Role of Cytoskeleton and Lipid Bilayer in Regulation of Cation Channels in Nonexcitable Cells

E. A. Morachevskaya and Yu. A. Negulyaev

*Institute of Cytology, Russian Academy of Sciences, Tikhoretsky pr., 4, St. Petersburg, 194064 Russia;
e-mail: elenmo@mail.cytspb.rssi.ru*

DOI: 10.1134/S1990747809030350

This study focuses on the role of submembranous actin cytoskeleton and lipid environment in function of two dominant types of cation-transporting channels identified in plasma membrane of nonexcitable cells: non-voltage-gated sodium channels and mechanosensitive channels. Using different modes of patch-clamp technique, we have shown that activation and inactivation of non-voltage-gated sodium channels is directly controlled by assembly–disassembly of microfilaments attached to cytoplasmic membrane surface. Actin-binding capping proteins have been found to modulate channel activity via modification of submembranous actin polymerization. Small G-proteins can regulate sodium channels and intracellular mechanism mediating their effect involves actin cytoskeleton rearrangements. The results suggest that uncapping of actin filaments caused by small G proteins is likely to be a key step in this regulation. Activation of sodium channels (conductance 12 pS) in response to cytochalasin B or D was also observed in cholesterol-depleted cells. Inside-out experiments with the use of globular actin indicated that filament assembly on cytoplasmic membrane side causes fast inactivation of sodium channels. These data imply that coupling of sodium channels with actin dynamics maintains after cholesterol depletion and presumable destruction of cholesterol-rich membrane microdomains (rafts). Notably, sodium channels activating in response to cytoskeleton disassembly are not

sensitive to mechanical stimulation. Local membrane stretch induces an activation of mechanosensitive cation channels permeable for physiological bivalent cations, calcium and magnesium. Interrelations of the channels with cytoskeleton and membrane lipids are generally considered to be of great importance for mechanotransduction. An adequate experimental model has been developed in our works to study cytoskeleton-related channel regulations using patch-clamp method. Consistent with our earlier studies, cytochalasins, known actin destructors, caused a decrease of the unitary conductance but did not promote mechanosensitive channel activation in K562 leukaemia cells. We found that cholesterol depletion inhibits mechanosensitive cation channels. Patch-clamp measurements and fluorescent microscopy have documented that suppression of mechanosensitive channel activation in cholesterol-depleted cells is due to F-actin rearrangement, presumably induced by lipid raft destruction. The data obtained indicate that actin cytoskeleton organization and dynamics are crucial factors in regulations of different types of cation channels plasma membrane of nonexcitable cells.

This work was supported by Russian Foundation for Basic Research (project nos. 08-04-00574a and 07-04-00679a).