YEAST LACKING ER CTA4 ATPASE EXHIBIT CALCINEURIN-DEPENDENT INCREASE IN CALCIUM INFLUX AND DECREASED GLYCOGEN CONTENT

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Widely conserved regulatory mechanisms known as capacitative calcium entry (CCE) become activated specifically in response to depletion of endoplasmic reticulum (ER) Ca^{2+} pool. Depletion of Ca^{2+} in ER leads to accumulation of unfolded proteins. In yeast CCE-like mechanism requires the high and low-affinity Ca^{2+} channels. ER Cta4 ATPase is involved in Ca^{2+} homeostasis in fission yeast and we study its role in signaling. Immunoblot showed that cells lacking Cta4p exhibited higher levels of the chaperone BiP, ER stress indicator. We found that cta4 mutant exhibited higher $^{45}Ca^{2+}$ uptake comparing to wild-type cells suggesting the stimulation of Ca^{2+} influx. Calcineurin (CaN) inhibition stimulated $^{45}Ca^{2+}$ accumulation in wt and cta4 mutant cells by ~4 fold indicating that there is CaN-dependent feedback inhibition of the Ca^{2+} channel. In turn, CaN is regulated by glycogen syntase kinase-3 (GSK3) which negatively regulates glycogen syntase (GS). Glycogen measurements revealed that Cta4p loss resulted in decrease of glycogen content. We propose the elevated Ca^{2+} levels in mutant increased GSK3 activity which diminished GS function. Our data suggest that Cta4p protects cells from ER stress and takes part in signaling network involving CaN and GSK3.

Key words: yeast, calcium, calcineurin, Gsk3. Supported by CAPES, CNPq, FAPERJ.