Calcium release-activated calcium current in rat hepatocytes

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Store-operated Ca^{2+} (SOC) channels play a central role in regulating intracellular Ca^{2+} concentration in hepatocytes and other nonexcitable animal cells (Gregory & Barritt, 2003). A major function of SOC channels appears to be to replenish intracellular Ca^{2+} stores when intracellular Ca^{2+} is lost from the cell during agonist-induced increases in the cytoplasmic Ca^{2+} concentration. One of the best-known store operated channels, Ca^{2+}release-activated Ca^{2+} (CRAC) channel has been extensively characterised in a number of immortalised cell lines. There is little evidence, however, that I_{CRAC} is activated in the physiological conditions in cells in primary culture. It has been speculated that the highly Ca^{2+}-specific CRAC channels are only expressed in blood cells and in transformed cells.

The aim of the present experiments was to elucidate the properties of the SOC channels in rat hepatocytes. Hepatocytes were isolated by collagenase digestion and plated on glass coverslips. Patch-clamp recording was conducted in the whole-cell mode using standard procedures after 24-48 hours.

Depletion of intracellular Ca^{2+} stores in rat hepatocytes activated a Ca^{2+}-selective inward current. Properties of this current, including high selectivity for Ca^{2+}, strong inward rectification, fast Ca^{2+} dependent inactivation at negative potentials and block by La^{3+} and 2-APB, were similar or identical to those of I_{CRAC} found in mast cells, RBL cells, Jurkat T lymphocytes (Zweifach & Lewis, 1993; Hoth & Penner, 1992; Bakowski & Parekh, 2002) and H4-IIE liver cells (Rychkov *et al.* 2001). The amplitude of I_{CRAC} in rat hepatocytes varied between −30 and −120 pA at −100 mV with an average density of about −1 pA/pF. Extracellular application of vasopressin or ATP activated a current with the same properties and the same size as that observed by $InsP_3$ induced depletion of the stores. I_{CRAC} developed more slowly with vasopressin than with ATP as agonist. Increasing the concentration of ATP shortened the delay in the development of I_{CRAC}, but did not change the amplitude of the current or the rate of its development. Concentrations of ATP (5-10 μM) that cause waves of increased cytoplasmic Ca^{2+} concentration also activated I_{CRAC}. So far, no other type of current activated by Ca^{2+} store depletion has been detected in these cells. It is concluded that CRAC channels are the major, and possibly the only, type of SOC channel in rat hepatocytes.

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