Regulation of V H^+-ATPase in Yeast: a Modulation of Coupling and Conformation Instead of V_0 Dissociation?

Monteiro R. M., Freitas F.P., Ribeiro C.C., Teixeira L.R.S., Souza G.S., Lima E.P.C and L.A. Okorokov.

[1]Lab. de Fisiologia e Bioquímica de Microorganismos, CBB, Universidade Estadual do Norte Fluminense Darcy Ribeiro, Campos dos Goytacazes-RJ

V H^+-ATPase is a proton pump involved in variety of the key processes such as ion homeostasis, solute transport, protein sorting, fusion/fission of membrane vesicles, proliferation of tumor cells, cell-cell fusion, hyphal growth and virulence of *Candida albicans,* establishment of left-right asymmetry of vertebrates etc. Its ATP hydrolytic activity increases by extra cellular glucose 2-3 fold and decreases again when glucose is exhausted. Unique and widely accepted explication of the phenomenon is a physical dissociation of the catalytic complex V_1 from the H^+ channel forming complex V_o and from membrane (Kane P., 1995). We reported recently that an initial velocity of H^+ transport in yeast total membranes can be reduced 9 fold while immunoreactivity of subunits A and B decreased only by 28 and 19 % instead of 50-90% predicted from the decrease of ATP hydrolysis or H^+ transport. We supposed that down regulation of the enzyme by low glucose does not require the V_1 dissociation from V_o and membrane but makes their interaction weaker. However, ATP hydrolysis by not activated pump did not show higher sensitivity to nitrate, known chaotropic ion, even under conditions of "cold inactivation". Unexpectedly, the low nitrate concentrations (1-10mM) caused an significant uncoupling of ATP hydrolysis and H^+ transport (initial velocity). The nitrate inhibition of the initial velocity and steady state of H^+ transport mediated by not activated enzyme was higher in comparison with activated enzyme suggesting the higher coupling stability of the activated pump.

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