The Second Tomoh Masaki Award (2013)

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ABSTRACT
Professor Katsutoshi Goto, PhD, a Japanese physio-pharmacologist born in 1943, is the recipient of the Second Tomoh Masaki Award, a bi-annual prize presented on the occasion of the International Conferences on Endothelin to scientists for outstanding contributions and achievements in the field of endothelin research. The Second Tomoh Masaki Award was presented to Professor Goto at the Thirteenth International Conference on Endothelin held at Tokyo Campus of the University of Tsukuba, Tokyo, Japan, in September 2013 in recognition of his scientific contributions in the 1980s that ultimately allowed to identify and characterize the endothelin peptides. Goto’s innovative work was quintessential in the discovery of endothelin which has led to the development of new therapies and new clinical applications in medicine and particularly pulmonary arterial hypertension. This article summarizes the career and the scientific achievements of Katsutoshi Goto, it includes statements of former students on his role as a mentor as well as the awardee’s personal quotes, including a message to young endothelin researchers.

The Second Tomoh Masaki Award (2013)

In September 2013, Professor Katsutoshi Goto, PhD, of the University of Tsukuba, Japan, was announced as the recipient of The Second Tomoh Masaki Award (Fig. 1) at the Thirteenth International Conference on Endothelin in Tokyo. The awardee Professor Goto had received a unanimous vote from the members of the Endothelin International Advisory Board to be the next recipient of this award. The award was presented by the ET-13 Conference Chairs during the conference’s Award Ceremony on September 11, 2013.

Katsutoshi Goto: an extraordinary physio-pharmacologist

Born in Aichi, Japan in 1943, after graduating from high school Katsutoshi Goto pursued studies in pharmacy at Nagoya City University and obtained his Bachelor of Pharmacy in 1966. In 1966, Katsutoshi Goto started to work in research at the Faculty of Pharmaceutical Sciences at the University of Tokyo as a graduate student with Professor Yutaka Kasuya to eventually obtain a Ph.D. degree. One day, Goto was invited to a dinner in the home of his mentor, Prof. Kasuya. At that time, Yoshitoshi Kasuya who was 10 years old (he would later join Professor Tomoh Masaki’s laboratory as a graduate student at the University of Tsukuba) saw the young Goto for the first time and thought that Goto was different from all the other graduate students working in his father’s laboratory. What made him special was that Goto listened to the little boy’s story with much patience without treating him as a child. Goto then also talked to him about the importance of having interests and questions towards different matters. This episode well exemplifies the style that Dr. Goto already had a very personal attitude to teaching which he continued to practice later as a supervisor of his students. Once a student presented an idea, Dr. Goto always listened to any idea or hypothesis – including primitive ones – without denying its right to be there. Then, he discussed a hypothesis with the student so he or she could make it a logically reliable opinion, and he would then further encourage the student to do a pilot experiment to test the hypothesis.

After receiving Ph.D., Dr. Goto accepted a position as research associate at the University of Tokyo in 1971 (Fig. 2). From 1974 to 1977 he obtained a research fellowship to continue his work the U.S. with Professor William W. Fleming at the Department of Pharmacology of the West Virginia University. Dr. Goto’s main scientific interest became the mechanisms underlying denervation– or drug-induced supersensitivity of the smooth muscle (Goto et al., 1976, 1978). After returning to Japan in 1977, Dr. Goto joined Professor Tomoh Masaki’s laboratory at the University of Tsukuba as an Associate Professor where he was in charge of...
a project entitled “supersensitivity of the smooth muscle by electrophysiological and pharmacological approaches”. Professor Katsutoshi Goto published several key papers in the field and identified the precise mechanisms of vascular supersensitivity in the early 1980s. Subsequently, he moved away from basic studies and cardiovascular pharmacology became his scientific interest (Goto, 1980, 1983). Just at the time, Professor Katsutoshi Goto started a collaboration with Sadao Kimura, an Assistant Professor of Basic Medical Sciences of the
University of Tsukuba and an outstanding biochemist skilled in deciphering the identity of bioactive peptides (Kimura et al., 1979; Lewis et al., 1980). This collaboration resulted in most impressive scientific discoveries, including the discovery and functional study of neurokinins A and B and a new concept of understanding how calcitonin gene-related peptide regulates the cardiovascular function by the sensory nervous system (Kimura et al., 1984; Saito et al., 1986; Kawasaki et al., 1988). When in 2013 Professor Goto discussed with the authors about those days long ago, he remarked that this collaboration with Professor Kimura was quintessential for the upcoming work related to the discovery of endothelin (Fig. 3).

