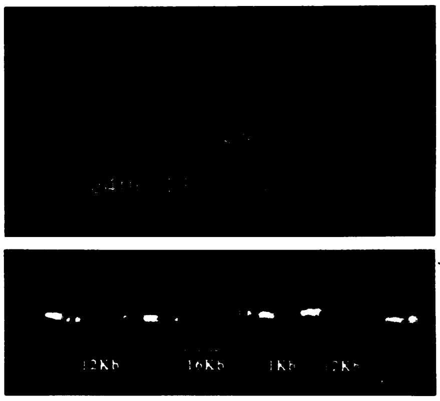
# Now in Vivid Color, Details of DNA



*Top: Stretched DNA shows relative order of different pieces of DNA labeled with different fluorescing tags. Averaging 41 samples of this DNA led to the distance in kilobases (kb) shown. Bottom: Repeating sequences of color reveal that when cancer cells make multiple copies of a gene that helps the cells resist the killing effects of chemotherapeutic drugs, these copies wind up close together but not regularly spaced.*

Parra and Windle/NATURE GENETICS

If one were to try to make sense of a note on a crumpled piece of paper, the first step would be to smooth the paper out. That same approach has now been applied to reading the genetic code.

By stretching DNA molecules across microscope slides, researchers have created more precise methods of pinpointing genes and analyzing their makeup.

Genes lie along chromosomes, DNA molecules that typically exist as long coiled helixes that can twist to form dense tangles. Thus, even though scientists can mark specific segments of these molecules with fluorescent tags, determining the order of those DNA snippets or their precise distances from either end of a chromosome can be difficult, says Bradford Windle, a molecular biologist at the Cancer Therapy and Research Center in San Antonio, Texas. Now, scientists can directly measure the spacing between fluorescing stretches, he and colleague Irma Parra report in the Sept. 1 NATURE GENETICS.

"It's a beautiful technique," comments Veronica J. Buckle at John Radcliffe Hospital in Oxford, England. "It's so much quicker than anything that's been tried before. I think any major lab that's into [gene] mapping is going to try it."

The "letters" in the genetic code, called nucleotide bases, are DNA's chemical building blocks. The bases that spell out a gene, a blueprint for a specific protein, fit in between strings of noncoding bases. Unlike most methods, which pinpoint the location of a specific gene to within a hundred thousand bases, the new procedure can map genetic sequences to within a few thousand bases, says Windle.

With the bases all in a straight line, "you can directly visualize in more detail the order of the DNA," adds Henry H.-Q. Heng at the University of Toronto. His group helped pioneer so-called linear DNA studies, which make it easier for scientists to tell the order of genes.

Indeed, several research teams in addition to Windle and Parra have developed strategies to stretch DNA, says Jeanne Bentley Lawrence of the University of Massachusetts Medical Center in Worcester.

These approaches harness a technique called *in situ* hybridization (SN: 3/20/93, p.188). Researchers first create genetic probes – short strands of bases with fluorescent labels attached. These probes seek out and bind to matching bases in a gene or RNA molecule and then glow a specific color under a fluorescence microscope or camera. But in unstretched DNA, "it would be a mix of colors; you couldn't see whether the [labels] were close or far apart," says Windle.

In their approach, Windle and Parra put some cells on the edge of a slide, break them up with detergent, and then tilt the slide so the viscous mixture of cellular components oozes down. The glass catches long molecules of DNA along the way. Some DNA stretches a little and accumulates near the starting point; a few strands reach all the way to the end. "It's like pulling cotton candy," Windle explains. "It gets thinner and thinner." Then the researchers label the stretched DNA.

DNA from several cells fills each slide, providing lots of material to look at and to compare, says Buckle. Thus researchers can assess distances between two probes on DNA from different cells and know with greater confidence that their observations are not artifacts.

Lawrence is not as sure as Buckle of the universal utility of these approaches. "There are faster ways to map genes and order sequences," she notes. "But there might be specific applications where one would want to study a particular region in detail."

By comparing normal with abnormal chromosomes, geneticists can more easily tell whether a faulty gene, especially a large one difficult to study otherwise, has lost a small – or large – piece of its code, reordered its bases, or added extra ones, Windle suggests. Also, the technique makes it possible to detect multiple copies of the same gene on a single chromosome.

Buckle warns, however, that while this mapping technique can provide resolution in the thousand base-pair (kilobase) range, confirming that level of detail will require much added work. "You have to be careful in interpreting what you see," she says. – *E. Pennisi*

## Unruly hair: No fairy tale

You think you've had a bad hair day? One U.S. woman has hair problems that go way beyond such ordinary complaints as split ends.

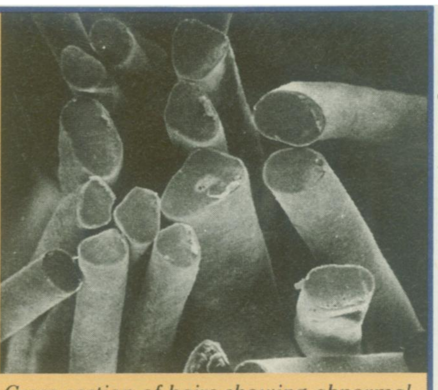
This true medical saga began when a 39-year-old woman with thick, light-brown hair complained to her doctor about hair loss. After she took the diuretic drug spironolactone for her treatable condition, the shedding decreased but the coarse, curly hair that grew back was so tangled she could not comb it, even with the liberal use of conditioners.

Dermatologist Wilma F. Bergfeld and her colleagues at the Cleveland Clinic Foundation describe the woman's plight in the August ARCHIVES OF DERMATOLOGY. It turns out that she suffers from uncombable-hair syndrome.

That's the actual name of a bona fide condition. The syndrome, also called spun-glass hair, may have inspired a German fairy tale about a boy with unruly hair who never touched a comb.

Dermatologists have reported 50 cases of the medical syndrome, mostly in children age 3 to 12. This is the first known case of the condition developing in an adult with previously healthy hair, Bergfeld and her co-workers say.

When the team used an electron microscope to examine the woman's hairs in cross section, the shafts appeared abnormal. Unlike the normally round cross sections of human hair, this woman's shafts appeared triangular or kidney-bean shaped, notes coauthor James T. McMahon. □



Bergfeld et al./ARCHIVES OF DERMATOLOGY

*Cross section of hairs showing abnormal shapes under electron microscope.*