COLLOQUIA IN CELLULAR SIGNALLING

Venue: Medical University Vienna, Center for Physiology and Pharmacology,
Institute of Pharmacology, Waehringerstrasse 13a, 1090 Vienna, "**Leseraum**".
(Harald Sitte, Tel.: (01) 01 40160 31323, harald.sitte@meduniwien.ac.at,
Christian Gruber, Tel.: 01 40 160 31392, christian.w.gruber@meduniwien.ac.at)

Friday **8.3.2013** **11:00 s.t.** **Mark Wheatley (host: Chr. Gruber)**

Chair of Biochemical Pharmacology
School of Biosciences
University of Birmingham
Edgbaston
Birmingham
B15 2TT, UK

"ACTIVATION OF G-PROTEIN-COUPLED RECEPTORS (GPCRs) BY PEPTIDE LIGANDS"

Mark Wheatley (m.wheatley@bham.ac.uk)

A fundamental issue in molecular pharmacology today is defining, at the molecular level, how G-protein-coupled receptors (GPCRs) are activated. Despite being activated by a wide variety of stimuli from photons to large glycoproteins, these receptors exhibit a conserved protein architecture comprising a bundle of seven transmembrane (TM) helices linked by extracellular loops (ECLs) and intracellular loops. Defining differences in the mode of binding exhibited by agonists and antagonists within this receptor structure will aid rational drug design and will provide insight into understanding their agonist-induced activation processes.

Our studies have addressed GPCRs for peptide ligands (peptide-GPCRs) and have focussed on the receptors for the neurohypophysial peptide hormones vasopressin and oxytocin in particular. Using systematic mutagenesis we have identified motifs and individual residues that are critical for high affinity agonist binding and receptor activation but not antagonist binding. Using a combination of peptide chemistry, site directed mutagenesis and molecular modelling, we have identified key agonist-specific contacts established between the receptor and ligand.