Two Human Chromosomes Entirely Mapped

In two of the earliest major advances in the mammoth international effort to identify and decipher all of the estimated 100,000 human genes, two groups of researchers have taken apart and put back together the smallest human chromosomes: the Y chromosome and chromosome 21.

The exercises have yielded for each chromosome a set of overlapping segments of DNA assembled in the correct order. Scientists expect both of these so-called physical maps to help them find new genes more quickly. They also predict that the map of the Y chromosome will shed new light on human evolution.

Scientists at the Whitehead Institute for Biomedical Research in Cambridge, Mass., constructed the physical map of the Y chromosome. The team, led by David C. Page, began by examining the Y chromosomes of individuals who had inherited only fragments of this rod-shaped structure, which bears the genes that make a male.

By comparing the different-size Y chromosome fragments of 96 such individuals, Page and his colleagues discovered naturally occurring breakpoints that they could use as molecular probes. This comparison also allowed the researchers to organize the probes into the order in which they would occur in an intact Y chromosome.

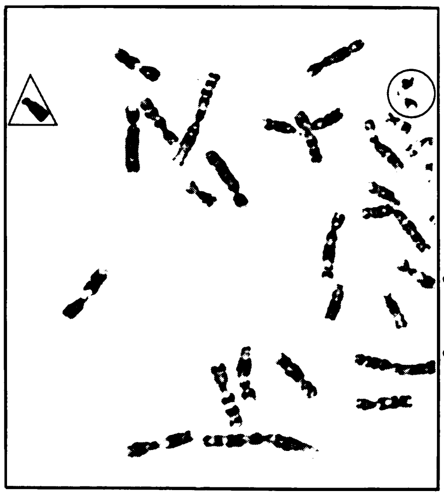
Page's group then used the probes to isolate long pieces of the Y chromosome from a man who had three extra Y chromosomes, which provided the researchers with an abundance of material for study. By assembling the pieces in the order of the probes, Page and his colleagues reconstructed 98 percent of the part of the Y chromosome that contains genes. They describe their work in two papers in the Oct. 2 SCIENCE.

Douglas Vollrath, a key member of Page's group, says the discovery should speed the Human Genome Project. "Until recently, the most difficult part was finding the DNA that you thought contained a particular gene," says Vollrath. "Now the problem shifts . . . you can go to the freezer and pull out a vial that contains the DNA you want."

Simon Foote, another key group member, adds, "This map and future maps will serve as the substrate for large-scale sequencing efforts" to read every letter in the encyclopedia of DNA that makes up the human genetic complement.

Vollrath and Foote say they plan to use detailed maps of the Y chromosome to shed light on the male side of human evolution. Several teams of evolutionary biologists have already used sporadic mutations in mitochondrial DNA — genetic material located outside the cell nucleus and inherited only from the mother — in attempts to trace human origins.

A team of 36 researchers from Europe, the United States, and Japan collaborated on the physical map of chromosome 21. Led by Daniel Cohen of the Paris-based Center for the Study of Human Polymorphism, they discovered 198 equally spaced landmarks on chromosome 21. These landmarks allowed the researchers to divvy the chromosome up into manageable chunks and to assemble the chunks in the correct order, they report in the Oct. 1 NATURE. Chromosome 21 is particularly important to human disease, Cohen and his colleagues state, because it contains the genes for amyotrophic lateral sclerosis (Lou Gehrig's disease) and for some forms of Alzheimer's disease and epilepsy. An extra copy of chromosome 21 causes Down's syndrome.



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Chromosomes from a normal man. The circle surrounds the usual two copies of chromosome 21. The triangle encloses the usual single copy of the Y chromosome.

The maps of the two chromosomes "represent a massive body of work," Peter Little of Imperial College in London comments in an editorial in the Oct. 1 NATURE. "The important message is that [such mapping] can be done and it is now only a matter of time (and money) before all human chromosomes are completed."

