



TECHNOLOGY

Genomes 'R' Us

Pacific Biosciences says it will soon be able to decipher the genetic code faster and cheaper than ever. **By Michael V. Copeland**

IT TOOK the Human Genome Project \$3 billion and 13 years to map the first genome and reduce it to a chemical code six billion letters long. Today, with faster computers and improved techniques, a research laboratory can sequence your DNA in about six weeks at a cost of \$100,000 to \$300,000.

Now a startup called Pacific Biosciences vows to do the job in 15 minutes for less than \$1,000. The Menlo Park, Calif., outfit says that by 2013 it will have a microwave-oven-sized machine on the market that could bring genomics to the masses.

The device's potential is sparking electric anticipation among some in the genetics community. "In all the things that I have seen in the past 20 years, I haven't seen anything as disruptive as what PacBio is cooking up," says Dr. Eric Topol, head of Scripps Genomic Medicine Program in La Jolla, Calif. "It changes everything in genomics." If a gene sequence could be ordered up as easily as an MRI—and the genetic blueprints of hundreds of thousands of individuals compiled—scientists could zero in on the mutations that cause Alzheimer's, leukemia, or prostate cancer; pharmaceutical companies could design more precise drugs; and doctors could predict what infirmities you are likely to face and start to head them off.

The prototype, slightly bigger than a

kitchen stove, bristles with tubes, lasers, lenses, and mirrors. It is a virtuoso feat of engineering that draws on optical networking, materials science, biophysics, and even a little videogaming. First, a solution made up of DNA that has been cut into tiny strips is introduced into the machine. Then those strips are scattered over a thin metal sheet punctuated with 3,000 tiny holes about 70 nanometers (1/1,000th the thickness of a human hair) in diameter. Anchored to each hole is a special enzyme called DNA polymerase, whose job in nature is to travel down a strand of DNA like a zipper, splitting the double helix and creating a complementary image of each strand.

What the PacBio device does, in the words of company founder and chief technology officer Stephen Turner, is "eavesdrop on nature" by washing the array of DNA polymerase molecules with a specially modified solution of nucleotides. Each has been labeled with a phosphorescent dye that can be detected in a tiny illuminated zone at the bottom of the metal sheet. Whenever a nucleotide is incorporated into the growing chain of DNA, its fluorescent label flashes a distinctive color. By detecting and recording these flashes, the PacBio

device builds a record of the precise sequence of base pairs in each strip of DNA. That record is fed into a computer that compiles the results from all the strips and reassembles them in the proper order.

PacBio's prototype can sequence a gene at the rate of ten base pairs per second. But the finished machine will be even faster. It will operate like a massively parallel computer, churning out genetic code at speeds approaching 10,000 base pairs a second.

PacBio is not the only company pursuing this market, which analysts say could jump from its current \$1.5 billion in revenues to tens of billions. Illumina, Applied Biosystems, and Helicos BioSciences have already gone public; Complete Genomics and Visi-Gen Biotechnologies are still private. But CEO Hugh Martin is confident that PacBio, which is backed by blue-chip venture capital firms including Mohr Davidow and Kleiner Perkins, will be the first to get a fast and cheap product on the market.

Indeed, such is the excitement about PacBio's device that one health-care

technology analyst even brings up the G-word. Says Ross Muken of Deutsche Bank: "These guys have a shot at becoming the Google of health care, the company that comes out of nowhere and dominates." ■

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