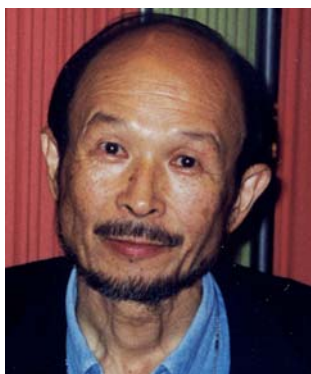


Introduction

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Professor Yasuo Inoue: 1934–2005

Prof. Yasuo Inoue was born in Taipei, Taiwan, on November 5, 1934, and passed away in Tokyo, Japan, on February 17, 2005. He was one of the greatest leaders in the field of glycoscience, as well as a wonderful teacher. The news of his sudden death one year ago shocked and saddened the science community. An excellent tribute, “A green thumb and a broad back: a tribute to the late Dr. Yasuo Inoue, 1934–2005,” has since been written by Dr. Yuan Chuan Lee (*Glycobiology* 15, 9G-14G, 2005). Here, we would like to further recollect our thoughts on a great man and his achievements in glycoscience, not only as those who are deeply indebted to Dr. Yasuo Inoue but also as his friends.

Prof. Yasuo Inoue was born of Japanese parents in Taiwan, where his father worked, and lived there during his boyhood. In 1946, after World War II, he returned to Japan. He was educated in the Mie Prefecture and, in 1954, after graduation from Tsu High School, entered the Department of Chemistry at the Nagoya University School of Science. He received further education at Nagoya University Graduate School, and obtained his Master of Science degree in

chemistry in 1960. He then went to Australian National University for advanced study in chemistry in the laboratory of Prof. Douglas D. Perrin, and was awarded a Doctorate of Philosophy in Chemistry in 1963. In the same year, he returned to Japan, and spent several years as an Assistant Professor in the laboratory of Prof. Koji Nakanishi in the Department of Chemistry at the Tohoku University School of Science. He studied mainly bioorganic chemistry of bioactive materials and the chemistry of nucleic acids. In 1969, he moved to the University of Tokyo, in the Department of Biophysics and Biochemistry in the School of Science as an Associate Professor, and shared a laboratory with Prof. Fujio Egami. From that time, he studied the physicochemical properties of carbohydrates and nucleotides. In 1971, Prof. Inoue began running his own laboratory to continue oligonucleotide chemistry and the related enzymology. In the 1980's, he performed many innovative studies on sialic acids and polysialic acids in collaboration with his wife, Prof. Sadako Inoue. For example, the discovery of KDN (2-keto-3-deoxy-D-*glycero*-D-*galacto*-nononic acid), which is one of the most important contributions to sialoglycobiology, was presented in 1986. In the 1990's until his mandatory retirement from the University of Tokyo in 1995, his contributions to the field of glycoscience were enormous in both quantity and quality. There were many discoveries and comprehensive studies on the structures and functions of sialoglycans and bulky multiantennary glycans, and de-*N*-glycosylation events in a biologic context. In 1996, he returned to his birthplace 50 years after he had left, and was invited to be a Distinguished Professor in the Institute of Biological Chemistry (IBC) at the Academia Sinica, Taiwan. Prof. Sadako Inoue was also invited to join the program. He continued first-rate research in sialoglycoscience for 7 years until he returned to Japan in 2003, 2 years before his eternal sleep.

An era of discoveries in glycoscience in Japan (1982–1995)

Scientifically, Prof. Yasuo Inoue will perhaps be best remembered for his numerous landmark discoveries published in the 1980s, a blossoming era of fruitful research during which he initiated the studies of fish egg polysialoglycoproteins (PSGP) with Prof. Sadako Inoue who discovered PSGP as the first example of a polysialic acid-containing glycoprotein in vertebrates in 1978. Together, they determined the complicated structures of polysialic acid-containing *O*-linked glycans of salmonid fish egg PSGP which formed the basis of their later pursuits and successes in glycoscience. At least four main branches of scientific quests extended from this seminal work.

