MELANOMA AND MELANOCYTIC NAEVI

THE FUNCTION OF NA+-CA2+ EXCHANGER IN HUMAN MELANOMA CELLS

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Background: Tumor cells are resting membrane potential-depolarized and enrich sodium and calcium, known to be associated with tumorigenesis and metastasis. Electrogenic Na+-Ca2+ exchanger or NCX has been suggested to participate in these processes.

Objective: In this study, we aimed to investigate whether NCX type 3 (NCX3) is involved in maintaining resting membrane potential, Na+ homeostasis and Ca2+ cycling in human melanoma cells.

Materials and Methods: NCX was detected by Western blot. Whole-cell voltage-clamp and perforated current-clamp were employed to record NCX currents and membrane potentials respectively. Cytoplasmic Ca2+ and Na+ were measured by loading Fluo-4 and CoroNa green respectively.

Results: Compared with normal human melanocytes (HMC), human melanoma cell WM 266-4 cells exhibited unexpected lower cytoplasmic Na+ (13.2%). Among NCX1, 2, and 3, only NCX3 was expressed in human melanocytes and WM 266-4 cells. And mitochondrial NCX was only detected in HMC. The average current density of voltage-dependent NCX3 was recorded in WM 266-4 with a maximum inward current of 0.24 pA/pF at −120 mV, a maximum outward current of 0.65 pA/pF at + 60 mV and a reversal potential of -42 mV. As KB-R7943 at 10μM was used to block NCX3 current, [Ca2+]i significantly decreased from 7.65 ± 0.65 to 5.19 ± 0.48 (F/Fo), [Na+]i increased from18.17 ± 2.67 to 22.38 ± 3.30 (F/Fo, $p<0.01$) and resting membrane potential gradually depolarized from -47.7 ± 4.4 to -38.3 ± 2.3 mV. These results suggest that NCX3 act in a reverse mode (3 Na+ efflux with 1 Ca2+ influx) in melanoma cell line WM 266-4 cells.

Conclusions: In melanoma cell WM 266-4 cells, NCX3 is involved in hyperpolarization of

resting membrane potential, decreasing cytosolic Na+ and increasing cytoplasmic Ca2+ by a reverse mode.