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Weekly News Reports on Key Research Applications

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Newsletter	Application Focus	Published On
BioArrayNews.com	▪ Microarrays ▪ Gene expression ▪ Functional genomics ▪ Molecular diagnostics	Tuesday

BioCommerceWeek.com	▪ Diversified research tools suppliers:
	  ▪ Management
	  ▪ Marketing
	  ▪ Product development
		Wednesday

BioInform.com	▪ Bioinformatics ▪ Computational systems biology ▪ Pathways and modeling ▪ Research computing	Friday
CBA-News.com	▪ High-content screening ▪ Cell-based assays ▪ Cellular imaging ▪ Functional genomics	Friday
PGxReporter.com	▪ Pharmacogenomics ▪ FDA Regulation ▪ Reimbursement ▪ Theranostics	Wednesday
ProteoMonitor.com	▪ Proteomics ▪ Protein biomarkers ▪ Mass spectrometry ▪ Protein therapeutics	Thursday
RNAiNews.com	▪ RNA interference ▪ Gene silencing ▪ Micro RNAs and siRNAs ▪ Therapeutic RNAi	Thursday

Every newsletter provides forward-looking coverage of its application focus, including:

- In-depth business, technology, and research news
- Updates on patents, licensing, and IP litigation
- Technology transfer and translational research
- Funding reports, including research grants and venture capital
- Exclusive interviews with business, technology, and research leaders
- New product launches and upgrades
- Summaries of relevant research papers
- Management news: hirings, firings, and promotions

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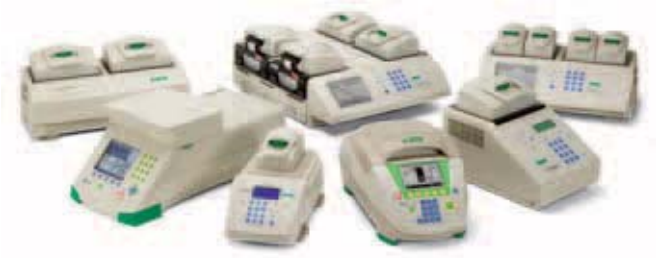

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BONUS: SNP GENOTYPING TECH GUIDE

June 2006

Genome Technology

Inside Integrated Biology

Exclusive! 4th Annual SALARY SURVEY

1,990 readers share salary, career, and benefits data.

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New Apps for Real-time PCR

Pathways: Welcome to BioPAX

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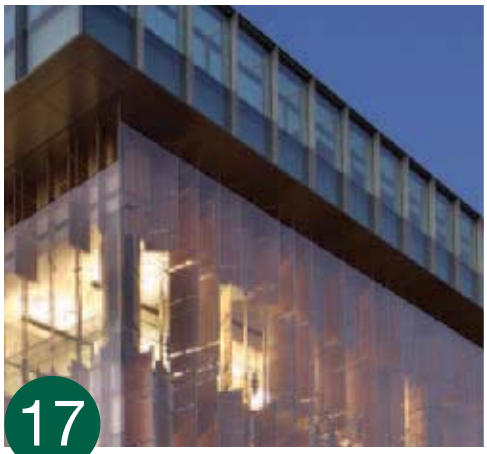
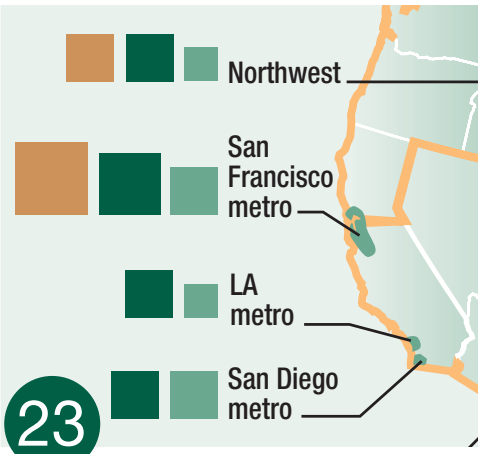
Genome Technology
Inside Integrated Biology

June 2006





UNDER ONE ROOF

Arizona's Answer to Systems Bio

TGen's Jeff Trent bills the new Center for Systems and Computational Biology as the home of 'multi-investigator, multi-institute teams with multimillion-dollar budgets.' It hasn't exactly been a tough sell.

By Jennifer Crebs

REAL-TIME PCR

PCR: The Conquests Continue

For 20 years, PCR has constantly evolved, making itself relevant to one new research field after another. The latest toeholds for real-time PCR: microRNAs, single-cell analysis, and clinical diagnostics.

By Meredith W. Salisbury

SALARY SURVEY

Your Money (and More)

Genome Technology's fourth annual salary survey shows that, for the most part, scientists are in better shape than they were a year ago. (Sorry, postdocs, not you.) A by-the-numbers look at the state of the field in 2006.

By Jennifer Crebs and Meredith Salisbury

ON THE COVER

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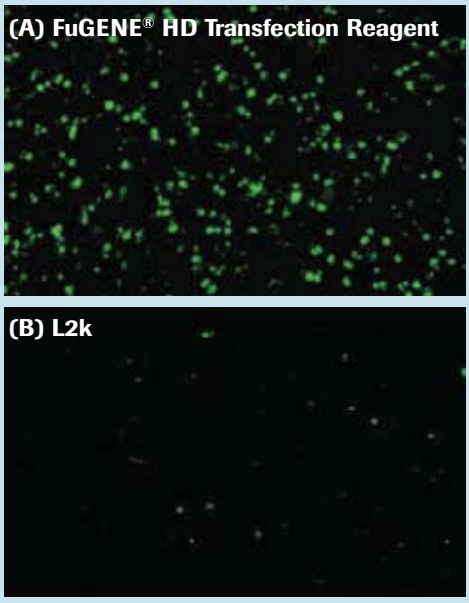

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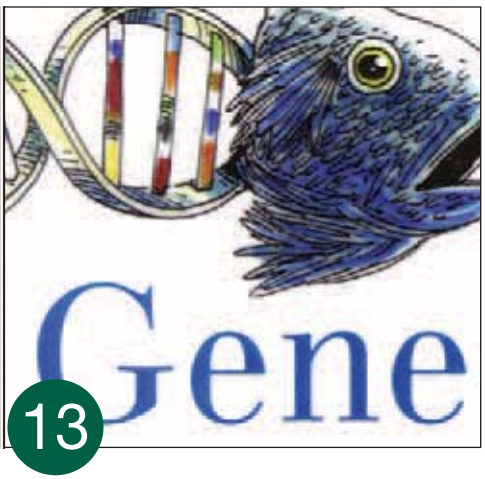
Inside Integrated Biology

June 2006



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columns

in every issue

spotlights

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Year Four: Still Going Strong

Wow. That's been the response around here as we tallied up the results of our fourth annual salary survey and saw just how many people took the time to share their job data. This year was our best yet for participant turnout, beating the previous record of about 1,500 with a whopping 1,990. Many thanks to all of you who filled out the survey — it's only with your cooperation that we can turn out such a useful resource for all of our readers. Let's face it: this may be the only earnings report of the year that you actually care about. You'll find it, seven pages of poked-and-prodded data goodness, beginning on p. 27.

Well, that probably cleared the room, but for the three of you who stuck around, we have lots of other great pieces in this issue. As a sidenote to our salary survey, we invited readers to submit their career-related questions to us so we could track down appropriate experts and get their advice for you. Again, response was overwhelming: as I write this, one of the piles on my cluttered desk is reserved for the six densely packed pages of questions you sent in. (Our favorite: "Why did I choose this field? What abnormality led me to low pay, long hours, zero hope of efficient training, a future postdoc and assurances that I will not have a stable [tenured] job until I am 45 years old — if even then?" Whoever you are, we're not sure what the answer is. If some diligent genotyper homes in on that abnormality anytime soon, we'll let you know.)

Not surprisingly, many of you want to know about negotiating tactics: increasing your salary, scoring a promotion or a raise, convincing an organization that you're the right person for the job. Another common query was about networking skills. (For what it's worth: after getting cornered by the bar at a conference dinner earlier this year, I realized that during the course of the evening I had seen and chatted with a good half the folks in the room, simply because I was standing nearby as they waited for their drinks. It's definitely an effective strategy for mingling.) We combed through the suggestions, pulled out the most commonly asked questions, and found people in the field who had experience in those areas. Their advice and practical tips for early career, late career, and everything in between can be found starting on p. 32.

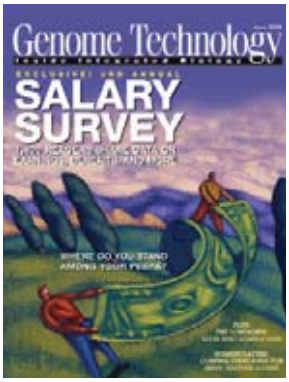
Also in this issue, you'll find a profile of the new Center for Systems and Computational Biology, a joint initiative between Jeff Trent's TGen and the Arizona State University's Biodesign Institute, headed up by George Poste (longtime readers may remember that both men appeared on *GT* covers in 2002 for their pioneering work). The center's unusual approach has even eschewed specialized core labs in favor of integrated technology facilities spanning many different disciplines — an interesting model that may very well gain proponents at other institutions as this kind of center becomes more common. You'll find that story, from senior editor Jen Crebs, on p. 17.

Meredith W. Salisbury, Editor

WHERE ARE THEY NOW?

GT In Years Past

Hello Salaries, Goodbye FGT, Welcome Standards



June 2005

One year ago in *Genome Technology*, the magazine featured its third annual salary survey, for which we boiled down salary data offered by 1,447 respondents. Compared with the results from two years back, which were based on the answers provided by 1,180 of you, last year's forecast indicated that the field's economic roller coaster had finally hit a brake run. As we reported at the time, salaries were holding, pay cuts weren't as widespread as before, and layoff rates were comparable to those in the previous year.

This year, we're continuing the salary survey tradition with our cover story, and it looks like the field is continuing to enjoy an economic springtime. Salary ranges are on the rise, company-wide layoff rates continue to drop, and raises are slightly up from last year. For those of you who did receive a recent bump up in pay, the percentage increases were significantly higher than those reported last year. Responses this year were also tracked in regions outside of the US and Canada, so we'll be able to report on global salary trends in this and future issues. For details on all of this and more, check out this year's results, starting on p. 23.

In last year's issue, we also spoke with Andy Feinberg about his work to trace loss of imprinting of the IGF2 gene, an epigenetic mutation that he found increases the chance of developing intestinal tumors. Soon after the issue published, Feinberg teamed up with Orion Genomics to develop a colon cancer molecular diagnostic test based on methylation patterns. Since then, Feinberg has joined in the call for a Human Epigenome Project, and most recently delved into the epigenetic bases of cancer for attendees at an AACR meet-the-experts session.

Five years ago, our cover story focused on the early days of First Genetic Trust, the biobanking business set up by Arthur Holden and Andrea Califano. Califano left the firm in 2003 for a faculty post at Columbia University, where he leads several bioinformatics and systems biology research efforts. First Genetic Trust, meanwhile, shuttered its operations late last year. Arthur Holden has been appointed as Illumina's senior vice president of corporate and market development.

Hiroaki Kitano appeared in these pages five years ago, back when his international conference on systems biology was still a newbie. The meeting kicked off in Tokyo in 2000 and will return to Japan — Yokohama, to be precise — for its seventh incarnation this October.

The Human Proteome Organization was also in the news five years ago, back when it was little more than 24 advisory members hashing out initial goals in a McLean, Va., conference room. HUPO has come a long way since then, having even established an international secretariat in Montreal last summer. Most recently, leaders of the organization's Proteomics Standards Initiative met to work out ways to integrate MIAPE standards with publication guidelines. Realizing that marrying disciplinary and presentation norms is hardly specific to proteomics, scientists at the meeting called for the construction of a central registry of reporting standards. We'll let you know as soon as more meta-information about minimum information comes to a white paper near you.

June 2001

— *Jen Crebs*

COMING UP

Next Month in GT

Don't miss these features in the July/August issue:

Funding: NIH & beyond

After years of double-digit increases in NIH funding, systems biology researchers are faced with an NIH budget crunch. *GT* will provide an in-depth look at where NIH dollars are going — and how readers can grab their share — as well as external funding opportunities available for this field.

Pharmacoproteomics

More and more, proteomics-based companies are proving their value through collaborations with big pharma. This story will examine how these partnerships work, and how pharma researchers are advancing their work thanks to the integration of proteomics data.

Roundtable

This year's roundtable theme: setting up the lab of the future. In this second installment, experts discuss informatics and data handling issues for the cutting-edge laboratory of tomorrow.

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25 YEARS ADVANCING SCIENCE

MARKERS
News Roundup

Short Reads

Thermo Electron and **Fisher Scientific** announced a $10.6 billion all-stock merger. The combined company will be called **Thermo Fisher Scientific**. Fisher's CEO **Paul Montrone** will step down, and Thermo CEO **Marijn Dekkers** will become president and CEO of the new entity.

The UK's **Biotechnology and Biological Sciences Research Council** has awarded £27 million to create three new centers for integrative systems biology at the **Universities of Edinburgh**, **Nottingham**, and **Oxford**. These will join the three other centers created last year at **Imperial College**, **Manchester**, and **Newcastle**.

In an attempt to settle their patent dispute, **ABI** parent **Applera** and **Beckman Coulter** have agreed to pay each other royalty-bearing licenses for their respective technologies. The settlement resolves "all outstanding legal disputes" regarding Beckman's CE and PCR technologies, as well as Applera's breach-of-contract allegations.

The **Virginia Bioinformatics Institute** and Brazil's **Oswaldo Cruz Foundation** have teamed up to develop drugs, vaccines, diagnostics, and other technologies for infectious diseases, which include dengue fever, HIV/AIDS, hepatitis C, influenza, pneumonia, and malaria.

