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) 4277-64123, *harald.sitte@meduniwien.ac.at*)

Friday **09.03.2012 11:00 s.t.** **Carsten Hoffmann (host: H. Sitte)**

PD Dr.
Institut of Pharmacology and Toxicology
University of Würzburg
Versbacher Strasse 9
97078 Würzburg

"Monitoring GPCRs activation in response to orthosteric or allosteric ligands in living cells"

Carsten Hoffmann (C.Hoffmann@toxi.uni-wuerzburg.de)

Abstract:
The G-protein-coupled receptors (GPCRs) represent target structures for almost 40 percent of all prescription drugs. Upon ligand stimulation the receptor conformation is rearranged which leads to a novel protein conformation that in turn can interact with different effector proteins. Significant knowledge has been gathered in the last decade about the nature of conformational changes that lead to receptor activation in general. Today it is widely accepted that different compounds can induce different conformational changes. However, the very details that may lead to different conformational changes are still poorly understood. Thus, it currently remains a process mainly based on trial and error to identify compounds that induce different conformational changes at a given receptor. Linking different conformational changes in a receptor to functional selectivity in signalling outcome could be a great step forward for a potential reduction of unwanted side effects of prescription drugs. However, this task is even more challenging since even less is known about how functional selectivity is achieved.
Fluorescence resonance energy transfer (FRET) techniques allow the sensitive monitoring of distances between two labels at the nanometer scale. Depending on the placement of the labels, this permits the analysis of conformational changes within a single protein (for example of a GPCR). These measurements can be done in living cells and with high temporal or spatial resolution. Using a FRET based approach we have studied conformational changes in differently labeled muscarinic acetylcholine receptor (M2AChR and M3AChR). The data discussed during this presentation will illustrate the power of FRET-microscopy in analysis of conformational changes of GPCRs in response to orthosteric and allosteric ligand exposure and illustrate novel techniques to study receptor signaling in real time.