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[\[PDF \(1234K\)\]](#) [\[References\]](#)**Changes of HCN gene expression and I_f currents in Nkx2.5-positive cardiomyocytes derived from murine embryonic stem cells during differentiation**

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ABSTRACT

Changes in the expression of hyperpolarization-activated cyclic nucleotide (HCN)-gated channels and I_f currents during the differentiation of embryonic stem cells into cardiac cells remain unknown. We examined changes of HCN genes in expression and function during the differentiation of Nkx2.5-positive cardiac precursor cells derived from mouse ES cells

using cell sorting, RTPCR, immunofluorescence and whole cell patch-clamp techniques. Cs⁺-induced inhibition of automaticity and transcription of HCN genes increased during differentiation. Expressions of Nkx2.5, a marker of cardiac progenitor cell, and Flk1, a marker of hemangioblast, were mutually exclusive. Messenger RNA and proteins encoded by HCN1 and 4 genes were predominantly observed in Nkx2.5-positive cells on day 15, although Flk1-positive cells did not express genes of the HCN family on that day. Cs⁺-induced prolongation of the cycle of spontaneous action potentials and I_f currents were predominantly observed on day 15. These results suggested that a fraction of Nkx2.5-positive cardiac precursor cells was committed to pacemaking cells expressing I_f channels predominantly encoded by HCN 1 and 4 genes.

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