Breakthrough biology: First synthetic chromosome for yeast created, capping month of biotech innovations

Imagine that a new drug to treat cancer is highly effective, but one of the compounds needed to create it is expensive and time-consuming to produce in the lab. No problem: yeast to the rescue. All scientists making the drug would need to do is go to their computer and boot up some genome-customizing software for yeast, pick their desired traits, and ask the software to gin up an artificial yeast genome for a strain of yeast that will mass-produce this compound as a part of their normal metabolism. From there it's a simple matter of manufacturing the genome in the lab and putting it into a waiting yeast cell; once the yeast takes up is its new instructions we'll have little living factories churning out whatever we need.

This is the fungal microbe used in break and beer-making the world over, now fully customized, ready to be kitted out with different versions of its genome for any number of roles.

Futuristic? Very. But not as much as it was last week. A team at the NYU Langone Medical Center's Institute for Systems Genetics has announced in *Science* the creation a fully functional synthetic chromosome for baker's yeast, *Saccharomyces cerevisiae*. This achievement is the latest milestone in a month filled with biotechnology firsts, including bionic plants and "living materials" and puts scientists in a position to push the boundaries of what yeast and synthetic biology are capable of doing for humanity.

Creating the First Synthetic Eukaryote Chromosome

Yeast is a eukaryote like humans, plants and animals — it has larger cells governed by a central nucleus, and its genome is accordingly larger and more complex than the viral and bacterial genomes that were used in previous synthetic genome efforts. *Nature* news's Ewen Callaway notes that it took 15 years and $40 million for geneticist Craig Venter to synthesize the genome of a bacterial parasite in 2010.

Though a notable achievement in its own right, the synthetic chromosome only represents about 2.5% of the entire yeast chromosome, according to Callaway. Already the NYU Langone team, led by synthetic biologist Jef Boeke, has formed an international effort to finish what they started and have a full synthetic genome of 16 chromosomes for *S. cerevisiae* within 5 years.

A completely synthetic genome isn't necessary for this research to have major practical benefits. Baker's yeast (also known as brewer's yeast) is one is already one of the best-known organisms in biology, and it may only take a few bits of "designer DNA" to unlock entirely new abilities in this multi-talented microbe.

The process of "biopharming" in yeast, bacteria, and even some plants and animals has not required the major syntheses of novel genetic material from scratch to make progress. Yeast has already been engineered, without synthetic genes, to produce artemisinin, an ingredient for an anti-malarial drug. But the demonstrated ability to create a significant portion of modified genetic material from scratch and insert it into living yeast heralds even greater possibilities. In genetic engineering today, we're largely limited by the fact that we're essentially borrowing traits from around the genetic world of nature and moving them around; synthetic biology at the genetic level as demonstrated by Boeke and his team promise to transcend these limitations.

These full possibilities of a synthetic genome are still a ways off, however. The cost of synthesizing genomes is still prohibitively high, Boeke told LiveScience. It took 7 years to create this synthetic chromosome, and the plan was originally to use commercial DNA-synthesis companies to build chunks of the genome. “But the first order,” writes Callaway, “cost roughly US$50,000 and took a year to arrive.”

So Boeke enlisted the aid of undergraduates at Johns Hopkins University via a “build-a-genome” class. Through Boeke’s course, Callaway writes:

> Each student makes their own stretch of the yeast genome, which involves stitching together very short lengths of DNA created by a DNA-synthesis machine into ever-larger chunks. These chunks are then incorporated into the yeast chromosome, a few at a time… Eventually, this results in an entirely synthetic chromosome.

The classes started in 2007 and many of the students are now co-authors on Boeke’s *Science* paper. Boeke is carrying forward this crowd-sourced structure into his five-year plan to create a full synthetic genome for *S. cerevisiae*.

A Month of Blurred Lines

This is the latest in a string of interesting developments in biotechnology over the last few weeks, all of which are blurring the lines between what we consider organic and artificial.

In a March 16 *Nature* Materials paper, an MIT team pioneered a field they’ve called “plant nanobionics” which infuses plant tissues with nanomaterials. For example, they infused plant leaves with carbon nanotubes, which embedded in the plant cells’ chloroplasts and acted as tiny antennas to pick up additional electromagnetic radiation (read: light) and enhanced the plants’ ability to photosynthesize.

On March 26, a different team at MIT announced the birth of “living materials” created through a mix of genetic engineering and nanotechnology. They modified E. coli bacteria so that they would take up nanoparticles of the researcher’s choosing — say, microscopic particles of gold. They were then able to control the growth of the bacteria and create a thin, living film of E. coli shot through with bacteria-assembled gold nanowires, creating a useful conductive surface.

In both of these previous experiments, and especially in the creation of a fully synthetic yeast chromosome, we’re witnessing the basic principle of biotechnology brought — literally — to life.

For biotechnology to work, biology and technology need to be compatible. We tend to sort “biology” and “technology” into two very discrete categories in our minds. One word conjures images of lush green leaves, the other of gunmetal gray wires. Indeed, the dissonance between these two ideas echoes the knock-down, drag-out global fight over how to handle genetically modified crops. Are nature and technology in opposition or can they work together?

But what these breakthroughs demonstrate, if one looks carefully enough, is that biology and technology are two sides of the same coin. Engineering metaphors are common in evolutionary science, implication of “design” notwithstanding. Likewise we get some of our best ideas from nature.

The further down in size scale you go—past tissues, past cells and the organelles in them, past gold nanowires—the clearer it becomes that the stuff of life and non-life is fundamentally the same. A chemist will tell you biology is just the chemistry of things we happen to call alive, and a physicist will tell you that chemists are just narrow-minded physicists.

This may seem trite. Most of us were taught about atoms. You may have developed hazy futuristic ideas about how, sure, if we know enough about the chemistry and physics underpinning biology we can probably bridge the gap between natural and artificial, open up a new world of possibilities.

I don’t know about you, but for me the exciting developments of the past month have brought those ideas out of the hazy future and into vividly photosynthesizing, biofilm-forming and fermenting life.

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Sources:

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- “First synthetic yeast chromosome revealed,” Ewen Callaway | Nature News
- “In a first, scientists create artificial chromosome,” Tanya Lewis | LiveScience