Abstract

Yeast *Saccharomyces cerevisiae* belongs to important models for alkali-metal-cation homeostasis research. As other cells, certain intracellular content of K^+ is necessary for *S. cerevisiae*, but Na^+ or other alkali metal cations (Li^+, Rb^+) are toxic for yeast cells. Uniporters Trk1 and Trk2 are responsible for K^+ accumulation, while efflux of Na^+, Li^+, Rb^+ and K^+ is ensured by Ena ATPases, $Na^+(K^+)/H^+$ antiporter Nha1 and K^+ specific channel Tok1. Several regulators of K^+ (Na^+) transporters are already known, but reciprocal regulation between transporters and overall picture of the maintenance of alkali-metal-cation homeostasis is still unclear. In this work, K^+ circulation (simultaneous uptake and export of K^+) was shown to be important in alkali-metal-cation homeostasis maintenance. K^+ circulation is maintained using reciprocal regulation and interactions between K^+ exporters and importers. Though obtained results showed that the alkali-metal-cation homeostasis and associated physiological parameters (e.g. membrane potential, cell size, salt sensitivity) are strain specific, Nha1p was verified to be important for cell survival in ever-changing natural environment. Furthermore, two novel positive regulators of Nha1p activity were found, 14-3-3 proteins and Cka1 kinase. 14-3-3 proteins interact physically with multiple parts of Nha1p. Cka1 kinase was previously known as *ENA1* expression regulator, moreover, regulation of Nha1p activity by Cka1p was observed in this work. Using knowledge and skills obtained during this work, *S. cerevisiae* strain lacking its own alkali-metal-cation exporters was used for characterization of human Nha1p homologue, Na^+/H^+ antiporter NHAoc/NHA2. Residues, whose mutation could be one of crucial points in the development of serious bone disease (osteopetrosis) in human, were identified in the NHAoc/NHA2 sequence. Altogether, results obtained in this work helped for better understanding the role of Nha1p and other transporters in maintenance of alkali-metal-cation homeostasis and its regulation, furthermore, an important progress has been made in methodology (especially in intracellular pH measurement) which will help in future studies.