T-cell development, activation and membrane potential

Yasuo Ishida (Japanese Foundation of AIDS Prevention)
Hiroshi Ohno (Molecular Genetics, Center for Biomedical Science, Chiba University)

Summery

Plasma membrane potential (Ψ) generated by inorganic ion permeation through the membrane is one of the most important cellular microenvironment. Several concentrated works during past two decades, in particular of excitable cells, have clarified the mechanisms of membrane physiology. We, however, have still limited knowledge in T cell physiology, especially roles of Ψ. We have focused on the points and studied the regulation of intracellular free calcium ion concentration ($[Ca^{2+}]_i$), how lymphocytes generate and maintain their Ψ, and analyzed how hyperpolalized Ψ influences T-cell activation.

Our findings are 1) T-cells possess calcium-dependent potassium channel, 2) the channel can be active at above 300 nM $[Ca^{2+}]_i$ and hyperpolarize the cell, 3) magnitude of calcium response, however, was constant throughout physiologic Ψ, and in even over 10 fold lower $[Ca^{2+}]_i$ level, 4) T-cell proliferation and lymphokine secretion were identical to calcium response, and 5) T-cell did not sensitively respond to TCR stimulation in hyperpolarized Ψ though the condition must enhance electro-chemical gradient that drives calcium ion influx. The results suggested that activation-induced hyperpolarization might play more important role rather than effective driving force of extracellular calcium ion though calcium elevation controls the condition.

We established Jurkat cell transfectants introduced by inward rectifier potassium channel gene (IRK1) to clarify physiologic role of hyperpolarized Ψ without $[Ca^{2+}]_i$ elevation. Transfectants initially showed strong hyperpolarization in low potassium medium. The condition, however, continued less than 5 minutes at 37 C. Chloride channels compensated to normal resting Ψ. Since expressed IRK1 channels could excessively permeate K^+ to force Ψ more negative, result suggests the presence of strong buffering reaction to maintain resting Ψ. We are planning to analyze the physiologic meanings of opposite Ψ regulation in the resting and activated T cells.