COLLOQUIA IN PHYSIOLOGY AND VASCULAR BIOLOGY

Venue: Medical University Vienna, Center for Physiology and Pharmacology, Institute of Pharmacology, Waehringerstrasse 13a, 1090 Vienna, "**Leseraum**"

(Johannes Schmid, Tel.: (01) 40160 31155, *johannes.schmid@meduniwien.ac.at,*
Harald Sitte, Tel.: (01) 40160 31323, *harald.sitte@meduniwien.ac.at*
Christian Gruber, Tel.: (01) 40160 31391, *christian.gruber@meduniwien.ac.at)*

Friday 20.12.2013 10:00 c.t. **Dan Larhammar** (host: Chr. Gruber)

Dept of Neuroscience,
Unit of Pharmacology Uppsala University,
Box 593
SE-75124 Uppsala
SWEDEN

"Multiplicity of vertebrate neuropeptides and receptors - why so many?"

Dan Larhammer (Dan.Larhammar@neuro.uu.se)

Abstract: The human genome encodes numerous neuropeptides and endocrine peptides and their corresponding G protein-coupled receptors (GPCRs). How did all these duplicates and subtypes arise and when did it happen? This is often difficult to tell because sequence analyses are difficult for short peptides and highly conserved GPCRs. By combining sequences comparisons with information about the chromosomal locations of genes, we have been able to deduce the origin of several peptide and receptor families. Our studies include NPY (neuropeptide Y), somatostatin, oxytocin/vasopressin and the opioid peptides (endorphin, enkephalins) and their respective receptor families. The conclusion is that all of these families expanded very early in vertebrate evolution some 500 million years ago as a result of two complete genome doublings. After these massive duplications, many genes have been lost, resulting in *fewer* genes in the human genome today than in the vertebrate ancestor as well as several presently living vertebrates. The evolutionary sequence comparisons have been very useful in our work to determine the binding interactions between NPY-family peptides and their receptors. Mutagenesis of human NPY receptors Y1 and Y2 exposes similarities and differences in their binding properties that can hopefully be utilized for development of subtype-selective ligands, both peptides and non-peptidergic compounds, for treatment of obesity, cancer and cardiovascular diseases.