

Low productivity of ribonucleotide reductase in *Saccharomyces cerevisiae* increases sensitivity to stannous chloride

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Genet. Mol. Res. 7 (1): 1-6 (2008)
Received October 25, 2007
Accepted December 11, 2007
Published January 8, 2008

ABSTRACT. Ribonucleotide reductase (RNR) of the yeast *Saccharomyces cerevisiae* is a tetrameric protein complex, consisting of two large and two small subunits. The small subunits Y2 and Y4 form a heterodimer and are encoded by yeast genes *RNR2* and *RNR4*, respectively. Loss of Y4 in yeast mutant *rnr4Δ* can be compensated for by up-regulated expression of Y2, and the formation of a small subunit Y2Y2 homodimer that allows for a partially functional RNR. However, *rnr4Δ* mutants exhibit slower growth than wild-type (WT) cells and are sensitive to many mutagens, amongst them UVC and photo-activated mono- and bi-functional psoralens. Cells of the haploid *rnr4Δ* mutant also show a 3- to 4-fold higher sensitivity to the oxidative stress-inducing chemical stannous chloride than those of the isogenic WT. Both strains acquired increased resistance to SnCl₂ with age of culture, i.e., 24-h cultures were more sensitive than cells grown for 2, 3, 4, and 5 days in liquid culture. However, the sensitivity factor of three to four (WT/mutant) did not change significantly. Cultures of the *rnr4Δ* mutant in stationary phase of growth always showed higher frequency of budding cells (budding index around 0.5) than those of the corresponding WT (budding index <0.1), pointing to a delay of mitosis/cytokinesis.

Key words: Ribonucleotide reductase; *Saccharomyces cerevisiae*; Mutagen sensitivity; Stannous chloride; Budding index