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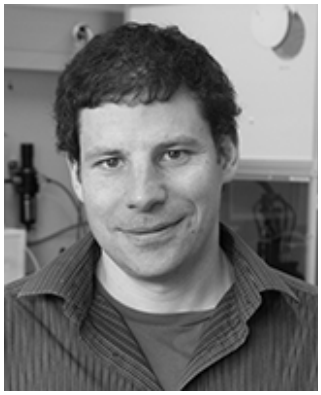
Regulation of Rps6 Phosphorylation by TOR Complexes in Saccharomyces cerevisiae.



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Nutrient-sensitive phosphorylation of the S6 protein of the 40S subunit of the eukaryote ribosome is conserved from yeast to man. However, despite four decades of research, the functional consequences of this modification remain unknown. We have revisited this enigma in *Saccharomyces cerevisiae.* We found that the regulation of Rps6 phosphorylation on Ser232 and Ser233 in yeast is surprisingly complex being mediated by both TOR Complex 1 and TOR Complex 2. TORC1 regulates phosphorylation of both sites directly via the poorly characterized AGC-family kinase Ypk3, and the PP1 phosphatase Glc7, whereas TORC2 regulates phosphorylation of only the N-terminal phosphosite via Ypk1 and Ypk2. Cells expressing a non-phosphorylatable variant of Rps6, Rps6^{AA}, have scorable phenotypes such as a significantly reduced growth rate and a 40S biogenesis defect. To characterize the effect of these variants on global translation we used ribosome profiling, however failed to detect any significant alterations. Curiously, Rps6 hyperphosphorylation appears to be toxic. Together, these observations depict the signaling cascades orchestrating Rps6 phosphorylation in budding yeast while challenging the role for Rps6 phosphorylation in translation.

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