COLLOQUIA IN PHYSIOLOGY AND VASCULAR BIOLOGY

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

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Friday 28.11.2014 12:30 s.t. **Bernhard Bettler** (host: E. Casanova)

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"Molecular insights into the regulation of $GABA_B$ receptor signaling"

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Abstract:
We are interested in the control of neuronal excitability by G-protein coupled receptors (GPCRs), in particular $GABA_B$ receptors, Trace Amine-Associated Receptors, mGlu5 receptors and dopamine receptors. These GPCRs are promising drug targets for mental health disorders. Research over the past couple of years showed that the heterogeneity of native GPCR signaling is not always faithfully reproduced in heterologous expression systems. We therefore initiated a search for proteins that regulate GPCR responses in their native context. In collaboration with Bernd Fakler (University Freiburg iBr) we used an unbiased proteomic approach that combines antibody-based affinity purification with high-resolution quantitative mass spectrometry to identify GPCR-associated proteins. Surprisingly, many of the identified proteins have not been implicated in GPCR signaling before. Finding the physiological functions of proteins that were identified in unbiased proteomic approaches is a challenging task. We adopted a strategy in which we systematically analyze the effects of proteins on receptor function and trafficking in a panel of assays in heterologous cells. We additionally probe the *in vivo* functions of these proteins in overexpression, knock-down and knock-out experiments. To address the molecular mechanism underlying functional effects of receptor-associated proteins we also identify their binding partners (besides the receptor) using reverse proteomics. This strategy is expensive and time-consuming but has enabled us to identify the physiological roles and mode of action of several novel receptor-associated proteins, which provided novel and unexpected insights into GPCR signaling. During my presentation I will present data on $GABA_B$ receptor-associated proteins.