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Influence of the ratio of co-expressed cardiac connexins Cx43 and Cx45 in the formation of gap junction channels and their electrical properties

Sebastien Dupuis, Sebastien Chaigne, Marion Constantin, Thomas Desplantez
IHU L'institut de rythmologie et modélisation cardiaque (LIRYC), Pessac, France

The cardiac action potential (AP) propagation is regulated to permit the coordinated and rhythmic atrial and ventricular contractions. This regulation requires several factors, especially gap junctions, which ensure a direct pathway for electrical and biochemical signaling. They are clusters of few to hundred intercellular gap junction channels (GJC) made of two hemichannels docked in the membrane of adjacent cells, which are composed of six connexins (Cxs). Their distinct electrical properties are a key factor regulating the propagation of the AP. Four cardiac Cxs, Cx40, Cx43, Cx45 and Cx30.2, exhibit specific patterns of expression that change in the healthy and diseased heart, which leads to different possible configurations of GJC. The aim of this study is to investigate the function of the distinct ratio of co-expressed Cxs in regulating the formation and function of GJC. Electrical properties of GJC (junctional coupling, voltage dependence, unitary conductance) are determined by performing electrical recordings on cell pair by applying the dual voltage-clamp method. Rat Liver Epithelial cells stably transfected to induce accurate Cx43:Cx45 ratios of 0 (single Cx43 expression), 0.5, 1 and 2, are used. The ongoing recordings show distinct electrical properties before and after the induction of Cx45: induction of Cx45 decreases the cell-to-cell coupling and rectifies the voltage dependence of GJC. Preliminary unitary recordings suggest a distinct formation of GJC of mixed Cx43/Cx45 composition in function of the Cx43:Cx45 ratio. Further investigations will provide better understanding on the distinct contributions of Cx43 and Cx45 in the GJC make-up, electrical properties and function of the Cx43/Cx45 expression pattern in regulating the cardiac impulse propagation in the healthy heart, and the pro-arrhythmic behavior in the diseased heart.