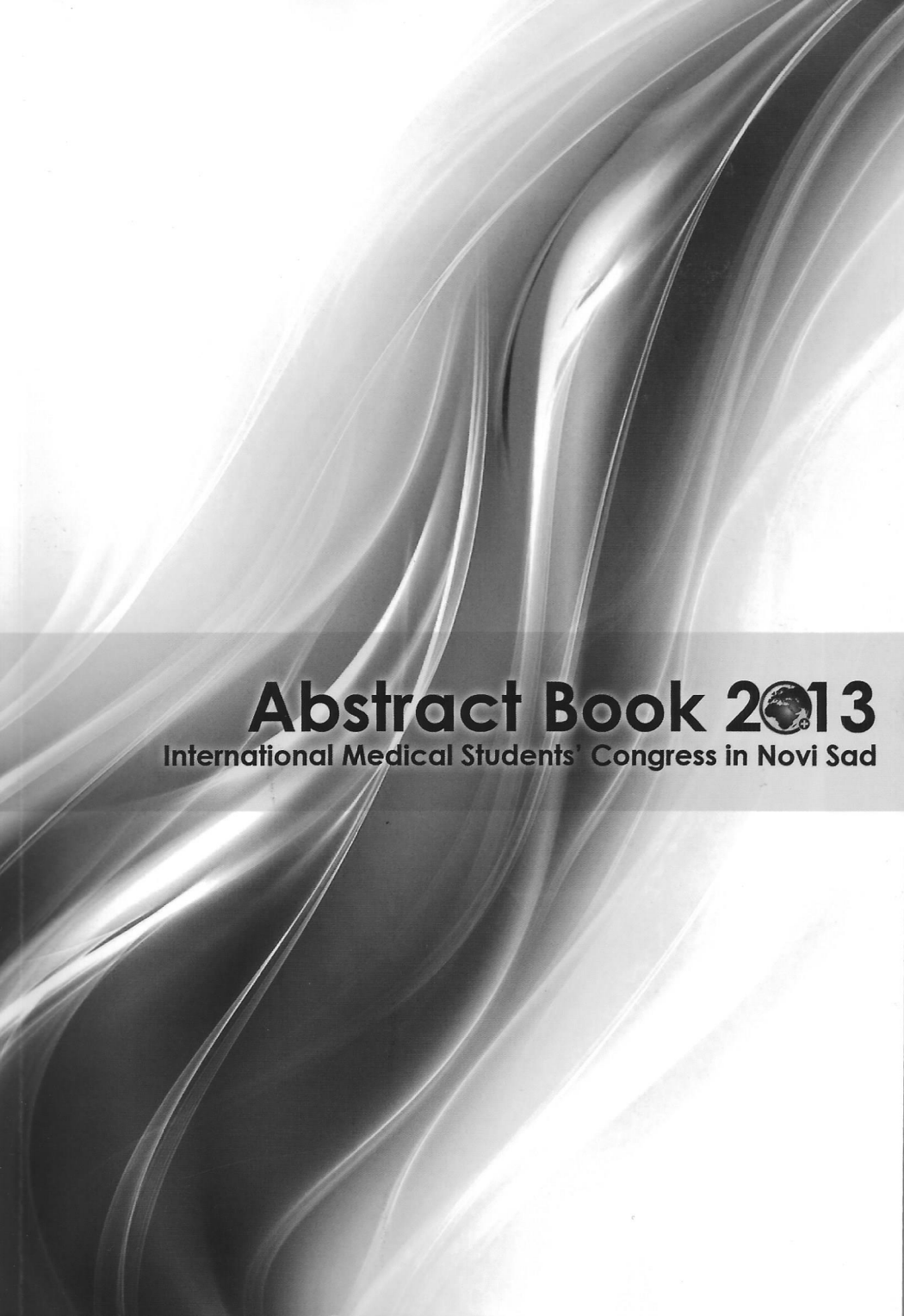




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INHERITED DISORDER OF CHOLESTEROL BIOSYNTHESIS (SLO SYNDROME) MODIFIES THE FUNCTION OF Kv1.3 CHANNELS AND PROLIFERATION OF LYMPHOCYTES

(Poster presentation)

Field of medicine: Pathophysiology

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Introduction: The Smith-Lemli-Opitz syndrome (SLO) is a multiple congenital anomaly, featured by reduced or complete lack of activity of 7-dehydrocholesterol (7DHC) reductase. Since 7DHC reductase catalyses the last step of the cholesterol biosynthesis people with SLO have lower serum cholesterol and higher 7DHC levels. The alteration of cholesterol/7DHC ratio also affects the biophysical properties of the cell membrane such as fluidity and raft organization. The change of these characteristics of the cell membrane may influence the function of the ion channels

Aim: In our present study we aimed to determine the effect of SLO on the gating of Kv1.3 channels and proliferation of T cells.

Material and methodology: T-lymphocytes were isolated from the peripheral blood of healthy age-matched control persons and patients with SLO. The biophysical properties of Kv1.3 were studied by means of the patch-clamp technique. We determined the kinetic and equilibrium parameters of Kv1.3 gating. Lymphocyte proliferation was monitored by use of CFSE-assay upon anti-CD3/anti-CD28 stimulation

Results: Our results showed that the activation and inactivation time constants were significantly higher in the patients with SLO than in the control group. Furthermore, the midpoint of the steady-state activation was shifted toward positive voltages in SLO T cells. The CFSE-based assay demonstrated that T cells of SLO patients challenged by anti-CD3 and anti-CD28 exhibited lower proliferation rate than control cells

Conclusion: We suppose that the modification in the biophysical properties of Kv1.3 and proliferation of T-cells may affect the physiological function of the lymphocytes

Key words: T-cells, Kv1.3, Smith-Lemli-Opitz