METAGENOMICS

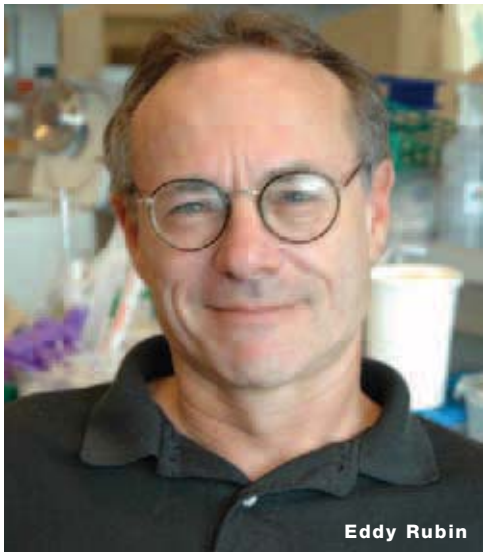
FROM JGI, COMMUNITY ARCHIVES FOR THE MICROBIAL SET

More than 250 microbial genomes have been sequenced to date and, with 700 more projects in the works, making sense of that flood of data has never looked more daunting. This is no surprise to scientists at the Joint Genome Institute, which has spearheaded nearly a quarter of the world's bacterial genome projects. To help researchers make sense of it all, the institute recently launched IMG/M, an experimental metagenome data management and analysis system.

"IMG/M arose from our interest in making it easier for users to access and analyze their data," says JGI Director **Eddy Rubin**. Advances in sequencing technology have made it possible to sequence a microbial genome in a day, he says, which presents the risk that some genomes will be neglected due to the sheer volume of data available.

Hence the creation of IMG/M, which builds on JGI's integrated microbial genomes (IMG) system and extends its comparative tools to metagenome data. The IMG system, built through a collaboration with Lawrence Berkeley National Lab, is updated quarterly and contains both draft and complete JGI genomes, in addition to other publicly available microbial genomes. Researchers interested in analysis, as opposed to just browsing the bank, can navigate the samples by phenotypes, ecotype, disease, and relevance.

According to **Victor Markowitz**, head of Lawrence Berkeley National Laboratory's Biological Data Management and Technology Center and the system's chief architect, the idea was always to broaden IMG's remit. "Once we had IMG, we asked what it would take to extend [the system] to metagenomes," Markowitz says. It took a lot, especially in terms of conceptual organization of the raw data. Whereas IMG charts isolate genomes for which assembly and gene prediction is done, IMG/M must contend with data from entire microbial communities for which assembly scaffolds come from different organisms.


Eddy Rubin

Given those complexities, the LBNL team forged ahead to create a repository capable of evolving with its diverse data sets. Working on the system mostly on weekends, the group built IMG/M over a period of five months, and a preliminary version was distributed for expert testing at the end of last year. One of the early users, JGI's **Phil Hugenholtz**, test drove the system to analyze enhanced biological phosphorus removing (EBPR) sewage sludge metagenomes, which yielded results slated to appear in an upcoming paper.

Hugenholtz also helped train the system on other microbial communities recently sequenced by JGI, including microbes colonizing the termite hindgut. "Termites are world-class biomass converters," says Rubin, and understanding those metabolic pathways may help meet "one of our greatest needs to convert cellulose into starch for alternative fuel development."

In addition to isolate genomes found in IMG 1.3, the current version of IMG/M contains metagenomic sequences generated from several environmental samples. At press time, there were data from two EBPR

sludge samples, three deep sea "whale fall" carcasses courtesy of Rubin's team, an agricultural soil sample, and an acid mine drainage biofilm. These samples are representative of a range of species diversity, dominant organism abundance, and sequencing depth.

The next version of IMG/M is slated for July 1, when IMG will also be loaded with more isolate genome data. After that, both repositories will be updated quarterly. "We're committed to progressively adding and annotating everything that [JGI] sequences or that is sequenced elsewhere," Rubin says, adding that the continual updates coupled with IMG/M's easily navigable interface make "it a really killer application." — *Jen Crebs*

OPTICAL MAPPING

OPGEN'S NEW PATH: SEQUENCE DEMAND, INSTRUMENT LAUNCH

Little OpGen, which made its debut in 2003 and the following year boasted a single customer, has by all accounts truly turned a corner. The company, which initially planned to have a service-only model for its optical mapping technology, recently announced a deal with an instrument manufacturer to turn that tool into a product customers could bring in-house. With close to 50 customers last year, the potential of demand from the next-generation sequencing market, and new scientific advisors **Bud Mishra** and **Thomas Anantharaman** from New York University, the OpGen of 2006 is a whole new animal.


Joe Shaw

In April, OpGen teamed up with Stratos Product Development to come up with a commercial instrument based on the four machines currently running at the company. A similar alliance with Micronics, meanwhile, is aimed at designing the disposable reagents for the instrument.

The new business model — a shift from services to placing instruments with customers — stems from a demand that OpGen couldn't meet, according to CEO **Joe Shaw**. "The service business is doing well, but demand, frankly, is exceeding our capacity," he says. Take that and combine it with the reluctance of potential customers to hand off their DNA samples or sequence information to an outside company, and you've got a good argument for selling instruments, Shaw says. Whether any single customer has high enough demand to justify buying an instrument, however, remains to be seen.

Shaw and his crew will first target the clinical microbiology community with the instrument, which is expected to run around $225,000 and be in beta testing by the first quarter of next year. Since optical mapping is often used to detect isolates of a particular organism, for instance, Shaw says it's a natural fit for situations such as identifying an infectious agent — and possibly even being used to help fit a particular antibiotic treatment to a patient.

Meanwhile, demand for OpGen's technology has gotten a somewhat unexpected boost with the next-generation sequencing tools on the market. Techniques like 454's, which produce much shorter reads than traditional Sanger sequencing, are helped

Seymour Benzer, **Caltech**'s *Drosophila* genomics pioneer, received the $500,000 Albany Medical Center Prize, which is the US's largest monetary award for medicine and biomedical research.

Danish drug developer **Santaris Pharma** has created a MicroRNA Research Consortium in partnership with the Department for Medical Biochemistry and Genetics at the **University of Copenhagen**. The new consortium is partially supported by a grant from the the **Danish Advanced Technology Foundation** worth €1.3 million, which will be matched by the University of Copenhagen and Santaris Pharma.

Millipore has plans to acquire **Serologicals** for $1.4 billion in cash — which is about how much revenue the combined company will make this year. The acquisition will close on June 30.

Pelican Life Sciences, one of the newer reagent shops on the block, has raised $100 million in private equity for acquisitions and development. The company also completed its first acquisition, that of **PML Microbiologicals**, originally announced last December.

Third Wave Technologies has made two new appointments to its senior management team: **Jorge Garces** has been appointed vice president of product and platform development, and **Cindy Ahn** has been appointed vice president and general counsel.

MARKERS

News Roundup

The Nasdaq exchange has given **Sequenom** until June 15 to comply with its minimum closing bid price requirement (that's $1.00) and remain listed on the exchange.

The times are a-changin' for **Affymetrix** management. **Susan Siegel** resigned from her position as president, but will stay on as an advisor reporting to chairman and CEO **Stephen Fodor**. **Thane Kreiner** is now senior veep of marketing and sales, while **Richard Rava** has been appointed head of product development. **Mitchell Kennedy**, previously VP of global technical support, has left the company.

The **NIH** has awarded a $1.58 million grant to researchers led by **Thomas Earnest** at **Lawrence Berkeley National Laboratory** to develop new robotic systems for high-throughput protein crystallography and related structural biology research.

UK-based **BioWisdom** has joined the AddNeuroMed project of the European Commission's Innovative Medicines for Europe consortium, where it will use its Sofia software platform to help identify and validate Alzheimer's disease biomarkers.

Reagent company **Panomics** has opened a wholly owned European subsidiary, **Panomics SRL**, located in Milan, Italy. **Bio-Rad** alumnus **Luigi Pirovano** was named managing director of the new unit.

along by a long-ranging scaffold from which to hang the reads. **Colin Dykes**, OpGen's CSO, says that optical maps "can certainly work as a scaffold" for this type of read, and complement the base-by-base information with higher-level data including rearrangements, insertions, and deletions. Shaw says OpGen has had "a number of clients" who have approached the company because they couldn't properly assemble 454 reads. Given that Solexa, Helicos, Agencourt, and other next-gen sequencing technologies nearing the market all share the short-read problem, OpGen could be well positioned to introduce its technology to a whole new clientele.

The company is currently in the process of closing a new round of funding worth about $15 million, Shaw says. In another change for the OpGen crew, longtime scientific collaborator **David Schwartz** is no longer closely tied to the company, Shaw confirms. Instead, Schwartz's former NYU colleagues Mishra and Anantharaman have joined the company's scientific advisory board. — *Meredith Salisbury*

MOLECULAR DIAGNOSTICS

INVITROGEN, BUILDING DX PLAY, WELCOMES COMPETITION

Invitrogen, aiming to expand into the molecular diagnostics market, made a deliberate splash in the field at this year's annual BIO meeting, held in Chicago. Three out of the seven sessions at which the company had speakers centered around diagnostics.

Todd Nelson, vice president of corporate development at the life sciences powerhouse, said at a molecular diagnostics session that what is now competition from small, private shops will eventually become "collaboration" opportunities for Invitrogen, which has grown in size and scope in recent years by adhering to a diet of steady acquisitions.

In fact, Invitrogen disclosed one such collaboration during the conference — a deal with Germany's Signalomics to develop nanocrystal reagents to identify tumors *in vivo* in patient tissue. The agreement continues a joint development program between Signalomics and the BioPixels business unit of BioCrystal, which Invitrogen acquired in October 2005.

Invitrogen's interest in the molecular diagnostics industry has been building over the past couple of years and the company has made a string of acquisitions to bolster that play. In particular, its purchases of Molecular Probes in 2003 and its acquisitions of Dynal, Caltag, and BioSource last year were made with an eye on grabbing a chunk of the molecular diagnostics market.

The firm furthered this goal in January when it realigned its BioDiscovery unit into two divisions, Life Sciences and Enabling Technologies. The Enabling Technologies division, which now primarily targets the research market, will focus on nanotechnology, imaging and microscopy, cell separation and analysis, labeling and detection, bead-based separations, and the firm's antibody center of excellence.

At BIO, Nelson said he was "thrilled" that privately held companies have been developing technologies to play in a space for which Invitrogen is gunning. Specifically, he said he was glad that as these companies grow, they are transferring the "burden" of risk to venture capital companies — and presumably off of potential suitors — which will enable them to develop a wide array of diagnostic technology.

To be sure, Nelson's remarks do not necessarily signal that Invitrogen has a molecular diagnostics acquisition in the works. But while Invitrogen remains tight-lipped about its plans for this arena, Nelson said that one area of interest for the company could be "enabling" pharmaceutical companies that want to partner with diagnostic shops to develop companion drug-diagnostic products, or so-called theranostics. According to Nelson, this is an area of "exceptional growth." — *Kirell Lakhman*

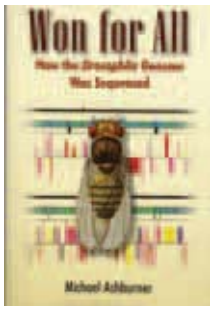
BOOK REVIEWS

In honor of summer, *Genome Technology*'s staff turned toward books that might make great beach reads. Here are a couple that won't weigh down your tote bag.

Won for All: How the *Drosophila* Genome Was Sequenced

By Michael Ashburner

Described by the publisher as a "nonfiction novel," Ashburner's memoiresque *Won for All* is aimed at people who were involved in, or at least intrigued by, the sequencing of the *Drosophila* genome. The book, roughly 100 pages, is the author's cathartic tale of what he went through during this period (including memories of hotels, flights, and limo service) and the main text refers to most fellow participants by first name only. It's an entertaining and quick read, but will likely be of interest mainly to people who are already fairly well acquainted with the field and events discussed.



Publisher: Cold Spring Harbor Laboratory Press
Publication date: March 1, 2006
ISBN: 0879698020

When a Gene Makes You Smell Like a Fish ... and Other Tales about the Genes in Your Body

By Lisa Seachrist Chiu

Chiu offers to take lay readers on an engaging road trip through the human genome with her debut book, pointing out sights both strange and fascinating along the way. The book's title hearkens to the story of a woman who suffers from trimethylaminuria, a metabolic disorder determined by mutations in the FMO3 gene. Plenty more genes, mutations, and their consequences are deftly explained via Chiu's anecdotal vignettes. Non-specialists will not only be entertained by a catalog of weird genes, but may also come away with a basic understanding of epigenetics, the HapMap project, and classic genetics.

Publisher: Oxford University Press
Publication date: May 1, 2006
ISBN: 0195169948

MARKERS

News Roundup

BIOMARKERS

NASA SOFTWARE AIDS CANCER RESEARCH

Cancer research and planetary science are fairly distant cousins in science's family tree, but that doesn't mean they have nothing in common. With help from researchers at CalTech's Jet Propulsion Lab, one technology is being used to organize and share data from both quarters.

Just as biologists mine clinical data for evidence of biomarkers heralding the early onset of cancer, planetary scientists must manage diverse physical samples to substantiate theories about what's happening in more remote corners of the universe. This analogy wasn't lost on the National Cancer Institute, which recruited JPL's **Daniel Crichton** to implement a software framework his group initially developed for NASA to share planetary data across geographically distributed research centers.

That effort, known as the Object Oriented Data Technology, plugs into existing systems and provides an architectural framework for integrating information across diverse networks. This key feature allows researchers from different sites in NCI's Early Detection Research Network to share clinical data that would otherwise be buried in a babel of homegrown terms.

The common data elements endorsed by the EDRN are harnessed by Crichton's OODT implementation, and provide a lingua franca for describing biospecimens. There are 90,000 specimens currently catalogued, which are parsed by more than 600 common data elements. So far, the informatics framework is live and connecting nine sites via the EDRN Resource Network Exchange, which is NCI's virtual specimen bank. Crichton says that 15 sites will be sharing data by the year's end.

