TOR1 and TEL1 Contribute to mtDNA Stability in *Saccharomyces cerevisiae*

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The mitochondrial DNA (mtDNA) encodes for only a few proteins, all essential for oxidative phosphorylation. As it localizes near the electron transport chain, a major site for reactive oxygen species generation, it is an important target for these species, and accumulates oxidized modifications in physiological and pathological conditions. These modifications are repaired by the base excision repair pathway. We and others characterized the core enzymes of this pathway, but its regulation in response to stress is still unclear. In this study, we investigated the roles of the Tor1p and Tel1p proteins from *Saccharomyces cerevisiae* in the cellular response to oxidative stress. These proteins are functional homologues of the mammalian proteins mTOR and ATM, respectively, whose roles include the control of energy metabolism, cell cycle, response to double strand breaks in nuclear DNA and oxidative stress. For that, we used wild type and mutant strains of *S. cerevisiae* lacking Tel1p and Tor1p. Both mutant strains accumulated significantly more *petits* colonies (lacking mtDNA) than the wild type strain $[8,446 \pm 1,463 \text{ (tor1)} \Delta \text{ vs. } 2,098 \pm 0,501 \text{ (WT), increase of } 4,025 \pm 1,658 \text{ times}; 7,040 \pm 1,148 \text{ (tel1)} \Delta \text{ vs. } 2,098 \pm 0,501 \text{ (WT), increase of } 3,355 \pm 1,348 \text{ times}], indicating that these proteins are involved in mtDNA maintenance. Moreover, *petits* accumulation after treatment with oxidants was altered in the mutant strains. The results suggest a direct role for these two proteins in mtDNA maintenance after oxidative stress, likely through a functional interaction with mitochondrial DNA repair pathways.

Keywords: TOR1, TEL1, *Saccharomyces cerevisiae*, mitochondrial DNA

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