ABSTRACT

Title: Leveraging the yeast genome to dissect conserved pathways in aging and disease

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Abstract content:
The complete sequencing and annotation of the *Saccharomyces cerevisiae* genome had a transformative impact on the yeast research community. It enabled the systematic use of reverse genetics alongside genome-wide resources such as the deletion collection, tagged-ORF libraries, epistasis mapping strategies, and transcriptomic and proteomic profiling approaches. This powerful experimental framework enabled us to dissect molecular mechanisms underlying fundamental cellular homeostasis, particularly on lipid metabolism, redox homeostasis, organelle dynamics, autophagy, ion homeostasis, stress responses and regulated cell death. In parallel, we explored the intricate signalling networks orchestrating these processes, predominantly on pathways governed by protein kinases, phosphatases and transcriptional regulators that coordinate cellular adaptation and stress-responsive gene expression. Our work has advanced the understanding of how cells integrate environmental and metabolic cues to regulate survival, and how disruption of these processes contributes to aging and disease. Importantly, the use of genome-wide methodologies and the integration of multi-omics data with functional genetics enable a shift toward systems-level analysis, allowing the identification of key regulatory networks and cellular functions that coordinate metabolism, stress responses, and survival, including during chronological aging. Moreover, the high degree of evolutionary conservation between yeast and human genes enabled us to develop and characterize yeast models for human diseases, such as Niemann-Pick type C and seipinopathies. These models facilitated the identification of genetic modifiers and potential therapeutical targets, highlighting the translational relevance of yeast research.
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