By providing a common language to describe biospecimens, the NCI hopes to foster collaborations across different sites to identify and classify putative biomarkers. To that end, JPL's team is currently at work on a system to capture and manage data coming out of biomarker validation studies. Known as the EDRN Knowledge Environment, this will provide "a one-stop shop for looking at information" like clinical data, protocol information, specimen descriptions, and details on the biomarkers themselves, Crichton says. The JPL team expects to have informatics tools and infrastructure in place by the end of the summer. *— Jen Crebs*

A Pathway to Pathways

When you could count the number of pathway databases on your fingers, parsing the data wasn't problematic. With the plethora of databases now, though, the BioPAX effort aims to help scientists make sense of it all. Participant Joanne Luciano outlines the initiative.

Wouldn't it be nice if you could load ligand, receptor, signal transduction, gene regulation, and metabolic pathway databases into your local database — and then be able to traverse them from a ligand binding to a cell surface receptor, through a signaling pathway that turns on a gene for an enzyme that catalyzes a metabolic reaction? We're not quite there yet, but an effort called BioPAX is making strides in turning this into a reality.

BioPAX is a community-based initiative founded to create a formal standard for data exchange and representation of biological pathways and their nuances. When there were only a handful of pathway databases, writing a few parsers was not an issue. But as the number and type of databases began to increase, researchers rallied to head off the impending integration nightmare. What emerged was BioPAX, whose ontology was created to enable integration of the increasing number of pathway databases that began mushrooming about five years ago.

THE PROBLEM WITH PATHWAYS

That biological pathways are central to biomedical research is no surprise to this community; they are the scaffold upon which we build our knowledge about biological mechanisms.

Pathway data is typically divided into metabolic pathways, molecular interactions, gene regulation networks, and signaling pathways. Metabolic pathways are characterized as a series of enzyme-substrate-product reactions. Molecular interactions, such as protein-protein interactions obtained from yeast two-hybrid experiments and used to identify the interacting components of complexes, are usually simplified as simple binary interactions. Meanwhile, gene regulation pathways show interactions between transcription factors and the genes whose transcription they activate or repress. And signaling pathway representations, the most varied, range from vague and general representations such as 'There's an activation chain in which A activates B activates C' to specific and detailed representations involving a series of complex binding reactions and protein post-translational modifications.

PathGuide, an online list of pathway resources, contains more than 200 biological pathway resources, and the list continues to grow in number as the databases grow in size. But how much of this pathway data is useful? If you're a biologist and need to order reagents for your experiment, or you are new to the subject and want a quick learn, then a visual representation of a pathway is most helpful. It is easy to understand, informative, and, after all, a picture is worth a thousand words. On the other hand, if you are a bioinformaticist or a research scientist and want to integrate these pathways into your knowledge base, then you'd rather have the thousand words. Images can't be read with computer programs, so they're essentially useless when it comes to computation.

Currently, to consolidate the knowledge required for many research projects, one must extract the relevant pathway data from each database, transform it into a standard data representation, and load it into an integrated repository. If you want to navigate through databases, then your best bet — and, in fact, your only hope at the moment — is to use gene and protein IDs.

But you still have a lot of work to do if you want to integrate data from different databases, because the semantics of those databases are not the same: different terms are used to describe the same thing, or in some cases the same name is used for two things. Without a human to do the mapping, there's no way for a computer to figure out the connections.

ENTER BIOPAX

And that's where BioPAX comes in. Its main goal is to create a formal representation whereby multiple types of pathway conceptualizations can be brought together into one framework. So far, only a few databases export their data in BioPAX format, allowing the aggregation of these data and queries across the datasets. Stanford has created the first public resource based entirely on BioPAX data, the Pathway Knowledge

INFORMATICS INSIDER

Base, which aggregates data from BioCyc, KEGG, and Reactome.

That's one type of integration, the aggregation of data. It is based on being able to tell whether two things are the same or different by comparing their database identifiers. The mapping of those identifiers, however, is done by humans; integration based on matching identifiers doesn't embed much in the way of semantics. For example: here's a BioCyc pathway, here's a KEGG pathway — are they the same? By contrast, an example of semantic integration is the ability to infer whether things are the same based on their descriptions. One plus one may equal two, but it's not identical to two. So is the reaction A + B ↔ C the same as C ↔ B + A?

We would also like a reasoner to be able to infer and properly map different levels of descriptions for the same entity. This would enable two sources with different levels of detail to be integrated, such as a database with protein-protein interactions with a database of kinases, or a database of chemical compounds structures with a database of reactions that involve those compounds.

BioPAX is also wrestling with more subtle issues in biological representation, such as how to handle incomplete knowledge of mechanism, the combinatorial explosion of protein states, and ambiguous representations such as polymerization reactions.

Currently, pathway data can be exchanged and aggregated in BioPAX format, but we're still working through representational issues of pathways in OWL in order to use an automated reasoner to determine whether two things are the same or different based on their descriptions rather than their identifiers. Furthermore, we want a reasoner to be able to point out when experts don't agree. BioPAX will never be able to resolve the differences of opinion, of course, but it can highlight them so that someone with the right skill and initiative can undertake the experiments that would be needed to resolve the disagreement. OWL, description logic experts, reasoners, domain experts (such as the database providers), and knowledge engineers and users are all required, and that's why BioPAX is a community effort — one that hopes to provide researchers with a pathway to pathways. GT

Joanne Luciano is a lecturer in the Genetics Department at Harvard Medical School, a visiting research fellow at the University of Manchester, and president and founder of Predictive Medicine. She is a co-organizer of the BioPathways Consortium and a member of the BioPAX Workgroup.

Arizona's Answer to Systems Bio

TGen's Jeff Trent bills the new Center for Systems and Computational Biology as the home of 'multi-investigator, multi-institute teams with multimillion-dollar budgets.' It hasn't exactly been a tough sell.

By Jennifer Crebs

Make room, Boston. Flush with cash dedicated to biosciences, Phoenix may be well on its way to becoming the biotech hotbed of the southwest. The latest in the Sun Belt arsenal is the Center for Systems and Computational Biology, a team solution to the challenge of team science.

The Center for Systems and Computational Biology is housed in Arizona State University's Biodesign Institute

Not yet even six months old, the center is the product of a close partnership between Arizona State University's Biodesign Institute and the Translational Genomics Research Institute. Its mandate is to jump-start advances in personalized medicine and diagnostics, a likely endeavor considering everything the center has going for it: top-tier faculty, both co-appointed and newly recruited especially for the job; access to one of the world's most powerful supercomputers; a roster of high-level genomic and proteomic technologies; and enviable funding streams from state, industry, and philanthropic sources. The only thing it lacks at the moment is a dedicated director.

In the interim, George Poste and Jeffrey Trent are jointly steering the center through its initial months. Trent, president and scientific director of TGen, was instrumental in rallying state and taxpayer support to build up Arizona's bioscience industry. Immediately prior to taking up his post at TGen, Trent spent nearly a decade as scientific director of the National Human Genome Research Institute. In 2004, he took on the lead role at TGen; not long after, George Poste was lured out of his retirement from SmithKline Beecham to man the helm at the Biodesign Institute. Trent says that the two have shared a good working relationship "for 25 years or so." Most recently, the two co-directors have concentrated on building the infrastructure and faculty to achieve "an endpoint of earlier diagnostics and smarter treatments."

To do so, the Center for Systems and Computational Biology is drawing on the strengths of both of its parent institutions. "TGen is unique from the standpoint that we have really focused on the translational window a little differently," Trent says. That is, instead of cobbling together an interdisciplinary program within the confines of a larger matrix, TGen has integrated its translational research efforts from the get-go.

This tack is complemented by a similarly cohesive strategy at the Biodesign Institute, which sports a research portfolio that defies standard classification schemes. The institute organizes its efforts around four key areas — biological systems, nanoscale systems, cognitive systems, and sustainable systems — and focuses on translating fundamental biological discoveries directly into real-world use. To this end, Biodesign works with ASU's commercialization body, Arizona Technology Enterprises, to strike up partnerships, license IP, and launch new companies.

Biodesign's commitment to commer-

UNDER ONE ROOF

Harnessing Diverse Research Tools

cializing technologies is echoed by TGen's focus on translating basic research to the clinic, and the underlying emphasis on moving research findings out of the lab is a part of the center's mandate as well. "Given some of the spinoff organizations we have, we're trying to move toward developing diagnostics or getting preclinical testing done on therapeutic leads — toward building all of that into the fabric of putting this together," Trent says. The Molecular Profiling Institute is one such spinoff company that provides prognostic testing facilities, services, and resources for genomic and proteomic profiling.

FORMALIZING THE INEVITABLE

While it's clear that researchers at Biodesign and TGen have already forged extensive working partnerships among research groups, the new center gives them a formal framework. "What we're trying to do is work on bigger projects, and those require multi-investigator, multi-institute teams with multi-million dollar budgets," says Trent. "I see [the center] begin to take its shape in the ability to capture the people for some of these larger projects."

One such person is Michael Bittner, co-director of TGen's computational biology division and head of the measurement and inference lab. Bittner is interested in flushing out background assumptions made about complex systems, wherein the sheer number of possible relationships outpowers the human faculty of tracking them. Enter high-performance computing, which Bittner uses to model, predict, and generate reliability estimates about gene interactions. The end goal of his work is to develop new measurement systems capable of identifying valid relationships within complex systems. Bittner, who already collaborates with Sudhir Kumar, director of Biodesign's Center for Evolutionary Functional Genomics, says that it was natural for him to get involved in being one of the partners of the center.

InfoSpot

Name: Center for Systems and Computational Biology
Hosts: The Translational Genomics Research Institute (TGen) and Arizona State University's Biodesign Institute
Leadership: Jeffrey Trent and George Poste head the center right now, while a newly recruited director will take the reins by summer's end.
Staff: Currently, the center is populated with about a dozen faculty members from Biodesign and TGen. Eventually, plans are to outfit the center with 20 faculty posts.
Funding stats: The center is one of the latest fruits of Arizona's heavy investment in bioscience research. Taxpayers voted in 2000 to drive $1 billion to state university research support. The center also benefits from the state legislature's pledge of $150 million to foster bioscience research, which was matched by industry investment. To recruit a dedicated director, the center will use $5 million from the Virginia G. Piper Charitable Trust's outlay of $50 million to attract personalized medicine leaders.
Key research areas: Computational biology, integrated cancer genomics, genetic basis of human disease, clinical translational genomics, applied nanobioscience, evolutionary functional genomics, innovations in medicine, protein and peptide therapeutics.
Notable technology: The ASU-TGen supercomputer, a 1,024-CPU IBM cluster ranked as one of the top supercomputers in the world.

"Typically, projects that deal with complex systems or complex problems do much better when there's a larger mass of people simultaneously attacking various aspects of it," he says. "We think the center will give us the chance to recruit some very smart people who are going to help speed the plow."

John Carpten, director of TGen's integrated cancer genomics division, agrees that more is merrier when it comes to speeding discoveries to the clinic. Carpten's research focuses on developing more sensitive cancer biomarkers by way of generating comprehensive profiles based on multiple data points. "I don't think any one scientist or any one technology will win the war on cancer," he says. Instead, he believes that successful cancer research requires a team research approach and an integrated technology model — two things that the center promises to provide in spades. "Having an entire center dedicated specifically to helping us integrate different technology platforms is going to be critical to moving these discoveries into the clinic," he says.

Specific tools in Carpten's arsenal include microarray and high-throughput sequencing technologies, as well as the strong collaborations he's initiated with facilities boasting high-resolution mass spectroscopy platforms. Whereas a number of institutions have strong programs in genomics or proteomics, he says, very few are performing comprehensive studies using one data set on multiple technology platforms. Carpten says his "hope is to bring to bear gene expression profiling, copy number analysis, promoter methylation, DNA mutation, as well as proteomics" on cancer research. Having access to the center's resources and infrastructure will therefore be a "huge advantage," he says.

Next up for the center will be the installation of a new director, which Trent expects to happen by the end of the summer. Additional faculty are also being recruited, and these investigators will have joint appointments with the founding research institutes. Getting funding to attract talent is hardly a problem. "At the moment, Arizona has a ridiculous wealth of opportunities to build the biomedical sciences," Trent says. "The bottom line is that Arizona is one of these remarkable places that's really growing and for which there is a lot of funding to facilitate research." GT

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Applied Biosystems

25 YEARS ADVANCING SCIENCE

PCR: The Conquests Continue

For 20 years, PCR has constantly evolved, making itself relevant to one new research field after another. The latest toeholds for real-time PCR: microRNAs, single-cell analysis, and clinical diagnostics.

By Meredith W. Salisbury

For people who aren't working on the cutting edge of the amplification field, it can be hard to get excited about PCR. Hey, it's understandable for a technology that's been a mainstay of this community for 20 years. But for people who pay attention to the tool as it continually expands into new research applications, each evolution of real-time PCR is a breakthrough unto itself. Thanks to the versatility of the amplification technology, it makes its mark on virtually each new research field, schmoozing with whole new groups of scientists until they, too, find they can't live without it.

This has been the modus operandi of PCR throughout its lengthy career. Beginning in 1985 with Kary Mullis' inspired plan to get strands of DNA to make copies of themselves, the tool has kept up with the times. One major evolution was the invention of reverse-transcription PCR, which allowed researchers to use RNA strands as the template; another was the development of real-time PCR, also known as quantitative PCR because it gave scientists the ability to quantify mRNA. Over the years, various other improvements, large and small, included finding a thermostable enzyme, specialty enzymes for higher fidelity and longer read length, hot start PCR, higher-throughput reactions, and identifying optimal concentrations and read lengths. These technical advances have all served to put PCR in the hands of people for whom it wasn't previously a viable tool.

