BIOTECHNOLOGY

The Ultimate Gene Gizmo: Humanity on a Chip

Commercial genomics reached a landmark last week, and several companies are jostling to share the limelight. Affymetrix Inc. of Santa Clara, California, announced that it is now selling the first research device that contains a complete set of 50,000 candidate genes covering the entire human genome. The GeneChip, as this microarray is called, can be used to measure the activity of all known human genes in a biological sample. Meanwhile, another California company, Agilent Technologies Inc. of Palo Alto, has begun distributing its own human genome array as an experimental prototype, and since June NimbleGen Systems Inc. of Madison, Wisconsin, has been using yet another whole-genome setup to support a DNA-scanning service at a lab in Iceland.

At a glance. Microarrays, such as Affymetrix's GeneChip (above), now include all known human genes.

These arraymakers use a variety of techniques to attach minuscule dots of DNA onto glass slides, silicon wafers, or nylon membranes. When exposed to a mix of RNAs from a biological sample, each DNA latches onto the RNA that matches its sequence. The RNA carries a fluorescent tag, marking the place where it attaches. Based on the location and intensity of the signal, researchers can tell which gene is the source and how active it is.

Affymetrix has adapted a form of semiconductor photolithography to create arrays that are similar to electronic chips; Nimble- Gen incorporates photochemistry and digital mirror technology; and Agilent uses ink-jet machines. All have been shrinking the DNAcontaining dots on their devices, thereby squeezing in more dots per array. For example, Affymetrix's first chips contained just a few thousand genes. More recently, the company developed a two-chip set covering most of the known human genes. The new version compresses the two chips into one and includes 6500 more genes. According to Stan Rose of NimbleGen, that company's array now covers 38,109 gene candidates. Agilent says its array will have more than 36,000.

These achievements "will reduce the [amount of] time and effort required to do an experiment, reduce the expense, and make the data more uniform," says Joseph Ecker, a plant scientist at the Salk Institute for Biological Studies in La Jolla, California, who has helped pioneer wholegenome chips for *Arabidopsis tumefaciens*. Needing less RNA for an experiment can be critical, he adds, because sometimes researchers can isolate only tiny amounts of it.

Whole-genome chips exist already for four other organisms: the yeast *Saccharomyces cerevisiae*, the nematode *Caenorhabditis elegans*, the fruit fly *Drosophila melanogaster*,

and the gut bacterium *Escherichia coli*. They have made possible wholesale scans that turn up new gene modifications and variations, says Ecker. The same should prove true for the new human gene arrays. In short, says Ernest Kawasaki, a molecular biologist who runs the microarray unit of the National Cancer Institute in Gaithersburg, Maryland, "we've come a long way."

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