The first branch was the establishment of KDN glycobiology (KDNology). During the course of research on PSGP, Prof. Yasuo Inoue discovered KDN and published a historic paper in the *Journal of Biological Chemistry* in 1986. KDN was a new sialic acid, in which the aminoacyl group in *N*-acetylneuraminic acid is replaced by a hydroxyl group. A series of comprehensive studies on the occurrence, unique structure, biosynthesis, and catabolism of KDN-glycoconjugates followed, leading eventually to the research field of KDNology. Together with Prof. Sen-itiroh Hakomori and Jürgen Roth, he published memorable contributions on the functional and histochemical aspects of KDN glycoconjugates. The second branch was the first demonstration of the structural diversity of polysialic acids. Besides α 2,8-linked polyNeu5Ac and polyNeu5Gc, α 2,8-linked poly(Neu5Ac,Neu5Gc), polyKDN, and their partially acetylated forms were discovered in fish egg PSGP by 1993. He also discovered a novel α 2,5-*O*-glycolyl-linked polyNeu5Gc in sea urchin egg jelly in collaboration with Prof. William J. Lennarz. Such a diversity of polysialic acid structures had never before been demonstrated. Prof. Frederic A. Troy II was one of his esteemed colleagues in polysialic acid research, and they spent wonderful and productive times together in the US as well as in Japan.

The third branch arose from their serendipitous finding of the dramatic structural change of fish egg PSGP at fertilization. This was actually the first description of the early fertilization event at a molecular level. In 1989, glycoproteins with structural and behavioral properties similar to PSGP were collectively named hyosophorin. Hyosophorin in fish other than salmonid fish contains a species-specific, bulky, multiantennary *N*-glycan (7–10 kDa), instead of polysialic acid. Prof. Inoue performed a series of challenging studies on the structural analyses of such huge glycans using conventional chemical methods as well as the newly emerging mass spectrometry technique, enjoying a fruitful collaboration with Prof. Anne Dell. His strong dedication to the studies of fish egg hyosophorin led to his next historic

discovery, which became the fourth branch. In 1991, he published a paper on the first discovery of peptide: *N*-glycanase (PNGase) in animals in the *Journal of Biological Chemistry*. During early development of the medaka fish embryo, the activity of this enzyme rises in accord with the increase in free *N*-glycans. Together with Prof. Sadako Inoue, Prof. Yasuo Inoue also found a large amount of free *N*-glycans possibly derived from yolk glycoproteins in fish eggs. The discovery of PNGase provided a clear mechanism for these interesting phenomena.

Prof. Yasuo Inoue worked for many years as a teacher at the University of Tokyo and many students received their doctoral degrees under his supervision. Many students were charmed by his fascinating and decisive teaching, because he led them through his thoughts on the most important current topics. In the 1970's, he published two textbooks in Japanese, titled "Chemistry of Nucleic Acids" and "Chemistry of Carbohydrates." These textbooks were unique and exceptional, because they were intensely focused on the physicochemical and chemical properties, and the conformational structures of these biomolecules. They were such unique and well-written textbooks that students referred to them as the "Old Testament" and the "New Testament." The students who joined his laboratory were often recommended to become experts in a given area within a month or two. They were simply inspired. Interested and well-prepared students were treated with respect as first-rate researchers and they would benefit greatly from fruitful and encouraging discussions with him. Prof. Yasuo Inoue was a philosopher, and as such, he was never perturbed when his thoughts deviated from those of the majority. Instead, he rather enjoyed the controversy. His thoughtfulness and decisive behaviors were the cornerstone of his scientific achievements. He was a high-spirited man who loved drinking, discussing, playing tennis, and driving. He was by turns explosive and gentle, humorous and philosophical. His optimistic and decisive way of thinking will live on in his scientific offspring.