These days, PCR — especially the real-time version — continues to extend its reach. According to experts who spoke with *Genome Technology*, three major areas into which real-time is currently taking hold are in RNAi, applications with smaller sample sizes, and the clinical and diagnostic arena. Beyond that, indicators show that real-time PCR has a whole host of other applications for which it's just starting to heat up.

RNA INTERFERENCE

Ask anyone who's running real-time PCR about what they're doing today that they weren't doing a year ago, and one term is virtually guaranteed to pop up: microRNAs. Vladimir Benes, who runs a genomics core facility at EMBL, says his lab has seen "microRNA profiling by qPCR, which definitely was not the case even a year ago."

"Before the RNAi explosion, people were looking at gene expression," says Tony Favello at Sigma-Aldrich. "Now they're looking at changes in gene expression and knockdowns."

But researchers' yen to quantify their microRNAs wasn't a technically simple feat for PCR vendors. Weighing in around just 22 bases, microRNAs proved an especially difficult target for amplification and detection. Applied Biosystems, which launched its microRNA assays this spring, finagled the technology to get it to work in this burgeoning field. "We do a little bit of a trick to use the real-time PCR for microRNA quantitation and detection," says Kathleen Shelton, senior product manager for microRNAs at ABI. The technique relies on an "RT-specific step where we extend the product … [so we are] able to get the specificity, sensitivity, and reproducibility that you get with regular TaqMan." So far, ABI has microRNA assays out for human, mouse, and rat, with plans to launch

Tony Favello, Sigma-Aldrich

Arabidopsis, *Drosophila*, and *C. elegans* shortly. Shelton says her team relies on the information deposited in public databases for sources on which to design their microRNA assays. Additional assays will be developed as data from more organisms is deposited in the public domain.

ABI certainly isn't the only vendor anticipating growth in this arena. PCR experts at Invitrogen, Qiagen, and Sigma-Aldrich all pointed to the same trend in their conversations with *Genome Technology*.

And microRNAs aren't the only genetic snippets to benefit from real-time PCR. Dirk Loeffert, director of R&D in the modification amplification technology center at Qiagen, says he sees customers using the technology to evaluate siRNA potency as well. "Researchers are validating more and more of the siRNA knockdown expression by real-time PCR," he says.

SMALLER SAMPLES AND SINGLE CELLS

As PCR companies have streamlined the sensitivity of their products, customers have been able to use the tool on smaller and smaller samples — down to the point where, today, scientists can use real-time PCR even on the single-cell level.

"People are doing more and more [studies with] pure samples collected by

Invitrogen's Ken Rosser

THE EXPLORATION CONTINUES

Experts who spoke with *Genome Technology* highlighted a number of trends in the expansion of real-time PCR. These include:

EPIGENETICS — Dirk Loeffert at Qiagen says the trend is still forming, but more and more researchers are coming around to the idea of using real-time PCR to study DNA methylation patterns. Reagents still have to be developed to really encourage this field, he says, but technically speaking, real-time is more effective in helping distinguish a specific from a nonspecific methylation event, he says — which could prove a real boon to epigenetics scientists.

NON-DNA ASSAYS — "There's been a slow but steady use of quantitative PCR for assays that aren't DNA at all," says Ernie Mueller at Sigma-Aldrich. Scientists interested in detecting antibodies, proteins, and other analytes are starting to tag those with DNA molecules and "piggy-backing off of PCR" to identify by proxy their target of interest, Mueller says.

IMMUNO PCR — This technique, a tool used for protein detection, is on the upswing, says Mikael Kubista at the TATAA Biocenter in Sweden. What was once an esoteric tool has become "an emerging field" in the real-time community, he says.

THE RISE OF MULTIPLEXING — Greg Shipley, a research assistant professor at the University of Texas Health Science Center, says multiplexing will become more and more common in the coming years. Many vendors don't handle anything higher-throughput than a 384-well plate, but "for any sort of normal screening, 1,536 is the standard in the field," he says, anticipating that as real-time PCR moves further downstream vendors will amp up their plexing to meet this demand.

NANOSCALE REACTIONS — Jo Vandesompele from Ghent University Hospital says current PCR protocols use "huge vessels" and need to be pared down to accommodate nanoscale reactions instead. Two companies he's got his eye on, BioTrove and Fluidigm, have products that seem promising in helping shrink the real-time reaction, he says.

MORE GENE EXPRESSION — Real-time is no stranger to gene expression, but scientists believe the demand for this application is on track to skyrocket. As more people realize that data from microarrays is not sufficient to detect lower-level changes, predicts Mikael Kubista, scientists will design their expression experiments to include real-time PCR. One such possibility, he says, would be doing a broad scan on a microarray to find a few dozen genes of interest, and then following up on those with real-time PCR. "It's more sensitive, the reproducibility is higher, and the dynamic range is much larger," he says.

MODEL ORGANISM STUDIES — Criss Walworth, a product line director at Applied Biosystems, says demand is growing for organism-specific assays, particularly in the comparative genomics field. Coming soon: targeted sets for rhesus and canine, according to Walworth.

SPEEDY PCR — Researchers are clamoring for the new, fast PCR techniques vendors have released recently. Some vendors have gotten what used to be an hour and a half process down to the neighborhood of 30 minutes. "Now the running of reactions takes less time than preparing your plates," says Vandesompele. *— MWS*

laser-capture microdissection," says Mikael Kubista at the TATAA Biocenter. "During the last year or so, a number of robust pre-amplification methods have appeared [making] it possible to analyze small sample amounts."

For the most part, this level of experiment means bypassing the RNA isolation steps, says Ken Rosser at Invitrogen. "Any type of RNA isolation method that you use is going to result in some kind of sample loss," he says. And for samples as small as his customers want to use, "you really can't afford to lose any of your nucleic acid because you compromise your sensitivity."

Criss Walworth, product line director for gene expression assays at ABI, says the company has a product in development right now that's a "kind of … sample stretcher." That type of tool, Walworth adds, will be "really enabling for people who are really sample-limited." Conceptually, of course, requiring less sample for these experiments opens the doors for customers in forensics or clinical research who previously couldn't make use of real-time PCR because their samples were simply too scarce or precious.

At the extreme, scientists are now focusing all the way down to the single-cell level. That's been made possible by new kits, many with isothermal enzymes, that work on whole transcriptome amplification, according to Jo Vandesompele at Ghent University Hospital. The idea is to do pre-amplification and a limited number of PCR cycles to prevent the introduction of any bias into the product, he says.

Kubista says this has allowed scientists to find whole new biological phenomena. His team published a paper late last year showing significant variation in the gene expression in individual cells compared to what shows up in expression studies of a cluster of cells. "That's very important in trying to understand how biological processes are controlled," he says, pointing out that even a year ago this kind of study would not have been possible.


Mikael Kubista

DIAGNOSTICS AND THE CLINIC

Like so many technologies in the systems biology field, real-time PCR is making its way downstream, with recent appearances in animal and human diagnostics. Dirk Loeffert at Qiagen says that veterinary tests in particular have picked up on real-time PCR as a replacement for some ELISA tests. It's likely that human diagnostics will follow more slowly, as they may be governed by the FDA. In the meantime, he says, the tool will likely be used to study infectious disease and in GMO detection.

"Today it's mainly used in research and to diagnose infectious diseases," says Kubista, "but it's reasonable that in a couple years' time we'll see the first diagnostic kits for complex diseases based on expression profiles."

In fact, a company called Genomic Health, led by Incyte founder Randy Scott, has introduced a breast cancer diagnostic test that analyzes the expression of a 21-gene panel to predict cancer recurrence.

"The application of real-time PCR in the clinic definitely has increasing popularity," says Vandesompele. What was once a primarily academic tool has been put to use for pathogen detection and, he believes, promises to provide the basis for a host of diagnostics based on expression pattern. GT

Your Money (And More)

Genome Technology's fourth annual salary survey shows that, for the most part, scientists are in better shape than they were a year ago. (Sorry, postdocs, not you.) A by-the-numbers look at the state of the field in 2006.

By Jennifer Crebs and Meredith Salisbury

To the survey respondent who wrote, "I am really not interested in salary. My job is very interesting and that is what matters," we'd like to say: more power to you. To the rest of our respondents, and indeed all of our readers, it seems that salary and overall compensation package are of much greater importance to you. One way we know this is that the response rate to our annual salary survey keeps going up: this year, 1,990 of you took the time to tell us how much you earn, what your perks are, and plenty of other great facts that served as the basis of the results you're about to read. Many thanks to all of you for your time and cooperation.

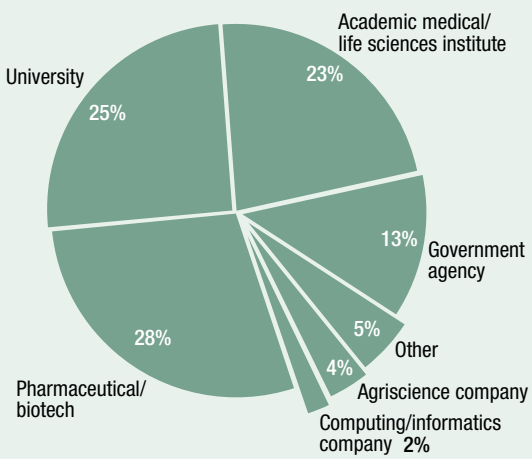
In our exclusive fourth annual salary survey, we have information for the first time from readers in Europe and Asia — allowing us to help you compare compensation data on a more global level. As always, we include results on layoffs, benefits, and more, broken out into public versus private sector, scientific tasks, and job title.

Finally, we added to the survey this year an invitation to readers to submit career-related questions. Boy, did we hit a nerve. We whittled down the list to the most common questions, and took those to experts in the field to provide you with practical tips and advice. That section begins on p. 32.

