POLYPHOSPHATE ACCUMULATED IN THE ACIDOCALCISOMES IS INVOLVED IN OSMOREGULATION IN TRYPANOSOMATIDS

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Acidocalcisomes are dense, acidic organelles with a high concentration of phosphorus present as pyrophosphate and polyphosphate complexed with calcium, and other cations. The acidocalcisome membrane contains a number of pumps (Ca^{2+}-ATPase, V-H^+-ATPase, H^+-PPase), exchangers (Na^+/H^+, Ca^{2+}/H^+), and channels (aquaporins), while its matrix contains enzymes related to pyrophosphate and polyphosphate metabolism. Acidocalcisomes have been found in several pathogenic microorganisms as well as in the green alga *Chlamydomonas reinhardtii*, and the slime mold *Dictyostelium discoideum*. The identification of acidocalcisomes in bacteria and the finding that human platelet dense granules are similar to acidocalcisomes, indicate that these are organelles that have been conserved from bacteria to humans. Acidocalcisomes function in the storage of cations and phosphorus, pyrophosphate and polyphosphate metabolism, calcium homeostasis, maintenance of intracellular pH homeostasis, and osmoregulation. Acidocalcisomes have been linked to the contractile vacuole complex in *C. reihnardtii*, *D. discoideum,* and *T. cruzi*). A microtubule- and cyclic AMP-mediated fusion of acidocalcisomes to the contractile vacuole complex in *T. cruzi* results in translocation of aquaporin and the resulting water movement, which, in addition to swelling of acidocalcisomes, is responsible for the volume reversal not accounted for by efflux of osmolytes. Polyphosphate hydrolysis occurs during hypo-osmotic stress and we have found an exopolyphosphatase present in acidocalcisomes and the contractile vacuole complex of *T. cruzi*. This is in agreement with the hypothesis that, when cells are submitted to hypo-osmotic stress, acidocalcisome polyphosphate is hydrolyzed after fusion to the contractile vacuole increasing its osmotic pressure and facilitating water movement. The gene encoding this exopolyphosphate has been cloned and the recombinant enzyme has been shown to hydrolyze preferentially short-chain polyphosphate. Ablation by RNAi of a small transmembrane protein of *Trypanosoma brucei* (TbPHM4) involved in the synthesis of polyphosphate alters acidocalcisome biogenesis, decreased the cells ability to respond to osmotic stress, and produced alterations compatible with an arrest of cytokinesis, followed by cell death. Taking together, these results provide support for an essential role of acidocalcisome polyphosphate in osmoregulation.

Keywords : acidocalcisome, polyphosphate, trypanosomatids