



Toshiharu (Toshi) Nagatsu: an appreciation

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Prof. Toshiharu Nagatsu—or “Toshi” as he is known to his many friends—has always harbored an interest in chemistry, dating back to his days at high school and to his medical studies at Nagoya University in Japan. It was during his time at the Nagoya University Medical Faculty, which was affiliated to a mental health hospital, that he came into contact with patients suffering from neuropsychiatric diseases and became fascinated in shedding light on the (bio)chemical basis of such disorders. Several important discoveries were made at that time—including Arvid Carlsson’s work in the field of brain dopamine actions and the discovery in the 1950s of the role of chlorpromazine in alleviating schizophrenic psychosis—which piqued his interest in neurochemistry and led him to immediately start laboratory practice at the Department of Biochemistry in the evenings beside his medical studies. Toshi began his research career in 1956 as a Ph.D. student working on catecholamines, a field that has determined his scientific life to this day.

Soon after receiving his doctoral degree he moved to the United States for postdoctoral research in the laboratory of Sidney Udenfriend. Together, in 1964 they discovered tyrosine hydroxylase (TH), the limiting enzyme of catecholamines. Of course, this landmark publication became a citation classic! Toshi continued the work on metabolism and its related enzymes in Nagoya, but his close connection to Sidney Udenfriend allowed him to visit that laboratory again and develop a photometric assay for dopamine- β -hydroxylase, the enzyme metabolizing dopamine to noradrenaline. Again, this paper became a citation classic.

In 1985, Toshi started studying the molecular biology of TH. He cloned and characterized the human TH gene and discovered four isoenzymes. These findings were the start of

an intense collaboration between his laboratory in Nagoya and the laboratory for clinical neurochemistry headed by one of us (PR) at the Department of Psychiatry at the University School of Medicine in Würzburg, Germany.

These human postmortem brain studies showed that (1) total TH activity, TH protein, as well as the mRNA of TH isoforms are significantly decreased in Parkinson’s disease (PD) and that (2) TH activity, when calculated on TH protein (homospecific activity), is greatly increased in the basal ganglia of PD despite reduced hTH1-hTH4 mRNA (Ichinose et al. 1994). Another successful cooperation with one of us (PR) consisted in detecting markers for neuroinflammation. Tumor necrosis factor (TNF)- α was significantly increased in the nigrostriatal system in PD (Mogi et al. 1994). Later, Toshi’s group reported on the increase of several other inflammatory cytokines as well as apoptosis-related factors (Nagatsu et al. 2000; Imamura et al. 2005).

A discovery of eminent importance was the causative gene of L-DOPA-responsive dystonia (Segawa’s disease), the encoding of GTP cyclohydrolase 1, and the enzyme synthesizing tetrahydrobiopterin, a cofactor of TH. Toshi’s publication record is outstanding and he still publishes on topics related to TH, inflammation, and apoptosis.

Toshi Nagatsu has been Chairman and Professor at Aichi-Gakuin University School of Dentistry, Nagoya, at the Tokyo Institute of Technology, Tokyo, at the Department of Biochemistry of Nagoya University School of Medicine, Nagoya, and he served as Professor and Director of the Institute for Comprehensive Medical Science of Fujita Health University, Toyoake. During various sabbaticals, he also carried out research at the University of Southern California School of Medicine as Visiting Professor in 1967, at the Roche Institute of Molecular Biology as Visiting Scientist in 1972, and at the National Institutes of Health as a Fogarty Scholar-in-Residence in 1999.

After his retirement from Fujita Health University in 2001, he continued his work as Visiting Professor at the Department of Pharmacology, Fujita Health University School of Medicine, Toyoake, and at the Department of Brain Functions, Nagoya University Research Institute of

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Environmental Medicine, Nagoya. His current interest lies in neurotransmitters and cytokines related to neurodegenerative diseases such as PD and Alzheimer's disease. He is also interested in the molecular pathology of neuropsychiatric diseases in relation to environmental factors, especially stress. He serves as an editor, an editorial board member, and as a reviewer of several international journals including the *Journal of Neural Transmission* (JNT).

Springer Nature and all who are involved in editing this scientific journal are extremely thankful and grateful for Toshi's outstanding cooperation in publishing and handling manuscripts and scientific works. Toshi is not only a superb scientist, he is a great human being—open-minded, full of energy, and willing to cooperate, to learn, and to help whenever necessary. He is truly an honorable man and it is therefore not surprising that Toshi is a respected scientist in Japan with friends all over the world. This list is indeed a long one and here we only mention Arvid Carlsson, Honorary Editor-in-Chief of JNT, and Keisuke Fujita, Founding President of Fujita Health University School of Medicine, Toyoake, Aichi, Japan, who collaborated with him and supported him for 30 years, 1965–1995.

Toshi Nagatsu is married to his beloved wife, Ikuko, a professor of histochemistry at Fujita Health University. He always expresses his deep admiration for her. She supported Toshi's scientific work from the very beginning in the 1950s while also tending to her own professional engagement and their family.

Toshi, we are honored and happy to have you on board at JNT but, more importantly, to have in you a close friend, a man of extraordinary capacity, and someone who is the example of a pure scientist. You are still focused on science, you still run a laboratory, and you have not given up your quest to clarify the basic mechanisms of neuropsychiatric disorders. The articles presented in this special issue are devoted to you and represent scientific topics you are interested in.

Ad multos annos!

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