bioArray News


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THE GLOBAL WEEKLY OF BIOCHIPS & MICROARRAYS

in this issue

FDA Preparing Draft Document to Help Guide Microarray Data Consideration

At PittCon, Beckman Coulter Rolls out New Microtiter Plate-Based Protein Array Platform

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THE GLOBAL WEEKLY OF BIOCHIPS & MICROARRAYS

volume 3, number 39
October 8, 2003

in this issue

GenomeWeb

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Less is Really More, Research Scientists Say in New York Bioarray Conference

WHAT do scientists want from a microarray platform?

Less, said participants at last week's inaugural BioArrays 2003 conference in New York City.

"The future of diagnostic prognostication involves a small number of genes — a small number, but one where quality counts," said conference attendee Steve Gullans, chief science officer of Woburn, Mass.-based US Genomics and an associate professor at Harvard Medical School, and Brigham and Women's Hospital, in Boston.

These sentiments emerged just as microarray giants Affymetrix and Agilent Technologies battled by press release on Oct. 2 to claim the lead in the race to commercialize microarrays that have the known coding content of the human genome on a single chip (see below).

But at the two-day conference, which was sponsored by GeneExpression Systems, a four-year-old genomics contract research company established by former PerkinElmer scientist Krishnarao Appasani, the message was clear: researchers are using microarray analysis to conduct thousands of assays, in order to create short lists of genes on which to base

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Affymetrix and Agilent Turn up the Volume To Market Single Whole Human Genome Chips

WITH A STATEMENT released released on Thursday morning, Affymetrix last week made its next move in commercializing a single microarray product containing probes that, in toto, represent the known gene content of the human genome.

The Affymetrix announcement, perhaps not coincidentally, came out hours before an announcement by Agilent, which stated that it, too, was in the early stages of commercializing its single microarray, whole-human-genome product.

Industry scientists and researchers said they welcome the tool, with more than one describing it as a means to cast a wide net. in genomic discovery.

Jeffrey Brockman, a senior scientist and microarray group leader for Psychiatric Genomics of Gaithersburg, Md., said his company has evaluated Affymetrix arrays and Agilent's cDNA arrays in its drug discovery efforts centering around brain diseases.

He said he is using both Agilent's cDNA arrays and Affymetrix's rat, mouse, and

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PEOPLE IN THE NEWS

David Hastings joins **Incyte** as executive vice president and chief financial officer, replacing John Vuko, the Palo Alto, Calif., and Wilmington, Del., company said last week. Hastings comes to Incyte from **ArQule**, where he has served as CFO and treasurer since 2000. Before joining ArQule, Hastings was vice president and corporate controller of **Genzyme**, and prior to that, was director of finance at **Sepracor**. Vuko, who has been Incyte's CFO since December 1999, will remain as an advisor to Incyte "for a period of time," the company said in a statement.

Steve Trevisan, executive vice president and a director of **Gene Logic**, will step down, but will continue in an advisory capacity until the end of the year, the company said last week. Trevisan joined Gene Logic in April as part of its acquisition of T**herimmune Research**, of which he was president and CEO. The resignation of Trevisan, which the company said was by "mutual agreement of the parties," comes as Gene Logic moves to fully integrate Therimmune Research under the Gene Logic brand name. Trevisan founded TherImmune in December 1998. Prior to this, he was president of **Perot Systems Communications**, which does billing systems for the telecommunications industry, and before that, was president and CEO of **CommSys**, an outsource billing provider. Trevisan also founded **National Clinical Resarch Centers** and was head of strategic business development at **Pansophic** systems.

Karen Dawes has joined the board of directors of **Genaissance Pharmaceuticals**, the New Haven, Conn., company said last week. Dawes is principal at the consulting group **Knowledgeable Decisions**, which focuses on biotech and emerging pharma companies. Previously, she worked as senior vice president and US Business group head at Bayer. She has also worked at **Wyeth Pharmaceuticals**, **Genetics Institute**, and **Pfizer**. She on the board of **Protein Design Labs**.