Living on a passionate devotion to glycoscience in Taiwan (1996–2003)

It was with both sentimentality and great courage that Prof. Yasuo Inoue, together with Prof. Sadako Inoue, chose to carry on their prolific research at the Institute of Biological Chemistry, Academia Sinica, Taiwan. From the onset, it was more than just a scientific devotion but also a passion to disseminate glycoscience on a soil he felt attached to as a second home. In addition to numerous publications continued to arise through previous and ongoing collaborative work largely carried out by their former students, their major accomplishment in this period (1996–2003) can be threaded in two inter-related directions. The first stems from their recognition that

further advances in analytical methodologies is critical to their chosen path of discoveries. Hence a great deal of effort was devoted, and paid off handsomely, on developing more sensitive methods in detecting various forms of oligo- and polysialic acids, culminating in their 2003 contribution to a chapter in *Methods Enzymol.* (vol 362, 543–560). The second encapsulates the continuation of a body of work in delineating the developmental regulation of polysialylation, applying the techniques they developed. Along this line, the discovery of an α 2,9-polyNeu5Ac glycoprotein in C-1300 murine neuroblastoma, sadly represents the final contribution of Prof. Yasuo Inoue to the field of sialobiology that was published as a full original research paper during his life time (*J. Biol. Chem.* (2003) 278, 8541–8546).

In retrospect, despite the retirement from Tokyo university and starting afresh in a less endowed glyco-milieu in Taiwan, Prof. Yasuo Inoue had managed a steady progress in a less traveled path, of which he would surely be credited as the pioneer and seer. He maintained his high standard and passion for science and life, and with it, imprinted his wisdom and vision on us. As we recollect the fond memories of him during his time in Taiwan, two other deeds must surely be commemorated. The first is his effort in organizing the international meeting “*Sialobiology and Other Novel Forms of Glycosylation*” in 1998, which for the first time, brought together most of the prominent glycobiochemists at work to Taiwan and through which introduced the Island he was born in, together with a handful of budding local glycoscientists, to the global map of glyco-world. The second is his major contribution through his own savings to the establishment of a *Foundation for Research and Education of Glycosciences* which aims to assist glycoscience students in Taiwan to travel to international glycoscience meetings. In fact, both acts reflect his vision and belief in helping the aspiring young glycoscientists to connect to the establishment, such that they will hear and be heard, and make their own mark, like he did. Prof. Yasuo Inoue has always been the one to dare, in the name of science and humanity, and with utmost sincerity as Prof. Hakomori would remember.

Ken Kitajima, Nagoya;
Kay-Hooi Khoo, Taipei

A few recollections of a sincere man

Time runs so fast. It is already a year since I heard the shocking news that Prof. Yasuo Inoue passed away, from hepatic cancer, in Feb 2005. I respect highly both Yasuo and Sadako, as an ideal scientist couple, making so many breakthroughs in the glycoscience area. I was not aware that they were working at the Dept. of Chemistry and Dept. of Biochemistry, respectively, at Tohoku Univ., Sendai—where I was educated and spent my youth. While I was working and struggling in

Sendai, they were not yet there. Yasuo was about 5 years younger than I, and because of this slight age difference, by the time they came to Sendai, I had already left for the U.S. I knew them mainly on a scientific basis in subsequent years, and my personal contact was somewhat limited—which I regret highly.

If I were asked to choose one word to express Yasuo’s personality, it would be “**sincerity**.” He was sincere in conducting his research, in educating his students, in relations with his friends, colleagues, and family. Sincerity is often associated with frank, well-justified opinions, and ignores some political consideration. What he expressed was always true, and justified.

He sent one of his colleagues, Yu Song, to my lab for collaborative studies. Since then, we had a few opportunities for more personal contact. Yasuo and Sadako kindly visited my lab and then came to my home. There were quite a few other occasions, including several Gordon Conferences and glycobiochemistry meetings, the “sialoglycobiochemistry” meeting (Taipei) which Yasuo organized, an international “neuroglycobiochemistry” meeting (Taipei), the International Symposium on Glycoconjugates (Bangalore, India), etc., during which we met and chatted together—occasionally with the help of some wine. On one occasion, Yasuo and Sadako invited me and Reiji Kannagi to the “best Chinese restaurant” in the best location of downtown Taipei. I really enjoyed this, and had to change my concept of Chinese cuisine. Before that time, I had no opportunity to try really first-class Chinese cuisine! These personal contacts steadily strengthened my impression of Yasuo as a man of true sincerity, with very warm humanity.

