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,*

Hannes Todt, Tel.: (01) 40160 31250, *hannes.todt@meduniwien.ac.at)*

Friday 26.06.2015 10:00 c.t. **Angelika Lampert** (host: H. Todt)

Universitätsklinikum Aachen, AÖR
Pauwelsstraße 30
52074 Aachen

"Sodium channel structure and function in pain"

Angelika Lampert (alampert@ukaachen.de)

Abstract: Voltage-gated sodium channels are responsible for the fast upstroke of the action potential and recently mutations in the subtype Nav1.7 were shown to cause inherited pain syndromes. These mutations, causing e.g. the burning hand and feed syndrome called erythromelalgia, reveal information of the channel's 3D structure and the potential conformational changes, which they undergo while opening and closing. Using patch-clamp, 3D structural homology modelling and site directed mutagenesis we revealed that the erythromelalgia mutation Q875E is likely to introduce a salt bridge, thereby stabilizing the channel's open state.

Prolonged or repeated sodium channel openings in nociceptors induce hyperexcitability and may thus provoke pain in the mutation carriers. Nav1.7 mutations causing the paroxysmal extreme pain disorder (PEPD) were shown to interfere with fast inactivation and thus increase resurgent currents. Erythromelalgia mutations on the other hand up now were never shown to enhance this type of current. Both diseases have clearly distinct clinical pictures and we hypothesize, that differences in the biophysical features induced by their mutations are responsible for this. In the presentation, I will discuss data showing that erythromelalgia typical gating features may prevent resurgent current formation, and thus may protect the patient from the more severe pain syndrome PEPD.