Topic 18 – Electrophysiology, rythmology and pacing – C

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0184
Distinct ratios of co-expressed Cx40 and Cx43 regulate a fine gap junction channel make-up and properties

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Co-expressed connexins (Cxs) can co-assemble to form gap junction channels (GJCs) of mixed Cxs composition characterized by specific electrical properties. To date the detailed GJCs make up in the distinct cardiac tissues that co-express distinct gradients of Cxs stays poorly understood. We aim to investigate whether and how the GJC make-up depends on the level and ratios of co-expressed connexin 40 (Cx40) and Cx43. Rat Liver Epithelial cells that endogenously express Cx43 and stably transfected to induce accurate ratios Cx43:Cx40 were used to perform electrical recordings on cell pairs by applying the dual voltage clamp method. We previously showed that the induction of Cx40 decreases the electrical coupling at high ratio Cx43:Cx40 while increasing at low ratios, decreases the voltage-dependence and slows the kinetics of deactivation and of recovery of GJCs. A deeper investigation at the single channel level permits to evaluate the Cxs composition and the distribution of different kinds of GJCs. Whereas non-induced cells, are coupled by homomeric-homotypic Cx43 or Cx43:Cx40 modifies the GJCs population in function of the ratio Cx43:Cx40: at high ratio GJCs made of Cx43 dominate the population, whereas lower ratios favor the contraction of Cx43:Cx40 heteromerization and the contribution of the Cx40. Our data show that the GJCs make-up is finely regulated in function on the ratio Cx43:Cx40 to form functional homotypic or heteromeric GJCs with distinct contributions of Cx40 and Cx43 properties and function in regulating the impulse propagation in the healthy heart and the pro-arrhythmic Cxs dysfunction. To correlate these results with the relative cardiac Cxs expression profiles, cell pairs of different Cxs expression pattern will be studied.

0295
TRPM4 is involved in excitation-contraction coupling regulation in healthy murine atrial cardiomyocytes

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Aims: The neuropeptide Endothelin-1 (Et-1), through the inositol triphos phate (IP3) pathway, is associated with a calcium release from the sarcoplasmic reticulum (SR). This RS depletion may open Store Operated Ca 2+ Channel (SOCs) leading to an additional calcium influx. TRPM4 is a calcium-activated non-selective cationic channel ubiquitously expressed. It is involved in many physiological processes including the negative regulation of SOCs. However, its physiological role in cardiac level remains unclear. Our purpose was to determine whether TRPM4 channel is involved during excitation-contraction coupling (ECC) at atrial level where its normally expressed and functional, in particular in response to the Et-1 during SOCs activation.

Methods and Results: Atrial cardiomyocytes were isolated from 8 weeks-old wild-type C57Bl/6 mice and ECC were analyzed by the Ionoptix® system with a 0.2mM Ca 2+ solution. LA was separated into branches. LA was perfused with a Ca2+-free solution (~10 min), then collagenase and protease solution (0.08mM Ca2+) and recirculated for ~25 min. Enzymes were washed out with a 0.2mM Ca2+ solution. LA was separated into

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