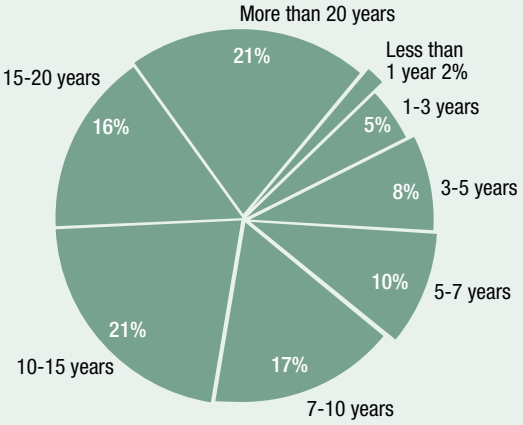
RESPONDENT DEMOGRAPHICS

Number of respondents: 1,990

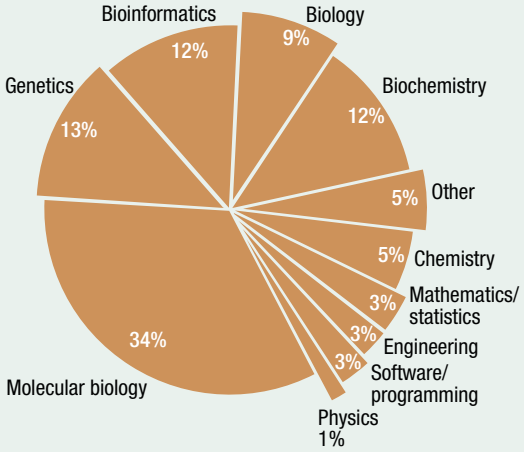
Type of organization



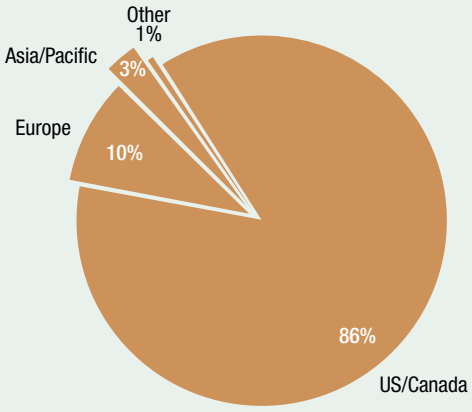
Years In Research



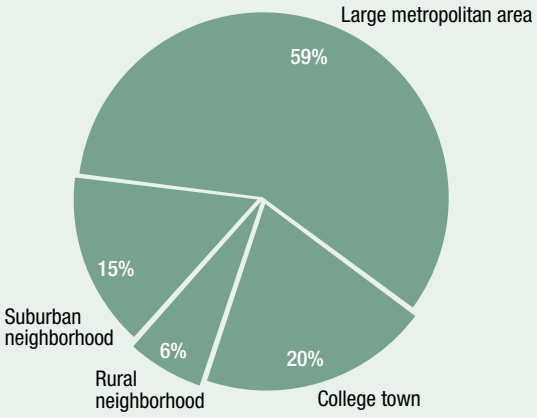
Primary Scientific Background



Respondents by Region



Type of Region



MEDIAN SALARIES BY ORGANIZATION AND SIZE

TITLE	MEDIAN SALARY 2006		MEDIAN SALARY 2005		MEDIAN SALARY 2004
SMALL PHARMA/BIOTECH (<500 EMPLOYEES)					
Chairman, president, CEO	$200,000-$299,999	↖	$175,000-$199,999	↙	$200,000-$299,999
CTO, COO, CSO, CFO	$150,000-$174,999		$150,000-$174,999	↖	$125,000-$149,999
VP, director, senior manager	$125,000-$149,999		$125,000-$149,999	↖	$100,000-$124,999
Senior scientist, senior researcher, senior technologist	$75,000-$99,999		$75,000-$99,999		$75,000-$99,999
Staff scientist, researcher, programmer	$75,000-$99,999		$75,000-$99,999	↖	$50,000-$74,999
Lab technician, technical specialist	$30,000-$49,999		≈ $30,000-$49,999		$30,000-$49,999
MIDSIZE PHARMA/BIOTECH (500-5,000 EMPLOYEES)					
VP, director, senior manager	$150,000-$174,999	↖	$100,000-$124,999	↙	$125,000-$149,999
Senior scientist, senior researcher, senior technologist	$75,000-$99,999		$75,000-$99,999		$75,000-$99,999
Staff scientist, researcher, programmer	$75,000-$99,999		$75,000-$99,999	↖	$50,000-$74,999
Lab technician, technical specialist	N/A		≈ $50,000-$74,999		N/A
LARGE PHARMA/BIOTECH (>5,000 EMPLOYEES)					
VP, director, senior manager	$150,000-$174,999		$150,000-$174,999		$150,000-$174,999
Senior scientist, senior researcher, senior technologist	$100,000-$124,999		$100,000-$124,999	↖	$75,000-$99,999
Staff scientist, researcher, programmer	$75,000-$99,999		$75,000-$99,999		$75,000-$99,999
Lab technician, technical specialist	N/A		$50,000-$74,999		N/A
UNIVERSITY/ACADEMIC LIFE SCIENCES INSTITUTE					
Dean, VP, director, senior manager	$100,000-$124,999		$100,000-$124,999	↙	$125,000-$149,999
Professor or principal investigator	$75,000-$99,999	↙	$100,000-$124,999		$100,000-$124,999
Associate or assistant professor	$75,000-$99,999		$75,000-$99,999	↖	$50,000-$74,999
Core lab manager	$50,000-$74,999		$50,000-$74,999		$50,000-$74,999
Senior scientist, senior researcher, senior technologist	$75,000-$99,999	↖	$50,000-$74,999	↙	$75,000-$99,999
Staff scientist, researcher, programmer	$50,000-$74,999		$50,000-$74,999		$50,000-$74,999
Lab technician, technical specialist	$30,000-$49,999		$30,000-$49,999		$30,000-$49,999
Fellow or postdoc	$30,000-$49,999		$30,000-$49,999		$30,000-$49,999
Graduate student	Less than $30,000		Less than $30,000		N/A
GOVERNMENT AGENCY					
VP, director, senior manager	$75,000-$99,999	↙	≈ $100,000-$124,999		$100,000-$124,999
Professor or principal investigator	$100,000-$124,999		$100,000-$124,999		$100,000-$124,999
Senior scientist, senior researcher, senior technologist	$75,000-$99,999		$75,000-$99,999		$75,000-$99,999
Staff scientist, researcher, programmer	$75,000-$99,999		$75,000-$99,999	↖	$50,000-$74,999
Core lab manager	$75,000-$99,999		$75,000-$99,999		N/A
Lab technician, technical specialist	$50,000-$74,999	↖	≈ $30,000-$49,999	↙	$50,000-$74,999
Fellow or postdoc	$50,000-$74,999		$50,000-$74,999	↖	≈ $30,000-$49,999

≈ median falls evenly between this level and next higher level
↖ median increased from previous year
↙ median decreased from previous year

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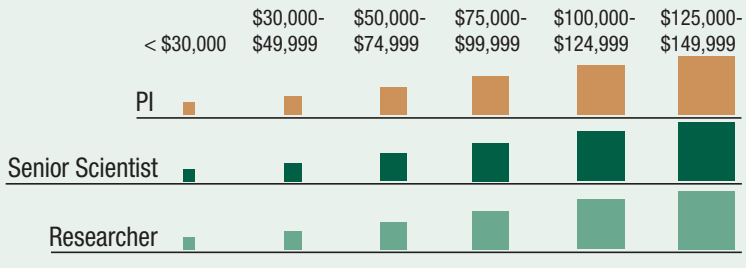
Typical Salaries by Region and Title

Median salaries reported by respondents who fell in the PI, senior scientist, or researcher categories



MEDIAN SALARY BY SECTOR AND YEARS OF RESEARCH EXPERIENCE

YEARS IN RESEARCH	PRIVATE SECTOR MEDIAN	PUBLIC SECTOR MEDIAN
Less than 1 year	$75,000-$99,999	$50,000-$74,999
1-3 years	$50,000-$74,999	$30,000-$49,999
3-5 years	$75,000-$99,999	$30,000-$49,999
5-7 years	≈$50,000-$74,999	$50,000-$74,999
7-10 years	$75,000-$99,999	$50,000-$74,999
10-15 years	$75,000-$99,999	$50,000-$74,999
15-20 years	$100,000-$124,999	$75,000-$99,999
More than 20 years	≈$100,000-$124,999	$100,000-$124,999

≈ median falls evenly between this level and next higher level

MEDIAN SALARY BY SCIENTIFIC TASK

BASED ON WHAT RESPONDENTS SAY IS THE PRIMARY SCIENTIFIC OR TECHNICAL TASK OF THEIR DAY

$50,000-$74,999	$75,000-$99,999
≈Microarray analysis or gene expression	SNP analysis or genotyping
Structural biology	Biostatistics/data analysis
DNA sequencing	Computing infrastructure/applications development
Functional genomics/RNAi	Proteomics or protein analysis
PCR or PCR-related tasks	Automation/robotics/engineering
	Quality assurance/quality control

≈ median falls evenly between this level and next higher level

JOB TENURE

MOST COMMONLY REPORTED JOB TENURE BY RESPONDENTS' PRIMARY SCIENTIFIC OR TECHNICAL TASK

1-4 YEARS	4-7 YEARS
Biostatistics/data analysis	Functional genomics/RNAi
Computing infrastructure/applications development	Structural biology
Microarray analysis or gene expression	SNP analysis or genotyping
Proteomics or protein analysis	DNA sequencing
Quality assurance/quality control	Automation/robotics/engineering
PCR or PCR-related tasks	

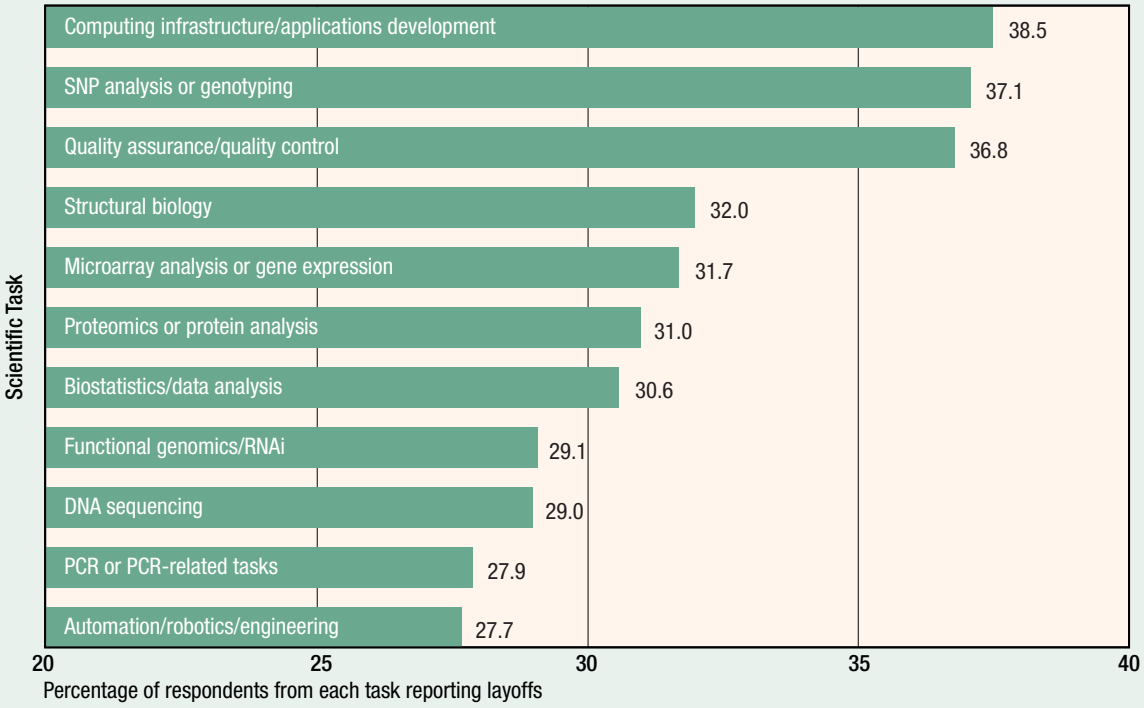
BENEFITS

BY RANKING AND REGION, MOST COMMONLY REPORTED BENEFITS IN RESPONDENTS' SALARY PACKAGES

	Asia/Pacific	Europe	US/Canada
Medical/dental insurance	1	2	1
Retirement plan	1	1	2
Annual bonus	3	3	4
Education/tuition benefit	4	4	3
Stock options	4	4	5

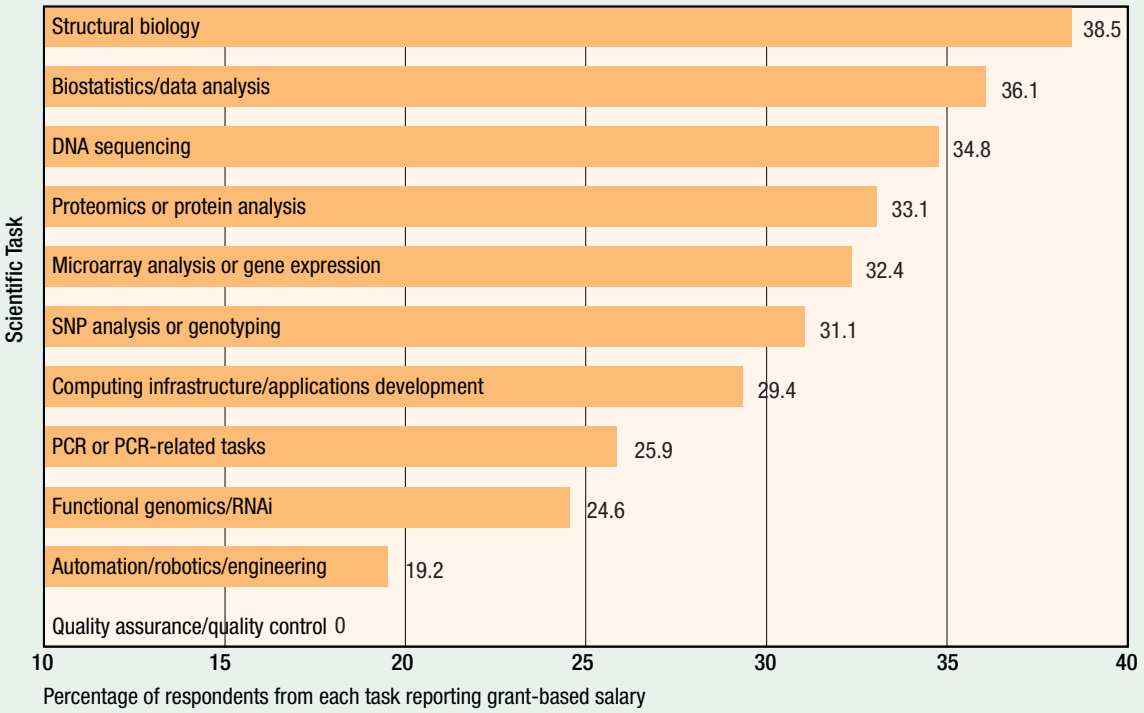
Reported Layoffs

Based on primary scientific or technical task of their day, percentage of respondents who reported that their companies had layoffs in the past year



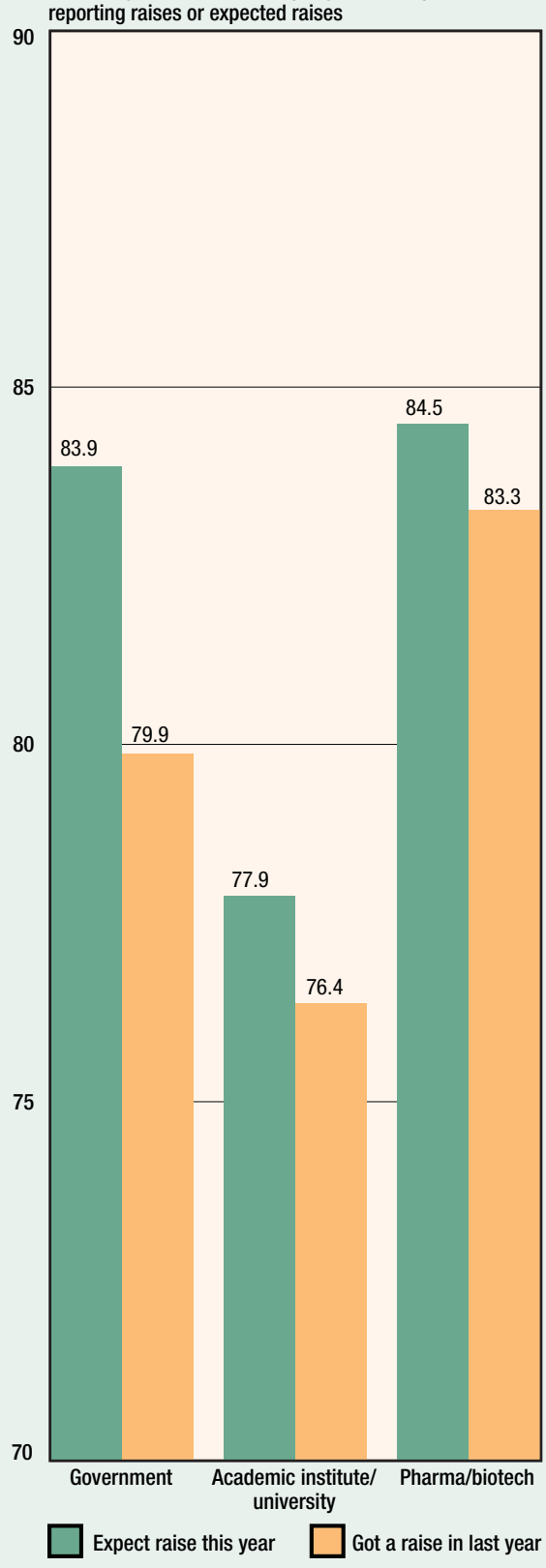
Salary from Grants

Respondents who say more than half of their salary comes from grants, based on primary scientific or technical task of their day



Raises and Expected Raises

Percentage of respondents by organization type reporting raises or expected raises



TENURE

Of the academics who responded, 18.7 percent have tenure, up slightly from last year's 16.2 percent

SALARIES BY ORGANIZATION

For salaries less than $50,000, respondents most frequently hailed from university settings. Respondents in the $50,000 to $74,999 range were most likely to be at an academic medical/life sciences institute. All higher salary ranges, from $75,000 on up, were most commonly populated by respondents from pharma/biotech.

