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OBITUARY

Professor Teruhiko Beppu (March 9, 1934–November 10, 2023) —the path he had walked

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Professor Teruhiko Beppu

Teruhiko Beppu, a Japanese microbiologist, passed from this life at 89 years of age. He long served as an Editorial Board Member (1987–2009) and Emeritus Member (2010–2023) of The Journal of Antibiotics and an Advisory Board Member of The Japan Antibiotics Research Association (1979–1995).

The scientific carrier of T. Beppu started in 1955 when he became an undergraduate student of the Laboratory of Fermentation at the Department of Agricultural and Biological Chemistry, The University of Tokyo. His supervisor, Kin-ichiro Sakaguchi, was the founder of the main field of applied microbiology in Japan.

The subject of T. Beppu's graduate research was the analysis of unique fungal metabolism. He completed his Ph.D. thesis in the same laboratory in March 1961, and subsequently became an assistant professor. Then, he was promoted to an associate professor (1969) and a full professor (1977) of the laboratory. After retiring from The University of Tokyo due to the official retirement age (1994), he moved to The College of Bioresource Sciences, Nihon University where he continued his research by supervising a new laboratory and a research institute until 2009. He was appointed to be a member of the Japan Academy as a representative of applied microbiology in 2004.

A wide variety of the research outcomes from efforts of T. Beppu and his colleagues was published including more than 500 original papers and book chapters. One of the accomplishments in his early days of research was the discovery of alloisocitric acid fermentation in fungi. He quickly introduced molecular biological techniques to his studies in the early 1970s. The milestone work during his career was the cDNA cloning of calf chymosin. He successfully generated its recombinant protein using an *Escherichia coli* host vector system and introduced it to the cheese manufacturing industry. He also worked on the characterization of many industrial enzymes and unique bacterial functions, such as the action of bacteriocin and the mechanism of protein secretion.

T. Beppu promptly worked on the screening for biologically active substances in microbial metabolites and identified various compounds that effectively inhibit specific cellular functions. Of these, the discovery of trichostatin and leptomycin and the subsequent identification of their molecular targets of action contributed greatly to the progress of eucaryotic cell biology. T. Beppu had foresight to perform the research approach today termed Chemical Biology.

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Another work area of T. Beppu related to microbial secondary metabolism was on the study of A-factor. A-factor (which stands for autoregulatory factor) is a gammabutyrolactone originally identified by Alexander S. Khokhlov to be a chemical factor involved in streptomycin production in *Streptomyces griseus*. First, T. Beppu investigated the cause of the frequent occurrence of streptomycin-nonproducing mutant, which was a significant issue in industrial production. He discovered that it is based on the loss of the ability to synthesize the A-factor. His detailed studies elucidated how the A-factor induces the expression of genes involved in the secondary metabolism and morphological development in *S. griseus*.

Today, the idea is widely accepted that microorganisms live by forming a community in nature, but T. Beppu had already proposed this idea in the 1980s. He studied various modes of microbe-microbe correlation and identified chemical factors involved in the unseen interaction that ranges from general substances such as carbon dioxide to specific organic molecules including siderophores. T. Beppu published more than 30 papers in The Journal of Antibiotics dealing new insights into microbial products.

In recognition of his significant achievements, T. Beppu was honored by awards from various societies, including the Japan Society for Bioscience, Biotechnology and Agrochemistry (1986), the International Union of Microbiological Societies (Arima Award, 1990), and the American Society for Industrial Microbiology (Charles Thom Award, 1995). The Japanese government honored his great contributions by awarding Medal with Purple Ribbon (1996), the Japan Academy Prize (1998), the Order of the Sacred Treasure, Gold and Silver Star (2009), Person of Cultural Merit (2012) and Order of Culture (2022).

T. Beppu left behind many suggestive words.

The application study sometimes opens the door to highly original basic science[1]. This saying opposes the conventional view that application is solely the result of accumulated basic knowledge. However, revolutionary advances in basic understanding have actually stemmed from discoveries made in application-oriented study. There are many such examples in the research on natural products. T. Beppu emphasized the importance of continuously performing microbial screening.

The heart seeks form, and the form propels the heart forward[2]. This is an old saying in Buddhism that reflects the relationship between religious devotion and figure creation. T. Beppu used this phrase as an analogy to explain his concept for the significant correlation between the understanding of chemical structure and biological function. He emphasized the importance of effective coupling of chemistry and biology.

The four Ps retained by an excellent researcher[3]. A Nobel laureate, Chen-Ning Yang (Physics, 1957), said that there are three Ps required in performing sophisticated research, i.e., Perception, Persistence, and Power. T. Beppu occasionally referred to the Yang's saying and proposed to add the fourth, Personality. He was good at finding out the unique personality aspects of his collaborators and effectively fit those aspects together to help guide his or her research in a direction which led each of those collaborators to great success.

T. Beppu was not only an excellent scientist, but a great mentor. His death is a great loss for science and related communities, but many followers will put his teaching into practice.

T. Beppu's words in Japanese are as follows.

[1] 応用から独創的な基礎が生まれる

[2] 心は形をもとめ、形は心をすすめる

[3] 優れた研究者に備わる４つのP

Compliance with ethical standards

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