

The Na/Ca exchange was affected by KB-R7943, nicorandil and monensin in breast cancer cells

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[Background] The Na⁺/Ca²⁺ exchanger (NCX) plays a pivotal role in regulation of intracellular Ca²⁺ concentration. NCX has been studied in a variety of cells, e.g. cardiac myocytes, smooth muscle cells, neurons, and recently, cancer cells as well. The aim of the present study was to assess the effect of agents affecting NCX on breast cancer cells. [Methods] Patch-clamp recording, Ca²⁺ imaging, MTT assay were used to evaluate the relationship of Ca²⁺ flux and cell proliferation. MCF-7 and HCC1937 breast cancer cells were used. [Results] Low (0.3, 5 mM) external Na⁺ solutions increased Ca²⁺ fluorescent intensity. KB-R7943 (10⁻⁵ ~ 2 x 10⁻⁵ M) also increased fluorescent intensity to some extent. The combination with low Na⁺ solutions and KB-R7943 increased fluorescent intensity drastically in HCC1937 cells. KB-R7943 in a concentration range of 10⁻⁵ ~ 5x 10⁻⁵ M reduced viability of HCC1937 cells in a concentration-dependent manner. Patch-clamp recording using ramp-clamp pulse (from +60 mV to -120 mV for 1.8 s) showed that KB-R7943 10⁻⁵ M reduced the reverse mode and the forward mode of NCX in MCF-7 cells. Other agents already reported to affect NCX by different mechanisms were studied in MCF-7 cells. Nicorandil 10⁻⁴ M and monensin 10⁻⁵ M increased NCX current. [Conclusion] We conclude that the NCX regulation system is working in [Ca²⁺]_i in breast cancer cells, and proliferation and viability are affected by agents modulating NCX. It is indicated that modulation of NCX might possibly become a therapeutic target in breast cancer.