Cardiac pacemaking is controlled by a mixed Na+/K+ current named If, which is activated by hyperpolarized membrane potentials. Recently, a family of hyperpolarization-activated cyclic nucleotide-gated cation (HCN) channels has been cloned. The members of this family exhibit the general features of If channels. This review describes the molecular diversity of the HCN channel family and the structural determinants of channel function including activation by voltage, modulation by cyclic nucleotides and ion permeation. The relationships between cloned HCN channel types and native cardiac If currents are explored.

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