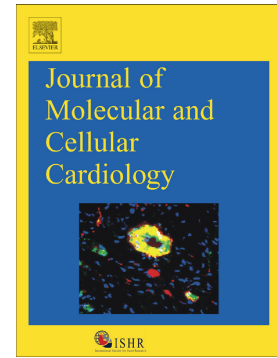


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Molecular simulations of cardiac IKs activation

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## Effects of $\beta$ -subunit on gating of a potassium ion channel: Molecular simulations of cardiac IKs activation

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### Abstract

Dynamic conformational changes of ion channel proteins during activation gating determine their function as carriers of current. The relationship between these molecular movements and channel function over the physiological timescale of the action potential (AP) has not been fully established due to limitations of existing techniques. We constructed a library of possible cardiac IKs protein conformations and applied a combination of protein segmentation and energy linearization to study this relationship computationally. Simulations reproduced the effects of the beta-subunit (KCNE1) on the alpha-subunit (KCNQ1) dynamics and function, observed in experiments. Mechanistically, KCNE1 increased the probability of “visiting” conducting pore conformations on activation trajectories, thereby increasing IKs current. KCNE1 slowed IKs activation by

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