A story about two copper proteins: Cu-sensing transcription factor, Mac1 and Cu/Zn superoxide dismutase, Sod1

Athanasia Stavropoulou[1], Maria Laskou[1], Dimitra Dialynaki[1#] and Despina Alexandraki[1,2*]

[1] University of Crete, University of Crete, Crete 70013, Greece

[2] Institute of Molecular Biology and Biotechnology, Foundation for Research and Technology, Foundation for Research and Technology-HELLAS,

Presenting author: Dimitra Dialynaki, email: d.dialinaki@gmail.com

* Corresponding author: Despina Alexandraki, email: alexandr@imbb.forth.gr

ABSTRACT

Copper is an important element for cell function, as it is cofactor of essential proteins. However, excess of copper ions leads to oxidative stress and ultimately cell damage. To avoid harmful effects due to the lack or excess accumulation of copper ions within the cell, regulatory mechanisms that ensure its homeostasis have been established.

One of the key players of copper homeostasis in *S. cerevisiae*, is the transcription factor Mac1, which is responsible for the regulated entrance of copper ions in the cell, in its deficient state, inducing the transcription of membrane copper reductase and transporter genes. Zinc and copper ions are essential for Mac1 DNA binding function, while excess of copper ions lead to its structural alteration and functional inactivation.

In contrast, the transcription factor Ace1 is activated in excess of copper ions and induces the expression of metallothioneins that contribute to copper ion chelation. At the same time, Cu/Zn superoxide dismutase Sod1 is a multipotent cytoplasmic/mitochondrial enzyme whose main known function is to detoxify the cell from superoxide ions. However, under specific oxidative stress conditions, Sod1 has been shown to enter the nucleus and affect the transcription of a number of genes, some of which are involved in copper homeostasis. Ccs1 chaperon is responsible for the transport of copper ions to Sod1, essential for its function.

The present work focuses on the study of the relationship between Mac1 and Sod1 proteins, as it has been observed that deletion of the *SOD1* gene results in reduced transcriptional activation of Mac1 transcription factor target genes. This observation led us to a series of experiments, aimed to examine the association and possible direct interaction of these two proteins in *S. cerevisiae.*