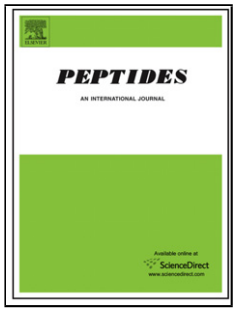

Kazuhiko Tatemoto – a homage to an outstanding scientist in peptide research

Karl-Heinz Herzig

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Kazuhiko Tatemoto – a homage to an outstanding scientist in peptide research

Karl-Heinz Herzig, MD, PhD – Editor in Chief
Institute of Biomedicine,
Medical Research Center and Oulu University Hospital,
University of Oulu, Finland
Email: karl-heinz.herzig@oulu.fi

Kazuhiko Tatemoto was born in 1940 in Tokyo, Japan, where he studied applied chemistry at Waseda University, Tokyo, and received his bachelor's degree in 1963. After his degree, he worked for a short time at a company in New York, USA. When he toured Europe for summer vacation, he fell in love with Sweden and its people. In 1967, he joined the laboratory of Hugo Theorell at the Karolinska Institute, Stockholm, Sweden, who had been awarded the Nobel Prize in 1955 "for his discoveries concerning the nature and mode of action of oxidation enzymes" while working on alcohol dehydrogenase. After Theorell's retirement, Tatemoto joined the laboratory of the brilliant and generous scientist Viktor Mutt as a PhD student. Mutt, a refugee from Estonia, had received his doctoral degree on the isolation of secretin under the supervision of Erik Jorpes, professor of medical biochemistry. Mutt succeeded Jorpes after his retirement and established a large-scale method for preparing concentrated starting material of thermostable intestinal peptides, in which proteases were destroyed by boiling, extracted by acetic acid, absorbed onto alginic acid, precipitated with NaCl and dissolved in alcohol. Furthermore, he established robust biological assay systems for their functional detection. Using this unique set up he was able for the first time to isolate large amounts of secretin and cholecystokinin. Another milestone of Mutt's work was the development of a chemical detection method with his new graduate student Kazuhiko Tatemoto using enzymatic degradation to release characteristic COOH-terminal amide fragments. The fragments were converted into fluorescent dansyl derivatives and identified by thin-layer chromatography (1). Using this assay, the team was able to isolate several novel peptides: Peptide Histidine Isoleucine (PHI), Peptide Tyrosine-Tyrosine (PYY), and Neuropeptide Tyrosine (NPY). In 1982, Tatemoto defended his thesis on the discovery of these three

peptides (2). In 1983, isolation of galanin (named after the N-terminal glycine and C-terminal alanine) followed (3). Many groups, around the world, have pursued his discoveries and are still exploring various aspects of these (neuro)peptides. For example, in July of this year the 12th NPY-PYY-PP meeting was held as a Gairdner International Symposium in Edmonton, Canada. Rarely have the results of a PhD thesis provided work for so many scientists around the world over such a long period and it is still ongoing.

After attaining his docentship at Karolinska, he joined to the Department of Psychiatry and Behavioral Sciences at Stanford University School of Medicine, Stanford, USA to investigate the newly discovered peptides as neurotransmitters in psychiatric diseases. In 1986, he published the isolation of pancreastatin (4), a peptide that inhibits glucose-induced insulin release from the isolated perfused pancreas.

Due to family reasons, he moved back to Japan and joined Gunma University in Maebashi, Japan, in 1991. During this time, sequence information of over 200 Gprotein-coupled receptors (GPCR) had accumulated, the vast majority without a natural ligand and therefore termed orphan receptors. Tatemoto and his team used this new field of reverse pharmacology to identify ligands for the orphan GPCR APJ, a putative receptor protein related to angiotensin receptor 1. They transfected CHO cells with the human AJP receptor and measured the extracellular acidification rate with various tissue extractions. Concentrate from bovine stomach gave the largest increase in acidification, leading to the isolation of a novel peptide called apelin (5). During this time, he also engaged in the drug discovery program of Takeda Chemical Industries and the Japan Tobacco Company until his retirement from Gunma University in 2006.

The retirement brought him back to the Nordic countries in Europe, which he loved so much. In 2007, he joined my team at the A.I. Virtanen Institute in Kuopio, Finland, to continue his work on reverse pharmacology and the discovery of novel endogenous ligands for orphan receptors. The following year he moved with the team to the Institute of Biomedicine at the Faculty of Medicine of the University of Oulu, Finland, where he inspired the team with his passion for science until his

death in 2011. He was an inspirational role model for young PhD students to persevere in their scientific quests in spite of all adversities and challenges until novel ligands have been identified (6-8).

In recognition of his achievements in peptide research, PEPTIDES is proud to announce the inauguration of the **Kazuhiko Tatemoto Best Paper Prize** for scientists within 10 years of receiving their PhD (maternity leave or shared parental leave during this 10-year period will be taken into account) for their contributions to PEPTIDES. The winning paper will be selected by a panel of members of the Editorial Board and awarded biennially.

References

[1] Tatemoto K. and Mutt V. Chemical determination of polypeptide hormones. Proc. Natl. Acad. Sci. USA 1978; 75: 4115-9.

[2] Tatemoto, K. Chemical detection: A new way of finding peptides. Discovery of peptide HI, peptide YY and neuropeptide Y. Thesis, Karolinska Institutet, Stockholm, Sweden, 1982.

[3] Tatemoto K, Rökaeus A, Jörnvall H, McDonald TJ, Mutt V. Galanin - a novel biologically active peptide from porcine intestine. FEBS Lett 1983; 164: 124-8.

[4] Tatemoto K, Efendić S, Mutt V, Makk G, Feistner GJ, Barchas JD. Pancreastatin, a novel pancreatic peptide that inhibits insulin secretion. Nature 1986; 324: 476-8.

[5] Tatemoto K, Hosoya M, Habata Y, Fujii R, Kakegawa T, Zou MX, Kawamata Y, Fukusumi S, Hinuma S, Kitada C, Kurokawa T, Onda H, Fujino M. Isolation and characterization of a novel endogenous peptide ligand for the human APJ receptor. Biochem Biophys Res Commun 1998; 251: 471-6.

[6] Karhu T, Akiyama K, Vuolteenaho O, Bergmann U, Naito T, Tatemoto K, Herzig KH. Mast cell degranulation via MRGPRX2 by isolated human albumin fragments. Biochim Biophys Acta Gen Subj 2017; 186: 2530-4.

[7] Karhu T, Akiyama K, Vuolteenaho O, Bergmann U, Naito T, Tatemoto K, Herzig KH. Isolation of new ligands for orphan receptor MRGPRX1-hemorphins LVV-H7 and VV-H7. Peptides 2017; 96: 61-6.

[8] Karhu T. Isolation of novel ligands for MAS-related G protein-coupled receptors X1 and X2, and their effect on mast cell degranulation. Acta Univ Oul D, 1426, 2017.

Figure 1:

Kazukiko Tatemoto 1940-2011