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GALANIN

GALANIN

A New Multifunctional Peptide in the Neuro-endocrine System

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at the Wenner-Gren Center, Stockholm, June 14-16, 1990

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Preface

During recent years the peptide galanin, which was discovered some years ago by Tatemoto, Mutt and collaborators, has received considerable attention among neurobiologists and endocrinologists. It was therefore decided to organize a meeting in Stockholm, which was sponsored by the Wenner-Gren Foundation and the Swedish Medical Research Council. It took place at the Wenner-Gren Center June 14-16, 1990. The present publication represents the proceedings of the meeting and is volume 58 in the Wenner-Gren International Symposium Series.

The meeting was held in honor of Viktor Mutt and we are most grateful that one of his closest friends and a collaborator in the early period, Professor Bertil Åberg, a leading Swedish scientist and a man of vision, has been willing to give a personal brief overview of Viktor Mutt's scientific life and achievements.

Stockholm in August 1990

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Viktor Mutt

by

Bertil Åberg

In 1946 the Department of Chemistry II at the Karolinska Institutet in Stockholm was housed in a building dating from the late 1850s. The head of the department was Erik Jorpes, who had fled from Finland during the First World War (he had been Minister of Health in the red revolutionary government of Finland, overthrown after the Civil War when Finland became an independent state). The same building also housed the departments led by Einar Hammarsten, Hugo Theorell and Ragnar Casparsson.

Jorpes had personally become rich by his association with the pharmaceutical house AB Vitrum, to which he had transferred his techniques for the production of bovine heparin and porcine insulin. This work in turn had aroused Jorpes' interest in 'natural' substances with a physiological action.

Jorpes had had a rough time during his first years in Sweden as a 'red' refugee, had often been hungry and had finished his medical studies chiefly thanks to his iron will. A long working day was natural to him and he expected the same from all his employees. The standard 'nine to five' day was, according to Jorpes, for 'bureaucrats and customs officials', and not for scientists. When Jorpes was in the lab, everybody should be in the lab — Christmas, Easter, Sundays and nights mattered little. Several of us were paid by Vitrum and many received pay or bonuses from Jorpes' own pocket. Many were refugees from the Second World War, and Jorpes, remembering his early days in Sweden, tried in every way to help them along. One of the refugees was Viktor Mutt.

My first glimpse of Viktor Mutt was of a young man with a boyish face, who in a corner of the 'big laboratory' was, as a laboratory technician, handling an enormous mass of animal organs. Viktor had fled from Estonia (he was born in Tartu in 1923) and had the same working habits as the Boss.

Very early in the morning he cycled to the slaughterhouse in the south of Stockholm (about 5 miles) with samples of heparin plus a glass bead in test-tubes kept in a wooden rack. Fresh bovine blood was poured into the tubes; they were then stoppered and the coagulation time was measured with a stopwatch. An increase in coagulation time was a measure of heparin activity (Jalling, Jorpes and Linden (1946), *Quart. J. Pharmacol.*, **19**, 96). The results were brought back by Viktor to the laboratory and formed the basis for the morning discussion with Jorpes.

The importance of measuring activity when purifying a substance was a lesson from Jorpes to Viktor Mutt. Later — when Jorpes feared lack of raw material for insulin production and turned to whale pancreas as a raw material — Viktor started to extract enormous masses of organ material. Turning to pig intestines, he isolated secretin and cholecystokinin, purified them and had them

transferred to pharmaceuticals (also sold by Vitrum, who were bought by Kabi, who 3 years ago sold the secretin to Ferring in Malmö).

Viktor realized that the intestinal extracts were a 'gold mine' for various peptides of which nothing was known about their structure or their action in the body. Historically all Viktor's marvellous achievements in the field of intestinal peptides are based on his early work with animal organ extracts.

Viktor would have remained a technician but he realized early on that in order to be able to do what he wanted in the future he must have an academic degree. I admit that I am breathless with admiration when I consider that he took an MB at the Karolinska Institutet in 1953 and defended a thesis for MD in 1959, nearly all the time keeping up hard laboratory work. Viktor was loyal to his old employer and benefactor, Erik Jorpes, until Erik died, and, luckily for the advancement of science, he has to this day been loyal to the field of intestinal peptides.

In Viktor's laboratory he and his guest scientists have isolated chymodinin, GIP (Gastric Inhibitory — or Glucose dependent Insulinotropic — Polypeptide), motilin, oxyntomodulin, a previously unknown form of somatostatin, VIP (Vasoactive Intestinal Peptide) and sorbin. In collaboration with T. J. McDonald, the bombesin-related GRP (Gastric Releasing Peptide) was isolated from porcine non-antralgastric tissue. In collaboration with K. Tatemoto, a chemical method was worked out for the determination of hormonal peptides with a C-terminal amidated alpha structure. This technique in turn led to the discovery of PHI (Peptide with N-terminal histidine and C-terminal isoleucine amide), NPY (neuropeptide Y (tyrosine)) and galanin (a peptide with N-terminal glycine and C-terminal alanine amide). At Viktor Mutt's laboratory, species varieties were studied (e.g. human secretin, bovine GIP), using radioreceptor assay techniques. Recently Viktor, together with Agerberth, Z.-W. Chen, Efendic and Östensson, have isolated from pig intestine a 60-residue polypeptide (PEC-60) (peptide with N-terminal glutamic acid (E) and C-terminal cysteine (C)). PEC-60 has a depressant activity on insulin secretion and a structural similarity to PSTI (pancreatic secretory trypsin inhibitor). Several antibacterial peptides have been isolated from pig intestine by Viktor Mutt in collaboration with Hans Boman and his co-workers. One of these has been characterized as a cecropin, a type of antibacterial peptide until now only known to occur in insects (Cecropia). The amino acid sequence determinations of Viktor's various peptides are largely carried out in collaboration with Hans Jörmvall.

Viktor Mutt's lifelong work with animal and human organ extracts has indeed opened a door to a vast field of physiologically active peptides of interest not only to the field of gastroenterology but also to that of the central nervous system. Many of the peptides will surely be shown in the near future to be of value for our understanding of the biochemical background of psychiatric diseases.

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