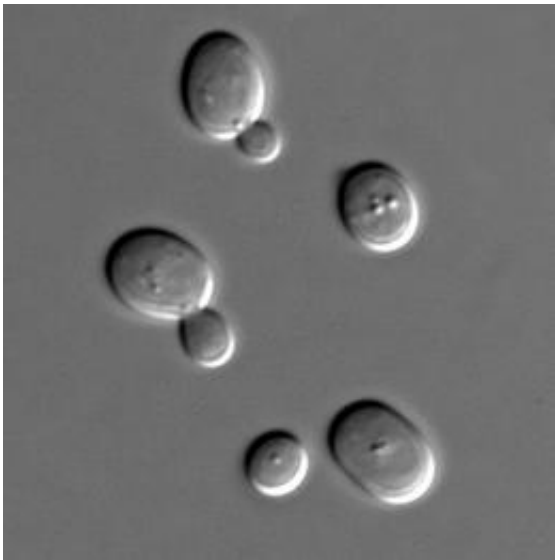


Biology team makes breakthrough in synthetic yeast project

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Sacharomyces cerevisiae cells in DIC microscopy. Credit: Wikipedia.

Led by Tianjin University Professor Ying-Jin Yuan, TJU's synthetic biology team has completed the synthesis of redesigned yeast chromosomes synV and synX with the two studies published in *Science* on March 10, 2017.

The publications are part of the effort to chemically synthesize the designer yeast genome (Sc 2.0), in collaboration with NYU and John Hopkins in the US, Tsinghua University, BGI-Shenzhen in China, the University of Edinburgh in the UK, and the Institut Pasteur and

Sorbonne Universités in France, as well as industry partners.

TJU is keen to integrate frontier science into student training. During the synthesis of the designer chromosome SynV, the "Build-A-Genome (BAG) China" course played a crucial role. In this innovative educational course, sixty-one students participated in the construction of building blocks and minichunks for synthetic chromosome V, although the majority of the students had little or no experience in DNA synthesis before. Through the BAG training, they advanced experimental skills, and obtained first-hand experiences essential to promote their troubleshooting ability. Several students became specialists in DNA synthesis and constructed DNA segments with significant complicated sequences. A selection of them went on to continue their education in the [synthetic biology](#) field by undertaking Ph.D programs in China, the US, Europe and other countries.

"The goal of the BAG course at TJU is to train the next generation of synthetic biologists with a global perspective, innovative spirit, and practical abilities", said Professor Yuan. This goal was reached during the process of the Sc2.0 project, linking the course to practical scientific work. The first authors of the synV and synX articles, Ph.D candidates from Yuan's team, Zexiong Xie and Yi Wu, were participants of the BAG course. As a combination of the international science community and the educational system, BAG provided an elegant model to inspire the next generation scientists towards future research on synthetic biology.

Pursuing construction of the synthetic eukaryotic chromosome perfectly matching the designer sequence, the research team overcame significant obstacles. With all the 3331 bp randomly distributed mutations and other unpredictable events corrected in the designed sequence and performing with a similar fitness compared with native strains, the completed synV chromosome supported the underlying design principles of Sc2.0. After

the paper was originally submitted, the team continued their corrections, leading to the title of the synV article being changed from "approaching a variant-free designer chromosome" to "'perfect' designer chromosome V". "Together with my colleagues, I spent almost 18 months mapping the bugs and correcting errors that led to the yeast being non-viable or having growth defects," says Xie, described the study of yeast chromosome synV.

Aiming to provide a model with which to study human ring chromosome disorders, the linear synV was converted to a ring synthetic chromosome, and it can extend genome design principles, as well as providing an insight into genomic rearrangement and ring chromosome evolution.

Certain genetic alternations in the chromosome would affect cell fitness and cause "bugs"; debugging is therefore imperative for successfully building a synthetic genome. The malfunction of synthetic genomes remains one of the most common obstacles, as it is difficult to uncover the underlying reasons. In a bid to tackle this problem, TJU developed a highly efficient debugging method called pooled PCRTag mapping (PoPM) by using a pooling strategy and the Sc2.0 PCRTag system, which is generalized to watermarked synthetic [chromosomes](#). PoPM is a powerful tool for synthetic yeast genome debugging which accelerated the progress of the whole Sc2.0 project. "During synX assembly, the PoPM method was applied to identify and eliminate genetic alternations that affect cell fitness, sequences we refer to as "bugs", and several details of yeast biology were uncovered by debugging. PoPM represents an efficient strategy for phenotype-genotype mapping which will be applicable for expanding understanding of yeast genomic and cellular functions" according to Wu.

More information: "Bug mapping and fitness testing of chemically synthesized chromosome X," *Science* (2017). [DOI: 10.1126/science.aaf4706](https://doi.org/10.1126/science.aaf4706)

"'Perfect' designer chromosome V and behavior of a ring derivative,"
Science (2017). [DOI: 10.1126/science.aaf4704](https://doi.org/10.1126/science.aaf4704)

Provided by Tianjin University

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