Scientifically, Yasuo had a strong background in chemistry and physics, while Sadako was strong in biochemistry and cell biology. I now fully appreciate how this combination allowed them to perform superior work in glycoscience. Yasuo was one of the first “sympathizers” for carbohydrate-carbohydrate interaction (CCI), which we proposed. He elegantly applied this approach, using KDN-GM3, to solve the problem of rainbow trout fertilization (in which complex acrosomal reaction is absent). Interestingly, several research groups are now working on CCI in Europe. All these scientists have a common strong expertise in chemistry and physics, rather than simply cell biology. One group was working in this area in Japan—and none in the U.S. I feel that glycoscience in the U.S. is unduly influenced by fashionable carbohydrate-protein interaction. It is natural that the current U.S. grant funding system cannot avoid this fashion. I am afraid that, with the loss of Prof. Yasuo Inoue, there are too few scientists having his unique combination of creativity and strong chemistry/physics background, who are not bound to fashion.

In retrospect, it has been a long journey, with a number of obstacles, but with good friendship and sympathy. I miss

Yasuo, as do so many of his colleagues and friends, but may his soul rest in peace.

Sen-itiroh Hakomori, Seattle

Preface for the special issue in honor of Professor Yasuo Inoue

It was with regret and a deep sense of loss that the glycoscience community noted the untimely passing away of Professor Yasuo Inoue, on February 17, 2005. In honor of his many great and irreplaceable contributions to the research of glycoconjugates, Prof. J. F. G. Vliegthart and the Associate Editors of Glycoconjugate Journal have jointly taken an initiative to publish a commemorative special issue carrying original work contributed by colleagues most closely associated with him scientifically and personally. We, in turn, are honored to be invited as the Guest Editors for this special issue which is now entering its printing stage, exactly a year after the late Prof. Yasuo Inoue closed the final chapter of a distinguished career and memorable life. His major contributions to Glycosciences are: a discovery of a new sialic acid, KDN (2-keto-3-deoxy-D-glycero-D-galacto-nononic acid) and comprehensive studies of KDN-glycoconjugates; a series of discoveries of new polysialic acid structures; precise determination of high molecular weight, multi-antennary *N*-glycan structures in fish egg hyosophorin; a discovery of peptide: *N*-glycanase (PNGase) in animals. Of these contributions, the discovery of KDN is well recognized as a landmark in the history of Glycosciences.

In accord with his research fields, we received two review articles and 13 original papers on the forefront research of Sialobiology concerning KDN, polysialic acid, and sialyl-transferases, unique insights into sulfated glycans, and challenging strategies for structural analyses using mass spectrometry and nuclear magnetic resonance spectroscopy. We are fortunate to invite and include Prof. Sadako Inoue as

one of the authors in this issue. She wrote the most updated and memorable review on KDN, as well as an original paper on the discovery of new mammalian KDN-containing glycoproteins that have been done in collaboration with Prof. Yasuo Inoue in Taiwan. Each article was strictly reviewed by first-rate scientists in the relevant fields. We believe this issue will make its own historical mark, not only in honoring a great scientist with top quality science, but also highly suggestive of the future directions to be taken. True to the late Prof. Yasuo Inoue's spirit—to dare traveling the hard route of scientific discoveries, with sincerity. This is how we remember Yasuo, and hope how this issue will be remembered.

On behalf of the editorial board, we thank all the authors for their indispensable contributions to this issue, and all reviewers enlisted for their professional critiques. Thanks also to all other potential authors who have expressed interest and enthusiastic moral support but failed to contribute to this issue *per se*, due to one reason or another. It was a most rewarding job editing this Special Issue, through which we found many kind words of affection and admiration to be spoken of a great man. This is the least we could do—paying our last respect to the late Prof. Yasuo Inoue, for the deeds he sowed during his 70-years' life.

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