TRP Channels in Agonist-Induced Proliferation of Prostate Cancer Cells

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Agonist-induced stimulation of $\alpha 1$ -adrenoreceptors ($\alpha 1$ -AR) of the cultured primary human prostate cancer (PCa) epithelial cells results in the enhancement of proliferative activity accompanied by the oscillations of the intracellular calcium concentration ($[Ca^{2+}]_i$), increase of store-independent calcium entry, and activation of the transcription factor NFAT (nuclear factor of activated T cells). Calcium entry in response to the $\alpha 1$ -ARs stimulation is primarily mediated by TRPC6 (transient receptor potential canonical 6) cationic channel: antisense TRPC6 depletion decreases calcium entry, suppresses $[Ca^{2+}]_i$ oscillations and slows down proliferation caused by the $\alpha 1$ -AR agonist phenylephrine. On the contrary, stimulation of purinergic P2Y receptors (P2Y-R) leads to complete cessation of proliferative activity of human PCa cells due to enhancement

of sustained store-dependent calcium entry, which is mainly mediated by TRPC1 and TRPC4 channels without NFAT involvement. Expression and channel-like function of another member of TRP channels family, cold/menthol-sensitive TRPM8 (melastatin 8), was dependent on the presence of functional androgen receptor and was characteristic of only apical phenotype of PCa epithelial cells. Our results establish TRPC6 and TRPC1/4 channels as important determinants in the control of PCa epithelial cells proliferation and TRPM8 channel as a marker of the PCa stages and androgen dependency.

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