— *C. Ezzell*

Dyslexia: Reading words, missing letters

By about age 9, children who encounter no major problems in learning to read attach a wide array of letters and letter combinations to their corresponding sounds within words. But this ability eludes dyslexics — even those who manage to become fairly good readers — and apparently impairs fluent word recognition throughout their lives, according to a report in the September DEVELOPMENTAL PSYCHOLOGY.

"Although dyslexics take longer to read and understand words, they can still improve their reading skills and accomplish much," asserts psychologist Maggie Bruck of McGill University in Montreal. "The bad news is that a core problem in dealing with letters and their corresponding sounds doesn't go away."

No good evidence exists as to whether instruction that emphasizes the ways in which "sounds hang on to letters" substantially improves the reading skills of adult dyslexics, Bruck notes.

The causes and exact nature of dyslexia remain uncertain. Bruck and many other researchers define it as a disorder in which a healthy person with a normal IQ exhibits word recognition and other reading skills far below standard levels for his or her age. Some educators view dyslexia as a condition that affects all facets of language, including reading, writing, and listening.

Bruck's sample consisted of 36 dyslexic children between ages 8 and 16 attending a reading disorders clinic, 39 adults with childhood diagnoses of dyslexia made at the same clinic, and 63 good readers (43 children between ages 8 and 10, and 20 college students).

Comparisons of dyslexics with good readers of the same age or the same reading level indicated that dyslexics always lag far behind in the ability to match letters to individual sounds that make up words. However, as dyslexics get better at recognizing words, they compare favorably with good readers on tests of knowledge about larger segments within words, such as syllables.

Even the 26 best readers among adult dyslexics, who read at nearly high-school level, matched letters to individual sounds within words less accurately than third graders, Bruck points out. That deficit contrasts with the fact that the third graders read and spelled more poorly than the adult dyslexics.

Third graders outscored adult dyslexics on a test in which they used blocks to indicate the number of sounds in spoken nonsense words, such as "tisk" (with four letters and four sounds) and "leem" (with four letters and three sounds). If third graders erred, they almost always reported too many sounds, such as four sounds in leem, reflecting a focus on the number of letters in the word, Bruck contends. Dyslexics often reported too few sounds, indicating a preoccupation with the way words sound.

Overall, the data suggest that no matter what their reading level, dyslexics do not easily connect letters to appropriate sounds within words, as good readers of all ages do, Bruck asserts. This deficit slows down reading and renders word comprehension more laborious, she says.

Dyslexics may harbor an inability to learn the associations between sounds and spellings, Bruck notes. Or they may learn these associations but fail to integrate sound and spelling knowledge rapidly while reading.

Dyslexics also displayed persistent problems with attaching letters to corresponding sounds in an unpublished study directed by pediatrician Sally E. Shaywitz of Yale University School of Medicine. But Shaywitz remains optimistic.

"Dyslexics can learn to compensate for this difficulty," she maintains. "We see remarkable progress in many adults who have been dyslexic since childhood and who are willing to work hard at becoming better readers." *— B. Bower*

Dimmer lasers brighten the photon's future

In efforts to create useful gadgets from the semiconductor layer cakes called multiple quantum well structures, researchers have already fashioned miniature lasers and optical switches that route information riding on light beams.

Now, in a significant advance, scientists at Purdue University in Lafayette, Ind., have decreased the intensity of laser light at which one such material allows light itself to change the rate at which it travels through the layers.

These so-called photorefractive materials have the ability to store holograms internally as a pattern of electrical charges. The patterns can hold a tremendous amount of information about an image projected into the crystal with laser light. This makes photorefractive materials ideal for use in the emerging technology of optical computing — controlling light with light.

Previous photorefractive materials required laser intensities 10 times greater than those demanded by the Purdue device. The new material's higher sensitivity to light bodes well for the use of photorefractive materials in optical computing, says physicist David D. Nolte, co-investigator on the Purdue project. "It means that the power requirements are way down, that you can use very low-power, low-cost, safe, compact laser diodes," he says.

Alastair Glass, a researcher at AT&T Bell Laboratories in Murray Hill, N.J., and co-holder of the patent on the material, characterizes the improvement in sensitivity as a welcome, though not unexpected, advance. These multilayer crystals, he says, "look like they're going to be the material of choice for image processing."

