ARE PRIONS ALWAYS DELETERIOUS TO THE HOST CELLS? STUDIES WITH THE YEAST PRION SUP35

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Prion proteins are associated with a pathologic condition, however, the wide conservation across almost all kingdoms of life, suggests that prions also encode heritable phenotypic traits. In *Saccharomyces cerevisiae*, Sup35 is translational release factor eRF3 acting on the suppression of nonsense codons. Sup35 can switch from the soluble state to a non-functional amyloid conformation denoted as [*PSI*+] that modifies cellular fitness and induces several phenotypes according to the genetic background. However, the molecular events altered by [*PSI*+] remain unknown. We observed that [*PSI*+] enhances thermo-tolerance of yeast cells after a pre-incubation at sub-lethal temperature (37 °C) when compared to normal cells [*psi*-]. In order to identify which factors are responsible for the increased thermo-tolerance of [*PSI*+] cells, we measured the accumulation of the thermo-protector disaccharide trehalose in cells submitted to 37 °C. [*PSI*+] cells accumulated more trehalose that [*psi*-] cells, a response controlled at transcriptional level as suggested by an enhancement of mRNA of *TPS1* (trehalose synthase) in [*PSI*+] cells. *TPS1* gene expression is controlled by the transcription factors Msn2 and Msn4. Our data showed that the expression of *HSP12* (controlled by Msn2/4) was increased in [*PSI*+] cells, supporting that the prion presence changes the expression and/or the activity of Msn2/4. We confirmed this result by using a *b*-gal reporter controlled by Msn2/4. Finally, we constructed two mutants lacking both *MSN2* and *MSN4* in a [*PSI*+] and [*psi*-] background and observed that the thermo-tolerance displayed by [*PSI*+] cells was lost in these mutants. These results demonstrate that the presence of prion in yeast cells is able to change their phenotype, through an improvement in the Msn2/4 dependent heat-shock response. Key words: yeast prion, heat shock, thermo-tolerance. Support: CNPq and FAPERJ.