Darlene Solomon has been named vice president and director of **Agilent Laboratories**, replacing the retiring Tom Saponas, the company said. Solomon is on advisory boards for the National Science Foundation's Nanobiotechnology Center and the **Defense Advanced Research Projects Agency** Center for Biochemical Optoelectronic Microsystems.

HOT NEW PRODUCTS

MWG Biotech of Ebersberg, Germany, this week announced the release of its **MWG Human 40K Array**, a pair of microarray chips containing 50-mer oligonucleotide probes for 40,000 human genes. The company's **A Array** consists of 20,000 genes with full functional characterization and content referencing. The 20,000 genes on the **B Array** are referenced against NCBI databases.

The company said the arrays include 11,000 genes classified into biological functional groups by the Gene Ontology classification system, mapping to 384-well microtiter plates to enable researchers to investigate subarray or oligo subsets. Additionally, the company created a non-redundant protein coding database, **CodeSeq**, with **NCBI's RefSeq** project serving as its primary sequence source.

bioArray News

The Global Weekly of Biochips & Microarrays

www.bioarraynews.com

ISSN 1534-9926

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SUBSCRIPTION INFORMATION

BioArray News is published weekly (50 times annually) by GenomeWeb LLC

Subscription rate: $895.

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PerkinElmer received US Patent No. 6,631,211, "Interactive system for analyzing scatter plots." The patent covers a system that can be used to analyze data from microarray experiments. A scanner system analyses data plotted in accordance with user-specified criteria or statistical measures from the data population, to produce a scatter plot that displays boundaries for the selection of outlier points and/or otherwise visually denotes in the plotted data which points are the outlier points. The scanner system analyzes the underlying data based on user-specified differential expression ratios, or based on criteria associated with the statistics of the data population, to produce outlier boundaries that are represented by diverging lines. Alternatively, the system may analyze the underlying data based on absolute expression levels, to produce boundaries that are represented in the plot by lines that meet at an identity line of slope 1. The scanner system may also combine several criteria and produce boundaries that denote as outliers the data that, for example, show both sufficient differential expression and also include individual expressions that are sufficiently above an associated noise floor.

Zyomyx received US Patent No. 6,630,358, "Arrays of proteins and methods of use thereof." The patent covers protein arrays technology and methods for the parallel, *in vitro* screening of biomolecular activity. The arrays include a number of proteins immobilized on one or more organic thin films on the substrate surface.

Affymetrix received US Patent No. 6,630,308, "Methods of synthesizing a plurality of different polymers on a surface of a substrate." The patent covers a method and apparatus for preparation of a substrate containing photoremovable elements. In the method provided, selected regions of the substrate are exposed to light so as to activate the selected areas. A monomer, also containing a photoremovable group, is provided to the substrate to bind at the selected areas. The process is repeated using a variety of monomers such as amino acids until sequences of a desired length are obtained. Detection methods and apparatus are also disclosed.

IatroQuest of Ontario received US Patent No. 6,630,356, "Photoluminescent semiconductor materials." The patent covers a method of manufacturing semiconductor materials with a porous texture, modified with a recognition element, to produce a photoluminescent response on exposure to electromagnetic radiation. The recognition elements, selected from biomolecular, organic, and inorganic elements, interact with a target analyte to produce a modulated photoluminescent response.

At GSAC 2003, Microarrays Take their Place Next To Sequencers As a Must-Have Tool

A COUPLE of years ago, at TIGR's Genome Sequencing and Analysis Conference, the microarray was an upstart technology that most speakers ignored because it had little to do with the main topic of discussion — sequencing.

But at this year's conference, held in Savannah, Ga. (Sept. 21-24), microarrays were almost a given: At least 12 of the 34 speakers wove microarray technology into their talks, more as a taken-for-granted-as-indispensable tool of genomic research than as the object of such research.

In the opening night's talks, Steffan Jansson of the Umea Plant Science Center in Umea, Sweden, discussed how he and his colleagues are using microarrays in their study of the *Populus* genus of evergreen trees — aspens and cottonwoods — as a model system for tree genomics. At the end of September, the group released a 25,000-EST *Populus* array, spotted with cDNAs from over 100,000 ESTs sequenced in 19 cDNA libraries. Jansson and colleagues are now using these arrays to study expression patterns in wood-forming tissues, the xylem of the tree. "We can find the genes expressed during different stages of wood formation," he explained. Understanding this process has potential economic value, according to Jansson, as the lumber industry is a major part of economies in countries such as Sweden and Canada.