Katsutoshi Goto and the discovery of endothelin

In May 1987, graduate student Masashi Yanagisawa who had recently completed medical school and obtained his M.D. degree, and the cardiology resident Hiroki Kurihara from Tokyo University – supervised by Professor Tomoh Masaki and in cooperation with Professor Goto and Professor Kimura – started the purification and characterization, and molecular identification of a recently reported endothelium-derived constricting factor (EDCF) activity (Barton et al, 2012; Barton and Pollock, 2012). The endothelin project, however, goes back almost exactly 30 years and began when Yanagisawa was inspired by a book that Professor Goto had brought back from the United States. Yanagisawa does not remember the precise title of the book, but remembers it had the words “coronary circulation” in its title. In the last paragraph of a chapter on “endothelium-derived vasoactive substances”, Yanagisawa found an abstract from Dr. Robert Highsmith’s laboratory published in the journal Federation Proceedings (now The FASEB Journal). The abstract with PhD student Kristine Hickey né Agricola as first author was presented at the 1984 FASEB meeting (now Experimental Biology) and reported the vasoconstrictor activity of a newly isolated EDCF (Agricola et al., 1984). The story behind Hickey’s PhD project has been reviewed elsewhere (Highsmith, 1998; Rubanyi, 2011; Barton and Pollock, 2012). The full article – which had not appeared in print yet when the book

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**“The collaboration with Professor Kimura was, in modern terms, a high-throughput screening to identify a new bioactive peptide. The combination of an established functional pharmacological assay and a high-performance liquid chromatography enabled us to isolate the target peptide. These systems became the basis of endothelin discovery in the short term. Above all, we and Professor Tomoh Masaki were full of enthusiasm to do something new at the Tsukuba University which was newly founded in October 1973.”**

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**Katsutoshi Goto**

The Thirteenth International Conference on Endothelin

Tokyo, September 2013

Fig. 3. A quote by Professor Katsutoshi Goto (2013) about the importance of his collaboration with Professor Kimura for the discovery of endothelin.

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**Fig. 4.** a. Photograph of Professor Katsutoshi Goto together with his students and the members of his laboratory at the University of Tsukuba in 1992. b. Photograph of Professor Katsutoshi Goto taken during a barbeque party held in his laboratory near Mt. Tsukuba, Japan, in 1992.
**“Do not pursue a trendy subject, rather think of what is important and investigate it persistently.”**

Katsutoshi Goto  
**The Thirteenth International Conference on Endothelin  
Tokyo, September 2013**

Fig. 5. A message by Professor Katsutoshi Goto to all young endothelin researchers after he received The Second Tomoh Masaki Award at the Thirteenth International Conference on Endothelin in Tokyo in September 2013.

was published – was referred to in that book chapter and attracted Yanagisawa’s attention. When Yanagisawa obtained a copy of the article after it was finally published (Hickey et al., 1985), he realized that the molecular structure of this EDCF had not been identified yet and proposed to identify and characterize it for his PhD thesis project (Barton and Pollock, 2012). Professor Masaki agreed, and the endothelin project was launched.

The organ bath assay system to measure isometric contraction of isolated vascular rings (also used elsewhere, Rubanyi, 2011) was routinely used in Professor Goto’s laboratory. Yanagisawa applied conditioned medium obtained from cultured porcine endothelial cells and for the first time observed very slow and potent contractions of porcine coro-

nary artery rings. When Professor Goto saw these contractile responses, he said to Yanagisawa: “I have never before seen such a vasoconstrictor activity. What is ahead of you should become very unique and special!” This comment further encouraged Yanagisawa and motivated him to increase all efforts to isolate and identify this substance. Within only seven months, the work of purification, identification, and sequencing the cDNA of the EDCF, which was designated as endothelin due to its en-

dothelial cell origin, was completed and a manuscript was submitted to Nature in December of 1987, where it was published on March 31, 1988 (Yanagisawa et al., 1988; Barton et al., 2012). The contribution and the knowledge of Professor Goto to this discovery had been essential.

Further achievements and a message to young scientists

In 1990, Goto was promoted to Full Professor and shortly thereafter began to organize Department of Pharmacology at the University of Tsukuba, as Professor Masaki had moved to Kyoto University (Fig. 4). In addition to his contribution to endothelin discovery, Professor Goto subsequently identified various aspects of the pathophysiolog-
al roles of endothelin in disease (Goto et al., 1996). In particular, an early article demonstrating an essential role of endogenous endothelin-1 in the pathogenesis of pulmonary arterial hypertension (PAH) with Takashi Miyauchi as first author paved the way to the first orally active therapy for patients with PAH using endothelin receptor antagonists (ERAs) as therapeutics (Miyauchi et al., 1993; Galié et al., 2009). Following his professorship at Tsukuba University, Professor Goto was appointed Director of the Innovation Satellite Tsukuba of the University of Tsukuba, including Head of the Cardiovascular Biosystem Project (1992); Director of Basic Medical Sciences (1995); Director of the Life Science Center of Tsukuba Advanced Research Alliance (2000); and Dean of the Graduate School of Comprehensive Human Sciences (2004). Following his professorship at Tsukuba University, Professor Goto was appointed Director of the Innovation Satellite Tsukuba of Japan Science and Technology Agency (2006), where he has continued to promote the advancement of science in an industrial–academic–gov-

ernment cooperation until 2011. As of 2014, Professor Goto is 71 years old and currently lives in Tsuchiura City, close to the University of Tsukuba where he was essential in the discovery of the endothelin peptide.

In September 2013, when Professor Goto learned from the Conference Chairs that he has been selected by the Endothelin International Advisory Board as the recipient of the Second Tomoh Masaki Award that was to be presented to him at the Thirteenth International Conference on Endothelin in Tokyo, he expressed his thanks. To all young endothelin researchers (Emoto et al., 2014), Professor Goto said, he would like to send a message. This message (Fig. 5) has implications for any young individual planning a career in biomedical research and even has general implications beyond science.

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