

Obituary

## In Memory of Professor Isamu Matsumoto, the Founder of JSBMS and Pioneer in Human Metabolome Science



The passing of Professor Doctor Isamu Matsumoto on February 15, 2004, has left his students and colleagues shocked and bereft. It is, nonetheless, some comfort to know that the wisdom and achievements of this remarkable man will remain with us.

Dr Matsumoto was born on October 8, 1929 in Tsingtao, China, and raised from boyhood in Toyama, Japan. After he graduated from the Gifu College of Agriculture in 1949, he served as Research Associate at Toyama University (1951–1960). To study Molecular Biology under his former teacher, Y. Takagi, he moved to Kanazawa University (1960–1961) and then to Kyushu University (1964–1966). From 1961 to 1964 he trained at St Louis University and Wayne State University in the USA. After receiving his Ph.D. in 1967 from Kyushu University, he served first as an Associate Professor in the Department of Medical Chemistry at Kurume University School of Medicine (1968–), and later as the Director of the Research Institute of Gas Chromatography–Mass Spectrometry (GC/MS) there (1972–1983). He completed his academic career as Professor of Biochemistry at the Institute of Human Genetics, Kanazawa Medical University (1983–1997).

During the Kurume days, Dr. Matsumoto eagerly pursued both his studies and the teaching of Molecular Biology, Metabolic Biochemistry, and Biomedical Mass Spectrometry. He had a warm and magnetic personality, which touched everyone who came in contact with him, and his Molecular Biology lectures fascinated medical and graduate students

alike. His office was always bustling with their comings and goings, even on weekdays and holidays. He had tremendous energy, and it seemed as though he never rested.

In the early 1970s, while at Kurume University, Dr. Matsumoto established the first Asian facility for the chemical diagnosis of inborn errors of metabolism (IEMs) using GC/MS. This technology was tremendously helpful in making early and rapid diagnoses of these disorders, and the results were important contributions to the field of Human Genetics. The discovery of new IEMs and the new research findings on proteins and genes were quickly disseminated from Japan to the rest of the world; those IEMs included tyrosinemia type III,  $\beta$ -ketothiolase deficiency, propionic acidemia, multiple cytochrome deficiency, and others. These achievements were owing in large part to Dr. Matsumoto's establishment of cutting-edge techniques for "metabolic profiling". Leading researchers came from around the world to visit with Dr. Matsumoto, and his efforts led to many Japanese scientists and students being able to study at such prestigious foreign research institutes as the Karolinska Institute, the University of Zurich, the University of Paris, the University of California, the University of Tennessee, and the National Institutes of Health.

From 1972 to 1985, Dr. Matsumoto published the "GC/MS News" which provided the information used by scientists across Japan to enter the field of mass spectrometry. His keen interest in the field of medical applications of mass spectrometry spurred him to found in 1976 the Japanese Society for Biomedical mass spectrometry (JSBMS), which he served as the president of from 1990 to 2000. Many renowned scientists, Drs. H. Brandenberger, J. Sjövall, C. Fenselau, C. Sweeley, J. McCloskey, S. Markey, L. Sweetman, D. Millington and N. Castagnoli were often invited to JSBMS meetings. JSBMS focused not only on the research of metabolites and small molecules, but also on protein chemistry. Many leaders in protein chemistry were invited to join the society, including like Drs. K. Biemann, D. Desiderio and R. Cotter. The greatest honor for the society to date came in 2002, when member Koichi Tanaka was awarded the Nobel Prize in Chemistry for proteome-related research. Dr. Matsumoto published the Proceedings of JSBMS for 23 years and he had an important goal for

JSBMS: He wanted the papers presented at the annual meeting to be published in an international forum, because the JSBMS is interdisciplinary and the research of international interest, despite the society's small size. Dr. Matsumoto's goal was achieved when Elsevier agreed to publish the papers in the Journal Chromatography B as an annual special issue. The first of these special issues was published in 1999.

