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The funny current channel HCN4 delineates the developing cardiac conduction system in the chicken heart

Vicente-Steijn R(1)(2), Passier R.(1), Wisse L.J.(1), Schalij M.J.(2), Poelmann R.E.(1), Gittenberger-de Groot A.C.(1), Jongbloed M.R.M.(1)(2)
Department of Anatomy & Embryology, Leiden University Medical Centre, Leiden (1); Department of Cardiology, Leiden University Medical Centre, Leiden (2), The Netherlands

Introduction - Hyperpolarization-activated cyclic nucleotide-gated channel 4(HCN4) in the mouse is expressed in the developing cardiac conduction system (CCS). In the sinoatrial node (SAN), HCN4 is responsible for the funny current. To date no data is available on HCN4 expression during chicken CCS development.
Objective - To determine the full-length sequence of Hcn4 and describe its expression pattern during development in relation to the CCS in the chicken embryo.
Methods - Hcn4 RNA expression was studied by in situ hybridization in sequential chick developmental stages (HH11-HH35) and immunohistochemical stainings were conducted for the myocardial protein cTnI and the cardiac transcription factor Nkx2.5.
Results - We obtained the full-length sequence of Hcn4 in chick. Hcn4 expression was observed early in development in the primary heart tube. At later stages, expression became restricted to transitional zones, comprising the sinus venosus myocardium where the SAN develops, the atrioventricular canal myocardium, the primary fold located between the developing ventricles to form the interventricular septum, and the developing outflow tract. These zones are flanked by the atrial and ventricular working myocardium. Further in development, Hcn4 expression was restricted to the SAN, the atrioventricular node, the common bundle, the bundle branches and the internodal and atrioventricular ring myocardium.
Conclusion - We have identified Hcn4 as a functional marker of the developing CCS in the chick. The primary heart tube expresses Hcn4, which is later restricted to the transitional zones and eventually the elements of the mature CCS. Furthermore, we propose that expression patterns during development might explain the occurrence of arrhythmogenic anatomical predilection sites in adults.