

In Memoriam:

Honorary Member, Yuzo Hayashi, M.D., Ph.D., 1930-2017

Dr. Yuzo Hayashi, Honorary Member of the Japanese Society of Toxicologic Pathology, passed away on May 23, 2017, at the age of 87. He was suffering from liver cirrhosis for the last several years. He also had surgeries with esophageal varix and received other treatment, gradually weakened, and deceased without regaining his health. I would like to express my sincere condolence.

The National Institute of Health Sciences (NIHS) which Dr. Hayashi used to belong to, is to be relocated to Tonomachi, Kawasaki, before the end of the Fiscal Year 2017. Dr. Hayashi moved to the residential area near NIHS at the current location in Kamiyoga, Setagaya-ku, several years ago. Soon after his relocation, I saw him occasionally within NIHS. I wanted very much to visit him at his new home, but could not make it, which I truly regret. I was a little too busy to visit him, but the real reason why I could not make it was that it took me too long to be ready for my meeting with him since I heard that he would always dress formally to welcome his visitors, and I wanted to be worthy of his formal welcome at least in my heart. I feel it very sorry to Dr. Hayashi for that I missed the best opportunity to spend time with him.



Dr. Hayashi graduated Tokyo Medical and Dental University (TMDU) in 1954, and joined the research institute of Shionogi and Co., Ltd., in 1960 after completing his graduate study at TMDU (majored in Pathology). In 1980, he assumed the position of Director Pathology Division of National Institute of Hygienic Sciences (the current NIHS), after having engaged in his research activities at Pathology Division, Medical School, Wisconsin State University in the United States, and Hatano Research Institute of Food and Drug Safety Center in Japan. In 1991, he was promoted to the Director of Biological Safety Research Center of NIHS (my current position), and took mandatory retirement in 1995.

Dr. Hayashi promoted the concept of risk assessment in drugs, food related substances, environmental chemicals, and etc., and it is no exaggeration to say that he was one of the key pioneers of regulatory science that has been advocated by NIHS. His philosophy of risk assessment is compiled and condensed in his book, "Toxicology Notebook: Co-existence with Chemical Substances" (in Japanese), which he kindly gave me with his signature. The book was published in 2001, six years after his retirement. Unfortunately, the book is not for sale, and it is difficult to obtain for general readers. The contents are still current and valid though it was published 16 years ago. In his book, Dr. Hayashi predicted the current trends of reducing the traditional animal testing with consideration to animal welfare, and in parallel developing new test methods with application of the state-of-art technologies. He referred to the application of in silico methods, toxicogenomics/pharmacogenomics, and others as well.

Dr. Hayashi's talk was always logical and reasoned, and we could hardly make any arguments.

However, he sometimes made a joke with a straight face. His famous jokes related to the two big misunderstandings of risk assessment: the first one is assuming risk assessment as a “magic bullet” with supportive evidences of the state-of-art technologies; and the other is assuming risk assessment as something to manipulate accounts, ; he said “rikutsu awasumento” in Japanese, meaning coming up with a convenient and plausible story. These two big misunderstandings of risk assessment were described in his book, Toxicology Notebook, mentioned earlier. As a scientist practicing risk assessment, I am truly convinced that the way Dr. Hayashi described risk assessment was perfect.

I had long known Dr. Hayashi by reputation, and the most unforgettable episode with him was a story that he told me about his encounter with Dr. Hideki Mori who was my mentor and senior researcher at Gifu University. With the exact words by Dr. Hayashi, “Dr. Hideki Mori, who is your senior at Gifu University is an eccentric person. He abruptly came into my room and asked me to give a seal on a document. I asked him what the document was for and found that it was a recommendation letter for him to apply a professor position of Gifu University.” This may embrace some dramatization by me, but Prof. Mori himself did not strongly deny the story, and thus I believe this was what happened between them. I understood intuitively that Dr. Hayashi was trying to express the brilliant of Dr. Mori by saying “eccentric.” It is also known that Dr. Mori served as President of Gifu University. While I was engaged in my research in the United State, Dr. Mori recommended me for a position at NIHS.

Dr. Hayashi demonstrated excellent leadership in committees within Japan and globally. Especially, I owe him very much in the International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and the Joint FAO/WHO Expert Committee for Food Additives (JECFA). At ICH, I was summoned to the meeting to discuss carcinogenicity studies organized soon after ICH was established, but the meeting ended before I could understand the ongoing discussions. I happened to sit next to the chairperson and was quite uncomfortable during the meeting. I remember regretting a lot wishing that I could have asked Dr. Hayashi about the meeting beforehand. At JECFA, I succeeded to the position of councilor from Dr. Hayashi. Soon after I assumed the position, a representative from Canada told me that she learned from Dr. Hayashi how to prepare the documents. Something I can hardly offer even now.

I learned the research achievements of Dr. Hayashi in his lecture given at the time when he retired from NIHS. I organized a lecture meeting outside NIHS, which was described in his book, Toxicology Notebook: “While I was busy handing down my duties to the successor and organizing the related materials, Dr. Akiyoshi Nishikawa of 2nd Section of Pathology Division told me that he was planning a lecture meeting for my retirement”. I am still very thankful to him for mentioning my name in his book. By the way, I was believing that I belonged to the 1st Section of Pathology Division since I started at NIHS, and thought that even Dr. Hayashi made a mistake in his memory. But I realized later that I started at the 2nd Section first and relocated to the 1st Section in NIHS. Dr. Hayashi’s memory always had unmatched accuracy. His achievements include comprehensive analyses of the carcinogenicity mechanisms of 4-nitroquinoline-1-oxide (4-NQO) using the methods including electron microscope and post-labeling, which contributed to elucidate its whole mechanisms. In addition to his studies in

carcinogenicity, Dr. Hayashi conducted detailed analyses of the mechanisms of pulmonary hypertension, lipidosiis, intrahepatic cholestasis, and etc., developed by chemical substances, which contributed to the advancement of toxicologic pathology.

As Dr. Hayashi had no children, one of my friends who was close to him was sorting through his possessions after his death, and he found numerous notes on how to assure safety of food-related chemical substances, written by Dr. Hayashi only about one month before his death. He must have been really frustrated with the incompetency of those who succeeded him including myself. May his soul rest in peace. We would do our best to succeed his wishes. Lastly, I would like to express my wholehearted gratitude to Dr. Hayashi for his guidance and support.

June 27, 2017

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