During his time at Kanazawa Medical University, Dr. Matsumoto, as a metabolic biochemist, quickly realized the significance of using the enzyme urease to simultaneously analyze organic acids, amino acids, sugars, sugar alcohols, and nucleotide bases, an idea originally described by J. Shoemaker and W. Elliott (1991). On the bases of his experiences with clinical applications, the practical yet comprehensive diagnostic procedure was developed which was extremely important for countless patients after disease onset, and so simplified as to allow the use even in the mass screening of newborns. The results on the chemical diagnosis for the high-risk patients and the pilot study of neonatal mass screening, which was started in 1995, marked a new page in the history of chemical diagnostics. In the post-genome 21st century, it appears that research in the Life Sciences will focus on proteomes and metabolomes, and Dr. Matsumoto's approach has initiated the use of metabolomics in a clinical setting. Dr. Matsumoto's work was even cited as the most advanced application by German plant physiologists in leading journals: *Current Opinions on Plant Biology* in 1999 and *Plant Cells* in 2001.

Dr. Matsumoto was very active, finding the time and energy to visit Ministry of Health officials, Dr. Shoichi Sakamoto (Professor Emeritus of Tokyo University and the former Director of the Japanese Society for Mass-Screening), and GC/MS makers and suppliers (JEOL, YAN, Shimadzu). He made it possible for four domestic organizations to conduct the pilot study of newborn urine screening. Thanks to his tireless efforts, Kurume University and Kanazawa Medical University are continuing this pilot study. Research in newborn mass-screening, beginning with metabolome analysis, will soon lead to the acquisition of extensive useful information that will help children worldwide to have healthier lives. Dr. Matsumoto would find this extension of his work especially gratifying, because he had an unbounded love for children.

Dr. Matsumoto was an editorial board member of the international journals *Biological Mass Spectrometry* (1974–1993) and *Mass Spectrometry Reviews* (1982–1997).

He was the first winner of the International Award in Mass Spectrometry and Biochemistry in Medicine in Alghero, Italy in 1975 (Organized by Dr. A. Frigerio). He was an important member of many leading associations, such as the American Society of Mass Spectrometry, the International Society Forensic Toxicologists, the International Society of Neonatal Screening, and the Japanese Societies of Biochemistry, Clinical Chemistry, Inherited Metabolic Diseases, Mass-screening, and Forensic Chemistry.

In 1997, Dr. Matsumoto was given the title of Professor Emeritus at Kanazawa Medical University. Even after he left academia, he continued to promote research and to build a network of people to carry on his life's work. After his retirement from Kanazawa Medical University, he established the Matsumoto Institute of Life Science (MILS), and its sister organization, MILS International in 1998. Despite his poor health, he made great efforts, with the support of the Foreign Ministry of Japan, to introduce a gas chromatograph-mass spectrometer at Mahidol University in Thailand to support chemical diagnoses there.

Dr. Matsumoto has left an impressive scientific legacy that stretches from the 1970s when he showed his frontier spirit by pioneering the first chemical diagnosis in Asia using metabolic profiling by GC/MS to the 1990s when he developed the simplified urease method that permitted the application of cutting-edge metabolic profiling to the early diagnosis and prevention of many diseases. He founded JSBMS and established a network for both domestic and international research. To continue his legacy, more improvements must be made to the GC/MS techniques. Despite its 30-year history of international use, chemical diagnoses based on organic acid profiling by GC/MS are not always reliable among laboratories in Japan. To conduct highly accurate chemical diagnoses with the simplified urease method, which paved the way for the development of metabolome research, Dr. Matsumoto's colleagues, including myself, have incorporated highly quantitative methods into the methodology, including statistical processing. To achieve Dr. Matsumoto's dream, my colleagues and I will continue to devote our energies to developing the field of Human Metabolome Science, for the benefit of people worldwide.

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