

## THE ROLE OF GLUCOSE REPRESSION IN YEAST LIFE SPAN

Graciele A. Oliveira<sup>1</sup>, Erich B. Tahara<sup>1</sup>, Mario H. Barros<sup>2</sup>, Andreas K. Gombert<sup>3</sup>,  
Alicia J. Kowaltowski<sup>1</sup>

<sup>1</sup>Departamento de Bioquímica, Instituto de Química, Universidade de São Paulo, São Paulo, SP, Brazil; <sup>2</sup>Departamento de Microbiologia, Instituto de Ciências Biomédicas, Universidade de São Paulo, São Paulo, SP, Brazil; <sup>3</sup>Departamento de Engenharia Química, Universidade de São Paulo, São Paulo, Brazil

*Saccharomyces cerevisiae* is used as a model to study the life span-enhancing effects of caloric restriction (CR), with the advantage of exhibiting short life spans and allowing simplified metabolic and genetic manipulation. A reduction from 2.0% to 0.5% glucose in the growth media leads to increases in oxygen consumption, decreased electron leakage and prolonged replicative and chronological life span in this organism. We studied CR effects in *Kluyveromyces lactis*, a Crabtree-negative yeast, with preferential respiratory energy metabolism. Interestingly, we observed that calorie-restricted *K. lactis* neither exhibited an increase in respiration nor a decrease in reactive oxygen species release when incubated under CR conditions. In addition, *K. lactis* chronological life span was shorter under CR conditions. We then investigated chronological life spans of *S. cerevisiae* growing with different carbon sources, including galactose, raffinose and glycerol. We found that carbon sources that do not lead to respiratory repression (glycerol and raffinose) do not lead to increments in life span when restricted. On the other hand, high levels of glucose and galactose promote shorter chronological life spans than lower levels, as is characteristic of CR. Altogether, these results suggest a strict dependence between the occurrence of the beneficial effects of CR and the attenuation of glucose repression in *S. cerevisiae*. Supported by FAPESP, CNPq, Instituto do Milênio Redoxoma and the Guggenheim Foundation.