PARTICIPATION OF NA/K-ATPASE IN INTRACELLULAR SIGNALING IN CEREBELLUM GRANULE CELLS

O. Brodskaya, E. Akkuratov, A. Boldyrev
Moscow State University Department of Biochemistry, M.V. Lomonosov Moscow State University, Moscow, Russia
olga3511@yandex.ru

Using cultured neurons obtained from cerebellum of 10 days old rats we have shown that the specific inhibitor of Na/K-ATPase, cardiotonic steroid (CTS) ouabain induces immediate activation of the ERK 1/2 signaling pathway. 1 nmole/L ouabain which affects only α3 (CTS sensitive) isoform of Na/K-ATPase results in transient activation of ERK1/2, whereas 100 μmole/L ouabain which suppresses both CTS sensitive and CTS resistant (α1) enzyme isoforms provides long term activation of ERK 1/2. The former type of ERK1/2 activation corresponds to adaptive response of the neurons while the latter corresponds to "pathological" reaction leading to programmed cell death. In both cases, Scr kinase and JNK are involved in the signaling mechanism. Interaction between Na/K-ATPase and glutamate receptors of NMDA class has also been demonstrated which may explain the excitotoxic effect of NMDA receptors enhanced by Na/K-ATPase inhibition. As the excitotoxicity of NMDA receptors usually accompanies human neurological diseases the interaction between these receptors and Na/K-ATPase may be the primary step of regulatory cell signaling in neuronal cells.