Meanwhile at the theoretical level, Lee Hood, founder of the Institute for Systems Biology, discussed in his plenary speech how systems biology involves studying a system within an organism — a "biomodule," by perturbing that system at a defined point, then seeing how the system changes — and how microarrays are one tool for detecting these changes. As an example, he cited ISB researcher Andrea Weston's work to study galactose metabolism in *Saccharomyces cerevisae*, in which she induced 20 galactose genes, then used microarrays to study the effects of these perturbations on gene expression in the galactose metabolism pathway. By studying the gene expression at different time points, Weston could observe how this biomodule operated in a tempo-

ral, dynamic manner, Hood said.

On Monday, Rick Wilson of the Washington University Genome Sequencing Center discussed how his group is using comparative genomic hybridization on microarrays that contain sequence from BAC clones tiled onto the array, to compare genomic DNA from patient and control samples in studies of genetic mutation in prostate cancer, non-small cell lung cancer, AML, and other diseases. These arrays can represent an entire chromosome of interest, he said, and can "reveal regions of a particular chromosome where there may be a disparity of copy number," or "deletions or amplifications between the two samples." Nigel Carter of Wellcome Trust Sanger Institute said in another talk that his group is also using CGH for studies of chromosomal disorders and chromosomal mutations in different cancers.

Stephen Chanock of the National Cancer Institute spoke on how microarray data provides a springboard for further study on gene expression, SNPs, and cancer. As part of an interdisciplinary program, the Cancer Genome Anatomy Project, his group has begun resequencing genes that were implicated in a 2000 *Nature* paper as differentially expressed in different subtypes of breast cancer [See Perou *et al*, Molecular portraits of human breast tumours, *Nature* 406, 747-752 (2000)]. "We've taken these particular genes which fall out of microarray analysis," said Chanock, and are resequencing them across the 5′ upstream region, the entire coding region, intronic segments with high similarity to other species such as mouse, and the 3′ region. They resequenced these genes in tumor DNA from 92 Norwegian breast cancer patients, along with 100 controls from the same population, looked at the SNPs to establish linkage disequilibrium and haplotype structure, and are currently comparing this data with expression array data, to get a better picture of the way genetic variation and gene expression interact in breast cancer. "I feel strongly we need to bring the world of haplotypes and SNPs" to expression arrays, he said.

Kam Man Hui of the Cancer Center in Singapore spoke about his group's use of spotted and Affymetrix arrays in gene expression studies of liver cancer; and Joseph Nevins, of Duke's department of molecular genetics and microbiology, brought microarray technology from bench to bedside, in detailing how gene expression profiles of breast cancer subtypes derived from microarray experiments are being used in a clinical setting as "clinico-genomic predictors of disease recurrence" to aid in treatment decisions. Nevins said applying genomic data to the clinic is only possible when "the higher ups" see that it is important.

— MMJ

Scientists...

continued from page 1

further research, and to simplify the task of analyzing the gigabytes of data that such wide efforts produce.

"Even 200 genes is a lot to think about," said Jose Walewski, an assistant professor at New York's Mt. Sinai School of Medicine who is conducting research on liver disease, concentrating on using microarray analysis to find pathways involving the hepatitis C virus and liver cancer.

"Microarrays have enormous value, but there is a real need to know the truth," said Thomas Vasicek of Lynx Therapeutics. Vasicek, a Harvard Medical School PhD in genetics and immunology, has cycled through thousands of microarrays in a career that saw him manage Millennium Pharmaceuticals' microarray technologies — followed by a stint as director of commercial technology for Corning's short-lived effort in microarray manufacturing — and a position as a visiting scientist at the Whitehead Institute, where he evaluated genomic technologies.

