Human Artificial Chromosome Created

For chefs, developing a new dish isn't an exact science. Guided by intuition and experience, they play with combinations of foods, herbs, and spices, hoping to come up with a culinary masterpiece.

Following a similarly adventuresome strategy, geneticists have now thrown several forms of DNA into human cells and created a long-desired prize: the first human artificial chromosome. "We put in three types of DNA and [the chromosome] self-assembled," says Huntington F. Willard of Case Western Reserve University School of Medicine in Cleveland.

The human artificial chromosome survived for as long as 6 months in cells, retaining its integrity while replicating during many cell divisions, Willard and his team report in the April NATURE GENETICS.

Examining such synthetic chromosomes may provide scientists with a more accurate recipe for the elements of a natural human chromosome. That knowledge may then elucidate how, during cell division, a chromosome replicates and the resulting pair segregates to different cells.

Moreover, by placing genes onto artificial chromosomes and then inserting them into cells, investigators hope to study how a gene's chromosomal surroundings regulate its activity.

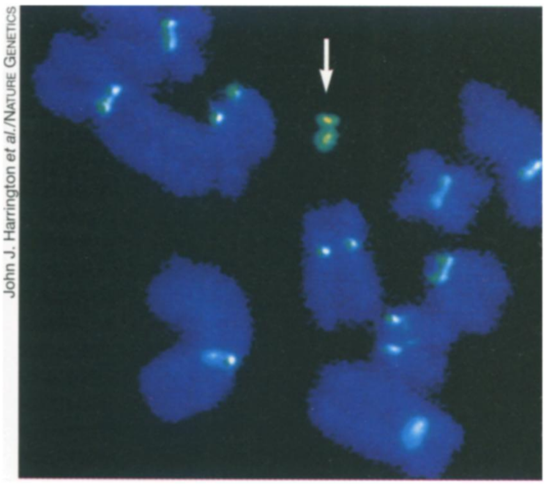
Gene therapy may also benefit from artificial chromosomes. Some researchers envision a day when they can slip into a person's cells synthetic chromosomes containing genes that correct a disease.

Although investigators have made yeast artificial chromosomes for more than a decade (SN: 6/5/93, p. 360), they struggled for years to synthesize the more complex human chromosomes.

Both yeast and human chromosomes appear to contain three main components. Capping the ends of chromosomes are telomeres, brief sequences of DNA repeated over and over (SN: 6/10/95, p. 360). Then there are the so-called origins of replication, DNA sequences that initiate the replication of a chromosome during cell division.

At the center of each chromosome is the mysterious centromere, which plays a vital role in the chromosome's segregation in a dividing cell. Ignorance of the structure, and even the size, of human centromeres has been the fundamental reason that scientists hadn't been able to create human artificial chromosomes.

In what Willard calls a "leap of faith," his team simply introduced into cells telomeric DNA, normal gene-containing human DNA, and alpha-satellite DNA, highly repetitive genetic sequences considered key to centromere function.



John J. Harrington et al./NATURE GENETICS

This artificial chromosome (arrow) replicates and functions like its much larger natural counterparts (dark blue).

In most cases, the added DNA interacted with the natural chromosomes in each cell, fragmenting them or appropriating pieces of existing chromosomal DNA to create small new chromosomes. In at least one case, however, a chromosome with a functional centromere seemed to form solely from the added DNA.

As they strive to improve the efficiency of the chromosome-building strategy, Willard and his coworkers are trying to answer questions about the nature of the artificial chromosome, such as whether its centromere is pure alpha-satellite DNA.

Artificial chromosomes tantalize gene therapists, who face serious problems using viruses and other means to add genes to cells. Some viruses integrate genes into preexisting chromosomes, which may cause mutations or affect the activity of the added gene. Other viruses shuttle genes into cells without integrating them, but the genes eventually disappear as the cells divide.

"In theory, an artificial chromosome would be a great advance because it wouldn't integrate but it would replicate and segregate," says Melissa A. Rosenfeld of the National Human Genome Research Institute in Bethesda, Md.

Artificial chromosomes could also deliver much larger genes than do the viruses now used in gene therapy. Yet Rosenfeld and Willard warn that gene therapists may not have this new tool quickly, if ever. One major hurdle that must be cleared is finding an efficient way to sneak the artificial chromosomes into cells. *— J. Travis*

NSF funds new computing partnerships

For more than a decade, university researchers could turn to one of the four supercomputer centers funded by the National Science Foundation for access to the fastest computers available. In recent years, however, the tremendous growth of computer networking and the increasing power of microprocessors have reduced the need for such centers.

In response to these changes, the agency has decided to restructure its original supercomputer centers program and introduce a new initiative focused on taking advantage of emerging computer technology and on broadening participation in computational science and engineering (SN: 12/23&30/95, p. 422).

Last week, NSF officials announced the two winners in its new Partnerships for Advanced Computational Infrastructure program. One group is led by the University of Illinois at Urbana-Champaign, the other by the University of California, San Diego.

In effect, the decision cuts from four to two the number of supercomputer centers supported by NSF. Funding for the facilities at the University of Pittsburgh and Cornell University will be phased out over the next 2 years.

At Illinois, the National Center for Supercomputing Applications becomes part of an alliance of diverse institutions, people, and companies in an ambitious venture to build a prototype of a "national technology grid." One of the alliance's main goals is to integrate computation, communication, visualization, and information storage, enabling researchers anywhere in the country to do sophisticated modeling and massive data crunching.

At San Diego, in addition to providing the resources needed for the highest possible level of scientific computation, the partnership plans to focus on the development of digital libraries and tools for manipulating huge data sets.

"This new program will enable the United States to stay at the leading edge of computational science," says Paul Young, adviser to NSF's computer and information science directorate. Both efforts include an educational component for students and teachers from kindergarten to graduate school. ***— I. Peterson***