Remembering Professor Toshihiko Ubuka (1934–2008)

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Satoko Ubuka

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Professor Toshihiko Ubuka was a distinguished Japanese biochemist, known domestically and internationally. In his scientific life, he researched various fields of sulfur biochemistry. Toshihiko Ubuka, Professor Emeritus from Okayama University Medical School, died of colon cancer on 4 April 2008, at the age of 74. Until he died, he worked in the Department of Clinical Nutrition in Kawasaki University of Medical Welfare: he was Vice-president of the University and Dean of Faculty of Health Science and Technology.

He was born on 31 January 1934, in a farmer's family in Okayama prefecture. The grandparents did the farming, but his father worked as a postal clerk and his mother was a high-school teacher. He suffered from diphtheria when he was 12 and was unable to attend school for a year because his lower limbs were paralyzed. He wanted to become a lawyer. However, in the last year of high school, when his father passed away because of stomach cancer, he decided to go to medical school. He studied medicine in Okayama University Medical School and graduated in 1959.

During his studies he had also started to learn kendo, which is a traditional Japanese martial art. Until the end of his life he regularly practiced kendo.

After graduation, he made a decision to be a biochemist and started studying biochemistry in Okayama University. He commenced his career as a researcher in Okayama Medical School in 1964, after obtaining his Ph.D. in biochemistry. He performed his scientific research work in the Department of Biochemistry in the Medical School of Okayama University under the supervision of Professor Shunji Mizuhara.¹ Professor Ubuka said at every opportunity how deeply grateful he was to Dr. Shunji Mizuhara, who stimulated his interest in sulfur biochemistry. The first papers co-authored by Professor Ubuka and published in 1962–1964 focused on isovalthine (2-amino-5-carboxy-6-methyl-4-thiaheptanoic acid), a branched-chain sulfur amino acid that was found in the urine of humans suffering from hypercholesterolemia by Professor Mizuhara. Ubuka (1962) described a method involving high-voltage electrophoresis combined with paper chromatography for the identification of isovalthine and its related compounds. Later, ion exchange amino acid analysis was used allowing for quantification of urinary isovalthine concentrations.

In the years 1967–1968, in parallel with the similar discovery of J.C. Crawhall, Ubuka found out that normal human urine contained small quantities of mercaptolactate-cysteine disulphide [*S*-(2-hydroxy-2-carboxyethylthio)cysteine; HCETC], and mercaptoacetate-cysteine disulphide [*S*-(carboxymethylthio)cysteine; CMTC]. Later on, in the 1970s, he synthesized *S*-(2-oxo-2 carboxyethylthio)cysteine (OCETC) and reduced it with lactate dehydrogenase to HCETC.

In 1960, he married Satoko, who was his college classmate, and later they had their first child, Takayoshi. Several years later, in 1967, he went to New York with his

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wife and son to work with Dr. Alton Meister in Cornell Medical School. Two daughters, Hiromi and Atsue, were born in New York.

From 1967, he worked as Research Associate at the Cornell University Medical School in the Biochemistry Department, which was chaired by Professor Alton Meister who made pioneering contributions to the study of glutathione metabolism. While working at Cornell, Dr. Ubuka studied asparaginase-sensitive and asparaginase-resistant leukemias.

He returned to Medical School of Okayama University in 1971 and worked in the Biochemistry Department as Lecturer and subsequently as Assistant Professor and Professor (from 1981) until 1999, when he retired.

After the stay in the USA, Dr. Ubuka's research field became sulfur biochemistry. Three main research themes that can be distinguished in his scientific work are the metabolism and function of cysteine, sulfur nutrition, and the modification and renaturation of proteins.

In the early 1970s, he investigated oxidative deamination for all available sulfur amino acids by the crystalline snake venom L-amino acid oxidase. He proved that rats fed a high protein diet metabolized cysteine to HCETC (determined in blood plasma). He confirmed L-cysteine transamination (first suggested by Meister et al. in 1954) in normal rat tissues and rat liver fractions. Subsequently, he purified cysteine aminotransferase (EC 2.6.1.3) from rat liver mitochondria, described it, and indicated that this enzyme was identical to aspartate aminotransferase (EC 2.6.1.1).

In the 1980s, Dr. Ubuka carried out studies of L-cysteine metabolism in guinea pig liver. He found that 3-mercaptopyruvate sulfurtransferase (MPST) activities in guinea pig tissues were very low compared with those in rat tissues and in effect a large HCETC production was observed when L-cysteine or 3-mercaptopyruvate was incubated with guinea pig liver or kidney homogenate.

In the 1990s, he examined the 3-mercaptopyruvate pathway of L-cysteine metabolism and sulfate formation, as well as hypotaurine and taurine formation in mitochondria. Subcutaneous injection of (aminoxyl)acetate, a potent inhibitor of transaminases, together with L-cysteine halved the sulfate excretion and doubled the taurine excretion.

In the years 2000–2008, on the basis of his previous publications he summarized mammalian cysteine metabolism pointing to the possible significance of cysteine metabolites, including hypotaurine, in antioxidation processes in liver cell mitochondria.

He remained actively engaged in research and scholarly activities and his passion for science continued until his death. He worked very hard every day. He usually went to work around 8 in the morning and came back home around 11 at night. He taught biochemistry to many students while he was a professor. Once he had a student whose entire body was largely paralyzed. Professor Ubuka constructed special devices for the youth so that he could perform biochemical experiments, which the Professor thought to be very important for all biochemistry students. The Professor's manners, diligence and knowledge evoked admiration among his co-workers and alumni.

In August 2007, Professor Ubuka attended the 10th International Congress on Amino Acids and Proteins (ICAAP) in Kallithea, Greece. He presented his data. We later found out that he had already developed colon cancer at this time and probably was not feeling well at times. However, he still vigorously worked after coming back to Japan and he even attended two more conferences in the fall. In Greece he also traveled to Kos Island and took a picture of the tree of Hippocrates—the platan tree under which, according to the legend, Hippocrates taught his pupils the art of medicine. On 4 April 2008, he passed away because of cancer, which metastasized involving many organs. However, what he taught us will remain in our memory forever; most likely, he has already started teaching biochemistry in heaven.

He is survived by three children, six grandchildren, and his wife.

CSA (cysteinesulfinic acid), KG (alpha-ketoglutarate), Pyr (pyruvate), ROS (reactive oxygen species), SP (beta-sulfinylpyruvate)

Reference

Ubuka T (2007) Hypotaurine biosynthesis in rat liver mitochondria. 10th international congress on amino acids and proteins. Amino Acids 33: I–LXX, p. IV