There is no doubt that microarrays have provided a previously unavailable insight into genomic functions and systems. But it is a technology that is still lacking the highest measures of accuracy and confidence that are to needed in the future — where it is seen as a key element to enabling the dream of personalized medicine.

Before the tool enters this personalized medicine arena, scientists said they want issues with hybridization-based assays solved.

"P53 chips miss mutations," said Francis Barany, a professor of molecular biology at Cornell's Weill Medical College in New York. "The commercial hybridization chips miss more than 25 percent of all mutations. If patients' lives depend on it, the chips need to be accurate."

Sam Hanash, a professor of pediatrics at the University of Michigan and the first president of the Human Proteome Organization, presented the following wish list for diagnostic tests:

"For the diagnostic tool set, you need to get samples in a non-invasive manner — blood, urine, or saliva, are easy to get; simple sample preparation; simple instrumentation; easily interpretable data; low cost; and, in the real world, something that is 100 percent accurate."

Hanash is a flag-bearer for the knowledge that proteomics will bring, as well as the orders of magnitude in complexity that accompany this logical next step in the exploration of systems biology.

"You are much closer to a

clinical outcome with proteins, rather than a hundred genes," he said. "but no single technology allows a researcher to study all aspects of proteins at once. "

Protein microarrays offer promise, but lack capture agents, he said, offering an optimistic prediction: "It's just a matter of time before we have those resources."

For David Munroe, director of the lab of molecular technology, and vice president of program management at the National Cancer Institute, Frederick, one promising technology is Nanogen's electronic microarray platform. NCI has an early-access relationship with San Diego-based Nanogen and is perhaps one of the company's key users.

"We have used it (Nanogen) for the admission of patients into clinical trials," he said. "It allows for exquisite determination between alleles. The only limitation with the platform is that it is not high throughput. But, it is simple to operate and we love it for diagnostics."

Other companies are targeting the space too.

US Genomics, which started up with the goal of enabling human genomes to be sequenced for $1,000 or less using its flow cytometry platform, is now looking to RNA analysis and is hoping to begin commercializing its instrument before the end of the year, said Gullans in a presentation entitled "Looking for a few Good Genes."

For the microarray industry, the opportunity is there to provide the answers that scientists are seeking next. Its advantage right now is that there are few substitute technologies available that can enable the numerous experiments that can be conducted using microarrays.

"Microarrays are the main tool, but certainly not the only one," said Jeffrey Waring, group leader for toxicogenomics for cellular and molecular toxicology at Abbott Laboratories. "Taqman assays would be quite good if we could get the list [of genes being studied] smaller."

MEETING NOTES

While all of the above are critical issues in the development path of the microarray technology, there are other issues at play too — intellectual property rights and funding.

The conference ended with a panel discussion on these topics by an academic technology transfer officer, a venture capitalist, and two lawyers specializing in intellectual property practice.

Joseph Lawler, an MD/PhD and a principal with the New York venture capital firm of JP Morgan Partners, did not paint a promising picture for those hopeful of earning early-stage funding for genomic platform technologies.

"Many investors are not as excited about platform technologies," he said. Entrepreneurs in this space would have to show that a platform is unique and can speed a drug's progress to the clinic, according to Lawler. Microarrays, which enable researchers to look at thousands of genes, might cast too wide a net for characterizations that can be based on 10 genes and can be done with another technology, Lawler said.

Entrepreneurs seeking funding should have a credible business plan, he said, and should know that the first decision-points an investor will analyze are the management team and the science involved. "If the science is bad, even the best management team won't help," he said

But while the hope of venture-capital funding might be dim, there are other funding vehicles available.

Kenneth Sonnenfeld, an attorney with the New York firm of Morgan & Finnegan, suggested partnerships for microarray content inventors. "Get it tested and get it out there, marketed on someone else's array," he said.

Sam Hanash, also participating on the panel, suggested taking financing through the public domain.

"Submitting a proposal to the NIH is an option," he said. "There are plenty of avenues with the NIH to get funding."

For many researchers in the audience, the principal question appeared to be about the viability of patenting genes.

