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.

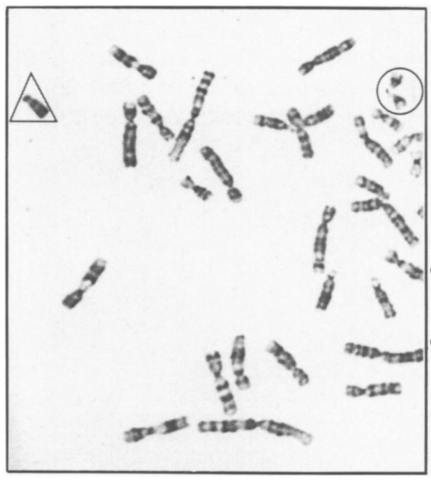
Page's group then used the probes to isolate long pieces of the Y chromosome from a man who had three extra Y chromosomes, which provided the researchers with an abundance of material for study. By assembling the pieces in the order of the probes, Page and his colleagues reconstructed 98 percent of the 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