COLLOQUIA IN CELLULAR SIGNALLING

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

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Friday **13.05.2016 12:00 s.t.** **James R. Hammond** (host: S. Sucic)

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"Phenotypes of the ENT1 (Equilibrative Nucleoside Transporter 1) - null mouse: Something for everyone"

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Abstract:
Equilibrative nucleoside transporter subtype 1 (ENT1, SLC29A1) is the primary mechanism for the transfer of adenosine across cell membranes. Pharmacological inhibition of ENT1 enhances the biological activities of adenosine including its vasodilation, cardioprotection, inhibitory neuromodulation, and anti-inflammatory activities. Therefore, it was anticipated that a global knockout of ENT1 would result in numerous aberrant phenotypes. Surprisingly, the ENT1-null mice were reproductively viable (via ENT1+/- breeding) with no overt biological disruptions. Nevertheless, a plethora of more subtle changes have since been noted in my laboratory and by other investigators. Dr Doo-Sup Choi and colleagues, who initially derived this mouse line, showed that the ENT1-null mice displayed less anxiety, had a reduced response to ethanol, and increased their preference for ethanol over water. Our lab subsequently identified a distinctive skeletal phenotype involving the aberrant calcification of the vertebral enthesis regions and intervertebral discs. We have also showed that hearts from the ENT1-null mice were partially protected against ischemia-reperfusion induced injury, and microvascular endothelial cells isolated from these mice were less sensitive to intracellular superoxide generation with enhanced catalase activity. Most recently, we found that aortas from the ENT1-null mice are 'stiffer' and show a reduced response to phenylephrine, but an increased response to general depolarization with KCl. ENT1-null mice also have a paradoxical increase (given that there is increased plasma adenosine) in blood pressure relative to wild-type mice. Some of these phenotypes may reflect enhanced adenosine signalling, but others are likely due to compensatory changes in other components of the purinergic signalling system. I will discuss these varied phenotypes and what they may be "telling us" about the biological roles of adenosine and the regulation of purinergic signalling.