Duncan Greenhalgh, an attorney and a PhD practicing with the Boston-based law firm of Testa, Hurwitz & Thibeault, said that patents can be granted for "new uses for old compositions of matter." Inventors, he added, are obliged to disclose to patent exam-iners all prior art they are aware exists in patent applications.

— MOK

Chips...

continued from page 1

human catalogue arrays.

"It's clear that each platform identifies a unique set of genes," he said. "One platform will not answer all questions.'

But it's still not clear how many platforms the microarray market, which is estimated to reach $800 million this year, can support.

The competition is just starting to heat up, and it's centering around this application.

Affymetrix, which is regarded as the market leader in mass-manufactured microarrays with a majority share outside of the self-spotting market, said in its Oct. 2 statement that it was ready to take orders for its GeneChip Human Genome U133 Plus 2.0 microarray, a single chip on the company's proprietary format, which it says contains 1.3 million

DNA probes to analyze the expression level of "nearly" 50,000 RNA transcripts and variants.

The arrays, Affymetrix said, would ship this month.

Meantime, Agilent Technologies, the No. 2 player among the companies that mass produce and market microarrays, announced that it had already shipped single, whole-genome chips to beta customers.

The Agilent array, the company said, contains 44,000 features and is printed on an 1x3-inch glass slide readable on any microarray scanner.

The dueling press releases clearly demonstrate the kinetics of competition in a market hurtling toward what perhaps may be a record financial quarter.

The whole human genome, arrayed on a single chip represents a technical achievement, and a milestone for an industry that is not a decade old but one that is reaching maturity, despite appearances of a spitting contest among the industry's largest players.

Meantime, Applied Biosystems, which ignited what some industry analysts are calling the 21st Century Chip Wars with a press release issued in late July (See, *BAN 7/30/2003*), remained on the sidelines. After issuing a press release promising a whole-human-genome single chip microarray by the end of the year, the company is keeping mum on details of its technology.

AFFYMETRIX PRODUCT DETAILS

The Affymetrix HG-U133 product is the next step beyond Affymetrix's two-chip microarray set, and contains the probes that represent the company's decision as to what is important in measuring transcripts from the the human genome. Pricing on the chip will range from $300 to $500, depending on volume purchased, the company told *The New York Times.* It did not respond to a *BioArray News* request for comment.

The company said that the content includes 10,000 new probe sets representing 6,500 new genes. The new information has been verified against the latest version of the publicly available genome map, the company said. The probe design strategy of the new array is identical to the two-chip set.

The company is also launching an 11-micron version of its HG-U133A array, which previously has been arrayed at an 18-micron format. The version 2 array contains probe sets identical to the previous product, the company said.

Affymetrix manufactures its microarrays using photolithography, the manufacturing method of the semiconductor industry, using ultraviolet light to deposit, *in situ,* bases at a length of 25 mers onto a quartz glass substrate.

The new arrays are only readable on the new Affymetrix scanner, which was released in January.

AGILENT PRODUCT DETAILS

Agilent spots onto one chip the genes it now sells as a two-array 60-mer oligonucleotide set — the Human 1A and 1B, released in June, and is adding additional content from Incyte and public databases.

The company's probe design seeks a perfect match to a sequence as its standard in probe design, Doug Amorese, biochemistry/chemistry R&D manager for the company's BioResearch Solutions group told *BioArray News*.

"Good [match] is not good enough," he said.

"What we have done is combined the expertise that we have developed in printing and probe design and validation with a maturing understanding of the human genome to generate a product that represents the genome as well as any product today can," he said.

Agilent, a Silicon Valley-based spin-off from Hewlett Packard, uses an ink-jet process to manufacture its microarrays, which are printed onto an open-format glass slide, readable in any commercial microarray scanners.

The company is regarded as the No. 2 industrial microarray producer with a product line that, anecdotally, is gaining share in a market where the majority of users spot their own slides.

While Agilent is not identifying its beta customers, no doubt one of them is Paradigm Genetics, which in October 2002, won a five-year contract from the National Institute of Environmental Health Sciences, worth up to $23.9 million, to produce gene expression data for a national reference database on the effects of chemicals on biological systems. The company uses Agilent Technologies' microarrays.