INVENTIONS

For those who are compensated in some way for their inventions, respondents in academia or government were most likely to get royalties, followed by ownership of the patent and monetary reward greater than $1. Respondents from pharma/biotech were most likely to receive $1, followed by monetary reward greater than $1 and ownership of the patent.

RAISES

Regardless of their primary scientific task, respondents across the board most commonly reported that their last raise fell in the 3 to 5 percent range.

Materials and Methods: A Career Improvement How-to Guide

In an added twist to the salary survey this year, *GT* invited respondents to submit their career questions to us. We followed up with experts in the field to get answers to the most commonly asked questions.

SALARY & COMPENSATION

How do I negotiate my salary and benefits package?

This was by far the most common question scientists asked; most experts responded with some variation of "it depends."

Linda Kirsch, a professional executive recruiter who specializes in the life sciences, says each person has to figure out what's most important to him and go from there. "For some people, money is number one; for some people, a title is really important," she says. She warns against "negotiating hard": "Be careful that you don't set the bar so high that if a manager hires you, they're always feeling that they've overpaid," she says. "Likewise, if somebody underpays for you, you as the employee always have this feeling [that] they're not giving me what I'm worth." She adds, "both parties at the end have to feel good about it or otherwise there's an undercurrent of discontent that rides throughout the relationship."

Pragmatically, she says, "the best time you can negotiate a salary is when you're coming in the door." She's seen people boost their incomes by 20 or 30 percent by changing jobs.

Jodi Greco, senior employment administrator at the Broad Institute, says, "A candidate should attempt to determine the hiring range for the position and obtain a copy of the job description [to] try to figure out where he/she fits in the range." She also indicates that while industry is fairly open to negotiation, it's much less so in academia, where successful negotiations are more likely to result in things like an extra week of vacation or flex time than in salary adjustments. For current employees, she recommends that people negotiate for salary increases tied to specific goals or added responsibilities.

I want to stay at my company, but I'd like a promotion. Is it wise to get an offer from another organization to use as leverage?

No way, says Laurie Irwin, a longtime biotech recruiter who works for Fortune Personnel Consultants. "It's like a cheating spouse," she says, pointing out that arriving on your supervisor's doorstep with a competing offer "could be perceived as a threat." The better course of action, she says, is to "sit down with your boss or manager and talk about reasons why you're feeling a little stale." She notes that in a case where somebody did use another offer as leverage, a company that six months down the road had to downsize might look at that person less favorably.

Which reference guides are used to establish salary baselines?

The formality of salary baselines varies considerably from one organization to another, says Kirsch. Some places actually set up salary grades corresponding to certain titles, and within those grades there may be very little flexibility.

At the Broad Institute, Greco says a number of factors go into salary ranges. These include external surveys as well as industry and market analyses. She also points to resources such as the Radford life sciences sector survey and monster.com as other potential sources of salary baseline information.

Jim Maus, grants coordinator at WashU, says that at the genome center there much of the salary guidelines are "handed down by the university." There's some wiggle room within that — in fact, the university just finished an extensive market analysis and regraded its salary ranges.

Baylor's genome center works similarly. Roxanne Beltran-Reyna, who heads up HR there, says the university standards are established by a compensation group that issues guidelines based on title, responsibility, education, and experience. Reyna says the genome center can sometimes justify slightly higher salaries in order to compete with industry compensation.

Do I have to disclose my current salary when I'm looking for a job?

Most likely. "I think you always have to disclose and you have to be honest about what you've made in the past," says Kirsch. In her experience, many companies will actually ask to see a potential employee's previous W2 forms to get a salary history. "They can't force you [to provide those], but if you don't they might not make you an offer," Kirsch says. Greco at the Broad Institute advises giving your prospective employer a salary range instead of an exact number.

TRANSITIONS

I'm a bench scientist but I'd like to get into the marketing or management side of the company. What's the best route? Should I get an MBA?

Nate Lakey, CEO of Orion Genomics, started out on the technology and science side of the field and made the transition to the business front. He credits much of that with the volume of business reading he did, including topics like statistical process control and total quality management. "I was interested in the processes behind science," he says. "Pretty quickly you find yourself getting into business questions." That led him to accept and excel at an operations position, which paved the way for his business career.

Kirsch says she considered getting an MBA when she realized she wanted to go from science to the business side, but decided that for her, the cost/benefit analysis didn't make sense. She recommends that scientists take executive classes and other business training classes when possible, noting that most highly regarded management schools offer short weekend or evening programs on very specific business topics.

Jane Krug, a former scientist who now runs her own marketing consultancy, says her path involved spending time in the sales department as her transition period. "I was really glad I had that experience." She also notes that this kind of move can be easier in a startup environment, where boundaries aren't as rigid.

I'm about to start my own lab. What factors should I consider?

Rob Mitra, assistant professor in the genetics department at Washington University, says that the most practical considerations are equipping your lab, choosing staff, and selecting a research goal. "Be focused and figure out exactly what you're going to do in the next two, three, four years," he says. That information will help you with the other key steps: "Figure out what equipment has to go in the lab. … [And] try to get the best graduate students and postdocs and technicians that you can," he says.

I am an unhappy postdoc. How do I get out of this lab before my project is completed?

Mitra at WashU advises people in this position to sit down with their PI and talk candidly about the situation. "I think it's important to have a frank discussion as to what it is that makes you unhappy," he says. "Your PI shouldn't be surprised." He says that in a case where there is no clear way to come to an agreement, a PI would be likely to release, and even help find a new position for, the postdoc. "It's the honorable thing to do," Mitra says.

How do I know when it's time to move on?

"If you're feeling stale or bored or underutilized, it's time to look," says Irwin. She says if you find that you're no longer being challenged, you've accomplished what you set out to do, or that the organization is not doing well, you should take stock of your situation and seriously consider a move to another place.

Kirsch says obvious situations include those where "your needs aren't being met [or] when there are situations that you know you can't correct." She says it's common for people to try to ride out bad times with a company, but it may be time to go in cases where that's actually hurting your livelihood or ability to provide for your family.

EDUCATION

Should I get a PhD? Will just having a master's limit my advancement?

"A PhD in the sciences really takes you a long way," says Linda Kirsch, noting that very few senior level people in academia or industry don't have a doctorate. She says opportunities are more open in fields like sales, marketing, or field operations for people who choose not to pursue a PhD.

Laurie Irwin says smaller organizations, like small pharma or biotech, are more likely to advance people who have a master's degree. Greco at the Broad says having a PhD is more critical for academic careers than industry ones.

"Often [organizations] still weed people out that don't have PhDs," says Rhonda Knudsen, HR director at the Institute for Systems Biology, adding that that trend is slowly changing. "It's fundamentally hard to change that bias."

NETWORKING

I know networking is important, but how do I do it?

There's no trade secret for how to become a well-connected person, but experts agree that many simple steps can help the process. Consultant Jane Krug says when she gets someone's business card, she writes a note on the back about where she met the person or about some aspect of their conversation that she wants to follow up on. In cases where she wants to keep in touch with the person, she says, "I'll often e-mail them right after and say it was great to meet you."

Krug also encourages people to walk the exhibit hall floors and attend social functions at conferences — and don't stand "with the people you know," she says.

Meeting people at a conference may seem about as appealing as cold-calling for a telemarketing firm, but once you get past any reluctance it can be quite painless. "If you're shy, you can overcome that by asking people questions about them — people like to talk," says Nate Lakey at Orion Genomics. "I try to really reach out. If I meet someone who's new I proactively introduce them to everyone I know. They'll return the favor and introduce you to people that they know." Lakey also cautions scientists to keep their expectations reasonable. "It takes about three to five years" for most people to feel solidly connected, he says. "You've got to pick a meeting and go to it for three to five years." At the end of that, he says, you'll come away "tired but with a great network."

ISB's Knudsen recommends joining associations — alumni, scientific, social — to meet more people. She points out that if you move, often associations have other regional branches and become a great way to plug in to a new community. "You have to put yourself out there," she says.

JOB SEARCH

I'm a scientist later in my career, and I'm concerned about looking for a new job. Do you have any advice for people in my position?

Experts agree that this topic has become a particular challenge in this field. "As you go up the pyramid, there are fewer jobs," says Kirsch, who encourages people to keep their networks active and always be open to opportunities. "Say you're 55 years old and you get laid off … you might have to take a step back, you might have to make less money."

Irwin recommends networking and keeping up with new trends and supplemental education, when possible. "With so much downsizing, people who have been secure in their positions for the past five to 10 years are suddenly out there looking," she says. "If they haven't kept up to date, if they haven't continued with their education … then they're going to be stale."

Greco from the Broad says contract work is one possible avenue of tracking down another job as a more senior person. Those "often lead to permanent positions," she says.

Which areas are poised for growth or slowdown in the next several years?

Laurie Irwin sees hiring trends in academia and government more so than industry at the moment. Within the field of bioinformatics, she says, she sees companies looking for expertise in specific therapeutic areas and statistics in particular.

Kirsch says that "employers are spending more money closer to the product, no matter what the product." She's noticed people who were in earlier-stage research heading down the pipeline to pharmacogenomics, for instance, or other clinical areas.

Are there opportunities for part-time positions or flex scheduling?

There may be such opportunities out there, but don't count on finding many, experts say. "I'm seeing organizations offering contract work," says recruiter Laurie Irwin. "I can't say that I've seen any part-time [work], not that it's not out there."

At ISB, Knudsen says she really hasn't seen part-time positions either. "Most of our people [work] more than a 40-hour week," she says. But as far as flexible scheduling goes, "people are just expected to get their work done" — there's no set schedule for staff, she says. GT

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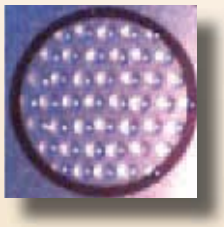

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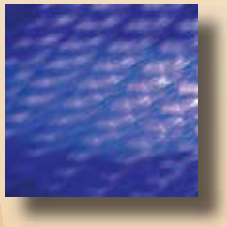

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Sowing Ag Dollars

For this fiscal year, the US Department of Agriculture was allocated some $95.4 billion, of which an estimated $19.4 billion will go toward discretionary spending, the broad umbrella under which the agency's research grant funding lies. That's a decrease from about $22 billion last year.

Researchers with an agricultural bent have found plenty of grant opportunities — especially for crop sequencing and pathogen genomics — for their science. We opted to look into USDA's records to see where the money is going. Using their grant search tool, we plugged in key words such as "bioinformatics," "RNAi," "genome," and "microarray" to track down the funding relevant to this field.

The list below shows the highest and most systems biology-targeted awards. It is by no means comprehensive and is meant to give you a sampling of the type of research USDA has chosen to support.

INSTITUTE/AWARD	PI	TITLE
Auburn University $690,000	Zhanjiang Liu	Mapping the Catfish Genome: BAC Contigs, End Sequencing, and Marker Development for Map Integration
Baylor College of Medicine $388,000	Sarah Highlander	Genome Sequencing of *Streptococcus Iniae*, an Emerging Pathogen of Aquaculture
Colorado State University $715,000	Jan Leach	Sequencing Multiple and Diverse Rice Varieties to Allow Connection of Whole Genome Variation with Phenotype
Institute for Genomic Research $1,000,000	Robin Buell	A Comprehensive Genome-based Diagnostics Resource and Pipeline for Identification of Threatening Plant Pathogens
Massachusetts Institute of Technology $1,872,774	Chad Nusbaum	The Genome Sequence of *Phytophthora Infestans*
Michigan State University $125,000	Ning Jiang	The Impact of Rice Mutator-like Elements on Gene Expression and Gene Function
Mississippi State University $403,000	Mark Lawrence	Genome Sequencing of the Fish Pathogen *Flavobacterium Columnare*
Mississippi State University $350,000	Shane Burgess	The Mechanics of Marek's Disease Lymphoma and Regression
National Center for Genome Resources $849,226	Stephen Kingsmore	Population Resource and Genome Sequence of the Vegetable Pathogen *Phytophthora Capsici*
North Carolina State University $700,000	Gary Payne	Gene Networks Controlling Development, Pathogenicity, and Secondary Metabolism in *Aspergillus*
North Carolina State University $354,500	Christina Grozinger	Molecular Mechanisms of Honey Bee Mating
North Carolina State University $321,773	Eric Davis	Functional Analysis of Cyst Nematode Parasitism Genes
North Carolina State University $762,000	Ralph Dean	Characterization of the Transcription Circuitry Regulating Pathogenicity in the Rice Blast Fungus
Oregon State University $577,000	Lynda Ciuffetti	Genome Sequence of *Pyrenophora Tritici-Repentis*: A Necrotrophic Fungus with a Complex Race Structure
Texas A&M University $438,096	Loren Skow	Haplotypes of the Bovine MHC
Tufts University $688,000	Stuart Levy	Genetics of Soil Survival and Persistence of *Pseudomonas Fluorescens*
University of California, Berkeley $1,500,000	Dan Rokhsar	Maize Missouri 17 Chromosome 10 Project
University of California, Davis $750,000	Venkatesan Sundaresan	Sequenced Insertion Lines for Rice Functional Genomics
University of California, Davis $715,000	Pamela Ronald	Elucidating the NRR/NH1 Mediated Resistance Signaling Network
University of Georgia $399,900	Richard Hussey	Root-Knot Nematode Parasitism Genes: Functional Analysis and Molecular Targets for Transgenic Resistant Crops
University of Illinois $5,000,000	Larry Schook	Porcine Genome Sequencing Project
University of Maine $350,000	Benildo de los Reyes	Cold Stress Response Gene Regulon in Rice
USDA Agricultural Research Service $548,372	Tad Sonstegard	Construction of a Gene Atlas for Cattle Tissues Using Sequence and Array-based Transcriptional Profiling
Virginia Polytechnic Inst. and State Univ. $545,000	Allan Dickerman	Highly Parallel Pathogen Microarrays for Plant Biosecurity
Washington State University $100,000	Michael Kahn	Respiration, Polymer Synthesis, and Effectiveness in Symbiotic Nitrogen Fixation
Washington State University $375,000	Michael Konkel	Comparative Genomics, Transcriptomics, and Proteomics of Pathogenic and Non-Pathogenic Isolates of *Campylobacter Jejuni*

