# NCCR TransCure Lecture in Physiology
# &
# DCR Cardiovascular Research Cluster Seminar

**given by**

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## *"TRPM4 in cardiac excitation and contractility. Lessons from knockout mice"*

**TRPM4 is a Ca2+-activated, but Ca2+-impermeable, non-selective cation channel and is an important regulator of Ca2+-dependent cell functions, including exocytosis, contraction and cell death. Trpm4 expression has been shown in atrial and ventricular cardiac tissue. Recently, gain-of-function mutations in the Trpm4 gene have been associated with conduction disorders, as Progressive Familial heart Block Type 1, Right Bundle Branch Block and Brugada Syndrome. The role of TRPM4 in the ventricular action potential and the effect on cardiac conduction was established by use of Trpm4-deficient (Trpm4-/-) mice. Patch-clamp experiments and membrane potential measurements showed that TRPM4 is activated during repolarisation of the ventricular action potential and that the duration of the action potential in cardiomyocytes of Trpm4-/- mice was significantly shorter compared to wild-type (WT) cardiomyocytes. Since TRPM4 influences action potential, and increased expression of Trpm4 (due to gain-of-function mutations) is associated with conduction disorders, we further investigated the effect of Trpm4 loss on signal conduction through the heart. Therefore, electrocardiographic intervals were determined in WT and Trpm4-/- mice. In conscious mice, II lead surface ECG was measured via telemetry. RR, PR, QRS and QTc intervals were calculated and no differences were found between the 2 genotypes. To look more in detail for impulse propagation and conduction disorders, intracardiac electrophysiological studies were performed on the mice. Atrial, His and ventricular potentials were analyzed in intracardiac electrograms and atrial-His and His-ventricular intervals were equal in WT and Trpm4-/- mice. Taken together, we conclude that loss of Trpm4 results in shorter ventricular action potentials, but this has no influence on impulse propagation and conduction properties of the heart muscle.**

## Monday December 14, 2015: 12.30

## MEM Building, Murtenstrasse 35, H-floor, H813

**Host: Prof. Dr. Hugues Abriel**

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