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IDENTIFICATION OF ION CHANNELS IN THE NUCLEAR ENVELOPE OF CARDIOMYOCYTES

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The nuclear membrane is semi-permeable barrier between the cytoplasm and nucleoplasm. Transport through the nuclear membrane is provided by numerous nuclear pores and ion channels with different biophysical properties. We previously recorded a large-conductance cation channels (LCC-channels) and other channels in the nuclear envelope of central neurons [Marchenko et al., 2005]. Now we have developed a method of isolating cell nuclei from the heart, suitable for the patch-clamp recording of ion channels. We hypothesize that nuclear ion channels are an integral part of Ca^{2+} signaling machinery and, as such, play an important role in the function of the heart muscle. Ion channels involved in intracellular Ca^{2+} signaling may be a target of completely new type of drugs for treatment of heart diseases.

The research was conducted on 2–3 weeks *Wistar* rats. The nuclei of cardiomyocytes were isolated by homogenization and subsequent centrifugation of received suspensions. Single-channel ion currents were registered in nucleus attached configuration and voltage-clamp mode of the patch-clamp technique. The results were analyzed using *Clampfit* and *Origin*.

We have found that the nuclear membrane of rat cardiomyocytes contains inositol 1,4,5-trisphosphate receptors with conductance of 384±5 pS (n=5). No ryanodine receptors, the most abundant intracellular Ca^{2+} channels of cardiomyocytes, have been detected in the nuclear membrane. The patch-clamp recording from the nuclear envelope of cardiomyocytes revealed the presence of large conductance cation channels (LCC-channels) characterised by large conductance (209±13 pS, n=44), slow kinetics and high open probability, similar to those, previously reported in neurons. The LCC-channels were permeable to K^+ and Na^+, but impermeable to Cl^- and Ca^{2+}. We also registered at least two types of ion channels with significantly higher conductance than that of LCC-channels — 312±8 pS (n=5) and 340±18 pS (n=2), which differ in kinetics. Our data indicate that nuclear membrane of cardiomyocytes contains also several types of ion channels with lower conductance (10–90 pS).

Summarizing, using the patch clamp technique in nucleus attached configuration we have found that the nuclear membrane of rat cardiomyocytes contains different types of ion channels with conductances in the range from 10 to 400 pS. Our data indicate that the nuclear envelope of cardiomyocytes is a Ca^{2+} store, sensitive to inositol 1,4,5-trisphosphate, but in contrast to sarcoplasmic reticulum of these cells, it does not contain ryanodine receptors. Therefore regulation of Ca^{2+} release in the nucleus differs from that in the cytoplasm. The numerous LCC channels may be involved in Ca^{2+} signaling by providing a route for counterflow of cations and thereby facilitating Ca^{2+} release from the nuclear envelope. The role of other, rarer nuclear channels is unclear and needs further investigation.