OTHERS IN THE GAME

Amersham Biosciences, the No. 3 player in the market, has refrained from entering the contest but said last week that it will bring to market a single CodeLink microarray product containing 40,000 probes in 2004.

NimbleGen Systems of Madison, Wisc., offers the whole human genome on an array for its microarray-analysis customers.

And, the European Molecular Biology Laboratory has created its own whole-human-genome microarray, comprised of cDNA probes, with hopes to offer the product to its scientific collaborators.

This rush to a product milestone, however, does not answer questions about the accuracy of the technology, the reproducibility of results, the sensitivity of the assays, and concordance between platforms that scientists as well as the FDA are increasingly echoing.

"Microarrays are a research tool to develop hypothesis, not a hypothesis tester," said Brockman.

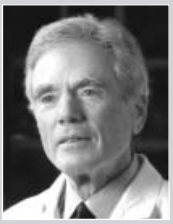
— *MOK*

Can Rich Guinea Pigs Change Health Care in the United States?

RALPH SNYDERMAN wants a pharmacogenomics revolution. But instead of the more traditional calls to use genotyping and gene-expression tools to revamp drug-discovery and -development protocols, Snyderman, CEO of Duke University Health Systems, wants to see PGx infiltrate the health-care continuum more quickly.

"We are now sitting on a great tsunami of biomedical research," he told attendees of last month's Genome Sequencing and Analysis Conference. Snyderman, who is also executive dean, Duke University School of Medicine, wants pharmacogenomics not only to treat disease, but to prevent it before it occurs — not a novel goal, to be sure, but one that may gain traction more readily thanks to a novel game plan, the help of a gene-sequencing pioneer, and some wealthy guinea pigs.

AT A GLANCE



NAME: Ralph Snyderman

TITLE: Chancellor for health affairs; executive dean, Duke University School of Medicine; president and CEO, Duke University Health System.

AGE: 63

EDUCATION: MD, Downstate Medical Center of the State University of New York

BACKGROUND: Vice president and later senior vice president at Genentech; assistant professor of medicine and immunology and chief of rheumatology at Durham Veteran's Administration Hospital

How do you think pharmacogenomics technologies can play a role in the health-care system in the United States, rather than just the drug-development continuum?

I think the first thing to make clear is the introduction of genotyping in regards to health care right now is more theoretical than practical. And one of the points that I made at the GSAC meeting in Savannah is that the major transformation of health care will be when we could develop and individualize risk assessment for individuals developing disease, so that we could truly try to practice preventative medicine in a personalized basis. In order to do this effectively, if you think of the time frame of disease, that most chronic disease develop over many, many years, that understanding an individual's susceptibility — even from the time of birth — will certainly inform an individual's personalized health plan.

So it stands to reason that at some point, genomics, by providing susceptibility information, will be part of a health-care system in which we try to intervene or prevent at the earliest possible time, rather than what we are doing now, which is treating after an event occurs.

The question is, 'How will genomic information be introduced?' We have a collaboration with Craig Venter to be thinking about, giving the power of sequencing anybody's genes, what do we do with [the sequence]? And if we were to sequence an individual's genes now, and say, 'How does that inform the practice of medicine,' today, that wouldn't be very helpful because we don't have a tremendous amount of insight as to truly what are the risk modifications in someone's genome. So we need to figure out how we're going to introduce genomic material in a way that makes sense.

Let me give you an example of what we're thinking about right now. We are beginning to engage in a project to try to determine individuals at risk at a very early age for developing obesity, and, as a consequence of obesity, diabetes, cardiovascular disease, and other things that are associated with obesity. And we're trying to develop risk-assessment tools.

