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Extracellular Zinc Modulates Cloned T-type Calcium Channels

Jung-Ha Lee[1], Byong-Gon Park[2], Jin-Yong Park[1], Joong-Woo Lee[2], and Seong-Woo Jeong[2]

[1]Department of Life Science, Sogang University; [2]Department of Physiology and Institute of Basic Medical Science, Yonsei University Wonju College of Medicine

In the present study, we investigated effects of extracellular zinc (Zn^{2+}) on T-type Ca^{2+} channel isoforms (α1G, α1H, and α1I) stably expressed in HEK 293 cells. Ca^{2+} currents were measured using 10 mM Ca^{2+} as a charge carrier under whole cell-ruptured patch configuration. Zn^{2+} blocked the α1H currents with a 100- and 200-fold higher potency (IC_{50} = 2.5 μM) when compared with those for blockade of the α1G and α1I currents, respectively. The blockade level by Zn^{2+} was much affected by varying test pulses (-60 mV to +40 mV), but not holding potentials (–110 mV to –70 mV). Zn^{2+} substantially slowed the inactivation kinetics of all the T-type currents. More interestingly, Zn^{2+} selectively prolonged deactivation of the α1I currents, while having little effect on that of the α1G and α1H currents. Taken together, our data suggest that (i) Zn^{2+} at low concentrations can be used for discriminating the α1H from the other two isoforms, (ii) extracellular Zn^{2+} blocks cloned T-type Ca^{2+} currents in voltage-dependent and state-independent ways. In addition, we speculate that the Zn^{2+}-evoked Ca^{2+} inflow through the α1I calcium channels during repolarizing phase of action potentials may play significant roles in regulation of neuronal functions in normal and pathophysiological conditions. *(Supported by the KOSEF grant R01-2000-00169)*