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OBITUARY

Remembering Professor Kiyoshi Isono (August 16, 1931–April 23, 2022)

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Photograph in his young days

Professor Kiyoshi Isono passed away on April 23, 2022, at the age of 90. Dr Isono was born in Kawasaki, Kanagawa, and was educated at the University of Tokyo (BS 1953).

He joined the Scientific Research Institute in Tokyo as a Research Associate and conducted research on natural compounds produced by microorganisms under the supervision of Professor Yusuke Sumiki. In 1958, the institute was relocated to Wako City, Saitama, and renamed the Institute of Physical and Chemical Research (RIKEN), where Dr Isono became a Research Scientist.

Subsequently, he joined Roy Curtis' laboratory at the Department of Plant Pathology, Purdue University, West Lafayette, IN, USA as a Postdoctoral Fellow (1961–1963), where he investigated the chemical synthesis of malformin, a fungal metabolite. Upon his return to RIKEN, he continued research on the isolation of new antibiotics for agricultural purposes.

Dr Isono became a Senior Scientist in 1968 and continued screening for antifungal antibiotics alongside Dr Saburo Suzuki, who was the successor to Dr Sumiki as the chief scientist at the Antibiotics Laboratory. Drs Isono and Suzuki discovered new antifungal antibiotics named polyoxins AL produced by *Streptomyces cacaoi* var. *asoensis* isolated from a soil sample collected by Dr Isono on Mt. Aso, Kumamoto, Japan. In 1984, he took me to Mt. Aso and showed me the location from which the soil sample was collected. I was impressed by his memory of the exact place where the soil was collected 20 years ago.

The polyoxins showed selective toxicity against plant pathogenic fungi because the target of the polyoxins is chitin synthetase which is essential for fungal cell wall synthesis but not for plants. Antibiotics researchers have exclaimed that "polyoxin looks like penicillin," because penicillin had been known as an inhibitor of bacterial cell wall synthesis. Polyoxin AL (polyoxin B as the main component and other derivatives) was marketed in 1967 as an antifungal antibiotic for plants and is still used worldwide. The discovery of polyoxins initiated further research into their mode of action, total synthesis, and biosynthesis studies. Based on his discovery of polyoxins, he was invited as a visiting researcher by Prof. Robert J. Suhadolnik to the Albert Einstein Medical Center, Philadelphia, PA, USA (1972–1973), where he studied biosynthesis of polyoxins with Prof. Suhadolnik.

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Dr Isono became Dr Saburo Suzuki's successor as the chief scientist at the Antibiotics Laboratory at RIKEN in 1978. He began screening novel antibiotics targeting cell wall biosynthesis based on the notion that the cell wall is essential for microorganisms (bacteria and fungi) and cell wall synthesis inhibitors are safe for humans and animals. The RIKEN Antibiotics Group, headed by Dr Isono, isolated several cell wall biosynthesis inhibitors, such as lipopeptin, neopeptin, neopolyoxin, cystargin, and liposidomycin.

After Prof. Isono's retirement, his former collaborators got together once a year. From the front left: Jun Eguchi (Kaken Pharm. Co.), Isam Yamaguchi (Food Agri. Materials Inspect. Center), Prof. Kiyoshi Isono, S. Funayama (Nihon Nohyaku Co.). From the rear left: H. Osada (RIKEN), N. Miyata (Snow Brand Milk Prod. Co.) M. Uramoto (Tamagawa U.), M. Ubukata (Hokkaido U.), T. Azuma (Kaken Pharm. Co.) (March 2001)

Professor Isono served as the chairman of the Chief Scientists Assembly of RIKEN in 1989 and retired from RIKEN in 1992. He served for the Department of Marine Science, Tokai University, Shizuoka, Japan as a professor until he was 65 years of age. After the retirement from Tokai University, he settled in Omiya-city, Saitama, and indulged in hobbies such as golf, photography, and spending time on his personal computer. In his later years, he spent his days in peace with his wife, Michiko. They enjoyed driving to Nikko, a beautiful place featuring magnificent historical architecture with beautiful lakes and mountains.

Professor Isono contributed significantly to The Journal of Antibiotics as a Member of the Editorial Board as well as an Emeritus Editorial Board member (1978–2022). He also served as a Member of the Editorial Board (1989–1991) of Agricultural and Biological Chemistry. He served as a Councilor to many societies, including the Japan Antibiotic Research Association, The Japan Society for Bioscience, Biotechnology, Agrochemistry, and the Okochi Memorial Foundation.

Professor Isono was a distinguished scientist and an expert in developing antifungal antibiotics, especially cell wall biosynthesis inhibitors. He discovered approximately 70 novel compounds and published approximately 180 research articles, reviews, and book chapters. In recognition of these successes, he was awarded the Research Promotion Award from the Agricultural Chemical Society of Japan (1969), Technical Prize from the Okochi Memorial Foundation (1970), Commendation by the Minister of the State for Science and Technology, Persons of Scientific and Technological Research Merits (1985), Japan Society of Agricultural Science Award (1989), and Yomiuri Agriculture Prize (1989).

He was a great mentor to his students and young scientists in the antibiotic research field. He never raised his voice, but the laboratory members respected his composed demeanor. When I first met him, right after completing my PhD (1983), he said to me that "there is no discrimination of age or position in science. You and I are equals as scientists." These words made me realize that I was no longer a student and had to become an independent scientist. I worked with him (1983–1992) and took over his position in 1992.

I pray for his peaceful eternal sleep while celebrating the stellar achievements of my respectful mentor, Professor Kiyoshi Isono.