I'd like to think … theoretically for a moment about how you can introduce genomics into that. To do a full sequence of everybody's genes would be nice, but it would exceed the capability of what we would be able to do [in regards to] costs and analyzing the information. However, from experiments at looking at knock-outs in mice, for example, it's already apparent that there are probably at least 40 genes that play a major role in determining susceptibility to obesity. These genes will probably affect different pathways and have different metabolic consequences. So what we are thinking about is based on the literature, maybe based on information with biotech companies that are doing knock-outs with many, many mice, identified genes of interest. For example, susceptibility to obesity, [or] susceptibility to diabetes. And if we are going to be dealing with a population to determine susceptibility to obesity, we would screen everybody in that group, initially for these particular genes — in other words, do genomic sequencing of these particular genes. And then follow over time, and see whether or not they really do predict the development of obesity, and, even more importantly, the association of obesity with other entities such as diabetes.

That's one of the ways we're thinking about introducing this now. The other thing that we will think about is, what are all the genes of interest that may be related to the development of cardiovascular disease, atherosclerosis? Then we would do a genotyping of these. What are the genes that may be associated with the development of prostate cancer? Ovarian cancer? We would do those as well. There are studies ongoing now at Duke where researchers are doing careful gene-expression analysis associated with breast cancer. And what is being found — this is work being done by Joe Nevins [director of the Duke Center for Genome Technology, one of five centers that make up the school's Institute for Genome Science and Policy] and Mike West [The Arts & Sciences Professor of statistics and decision sciences] — is that there are quite discrete patterns in gene expression in tumors that either do or do not metastasize, do or not have a very high mortality associated with them. Once we identify what these genes are, we would probably do a genotype analysis to see if the level of expression in the tumor is inherently based in the genomics of that individual. We would do this rather than just gene expression.

I guess what I'm saying is that we expect to introduce genomics analysis in a piecemeal basis based on diseases of interest, based on what we know very largely from other information as to what the genes of interest are. And then we will track people over time.

We are also thinking, but haven't yet decided whether this makes sense in individuals who come to us for executive health physicals. These are individuals who are usually senior officers of major corporations — people who can afford to get the very best for analyzing their own health; they come to Duke, or they may go to the Mayo Clinic, or other places. We're thinking of offering the option of a genotypic analysis of either all their genes, or genes of special interest to them, but the reason we haven't done it yet is that we don't know what the individuals can usefully do with this information since, other than worry about it, there isn't enough information there to know what is truly meaningful so that one would modify their behavior. But when Craig Venter and I initially started talking about how we might partner his … technology and understanding of genomics and Duke's capability of delivering … healthcare, one of the things we were thinking about is doing full genotypic analysis of all reading frames of genes for individuals who wanted to have this information. We just haven't gone ahead and done this yet.

Tell me about the pilot study at Duke that you mentioned during your GSAC presentation.

We're doing a few things in trying to develop tools to anticipate risk, and trying to intervene prior to adverse outcomes—what we're calling prospective medicine. And with CMS, we were given a grant to see whether r not early intervention as a development of a risk-assessment tool so that we could provide individuals with highly personalized information saying, 'Compared to a normal population, you have a 40-fold increased risk of having a heart attack within three years,' whether or not that would be helpful in modifying the outcome. Initially in that study, we are not using genomic information; we are using family histories. We expect down the road that that is exactly what we are going to do.

Let's say you wanted to know what are your risks for the top 10 major, potentially preventable diseases. What are you most susceptible to, and what do you need to do about it? Currently, we don't know how to use genomic information to get you that risk assessment. But we feel it's inevitable that within the next five years that more and more genomic analysis will be informing in determining an individual's risk. What we're trying to do is to develop the template in which we could insert genomic analysis. And that's what we're doing right now.

You said using genomic information for medicine is in the theoretical stage. What about the use of genotyping and gene-expression technologies in molecular diagnostics? Doesn't a test based on a cytochrome P450 mutation — a test used by many reference labs today — rely on genomic tools and information?

I wouldn't argue that there aren't ones [products based on genomic technologies or data] already on the market. And I think that's a very good example — the P450 series. I think that if you were to ask, 'Where will genomic analysis have the initial impact in the practice of medicine?' I think pharmacogenomics very likely is going to be an early use.

Back to your research with Venter: Is the aim to learn as much as you can from applying these technologies to wealthy executives, and then to move those discoveries and applications to, for lack of a better term, normal people?

