Biology

Brewing up a double genome

Beer lovers owe a debt of gratitude to *Saccharomyces cerevisiae*, the yeast commonly used to generate the alcohol in beer. Now, a new genetic analysis suggests that the organism's alcohol-making ability developed as a result of an accidental duplication of the entire yeast genome millions of years ago.

In the June 12 NATURE, Kenneth H. Wolfe and Denis C. Shields of Trinity College in Dublin contend that two yeast cells once merged to create a cell that had four sets of chromosomes. This ancestor of S. *cerevisiae* quickly eliminated most, though not all, of the extra genes and settled back to two sets of chromosomes. "What we see now is the remains of an event that happened a long time ago," says Wolfe.

The researchers base their conclusion on finding more than 370 instances in which S. *cerevisiae* has two almost identical copies of a gene on a single chromosome. The orientation and placement of these gene pairs suggests that they did not result from the copying of individual genes but from the duplication of an entire genome, say Wolfe and Shields.

The extra genes that S. *cerevisiae* did hold onto may have evolved to endow the yeast with new abilities. Several of the gene pairs, for example, contain a gene activated in the presence of oxygen and one activated when no oxygen is present. This may help explain why, unlike its close relatives in the yeast world, *S. cerevisiae* prefers fermentation—which uses sugars but no oxygen to generate energy and alcohol—to forms of respiration that use oxygen, says Wolfe. —*J.T.*

Protein of cancer enzyme identified

Scientists have found a protein component of the enzyme telomerase, an RNA and protein complex that stitches protective pieces of DNA onto the ends of chromosomes. Without this enzyme, chromosomes grow shorter with every cell division (SN: 11/25/95, p. 362).

The researchers discovered the protein, called p123, in the telomerase of the protozoan *Euplotes aediculatus*. They have also determined its yeast counterpart. If that protein's gene is mutated, yeast chromosomes shrink with every cell division, eventually shutting down the yeast cells.

The structure of the telomerase protein resembles that of reverse transcriptase, an enzyme used by HIV and other retroviruses, report Joachim Lingner, a Howard Hughes Medical Institute investigator at the University of Colorado in Boulder, and his colleagues in the April 25 SCIENCE. They suggest that some of the many compounds developed to inhibit the viral enzyme may also inhibit telomerase. Such drugs could prove useful in battling cancer, since many tumors depend on telomerase for growth (SN: 5/31/97, p. 333). —*J.T.*

How much human DNA can mice hold?

For many years, scientists have created transgenic mice by adding individual human genes to the mouse genome. A research group in Japan has unexpectedly found that it can also introduce large fragments of human chromosomes, some probably containing more than 1,000 genes.

When single genes are added to the mouse genome, they fit into mouse chromosomes at random locations, which may alter the timing, location, and intensity of the human gene's activity. In contrast, the chromosome fragments remain independent, they are copied and distributed normally when cells divide, and their genes appear to behave as they do in people, report Kazuma Tomizuka of Kirin Brewery Co. in Kanagawa, Japan, and his colleagues in the June NATURE GENETICS.

Moreover, in several cases, a human chromosome fragment made it into the germ cells of a mouse, enabling the mouse to pass the fragment to its offspring. —*J.T.*

Biomedicine

Cow protein may help eye inflammation

Uveitis, an eye inflammation, is responsible for about 10 percent of all cases of severe vision impairment and blindness in the United States. It can arise from injury or infection, but it sometimes attacks mysteriously via an autoimmune reaction—the body turning against itself. To suppress the immune system in such cases, patients need to take powerful steroids for long periods, a treatment that can cause harmful side effects, including kidney damage, glaucoma, cataracts, and brittle bones.

Scientists at the National Eye Institute in Bethesda, Md., report in the May AMERICAN JOURNAL OF OPHTHALMOLOGY that retinal S antigen, a purified protein derived from cow eyes, may enable physicians to wean some patients off steroids without their uveitis flaring up.

Of 45 people whose autoimmune-based uveitis was being held in check with steroids and other medication, 10 received pure retinal S antigen orally, 10 got a mixture of other cow retinal constituents, 10 took a combination of the S antigen and the bovine mixture, and 15 received a placebo. Over 11 weeks, doctors tried to taper off the patients' steroid dosage while keeping inflammation at bay. The 10 patients receiving pure retinal S antigen fared markedly better than those in the other groups. Some were able to stop taking steroids. Surprisingly, the 10 patients who received the mixture without the S antigen fared badly, even worse than the placebo group, says Robert Nussenblatt, leader of the research team.

How S antigen works is unclear, Nussenblatt says. It may produce substances that "turn off" the immune response in the eye, he says, or it may paralyze T cells, the immune system's roving soldiers.

Uveitis can lead to glaucoma or irreversible destruction of the retina. Although the study population was small, the researchers consider the findings promising and are preparing for a larger clinical trial. S antigen may also prove useful in preventing rejection of corneal grafts, they suggest. —*N.S.*

Corneal dystrophy genes mapped

Nearly 60 years ago, German scientist Alois Meesmann identified a hereditary eye disease that causes irritation, blurry vision, and sensitivity to light. Now, researchers have tracked descendants of the German group Meesmann originally studied, as well as two extended families in Northern Ireland that carry the trait. By means of eye examinations and tissue samples, they have discovered that genetic mutations in either of two genes are responsible for the disease, which has come to be known as Meesmann's corneal dystrophy.

In this disease, tiny round cysts form on the cornea and begin to rupture during adulthood. People with the condition usually cannot tolerate contact lenses, although some people who carry the mutated genes show few effects. Gene mapping opens the door to genetic testing for this corneal dystrophy, which carriers pass on to roughly half of their children, says W.H. Irwin McLean of Thomas Jefferson Medical College in Philadelphia. He and his colleagues in Germany and Northern Ireland report their findings in the May NATURE GENETICS.

The flawed gene causes a crucial error in the sequence of amino acids of some keratins—tough proteins that form protective surfaces for mammals' cells, especially on exposed outer parts of the body, including the eyeball. Without the normal, sturdy keratins, cells in the cornea are weakened and cysts form.

Not everyone who cannot tolerate contact lenses has corneal dystrophy. The genetic mapping may help future research on these people, who the researchers suspect have a genetic mutation that creates a milder abnormality. Also, the study "brings us closer to the complete picture of these protein mutations," McLean says, which could aid research into other keratin disorders. —*N.S.*