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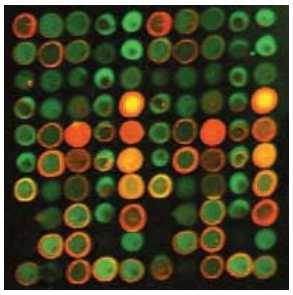

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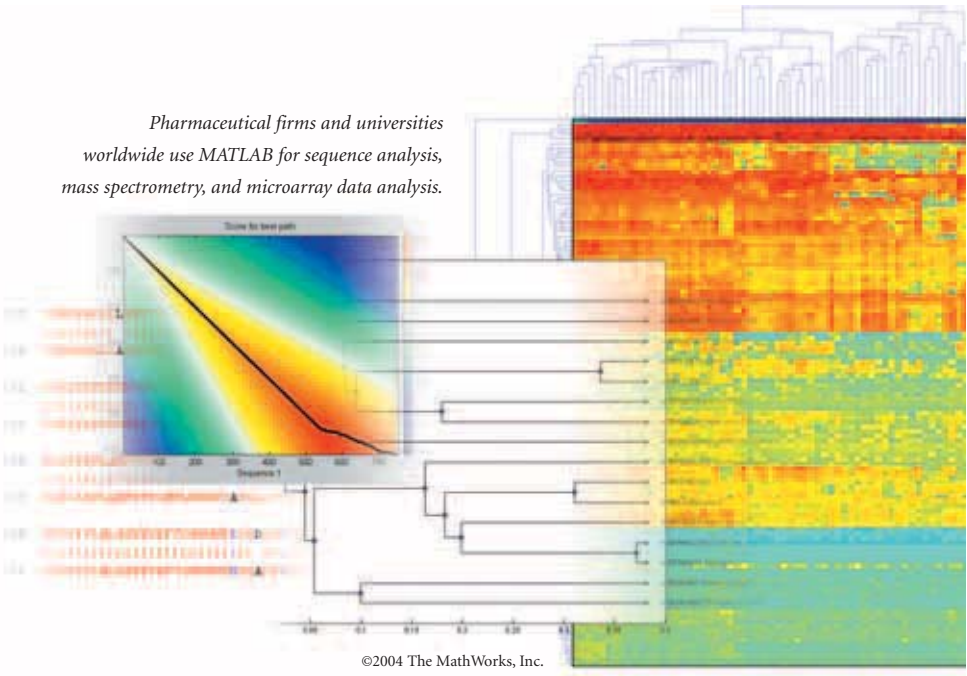

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After Uncertainty, EMBOSS Secures Long-Term Funding

Plans are underway to celebrate the 10th birthday of the EMBOSS software package this summer, now that its developers have received word that their funding is secure for at least three additional years — a decision that ends two years of uncertainty around the popular open source bioinformatics suite.

In April, the European Bioinformatics Institute announced that the UK's Biotechnology and Biological Sciences Research Council had agreed to support the project. While the amount of the funding was not disclosed, project leader Peter Rice says that it is enough to support two developers at the EBI, in addition to himself, for three years as of May 1.

But the funding means more than just three jobs. Rice says the support guarantees that the core software will remain stable, which should encourage developers from academia and industry to begin contributing to the open source project and eventually expand its capabilities.

"We hope in coming years that we'll have a lot more outside collaborators," Rice says. "Obviously, nobody wanted to collaborate too much if we could disappear in a few months. It wasn't a great time to set up collaborations. … Now we'll be really looking to see who'd like to use EMBOSS as the basis for development."

Since the UK's Medical Research Council in 2004 closed the bioinformatics division of the Rosalind Franklin Center for Genomics Research, which housed the bulk of the EMBOSS development team, the three core developers have managed to keep the project alive through "interim" funding from the EBI, but the effort has largely been "on hold," according to Rice.

The impact of this holding pattern on users and collaborators is unclear, but it appears that many remained loyal to the effort despite the funding uncertainty. Rice notes that letters of support from dedicated EMBOSS users across the world helped convince BBSRC to fund the project.

— Bernadette Toner

PATENT WATCH

US Patent 7,031,847. **Method and apparatus for displaying gene expression patterns**. Inventors: Yasuyuki Nozaki, Ryo Nakashige, Tsunehiko Watanabe, and Takuro Tamura. Assignee: Hitachi Software Engineering. Issued: April 18, 2006.

This patent "discloses a method for displaying gene expression patterns of multiple genes that change according to the experiment cases, where a first axis represents the genes and a second axis represents the experiment cases," according to the abstract.

US Patent 7,031,846. **Method, system, and computer software for the presentation and storage of analysis results**. Inventors: Shantanu Kaushikkar, Teresa Webster, Rui Mei, and Linda McAllister. Assignee: Affymetrix. Issued: April 18, 2006.

This patent describes a computer program "that processes emission intensity data corresponding to probes of a biological probe array. [It] includes a genotype and statistical analysis manager that determines absolute or relative expression values based, at least in part, on a statistical measure of the emission intensity data and at least one user-selectable statistical parameter. … The analysis manager may further display the absolute or relative expression values based, at least in part, on at least one user-selectable display parameter and/or a measure of normalized change between genotype calls."

DATAPOINT

58 percent

Decline in Compugen's first quarter revenue compared to the same quarter a year ago, down to $200,000 from $481,000. Meanwhile, R&D spending decreased 22 percent and net losses declined 19 percent.

The **European Bioinformatics Institute** is planning a format change for the EMBL Nucleotide Database scheduled to take place this month. In a notice to users, EBI said that the "ID" line will have a different structure and the "SV" line will be removed beginning with release 87 of the database.

Ariadne Genomics joined the **Affymetrix** GeneChip-compatible Applications Program and says that its PathwayStudio 4.0 pathway analysis software has earned GeneChip-compatible status.

Organizers of the **BioCreative** (Critical Assessment of Information Extraction Systems in Biology) text-mining challenge have issued the first call for participation in BioCreative II, which will be held in October, with the workshop to be held next spring. Training data will be released this month. The evaluation's three tracks will focus on finding the mentions of genes and proteins in sentences drawn from Medline abstracts; producing a list of Entrez Gene identifiers for all the human genes and proteins mentioned in a collection of Medline abstracts; and identifying protein-protein interactions from full text papers for curation into the IntAct and MINT databases.

GeneGo and **XB TransMed Solutions** integrated their platforms — MetaCore pathway software and XB-BioIntegration Suite translational medicine software — to allow shared customers to capture, manage, and mine integrated clinical, preclinical, and molecular data.

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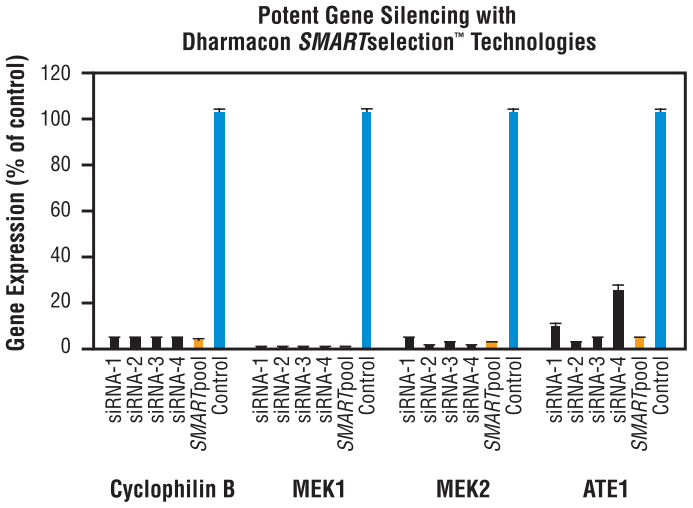

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Sigma Targets Academics with Partnership Program

Sigma-Aldrich has established a partnership program designed to strengthen ties between the company and academic users of its RNAi and other functional genomics products, as well as boost the company's visibility in the RNAi space.

The first alliance under the so-called RNAi Partnership Program has been formed with Rutgers University, according to Sigma-Aldrich.

The deal also represents the latest step in a trend among some RNAi reagent firms that want to set themselves apart from their competitors — an important point for Sigma-Aldrich, which is a relative latecomer to the RNAi party.

According to Doug Johnson, market segment manager for functional genomics at Sigma-Aldrich, the company set up the program as "a way to develop partnerships with academic institutions."

Participants in the program will get early access to new Sigma-Aldrich technologies, and will have a dedicated support team to assist with products from the company's functional genomics product portfolio, which includes the Mission TRC shRNA libraries developed in conjunction with the Broad Institute's RNAi Consortium.

"We wanted to be more than just a supplier of reagents," Johnson says. Additionally, Sigma-Aldrich hopes the program will educate researchers who previously hadn't thought of the company as a life sciences player.

"One of the things we had heard in the past was … people saying, 'I didn't realize Sigma provided these kinds of reagents. I didn't know Sigma had quantitative PCR or reagents … for proteomics'" or any of the other tools used in gene-knockdown experiments, Johnson says. "There are still a lot of people who think of us … as [providing] chemicals first and not necessarily some of the more biotech-related products. [The program] definitely helps us let them know about those sorts of things."

— *Doug Macron*

PATENT WATCH

US patent application 20060089324. **RNAi modulation of RSV, PIV, and other respiratory viruses and uses thereof**. Inventor: Sailen Barik. Filed: June 14, 2005.

This invention is based on an *in vivo* demonstration of RSV and PIC inhibition via the intranasal and parenteral administration of RNAi agents. The application suggests that viral reduction can be achieved with more than one virus being treated concurrently. Based on these findings, the invention provides compositions and methods that are able to reduce respiratory virus mRNA levels, protein levels, and viral titers in subjects.

US patent application 20060073127. **Therapeutic alteration of transplantable tissues through *in situ* or *ex vivo* exposure to RNA interference molecules**. Inventors: Timothy Kowalik and Marc Uknis. Assignee: University of Massachusetts Medical School. Filed: July 11, 2005.

This invention concerns the discovery of methods of effectively delivering an RNAi agent (which includes siRNAs) to a transplantable tissue. Agents described in the application can be delivered as "naked" molecules or by using liposomal and other modes of delivery to tissues. Delivery can occur either via perfusion of the RNAi agent in solution through the vasculature of whole or partial organs, or else through the bathing, injection, or other treatment of transplantable cells with RNAi agents.

DATAPOINT

~7,500

For a sub-genomic library representing roughly one-tenth of the human genome, Louis Staudt of the NCI's Center for Cancer Research has cultivated about 7,500 shRNA vectors used to identify cancer-relevant pathways.

Publishing in *Nature Methods*, **EMBL** researchers have described their development of an automated, high-throughput platform that incorporates video imaging to bring time-lapse microscopy to genome-wide RNAi screens. The team, led by **Jan Ellenberg**, is collaborating with other European researchers to make the technology widely available.

Merck Research Laboratories, hoping to improve the efficiency of siRNA assay runs in its Automated Biotechnology Laboratories, will help **Cerionx** optimize its cold-plasma process for automated pipette tip cleaning.

Australian RNAi drug firm **Benitec** has cut half of its US workforce and begun moving to a less-expensive facility as part of a cost-reduction effort expected to save about $4 million a year. The company has also begun exploring the possible merger, acquisition, or divestiture options for its US operations.

Alnylam Pharmaceuticals has signed a cooperative research and development agreement with the **United States Army Medical Research Institute of Infectious Diseases** to collaborate on the discovery of RNAi-based drugs for biodefense.

Following the company's sale of its RNAi therapeutics assets to **Nastech Pharmaceuticals** in February, **Galenea** has officially realigned itself to focus exclusively on discovering and developing non-RNAi drugs to treat central nervous system diseases.

Gene Logic plans to help **Organon Pharmaceuticals** find new uses for a number of failed compounds, though it is not yet decided which or how many compounds are up for repositioning. In a twist on Gene Logic's standard repositioning deal, the company will own half of any compound that Organon decides to pursue.

Writing for *Nature*, **John Lindon** and colleagues at **Imperial College London** and **Pfizer** have reported a proof-of-concept study using metabolomic profiles to predict the extent of liver damage in rats receiving acetaminophen.

Biocon intends to file for regulatory approval of its EGFR-targeting drug Biomab from the government of India. Meanwhile, the company's subsidiary **Biocon Biopharmaceuticals** recently finished clinical trials for the head-and-neck anticancer compound. Biocon Biopharmaceuticals is a joint project with the Cuba-based **Center for Molecular Immunology**.

Canada-based **Warnex** has agreed to acquire PRO-DNA Diagnostic for $2 million. The genetic-testing service provider will operate as a division of Warnex Medical Laboratories and will be relocated from Montreal to the Warnex facilities in Laval, Quebec.

Digene has announced plans to market and distribute cystic fibrosis screening products made by **Asuragen**, the newly formed molecular diagnostic company spun out of **Ambion**.