We would like to. I don't know whether the volumes will be enough. What's ironic is that, one of the question you posed — How do you put genomic analysis into the current health-care system? — I think what you have behind that is, 'Will the current health-care system reimburse it or support it?' The answer is a resounding no. Absolutely no. So we have to find ways in which we have to deal with the reimbursement system and make progress.

In the executive health program, we have people who are paying their own freight. Ironically, at the other end of the spectrum — the indigent, or who have very little access to health care — there we could try to receive foundation funding, or funding from other entities to … put these analyses into large-scale pilot clinical project. Right now, the health-care system doesn't reimburse for this.

So the answer to your question is yes; we would try to do that. In order to get sufficient volumes to study, it's likely we'll have to do other things — such as having focused studies on obesity, cardiovascular disease, or maybe certain forms of cancer.

— Kirell Lakhman, Editor, SNPTech Reporter

BIOARRAY BRIEFS

LARK TECHNOLOGIES INC. ANNOUNCES TRADING SYMBOL CHANGE

Houston-based Lark Technologies, a microarray services provider which trades over the counter on the Nasdaq exchange, has changed its trading symbol to LRKT from LDNA as a result of the company's reverse/forward split.

ACCELR8 TECHNOLOGY CORPORATION TO TRADE ON AMEX

Denber-based Accelr8 Technology announced last week that it will begin trading its shares on the American Stock Exchange under the symbol AXK.

Accelr8 sells microarray slides and microtiter plates coated with its OptiChem activated surface chemistry.

EPIGENOMICS, SANGER INSTITUTE LAUNCH FIRST PHASE OF HUMAN EPIGENOME PROJECT

Epigenomics and the Wellcome Trust Sanger Institute announced this week the start of the first phase of the Human Epigenome Project (HEP) — an effort to map all the sites in the human genome where cytosine bases are modified by DNA methylation. The announcement follows the completion of an HEP pilot project that studied methylation patterns within the Major Histocompatibility Complex in chromosome 6 to determine the methylation status of over 100,000 sites. Data from the pilot study, which was funded by the European Union, was released today on the *HEP's website*. Commercial and academic partners will supply tissue samples for the project. Epigenomics will prepare the tissue samples with its high-throughput methylation analysis technology before they undergo sequencing by the Sanger Institute.

NATIONAL SCIENCE FOUNDATION ANNOUNCES 31 GRANTS FOR PLANT GENOME RESEARCH

The National Science Foundation announced late last week that it has provided 31 new grants worth a total of $100 million to support plant genome research. According to NSF, the two-to-four year grants, worth between $600,000 to almost $11 million, were provided to universities and institutions across the nation, including Indiana University, Florida State University, Rutgers University, the Fred Hutchinson Cancer Research Center, Yale University, and Cold Spring Harbor Laboratory. Among the projects being funded by the grants, said NSF, are six new plant genome "virtual centers," collaborations of various investigators to focus on a particular research goal. One, for example, will develop a scientific-community resource for studying genome-wide gene expression in corn, said NSF. A complete list of the grant recipients, as well as abstracts detailing their work, can be found on the *NSF website*.

EPOCH TERMINATES MGB ECLIPSE PROBE DISTRIBUTION DEAL WITH AMERSHAM

Epoch Biosciences said last week that it has terminated an arrangement under which its MGB Eclipse genetic analysis probe systems was distributed by Amersham Biosciences.

According to Epoch, it ended the deal because Amersham failured to meet contractually established sales goals for the system. In August, the company disclosed that it anticipated revenues from Amersham would be insignificant for the rest of the year and that its projected revenues for the full-year 2003 would be between $8.5 million and $9.5 million.

AGILENT AND STANFORD'S REYNOLDS CENTER COLLABORATE ON HEART DISEASE RESEARCH

Agilent Technologies announced last week a collaboration with Stanford University's Donald W. Reynolds Cardiovascular Clinical Research Center to study the basic mechanisms of heart disease.

Under the arrangement, the partners will use Agilent's gene expression and computational technologies to identify, characterize, and validate potential diagnostic and drug targets that could help prevent, diagnose, and treat heart disease.

Financial terms of the agreement were not disclosed.

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