

A bioprint visualization of the 16 yeast chromosomes. Yeast incorporating specific pigment genes is printed onto an agar plate so that it grows to give the desired image. The image grown here highlights the generation of synthetic (yellow) versus wild-type (blue) yeast chromosomes.



BUILDING ON NATURE'S DESIGN

By Laura M. Zahn and Guy Riddihough*

In 1996, a breakthrough was achieved when the sequence of ~12 million base pairs, divided among 16 chromosomes, was reported for baker's yeast (*Saccharomyces cerevisiae*). Now, some 20 years later, the Synthetic Yeast Genome Project (Sc2.0) reports on five newly constructed synthetic yeast chromosomes, advancing efforts to substantially reengineer all 16 yeast chromosomes with the goal of creating a fully synthetic eukaryotic genome.

Genomes are in constant flux: They are prone to deletions, duplications, and insertions; recombination and rearrangement; and invasion and disruption by selfish genetic elements such as transposable elements. These many changes are subject to the vagaries of natural selection, resulting in a genome organization not based on principles of efficiency or economy of space, but instead contingent on the evolutionary history of the organism.

Sc2.0 has set out to untangle, streamline, and reorganize the genetic blueprint of one of the most studied of all eukaryotic genomes. Here they report on their development, design, construction, testing, and curation principles, which may be scalable to other, larger genomes. Ultimately, researchers aspire to remove all transposons and repetitive elements, recode UAG stop codons, and move transfer RNA genes to a novel neochromosome without causing fitness defects, while simultaneously adding features to facilitate chromosome construction and manipulation. When complete, the final synthetic yeast strain will be another milestone in our ability to work with and understand the eukaryotic genome.

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