The Role of Glucose Restriction on Amino Acid Metabolism and Lifespan in Yeast

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Calorie restriction (CR) is a dietary intervention capable of extending life span in a wide range of organisms. A yeast model of CR has been developed in which limiting the concentration of glucose in growth media of *Saccharomyces cerevisiae* leads to enhanced replicative and chronological longevity[1]. We have previously reported that life span extension promoted by CR is due to mitigation of glucose repression pathway[2]. We now study the relationship between CR and amino acid metabolism. We measured the activity of enzymes related to amino acid metabolism and chronological life span of the BY4741 yeast strain and its null mutants *bat1?*, *gdh1?*, *gdh2?* and *gdh3?*, which encode cytosolic branched-chain amino acid aminotransferase, cytosolic NADP glutamate dehydrogenase, mitochondrial NAD^+ glutamate dehydrogenase and mitochondrial NADP glutamate dehydrogenase, respectively. We found that the activity of NAD^+ glutamate dehydrogenase is enhanced in cells grown under CR, but the activity of $NADP^+$ glutamate dehydrogenase is not. Increases in chronological life span were observed in *bat1?* and *gdh1?* mutants due to CR, but no significant difference was observed in null mutants for gdh2p and gdh3p, indicating these proteins are essential for the beneficial effects of CR. In these cells WT and null mutants grown under control conditions presented equal life spans. Altogether, our results indicate that *S. cerevisiae* life span extension promoted by CR depends on the interaction between glucose signaling and mitochondrial amino acid metabolism.

Supported by FAPESP, CNPq, *Instituto do Milênio Redoxoma* and The John Simon Guggenheim Foundation.

Keywords: Caloric restriction, amino acid metabolism, *S. cerevisiae*

1. Lin SJ, Kaeberlein M, Andalis AA, Sturtz LA, Defossez PA, Culotta VC, Fink GR, Guarente L (2002) *Nature* 418:344-8.
2. Oliveira GA, Tahara EB, Gombert AK, Barros MH, Kowaltowski AJ (2008) *J Bioenerg Biomembr*. [Epub ahead of print]