Letter to the Glyco-Forum

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A Green Thumb and a Broad Back:
A Tribute to the late Dr. Yasuo Inoue
(1934–2005)

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On February 6, 2005, Dr. Yasuo Inoue sent me an email message about his failing health, ending with, “I am sorry to inform you of this unpleasant matter at a joyful festival season [lunar New Year]. — Tomorrow I’ll have to return to the hospital and I would not be able to write directly to you in coming days.” Alas, that was the last message I received from him. He closed his wonderful life and splendid career in glycobiology on February 17, 2005, succumbing to hepatic cancer and cirrhosis.

Dr. Yasuo Inoue was born in Japanese-occupied Taiwan, in a town south of Taipei, where his father was a director of a brewery. After WWII, when Japan relinquished control of Taiwan, Yasuo returned to Japan with his family to continue his education in middle and high school. After obtaining BS and MS degrees in chemistry from Nagoya University, he traveled to the Australian National University for advanced study in chemistry in the laboratory of Professor Douglas D. Perrin and was awarded a PhD in chemistry in 1963. Although it was an unusual move (since most of the graduate studies by Japanese students were pursued in the U.S. or Europe in those days), it was a perfect choice for him because he met his future wife and lifelong collaborator, Sadako (an excellent glycobiologist in her own right) at the University. They were married upon returning to Japan, and Yasuo spent several years as Assistant Professor in the laboratory of Dr. Koji Nakanishi at the Tohoku University in Sendai, where his interests were mostly nucleotides and NMR. In 1971, Yasuo moved to the University of Tokyo to become Associate Professor in biophysics and biochemistry.

Although his first publication on carbohydrate materials was with Sadako on NMR measurement of sulfated polysaccharide (Inoue and Inoue, 1966) during his Sendai era, his serious interest in glycobiology was not aroused until he helped Sadako (without requesting to be a co-author) on the structural elucidation of trout egg polysialoglycoproteins (Inoue and Iwasaki, 1978) by determining the presence of NeuGc. The “sweet” taste once acquired could only intensify, and as he became more involved in polysialoglycoprotein, he started to publish collaborative works with Sadako (Nomoto et al., 1982), an arrangement that would last throughout the rest of their careers. Thus began an era of a brilliant glycobiology research team, which would continue for a quarter of a century. Further exploration of fish egg glycoproteins led to a succession of amazing findings, such as: a unique structure, β-GalNAc(1-4)-(NeuGc2-3)β-GalNAc, which was resistant to sialidase (Iwasaki et al., 1984); novel sialoglycoproteins (hyosporhin) from the eggs of Medaka, Oryzias latipes (Iwasaki et al., 1987); large amounts of free bi-, tri-, and tetra-antennary sialooligosaccharides in the unfertilized eggs of a freshwater trout (Ishii et al., 1989) and from unfertilized eggs of dace (Inoue et al., 1989). These findings further guided them to discover peptide:N-glycosidase (glycoamidase) activity in the early embryos of Medaka, the first demonstration of such an enzyme in animal cells (Seko et al., 1991). Isolation of a similar enzyme from fibroblasts led them to suggest possible widespread occurrence of post-translational N-deglycosylation (Suzuki et al., 1994, 1997).

Another new frontier pioneered by the Inoues was their discovery of “deaminated” sialic acid, commonly known as KDN (Nadano et al., 1986). Initially, it was found only at the non-reducing termini, but later it was also found in α(2-8)-linked polymeric forms (Kanamori et al., 1989, Ziak et al., 1996). Discoveries of CMP-KDN synthetase (Terada et al., 1996), chain-terminating α(2-8)-KDN-transferase (Angata et al., 1994) and “KDNase” (Kitajima et al., 1994) followed. Enviably, Yasuo had a green thumb in experimental sciences.
After his mandatory retirement from the University of Tokyo, he took the position of Distinguished Professor in 1996 at the Institute of Biological Chemistry (IBC) of Academia, Sinica, Taiwan, where the director at the time, Dr. Darrell Liu, was anxious to establish a strong glycobiology program. Sadako was also invited to take part in the program, and for the first time, the Inoues were working side by side in adjoining laboratories. Although Academia Sinica is not an educational institution, and availability of graduate students is less than ideal, the Inoues did not slacken their pace of research. Some of the notable accomplishments during this period are: deciphering of developmental pattern of polysialylation (Poongodi Geetha et al., 2002); demonstrating the presence of KDN in human red blood cells (Inoue et al., 1998); implicating KDN(GM3) in carbohydrate-carbohydrate interactions (Yu et al., 2002); demonstrating the developmentally regulated expression of a peptide:N-glycanase in rice seeds (Chang et al., 2000); and the discovery of an α-(2-9)-polyNeu5Ac glycoprotein in murine neuroblastoma (Inoue et al., 2003).

