The role of transient receptor potential channel blockers in human gastric cancer cell viability.


Source

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Abstract

Transient receptor potential cation channel, subfamily M, receptor 7 (TRPM7) is a ubiquitous divalent-selective ion channel with its own kinase domain. Human gastric cancer cells express the TRPM7 channel, and the presence of this channel is essential for cell survival. Recent studies have suggested that 5-lipoxygenase (5-LOX) inhibitors are potent blockers of the TRPM7 channels. The aim of this study was to show the effects of 5-LOX inhibitors on the growth and survival of gastric cancer cells. Among 5-LOX inhibitors, nordihydroguaiaretic acid (NDGA), 2,3,5-trimethyl-6-(12-hydroxy-5,10-dodecadienyl)-1,4-benzoquinone (AA861), and 3-[1-(p-chlorobenzyl)-5-(isopropyl)-3-tert-butyliothiindol-2-yl]-2,2-dimethylpropanoic acid (MK886) were potent blockers of TRPM7-like currents in gastric cancer cells and also induced cell death. However, zileuton was ineffective in suppressing TRPM7-like current activity and inducing cell death. Moreover, a specific transient receptor potential cation channel, subfamily C, member 3 (TRPC3) inhibitor, a pyrazole compound (Pyr3), and a specific melastatin TRP (TRPM4) inhibitor, 9-phenanthrol, did not affect TRPM7-like currents or induce cell death. We conclude that TRPM7 has an important role in the growth and survival of gastric cancer cells and a likely potential target for the pharmacological treatment of gastric cancer.

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