all living organisms. This discovery has profound implications for biology and medicine, particularly in the development of antibiotics that selectively target bacterial ribosomes. Beyond his scientific achievements, Ramakrishnan has been a prominent leader in the scientific community, notably serving as President of the Royal Society, where he advocated for evidence-based policy and the democratization of science.

Keywords: Molecular biology; X-ray crystallography; Ribosome; Democratization of science

Introduction and Background

Venkatraman "Venki" Ramakrishnan is a distinguished scientist whose groundbreaking research has revolutionized our understanding of molecular biology. Born in 1952 in Chidambaram, India, Ramakrishnan's early life was steeped in an environment that valued education and scientific inquiry. This upbringing, combined with his innate curiosity and determination, propelled him to become one of the most influential figures in modern science. His work on the ribosome, the molecular machine responsible for synthesizing proteins in all living cells, earned him the Nobel Prize in Chemistry in 2009, placing him at the forefront of molecular biology. Ramakrishnan's journey from a student of physics in India to a global leader in biological research highlights the power of interdisciplinary study and the relentless pursuit of knowledge. This introduction explores the life, career and lasting impact of a scientist whose contributions have reshaped the landscape of molecular biology and medicine.

Early life and education

Born in 1952 in Chidambaram, India, Ramakrishnan **(Figure 1)** was raised in a family that valued education and science. His parents were both scientists, which undoubtedly influenced his early interest in the field[1]. He earned his undergraduate degree in physics from Maharaja Sayajirao University of Baroda, where he completed his schooling. He then moved to the United States to pursue graduate studies, obtaining a PhD in physics from Ohio University. After this, he shifted his career from physics to biology at the University of California.

Career and contributions

After transitioning to biology, most of Ramakrishnan's work throughout his career focused on the ribosome. Following two years at the University of California, he applied for postdoctoral research positions and was offered one at Yale University. Here, he met Peter Moore, with whom he participated in mapping the

location of proteins within the 30S subunit, one of the two major components of the ribosome[2].

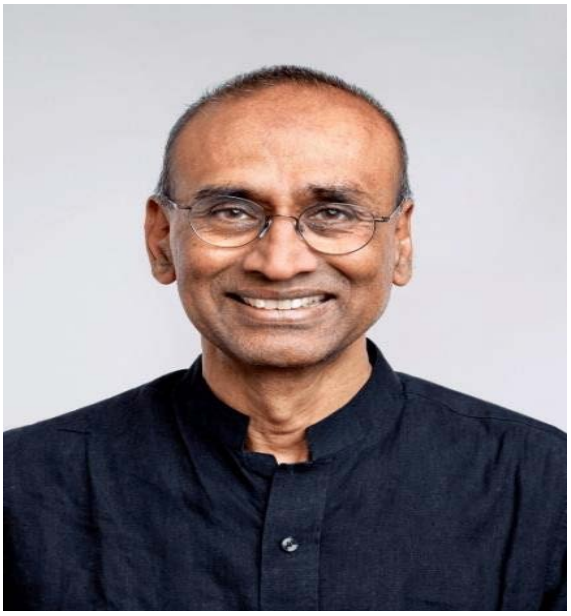

Figure 1: Venki Ramakrishnan.

Upon completing his fellowship at Yale, Ramakrishnan applied to several American universities but was not offered any interviews due to his unusual career path. He was offered a position at Oak Ridge National Laboratory before moving to Brookhaven National Laboratory. At Brookhaven, he published his first independent paper in Science. During this time, he worked on both the ribosome and chromatin using neutron scattering.

After a few years at Brookhaven, Ramakrishnan sought better ways to study the ribosome.

A colleague at Brookhaven suggested that he learn X-ray crystallography, so he went to the MRC Laboratory of Molecular Biology in Cambridge, England, for one year, supported by Brookhaven and a Guggenheim Fellowship. At MRC, he learned about crystallography. After returning to Brookhaven, he completed his last neutron scattering experiments and concentrated entirely on the crystallography of ribosomes and factors. He was then offered a job at the University of Utah, which he accepted.

Ramakrishnan, along with Bob Dutnall, went on to solve the first structure of a histone acetyltransferase. After this, Ramakrishnan worked on solving the entire molecular structure of the ribosome, but it was ambitious for the resources and facilities available at the university. While on his way to a conference in Sweden, he met again with sympathetic colleagues at Cambridge. A position had opened up at the LMB and Cambridge had resources and facilities better suited to a head-on assault on the ribosome, so he moved there.

At MRC, he focused entirely on the ribosome, continuing to send work to colleagues in Utah for analysis. This transatlantic, transcontinental teamwork paid off. Within a few months of his arrival in Cambridge, Ramakrishnan reported a major breakthrough: the entire central domain of the 30S subunit[3]. He shocked the audience at an international ribosome conference in Denmark with his findings, which were published in Nature in August 1999[4].

As he continued his efforts to map the entire 30S subunit, Ramakrishnan was aware that his old Yale colleagues Tom Steitz and Peter Moore, as well as Ada Yonath, were working on the same problem. The only laboratory where his team could harvest the data, they sought from the crystals they had created was the beamline at the Advanced Photon Source (APS) at Argonne National Laboratory in Illinois[5]. In February 2000, Ramakrishnan and a team of four booked time there, working around the clock in 12-hour shifts. Within weeks, they had the complete atomic structure of the 30S ribosome subunit.

The structure of the 30S subunit led to several follow-up studies on antibiotics and ligand binding[6]. The most important of these, largely carried out by James Ogle, led to an understanding of how the ribosome ensures the accuracy of translation during the decoding of the genetic message[5]. This discovery will enable the creation of more and better antibiotics and possibly bypass the risk of creating antibiotic-resistant microbes[6].

Awards

In 2009, Ramakrishnan was awarded the Nobel Prize in Chemistry, along with Tom Steitz and Ada Yonath, for mapping the ribosome. In 2007, he received the Louis-Jeantet Prize for Medicine, which is a major European scientific honor. He was elected as a member of the European Molecular Biology Organization in 2002, a Fellow of the Royal Society in 2003 and a member of the U.S. National Academy of Sciences in 2004.

In 2010, Ramakrishnan was awarded the Padma Vibhushan, India's second-highest civilian honor. In 2008, he won the Heatley Medal of the British Biochemical Society and became a Fellow of Trinity College, Cambridge and a Foreign Fellow of the Indian National Science Academy[1]. He has been a member of the German Academy of Sciences Leopoldina and an Honorary Fellow of the Academy of Medical Sciences (Hon FMedSci) since 2010. He was knighted in 2012 for his service to molecular biology.

Leadership and authorship

Ramakrishnan was elected as the President of the Royal Society for a five-year term in 2015[7]. He has also given many seminars and lectures at different colleges in various countries for young students. Additionally, he has distinguished himself as an author. His book Gene Machine, published in 2018, offers an insider's view of the discovery of the ribosome's structure and his journey[6]. In 2024, he released Why We Die: The New Science of Aging and the Quest for Immortality, which questions the inevitability of death and explores the potential for extending human life.

Conclusion

Venki Ramakrishnan's journey from a physicist in India to a noble laureate and global leader in science exemplifies the power of curiosity and persistence. His work on ribosomes not only helped us understand the processes of life but also laid the foundation for the development of novel antibiotics. Ramakrishnan's influence is not only in scientific experiments but also in leadership and education. He also shapes the future of research by encouraging a culture of collaboration and transparency that is important for the most pressing challenges in biology and science. His impact on science and society will endure for many years to come.

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