During these studies, the Inoues were compelled to refine the tools for determination of polysialic acids, which culminated in various procedures of capillary electrophoresis, and liquid chromatography (Cheng et al., 1998; Inoue et al., 2000, 2001; Lin et al., 1999). The last published method, combining sensitivity of fluorescence detection and high resolution of HPAEC, achieved detection of as little as a few fmols per resolved peak (Inoue et al., 2001) and resolving polymers approaching degree of polymerization of 100. While in Taiwan, Yasuo organized an international conference, “Sialobiology and Other Novel Forms of Glycosylation” in 1998 (Inoue et al., 1999), which was very adedly executed and was highly acclaimed.

Yasuo was a tireless worker with total devotion to the work in his chosen area, which was shared by Sadako. Their passion for research can be seen from the opening statement in the Japanese review on the discovery of polysialylglycoprotein (PSGP): “In Nature, there exist some substances of extraordinary chemical structures far beyond the investigator’s knowledge and imagination, which excite its discoverer and structural analyst to no end. Especially when such substances are related to important biological phenomenon and manifest great biological activities, the delight of the investigator is beyond description.” (Inoue and Inoue, 1985). He was also a man of few words. I often heard Yasuo uttering a Japanese proverb, “Children grow up by watching the backs of their parents,” meaning children learn from the examples set by parents. What a broad back he had! The examples he set had great impact on his students, the cream of the crop at the renowned University of Tokyo, who were fortunate enough to spend time in his laboratory. Nearly all of them are now outstanding researchers highly active in the glycosciences. Yasuo was very generous in supplying his superbly trained and highly inspired students to other outstanding glycobiology laboratories in the world. For example, Drs. Akiko Kanamori, Akira Seko, Shinobu Kitazume, Chihiro Sato, Tadasu Suzuki, Tomohiko Taguchi, Takashi Angata, Mariko Kudo, and Yoko Funakoshi have made or are making important contributions in the laboratories of Drs. Ajit Varik, Richard Cummings, Yoshito Hirabayashi, Minoru Fukuda, Katsuko Yamashita, Rick Troy, William Lennarz, Karen Colley, Kiyoshi Furukawa, Naoyuki Taniguchi, and others. Dr. Ken Kitajima, the most senior of the pack from the Inoue laboratory, currently Professor at Nagoya University Bioscience and Biotechnology Center, embraces a few of them as well.

Yasuo’s generosity was not limited to supplying talented students to other laboratories. Near the end of his stay in Taiwan, he and Sadako donated a sizable sum to establish the Foundation for Research and Education of Glycosciences, which aims to assist glycoscience students in Taiwan to travel to international glycoscience meetings. Although the foundation was helped by additional contributions from industry, the fact that the Inoues were so munificent as to donate their savings, accumulated by living rather simply and frugally, is enormously admirable.

Yasuo has departed us now, but the flame of Yasuo’s great enthusiasm for science, especially for glycosciences, will no doubt be kept kindling by his former students and associates from Japan and Taiwan for many years to come. This man with a green thumb and a broad back made a big difference to this world.

References
Ishii, K., Iwasaki, M., et al., (1989) Free sialooligosaccharides found in the unfertilized eggs of a freshwater trout, Plecoglossus altivelis. A large


