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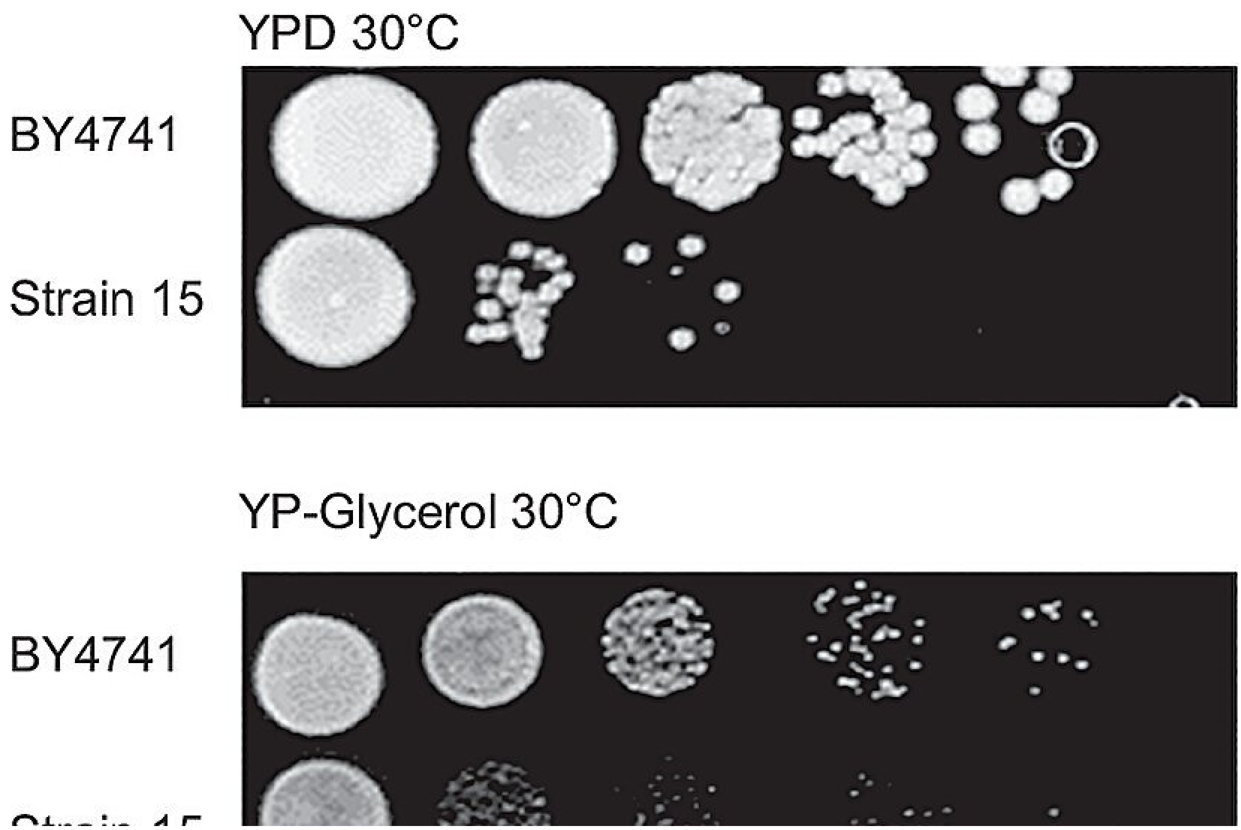
Final synthetic yeast chromosome completed, paving way for biotech advances

January 22 2025



Strain harboring synthetic megachunk exhibits reduced growth. Credit: *Nature Communications* (2025). DOI: 10.1038/s41467-024-55318-3

Macquarie University researchers have worked with an international team of scientists to achieve a major milestone in synthetic biology by completing the creation of the final chromosome in the world's first synthetic yeast genome.

This achievement represents the completion of the global Sc2.0 project to create the world's first synthetic eukaryotic genome from Saccharomyces cerevisiae (baker's yeast) and a new-to-nature tRNA neochromosome.

Using cutting-edge genome-editing techniques, including the CRISPR D-BUGS protocol, the team identified and corrected genetic errors that impacted yeast growth. These changes restored the strain's ability to grow on glycerol, a key carbon source, under elevated temperatures.

The breakthrough, published this week in *Nature Communications*, demonstrates how engineered chromosomes can be designed, built and debugged to create more resilient organisms that could help secure supply chains for food and medicine production in the face of climate change and future pandemics.

"This is a landmark moment in synthetic biology," says Professor Sakkie Pretorius, Co-Chief Investigator and Deputy Vice Chancellor (Research) of Macquarie University.

"It is the final piece of a puzzle that has occupied synthetic biology researchers for many years now."

Distinguished Professor Ian Paulsen, Director of the ARC Centre of Excellence in Synthetic Biology, who co-led the project, says, "By successfully constructing and debugging the final synthetic chromosome, we've helped complete a powerful platform for engineering biology that could revolutionize how we produce medicines, sustainable materials and other vital resources."

The research team used specialized gene editing tools to identify and fix problems in the synthetic chromosome affecting how well the yeast could reproduce and grow under challenging conditions.

They discovered that the placement of genetic markers near uncertain gene regions accidentally interfered with how essential genes were turned on and off, particularly affecting crucial processes like copper metabolism and how cells divide their genetic material.

"One of our key findings was how the positioning of genetic markers could disrupt the expression of essential genes," says co-lead author Dr. Hugh Goold, research scientist at The NSW Department of Primary Industries and Honorary Postdoctoral Research Fellow from Macquarie University's School of Natural Sciences.

"This discovery has important implications for future genome engineering projects, helping establish design principles that can be applied to other organisms."

The completion of the chromosome known as synXVI allows scientists to explore new possibilities in metabolic engineering and strain optimization. The synthetic chromosome includes features that enable researchers to generate genetic diversity on demand, accelerating the development of yeasts with enhanced capabilities for biotechnology applications.

"The synthetic yeast genome represents a quantum leap in our ability to engineer biology," says Dr. Briardo Llorente, Chief Scientific Officer at the Australian Genome Foundry.

The construction of such a large synthetic chromosome was only possible using the robotic instrumentation in the Australian Genome Foundry.

"This achievement opens up exciting possibilities for developing more efficient and sustainable biomanufacturing processes, from producing pharmaceuticals to creating new materials," says Dr. Llorente.

The research provides valuable insights for future synthetic biology projects, including potential applications in engineering plant and mammalian genomes. The team's new design principles for synthetic chromosomes to avoid placing potentially disruptive genetic elements near important genes will help other researchers working on synthetic chromosomes.

More information: Hugh D. Goold et al, Construction and iterative redesign of synXVI a 903 kb synthetic Saccharomyces cerevisiae chromosome, *Nature Communications* (2025). DOI: 10.1038/s41467-024-55318-3

Provided by Macquarie University

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