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TRANSIENT RECEPTOR POTENTIAL CHANNELS IN GASTROINTESTINAL TRACT

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Transient receptor potential (TRP) channels are molecular candidates for nonselective cation channels (NSCCs) like receptor-operated channels or store-operated channels in nonexcitable cells as well as excitable cells. TRP channels are usually calcium permeable channels and play important roles for calcium influx together with voltage-gated calcium channels. TRP channels are mainly classified into classical type (TRPC), vanilloid type (TRPV) and melastatin type (TRPM). NSCCs activated by muscarinic stimulation induce depolarization and increase the frequency of the slow waves in gastrointestinal (GI) tract. The depolarization activates voltage-gated calcium channels and in turn enhances smooth muscle contraction. When TRPC4 or 5 were expressed in human embryonic kidney (HEK) cells, the electrophysiological properties were similar to those of NSCCs activated by muscarinic stimulation in murine gastric smooth muscle cells. In addition, NSCCs activated by muscarinic stimulation were not recorded in gastric smooth muscle cells of TRPC4 knockout mice. However, there is still a possibility that TRPC4 forms functional channels as heteromultimers with TRPC5 or TRPC1 because the response of TRPC4 or TRPC5 to extracellular pH was different from native NSCC activated by muscarinic stimulation in murine gastric smooth muscle cells. NSCCs are also involved in pacemaking activity in interstitial cells of Cajal in GI tract. Initially, NSCCs responsible for pacemaking activity are considered as calcium-inhibited channels like store-operated channels and TRPC4 as molecular candidates for NSCCs responsible for pacemaking activity. In contrary, we showed that TRPC4 is responsible for NSCCs activated by muscarinic stimulation and pacemaking activity was maintained in TRPC4 knockout mice. Considering the expression of TRPM7 in interstitial cells of Cajal, the ionic permeability to divalent cations, the inhibitory effect of internal magnesium on channel activity, and the effect of TRPM7 siRNA on pacemaking activity, TRPM7 appears to be a molecular candidate for NSCCs responsible for pacemaking activity. In conclusion, TRP channels are playing important roles in GI tract, i.e., muscarinic modulation of GI motility and pacemaking activity.

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DISTRIBUTION AND FUNCTION OF TRPV1 CHANNELS IN THE UROGENITAL TRACT IN NORMAL AND PATHOLOGICAL CONDITIONS

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