Molecular Basis of Cardiac Action Potential Repolarization

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ABSTRACT: The action potential (AP) is generated by transport of ions through transmembrane ion channels. Rate-dependence of AP repolarization is a fundamental property of cardiac cells and its modification by disease or drugs can lead to fatal arrhythmias. Using a computational-biology approach, we investigated the gating kinetics of the slow K^+ current (I_{Ks}) during the AP in order to provide insight into the molecular basis of its role in rate-dependent repolarization. Results show that I_{Ks} builds an available reserve of channels in closed states near the open state that can open rapidly to generate current during the AP repolarization phase. By doing so, I_{Ks} can also provide repolarizing current when other currents (e.g., I_{Kr}) are compromised by disease or drugs, thus preventing excessive AP prolongation and arrhythmic activity. Supported by NIH-NHLBI grant RO1 HL49054 and Merit Award R37 HL33343

KEYWORDS: cardiac action potential, cardiac repolarization, ion channels, cardiac arrhythmias

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