Yeast genetic blueprint publicly unveiled

The entire genetic blueprint of *Saccharomyces cerevisiae*, a yeast commonly used by bakers and brewers, was made public at press conferences in the United States and Belgium last week. The unveiling marks the first time scientists have sequenced all the genes of an organism with cells similar to humans cells.

Investigators expect the achievement to provide significant insight into how human cells operate and why they go awry in some diseases. "When we understand how [yeast] works, it's remarkable how often that explains how we work," says Ronald W. Davis of Stanford University School of Medicine.

"All of yeast biology will be effectively divided between the pregenome era and the postgenome era, and today we cross that threshold," remarked Francis S. Collins, head of the National Center for Human Genome Research in Bethesda, Md., at the U.S. press conference announcing the achievement.

Investigators say the experience gained in sequencing yeast's DNA will facilitate the sequencing of the much larger human genome, a task they predict will be finished in 7 to 9 years.

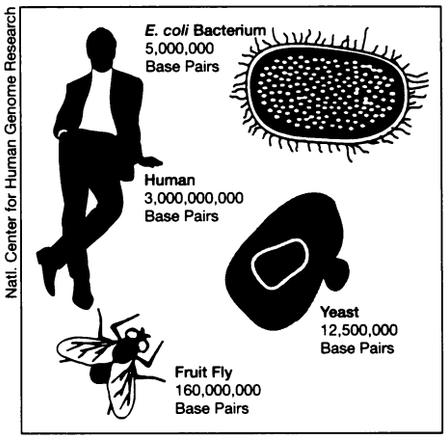
To emphasize the relevance of yeast biology, Collins compares the human body to a skyscraper such as the World Trade Center. Someone with no experience in construction and without access to the blueprint could not hope to grasp how so complicated a structure was built, he says.

If that person first learned how to build a one-bedroom house, many principles behind the World Trade Center's construction would be clearer, notes Collins. "Yeast is our one-bedroom house."

The yeast sequencing effort began in 1989 as a loose collaboration among a few dozen European laboratories. The European-led project quickly expanded to include nearly 100 research groups worldwide, among them DNA sequencing centers at Stanford and at Washington University in St. Louis. This division of labor enabled investigators to finish the sequencing years ahead of schedule.

Researchers found that the yeast genome contains more than 12 million nucleotide base pairs, the chemical subunits of DNA. Parceled into 16 chromosomes containing some 6,000 genes, these bases encode the information that yeast cells use to create the myriad proteins they need.

Before the yeast triumph, only the much smaller genomes of viruses and bacteria had been completely sequenced. The yeast genome is nearly seven times the size of the genome of *Haemophilus influenzae*, the first bacterium to be sequenced (SN: 6/10/95, p. 367), and more than double that of *Escherichia coli*, the popular laboratory bacterium whose sequence is nearing completion.



Sizes of various genomes.

Unlike bacteria, however, yeast cells possess many of the features of human cells. Both yeast and human cells store their genetic material in an internal envelope called a nucleus. Furthermore, yeast genes required for cell division and sexual reproduction resemble those active in comparable human cellular processes. Yeast "is much more similar to humans than bacteria [are]. That's what gets us so excited," says Davis.

The completed yeast sequence is likely to help identify the roles of newly discovered human genes. Testing this idea, investigators recently searched a partial yeast genome database for DNA sequences similar to 52 human disease genes. One in four of the human genes matched a yeast gene, says Philip Hieter of the Johns Hopkins University School of Medicine in Baltimore.

The disease neurofibromatosis offers an example of how yeast genetics has helped explain a human disease. In 1990, investigators pinpointed the human gene at fault in this nerve cell cancer. The gene resembles two yeast genes whose proteins inhibit the activity of ras, a molecule known to regulate cell division. The match immediately suggested that ras is overactive in neurofibromatosis patients, leading to uncontrolled cell division.

Without this match to the yeast genes, "we'd still be pretty much in the dark about how the disease comes about," Collins notes. Physicians, he says, can now consider treating neurofibromatosis patients with ras inhibitors already developed for other cancers.

Completion of the yeast sequence does not signal an end to ambitious yeast projects. Researchers already plan to determine the interactions among all the proteins encoded by the thousands of yeast genes. — *J. Travis*

Early life: In the soup or on the rocks?

In most scenarios of the origin of life, precursors of biological molecules formed in a rich brew of amino acids. Then, on the beaches of primitive Earth, these raw materials of life somehow linked into longer, self-replicating molecules. Reproducing these events in the laboratory has proved challenging, however.

In experiments designed to mimic primordial chemistry, scientists have demonstrated that biological precursors form when simple organic compounds are blended and cooked. Yet these prebiotic molecules rarely combine into chains of more than 10 to 20 links. To replicate, researchers believe, molecules must contain close to 60 molecular segments—the minimum necessary to sustain a primitive genetic code.

Now, James P. Ferris, a chemist at Rensselaer Polytechnic Institute in Troy, N.Y., and his colleagues have shown that long, chainlike molecules called oligomers can assemble themselves on mineral surfaces. Describing the chemical feat in the May 2 NATURE, the researchers contend that "the minerals on the primitive Earth would have provided a 'library' of surfaces for the exploration of molecular evolution."

Ferris' group mimicked conditions in which a warm broth of prebiotic molecules repeatedly splashed up on rocks and dried in the sun. The researchers poured solutions of amino acids and nucleotides over each of three materials: a clay called montmorillonite and two porous, bonelike minerals known as illite and hydroxylapatite. Many cycles of incubation, evaporation, and replenishment yielded oligomers up to 55 units long.

From those molecules, the scenario continues, others would have emerged—still larger molecules capable of carrying enough information to replicate. Eventually, these prebiotic molecules could have mutated into more advanced forms, including, ultimately, the nucleic acids and proteins that make life possible.

Ferris' results represent "quite an achievement," says Andrew D. Ellington, a chemist at Indiana University in Bloomington. "In terms of the chemistry, it's a significant step ahead of what's been achieved before."

If organic molecules solidified on warm stone, says chemist Günter von Kiedrowski of the University of Ruhr in Germany, "the polymers of life were more likely to have been baked like prebiotic crepes than cooked in a prebiotic soup."

"The message," he adds in a commentary accompanying the report in NATURE, "is that the earliest forms of life may have proliferated by spreading on surfaces." — *R. Lipkin*