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Poster Presentation

The Role of HCN Channels in T Cell Function

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Abstract

Ion channels play a major role in the regulation of T cell function in health and disease. In a computer-based model, established to simulate T cells' membrane potential (VM) generation, we discovered a discrepancy between the simulation and patch-clamp recordings. The predicted VM was more hyperpolarized than the measured VM, indicating that a yet unknown, depolarizing ion current might contribute to the T cells' VM. Since TASK2 and TASK3 channels are known to be expressed on T lymphocytes and the fact that the depolarizing I_h , mediated by HCN (hyperpolarization cyclic nucleotide activated) channels, was identified as a key antagonist of ITASK in previous studies, HCN channels seem to be an ideal candidate to explain the discrepancy between measured and simulated VM. HCN channels belong to the family of pore-loop ion channels and appear in four isoforms (HCN1-4) differing in activation kinetics, voltage and cAMP dependency and size. Their role for pacemaking activities in the heart and central nervous system is well known, however their expression and potential function in T cells has not been investigated so far and is subject to this study. In PCR and Western Blot experiments we could show the expression of HCN1-4 on T cells. HCN2 channels were upregulated upon stimulatory conditions both on mRNA and protein level. Quantification for HCN1 and HCN3-4 expression is currently pending. The pharmacological blockade of I_h by ivabradine (reversible) and ZD7288 (irreversible) resulted in differential, dose-dependent effects on cell viability and altered cytokine patterns as assessed by flow cytometry or ELISA respectively. Overall these findings support a regulatory role for HCN channels in T cell function and warrant further investigations.

Keywords: Channels, Health, Disease

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