A TR(I)P through the world of epithelial calcium and magnesium channels

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Ca^{2+} and Mg^{2+} are of great physiological importance by their intervention in many enzymatic systems and their function in neural excitability, muscle contraction, blood coagulation, bone formation, hormone secretion and cell adhesion. The human body is equipped with an efficient negative feedback system counteracting variations of the Ca^{2+} and Mg^{2+} balance. This system encompasses parathyroid glands, bone, intestine and kidneys. These divalents are maintained within a narrow range by the small intestine and kidney which both increase their fractional (re)absorption under conditions of deprivation. If depletion continues, the bone store assists to maintain appropriate serum concentrations by exchanging part of its content with the extracellular fluid. After years of research, rapid progress has recently been made in identification and characterization of the Ca^{2+} and Mg^{2+} transport proteins contributing to the delicate balance of divalent cations. Expression cloning approaches in combination with knockout mice models and genetic studies in families with a disturbed Mg^{2+} balance revealed novel Ca^{2+} and Mg^{2+} gatekeeper proteins that belong to the super family of the transient receptor potential (TRP) channels. These epithelial Ca^{2+} (TRPV5 and TRPV6) and Mg^{2+} channels (TRPM6 and TRPM7) form prime targets for hormonal control of the active Ca^{2+} and Mg^{2+} flux from the urine space or intestinal lumen to the blood compartment. The function of these distinctive epithelial Ca^{2+} and Mg^{2+} channels is believed to be relevant to various (patho)physiological situations.