

Analysis of the K⁺ current in human T cells in hypercholesterinaemic state

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It is well documented in the literature that the changing the cholesterol content of the cell membrane may influence the functioning of the membrane proteins, including that of the ion channels. In most of the relevant studies the cholesterol content of the membrane is altered artificially, using various forms of cyclodextrins. Our laboratory has reported previously that the increase of the cholesterol content of the cell membrane (*in vitro*, using cholesterol/cyclodextrin inclusion complex treatment) modified the biophysical parameters of the gating of Kv1.3 K⁺ ion channels in human T-lymphocytes.

As Kv1.3 channels have a pivotal role in the regulation T cell proliferation and function we addressed whether the changes described in the model experiments could be observed for Kv1.3 channels of T cells isolated from patients with hypercholesterinaemia.

T-lymphocytes were isolated from the peripheral blood of patients with cholesterol level considered normal (< 5.2 mmol/l) according to the laboratory standards (control group) and patients with hypercholesterinaemia („hc”, the cholesterol level is the 1.5 – 2-fold of the normal one, n = 5). Patient samples („hc” samples) were obtained from untreated (first-visit) outpatients of the Department of Medicine and they did not suffering from any additional other diseases.

The biophysical characteristics of the Kv1.3 ion channel were studied using the whole-cell configuration of the patch-clamp technique. We determined the kinetic (activation and inactivation kinetics, time constants for recovery from inactivation) and equilibrium parameters (voltage-dependence of steady-state activation and inactivation) characterizing the gating of Kv1.3 channels. The expression level of the channels was characterized by current density (pA/pF) calculated as the peak current normalized to the membrane capacitance, the latter being proportional to the membrane surface area.

Our results indicate that the biophysical parameters of Kv1.3 gating are similar in the control group and in the „hc” samples (p= 0.05). Thus, the increase of the serum cholesterol level does not result in such biophysical changes in Kv1.3 gating as those that we measured in model experiments using cholesterol/cyclodextrin inclusion complex treatments. On the other hand the current density measured in T cells isolated from the „hc” sample (CD_{hc} = 610 ± 98 pA/pF) was significantly higher than in the case of the control cells (CD_c = 398 ± 10.8 pA/pF). This increase in the current density may reflect chronic inflammatory processes coupled with hypercholesterinaemia and the cytokines produced.