This is the first time researchers have demonstrated experimentally the low power requirements of the material, Nolte says. The Purdue team describes its results in the September JOURNAL OF THE OPTICAL SOCIETY OF AMERICA.

In an ordinary material — glass, for example — intersecting beams of photons pass right through each other unperturbed. Photorefractive materials, however, allow researchers to modulate one light beam with another. In the device tested at Purdue, ultrathin semiconductor layers — the multiple quantum wells — confine photons, enhancing certain optical properties of the material.

The Purdue researchers demonstrated significant modulation at intensities comparable to the illumination in a dimly lit room. Moreover, the device redirects an unprecedented 10 percent of one beam's energy into the other. Nolte says this dual result — a high degree of modulation at a relatively low laser intensity — is a "world record" for photorefractive materials.

In their experiments, the researchers place the device at the intersection of two laser beams. The beams interfere with each other, generating a pattern of bright and dark fringes. Electric charges move into these fringes and form a holographic impression of the information projected in the laser beams.

The laser beams also interact with the hologram. This allows one beam to control another: A change in the light entering the crystal changes its optical properties, which in turn affect the behavior of the other beam.

Nolte says these photorefractive materials — whose applications include holographic memories and robot vision — are drawing the attention of other researchers. He cites well-attended sessions on the subject at last week's meeting of the Optical Society of America, held in Albuquerque, N.M. "More and more people are getting interested in these devices," he says. *— D. Pendick*

Protein identified in dinosaur fossils

A team of molecular biologists and paleontologists has identified a protein preserved in dinosaur bones, opening up the possibility of using ancient molecules to help sort out the controversial relationships among dinosaurs and other vertebrates.

Scientists have long considered it highly unlikely that they would find proteins in material more than a few million years old, because such organic molecules usually decay far sooner. Yet several research teams in the past few years have reported detecting proteins in very old fossils, including dinosaur bones (SN: 5/4/91, p.277). In the dinosaur case, however, the researchers did not know which proteins they had detected, and many scientists wondered whether the proteins had come from bacteria or other sources of contamination.

Now, Gerard Muyzer of Leiden University in the Netherlands and his colleagues report using immunological tests to identify a specific bone protein called osteocalcin in several dinosaur fossils that date back 75 million and 150 million years. They discuss their work in the October GEOLOGY.

"If it is indigenous, then it is the oldest protein," says Lisa Robbins, a micropaleontologist at the University of South Florida in Tampa.

Muyzer's group identified the dinosaur protein through an antibody that binds to osteocalcin, a small molecule present in the bones of vertebrate animals. The antibody test found osteocalcin in the bones of hadrosaurs, a ceratopsian, and a sauropod dinosaur. It also detected the protein in several mammal fossils and an ancient turtle bone.

The researchers believe the osteocalcin is indigenous to these fossils because invertebrates and bacteria do not produce this protein. Their tests did not show any osteocalcin present in fossilized seashells. Another procedure showed that the dinosaur fossils contained relatively high concentrations of gamma-carboxy glutamic acid (Gla), an amino acid absent in invertebrates and microbes, say the researchers.

Other researchers, however, remain skeptical about the possibility of finding proteins from so far back. Jeffrey L. Bada from the Scripps Institution of Oceanography in La Jolla, Calif., says a study he did on Gla shows that it doesn't last more than 100,000 years. "I worry greatly about the stability of Gla. Why would it remain unaltered over tens of millions of years?" he wonders.

Muyzer and his colleagues had hoped to isolate the osteocalcin and then determine its amino acid sequence. By comparing that with osteocalcin sequences from birds and crocodiles, the researchers could address the long-standing question of how closely birds and dinosaurs are related. At present, paleontologists can only use dinosaur bones to make comparisons.

Muyzer's group did not succeed in isolating the protein. But advances in laboratory procedures may soon make the job easier. "The techniques are improving daily. It's just a matter of the techniques catching up with what we want to do," Robbins says. *— R. Monastersky*