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New Tools Highlighted at ASHG Conference

Stimulating Discovery and Accelerating R&D

Several companies introduced new tools for advancing genomics research at the "55th Annual Meeting of the American Society for Human Genetics," held recently in Salt Lake City. The offerings are expected to help to stimulate genomics studies and speed the development of new predictive diagnostic tests and treatments for human diseases.

The release of 400,000 PCR primer pairs for more than 16,000 human genes, which will be made available through a new Probe Database developed by the National Center for Biotechnology Information (NCBI), was announced by David Ginzinger, Ph.D., director of advanced research and technology at Applied Biosystems (www.appliedbiosystems.com).

"Sequencing the human genome was a great accomplishment,"said Dr. Ginzinger, who moderated the "12th Annual Advancing Genomics Symposium" sponsored by Applied Biosystems. "But it's the first step in a long journey that needs innovative tools, which Applied Biosystems can provide to make the process easier."

The NCBI Probe Database is publicly accessible at www.ncbi.nlm.nih.gov/

genome/probe.

Dr. Ginzinger also described some other relevant products. The Tempus blood RNA collection tubes preserve RNA in whole blood and maintain expression levels for use in real-time PCR and microarray analysis. The technology was inspired by clinical researchers who had trouble keeping RNA stable in samples collected from patients enrolled in drug trials.

The Tempus tubes contain reagents that immediately inactivate RNAase and stop all metabolic activity. The high-quality RNA remains stable for up to five days at room temperature. "It's a critical step for getting good gene expression data in studies," noted Dr. Ginzinger.

Non-coding RNA, also known as micro or miRNA, "is fashionable these days," he said. Found in all mammals and plants, about 330 microRNAs have been discovered in humans, and some experts predict that up to 1,000 types will be found.

MicroRNAs operate during translation and can repress panels of other genes downstream. The TaqMan microRNA assays human panel early-access kit provides 180 microRNAs, and the offering will grow as more are discovered.

Multiplexing

Promega's (www.promega.com) new Plexor technology for gene-expression analysis and SNP profiling allows users to multiplex real-time quantitative PCR (RTQPCR). The method requires only two novel primers for sensitive and specific quantitation, according to the company.

In addition, Plexor runs on most commercial RTQPCR instruments, including those made by Applied Biosystems, Roche, Bio-Rad, Cepheid, and Stratagene. Whereas other RTQPCR systems produce an increase in fluorescence, Plexor reportedly quenches fluorescence.

The Plexor chemistry can be used to identify and quantitate specific DNA sequences in genomic DNA, mitochondrial DNA, cDNA, or viral DNA samples. In multiplex reactions, one primer for each target must carry a different fluorescent label.

The types and number of fluorescent labels that can be used depend on the detection capabilities of the real-time instrument. While developing Plexor, Promega experts worked with scientists at the University of Wisconsin, who were skeptical that multiplexing was possible. The current dogma is that quantitation of high-copy number transcripts interferes with quantitation of low copy-number transcripts.

The Promega team proved that for up to four primer pairs, Plexor's primer chemistry detects low copy-number genes in the presence of high copy-number genes.

Because many bench scientists share real-time instruments, they are often limited to running one or two plates a week. Plexor's multiplexing ability allows them to move control reactions into target reactions as internal controls, which "opens up half a plate to run more experiments and increases productivity," said Kyle Hooper, Ph.D., genomics product manager at Promega.

Alpha testers gave Promega the first targets tested in Plexor. To further validate the new platform for SNP genotyping, "we need help from researchers with thousands of samples," said Dr. Hooper.

Promega plans to release Plexor by the end of 2005. Customers will design their assay primers at a special website, then select a collaborating oligonucleotide manufacturer to construct the

primers with the novel primer chemistry. A Plexor kit contains all the reagents needed to run the reactions, notes the company.

The Plexor software imports raw data that is exported from current real-time PCR instruments and converts it to analyze fluorescent quenching.

One-Color Microarrays

Agilent Technologies (www.agilent.com) introduced its One Color Gene Expression microarrays based on the same platform as its Two Color Gene Expression platform.

"Instead of indirect comparisons made with two colors co-hybridized on one microarray, we're providing this one-color capability to simplify comparisons across multiple microarrays to make broader comparisons," said Erik Bjeldanes, product manager for gene expression.

Although two-color microarrays more accurately measure small changes of expression levels, one-color microarrays are more straightforward and cost effective for experiments that involve large numbers of samples or time-course experiments, he explained.

For instance, to compare drug activity at time zero (control) and at various time points, one-color microarrays allow users to prepare just one control, then compare it to each time point. With two-color microarrays, a control must be prepared and co-hybridized with each time point.

One-color microarrays "give our customers greater flexibility in designing experiments on our platform," said Bjeldanes. Customers can switch between the protocols without much change in workflow.

DNA Diversity Map

Francis Collins, M.D., director of the National Human Genome Research Institute, announced the completion of HapMap, a collection of haplotypes identified in 269 individuals.

The International HapMap Consortium involved 200 scientists from six countries who analyzed SNPs in people from Nigeria, Utah, China, and Japan. This SNP database, containing nearly 10 million SNPs, will be useful for mapping regions of chromosomes associated with chronic illnesses. Researchers can zero in on particular gene variants and ignore large portions of DNA that do not contain diseased genes.

Although officially unveiled at the conference, researchers already used HapMap to link a variant of the gene called complement factor H (CFH) to age-related macular degeneration (AMD). CFH plays a role in inflammation.

"Who knew an eye disease had anything to do with inflammation," said Dr. Collins. The finding suggests new ways to prevent or treat AMD.

All data from the HapMap project are publicly available at www.hapmap.org.

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