

C5

Effects of Cofilin and PMA on Na⁺-K⁺ Pump Current in Guinea-pig Ventricular Myocytes

So-Young Lee, Jaehoon Jung*, Chin O. Lee, and Kyunglim Lee*

Department of Life Science, Pohang University of Science and Technology, Pohang 790-784, *College of Pharmacy, Center of Cell Signaling Research and Division of Molecular Life Science, Ewha Woman's University, Seoul 120-750

The Na⁺-K⁺ pump, a plasma membrane Na⁺-K⁺ ATPase is plays a key role in the regulation and maintenance of Na⁺ and K⁺ ion concentration gradients across cell membranes. This enzyme pumps three Na⁺ out of and two K⁺ into the cell against their electrochemical gradient by utilizing the energy derived from ATP. Therefore, the Na⁺-K⁺ pump generates a net outward electrical current. The Na⁺-K⁺ pump currents was determined as that abolished by 0.5 M strophanthidin in myocytes internally dialyzed via wide-tipped pipettes perfused with solution containing 50 mM Na⁺, 10 mM MgATP and 15 or 100 nM Ca²⁺. The steady-state Na⁺-K⁺ pump current-voltage (I-V) relationship was obtained by subtracting the I-V relationship determined in the presence of strophanthidin from that determined just before in its absence.

It was reported that cofilin interacted with a large cytoplasmic loop of Na⁺-K⁺ pump (1). Cofilin, an actin-binding protein, increased the Na⁺-K⁺ pump current over the entire voltage range (-100 to +40 mV) examined. At 0 mV holding potential, cofilin increased Na⁺-K⁺ pump current by 52.7 ± 16.2 % (mean ± S.E., n=3). The ratio of the pump current amplitude in the presence of cofilin to that in its absence did not change with voltage. The result suggests that cofilin might stimulate the Na⁺-K⁺ pump by interacting with its cytoplasmic loop.

Gao et al.(2) reported that activation of PKC increased Na⁺-K⁺ pump current. We examined if PKC activator, PMA at low and high concentration influenced the Na⁺-K⁺ pump current. Our study revealed that PMA did not change the Na⁺-K⁺ pump current (n=13). The Na⁺-K⁺ pump current was not changed by even 15 μM PMA that was reported to cause a maximum increase in Na⁺-K⁺ pump current, regardless of cytosolic [Ca²⁺].

(1) Lee Kyunglim et al, Interaction of the α subunit of Na,K-ATPase with cofilin, *Biochem J.* (2001) 353:377-385

(2) Gao J et al, Activation of PKC increase Na⁺-K⁺ pump current in ventricular myocytes from guinea pig heart, *Pflügers Arch* (1999) 437:643-651