Clinical Data to Launch Clozapine Dx Later in '06

Pharmacogenomics Reporter

Clinical Data plans to launch its first molecular diagnostic later this year, a product designed to identify patients at risk for developing severe adverse events to the third-line schizophrenia drug clozapine, says Carol Reed, the company's chief medical officer.

Clinical Data will offer the test before the end of the year through its CLIA lab, but the company is not discounting plans to talk about the test with US regulators. "We certainly have plans to discuss the implications of this with" the US Food and Drug Administration, Reed says. "Some of the groups at FDA are already aware of what we've been doing, and we look forward to continuing those relationships, as well as cultivating some other groups within FDA who need to know, but might not be as familiar with it."

Approximately 0.8 percent of patients taking clozapine develop agranulocytosis, which is an inability to create white blood cells that can quickly lead to infections and death. Patients prescribed clozapine must have failed at least two other treatments, and they are required to undergo weekly blood testing to detect white blood-cell depletion.

"I think the need to seek FDA approval for [the test] will depend on the life-cycle management issues … as well as discussions with FDA and where they might like to see it go," Reed says.

Sales for clozapine amount to approximately $200 million per year. Between 80,000 and 90,000 people in the United States take the drug, with "at least that many" in Europe, Reed estimates.

The company says it hopes the test will encourage US regulators to consider upgrading clozapine to a first-line, and thus more widely prescribed, treatment. However, the firm has not begun discussing with the FDA whether its test can play a role in the agency's decision to make the drug a first-line therapy.

— Chris Womack

DATAPOINT

11

In the first study of its kind, Pharmacogenetics Research Network scientists measured 11 different protein markers of tumor response to Pfizer's chemotherapeutic Camptosar. The markers didn't jibe with tumor location, implying that cancer treatment may be better guided by diagnostic data.

PATENT WATCH

US Patent 7,033,755. **Diagnostics and therapeutics for glaucoma**. Inventors: Abbot Clark, John Fingert, Loretta McNatt, Edwin Stone, and Wan-Heng Wang. Assignees: Alcon and the University of Iowa Research Foundation. Issued: April 25, 2006.

This patent covers methods for diagnosing and treating glaucoma, including a diagnostic method by which the expression level of mRNA encoding human frizzled related protein-1 is detected in a patient sample of trabecular meshwork cells, and wherein an aberrantly high level of the mRNA relative to that of a normal person is diagnostic of a glaucomatous state.

US Patent 7,034,135. **Molecules of the NBS/LRR protein family and uses thereof**. Inventors: John Bertin, Weiye Wang, and Maria Blatcher. Assignees: Millennium Pharmaceuticals and Wyeth. Issued: April 25, 2006.

Novel NBS-2, NBS-3, PYRIN-12/NBS-4, and NBS-5 polypeptides, proteins, and nucleic acid molecules are disclosed in this application. Each of the described genes has a nucleotide binding site domain, which is present in a number of proteins that transmit signals which activate apoptotic and inflammatory pathways in response to stress and other stimuli. Diagnostic, screening, and therapeutic methods using compositions of the invention are also provided.

Microdevice Relies on Tried-and-True Sanger

Is Sanger sequencing on its way out? Developers of alternative DNA-sequencing technologies might suggest it is, but other innovators believe the technique will evolve much like computers have: from a roomful of expensive and labor-intensive equipment to integrated microdevices requiring little oversight.

In April, a team of academic scientists working with Microchip Biotechnologies, a Dublin, Calif.-based startup founded by three Amersham veterans and a UC Berkeley researcher, published details of an integrated, Sanger-based micro DNA sequencer they developed that fits into the palm of your hand. The company is one of at least three groups trying to lower the cost of and miniaturize Sanger sequencing.

Developers say these devices will cut reagent and personnel costs while maintaining the high accuracy and long sequence reads for which the Sanger method is known. By using tiny amounts of starting material, they also plan eventually to abolish clonal libraries, a cumbersome step in sample preparation, and replace them with bead-based amplification.

At the moment, the technology has enabled its inventors to create a 556-base sequence read with 99 percent accuracy. So far, none of the rival emerging sequencing technologies, like those developed by 454 Life Sciences and Solexa, has published similar read lengths. Such read lengths are required to detect structural genome variations — including repetitive sequences, gene inversions, deletions, and duplications — that play an important role in diseases like cancer, according to Richard Mathies, a professor of biophysical and bioanalytical chemistry at Berkeley.

"This is one of the reasons why we thought it was important pushing Sanger to its ultimate limit," says Mathies, senior author of the paper, which appears in *PNAS*.

Microchip Biotechnologies CEO Stevan Jovanovich says he wants to commercialize an integrated, microfabricated DNA sequencer based on Mathies' developments that includes bead-based template amplification, sample prep, and separation, in 2008.

— Julia Karow

PATENT WATCH

US Patent 7,034,143. **Systems and methods for sequencing by hybridization**. Inventors: Franco Preparata and Eliezer Upfal. Assignee: Brown University Research Foundation. Issued: April 25, 2006.

This patent covers a method related to "nucleic acid probes comprising a pattern of universal and designate nucleotides, or 'gapped' probes, and the use of sets of gapped probes in sequencing by hybridization to determine the sequence of nucleic acid sequences. The inclusion of universal nucleotides in the probes allows for efficient and rapid sequencing of longer nucleotide sequences than can be sequenced using traditional probes."

US Patent 7,041,455. **Method and apparatus for pattern identification in diploid DNA sequence data**. Inventors: Charles Magness and Dake Sun. Assignee: Illumigen Biosciences. Issued: May 9, 2006.

This provides methods for (1) obtaining two parental allele sequences from diploid DNA sequence signal data, (2) identifying the mutation and haplotype patterns in the two parental allele sequences, (3) assigning likelihood scores for the mutations thus identified, and (4) identifying patterns of methylation.

DATAPOINT

$8.8 MILLION

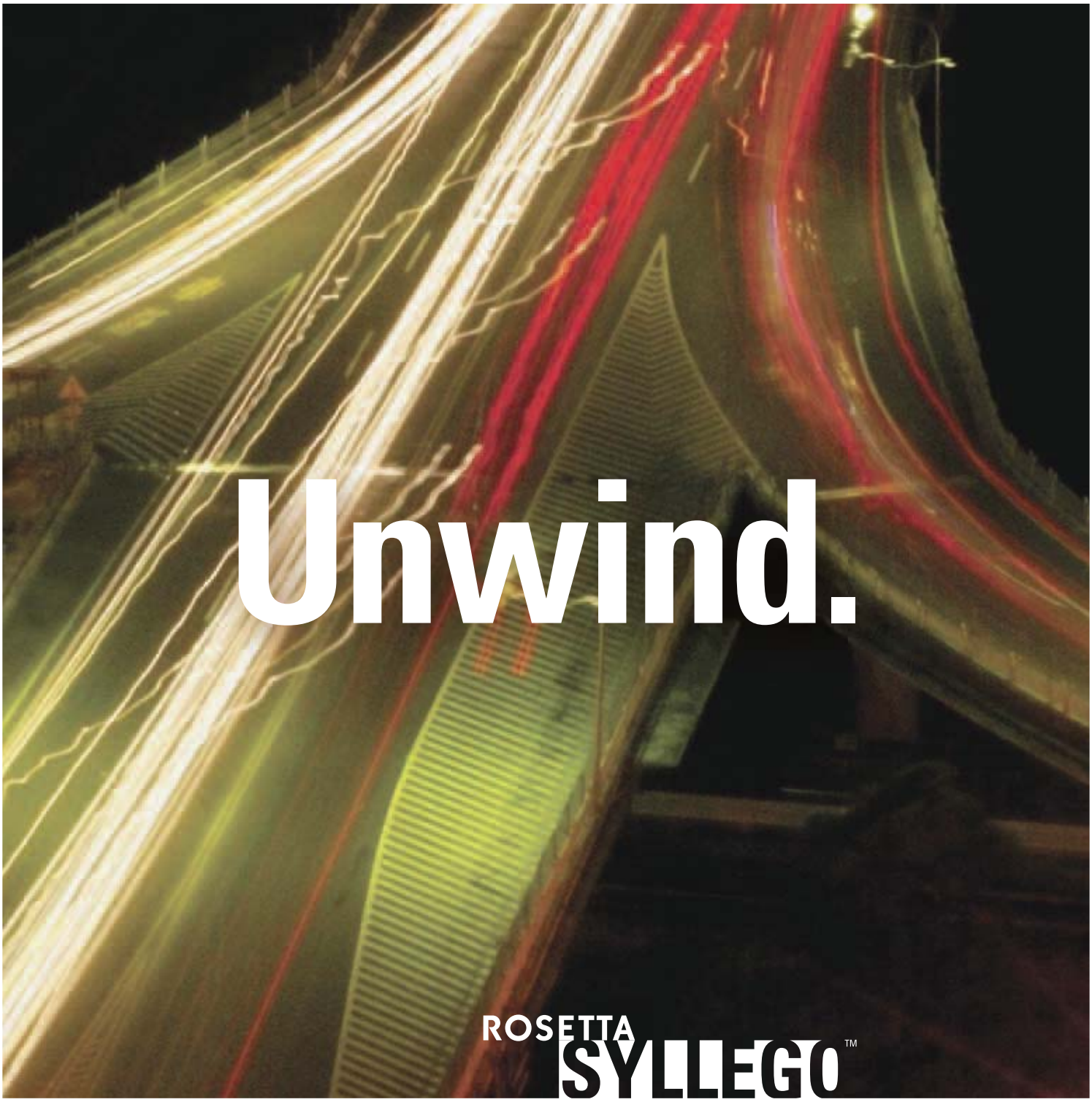
Revenues generated by 454 Life Sciences from sales of instruments, reagents, fee-for-service sales, and milestone and royalty payments for the first quarter of this year, up from $1.3 million a year ago.

During its quarterly earnings report this spring, **Applied Biosystems** noted that revenue from its DNA sequencing segment declined 4 percent to $136.5 million. Overall, the company reported an 8 percent increase in sales, buoyed by its mass spec and real-time PCR divisions.

DNAStar introduced its "Rising Star" grant program for small colleges, aimed at helping smaller academic institutions buy the company's Lasergene sequence-analysis software. Colleges or universities meeting the terms of the program can receive up to $2,500 in matching funds toward the purchase of the software.

454 Life Sciences and distribution partner **Roche Diagnostics** expect to release the beta version of a new sequencer, called the Genome Sequencer 100, that they say will be better at sequencing larger genomes. Meanwhile, the companies also introduced a new version of the current Genome Sequencer 20 machine that has improved single-read accuracy, software algorithms with additional applications, better reagents, and a LIMS interface.

Reveo, an R&D firm based in Elmsford, NY, announced that it has partnered with the **University of Washington** to develop a portable DNA sequencer based on nanoprobe arrays. **Babak Parviz**, director of the Nanosystems Laboratory and a faculty member in the Department of Electrical Engineering at the University of Washington, will lead the university's participation.



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Researchers Now Testing PSI's GE MIAPE Module

Proteomics researchers are currently testing preliminary guidelines released by the gel electrophoresis module of the Proteomics Standards Initiative's Minimum Information About a Proteomics Experiment standard, according to PSI officials.

Frank Gibson, the leader of MIAPE's gel electrophoresis module, reported during the PSI's spring workshop in San Francisco this April that the MIAPE-GE committee had finished gathering a requirements list, and had obtained comments about the list from a panel of experts on gel electrophoresis. Proteomics researchers are now testing the guidelines.

"The external reviewers said in general that the coverage [of the guidelines] is comprehensive and the clarity is excellent," said Gibson. "Overall, they said, 'Keep it at a minimum. Don't add more.'"

Some of the MIAPE-GE reporting requirements include disclosing the date the experiment was performed; the person who performed the experiment; the name of the electrophoresis process used; the sample name; a description of the loading buffer; the number of dimensions of the electrophoresis process; the separation method employed for each dimension; a description of the gel matrix; the physical dimensions of the gel; a description of the protocol used to run the gel; a description of what was done between gel dimensions; a description of the protein/peptide detection process; the name of the image acquisition process; and a description of the gel image, including image name, dimensions, and resolution.

In the first stage of the MIAPE-GE testing, the requirements were simply listed in a Microsoft Word document, Gibson said. However, it would be a goal in later stages to have software programs that can automate the information-gathering process.

The gel electrophoresis module is one of nine MIAPE modules that have been formed so far. The PSI created the MIAPE guidelines in order to enable researchers to reproduce proteomics experiments originally performed by their peers, and to be able to reanalyze data from those experiments to answer different questions.

— *Tien-Shun Lee*

PATENT WATCH

US Patent 7,034,287. **Mass spectrometer and method of use**. Inventors: Akihiko Okumura and Izumi Waki. Assignee: Hitachi. Issued: April 25, 2006.

This patent pertains to "a mass spectrometer combining an ion trap and a TOF/MS non-coaxially, wherein ion trapping efficiency, mass resolution, and CID efficiency can be maximized. [This includes] having a mass filter disposed between an ion source and an ion trap and a controller for controlling the gas pressure inside the ion trap and the gas pressure inside the mass filter independently, wherein the gas pressure inside the ion trap is set to the level higher than that inside the mass filter."

US Patent 7,030,373. **MALDI plate construction with grid**. Inventors: Marvin Vestal and Timothy Hutchins. Assignee: Applera, MDS. Issued: April 18, 2006.

A MALDI plate construction is provided to support a sample in a manner to effect mass spectrometry of the sample. The plate construction comprises a sample receiving surface, a plate holder for retaining that surface, and an electrically conductive grid positioned adjacent to the sample receiving surface and in electrical contact with the plate holder.

DATAPOINT

$13.7 million

Value of NIH award to a team of scientists led by the Texas Agricultural Experiment Station to determine the three-dimensional structures of a "large number" of *Mycobacterium tuberculosis* proteins. The five-year project will use protein crystallography to identify potential drug-binding sites.

Thermo Electron reported that first-quarter revenues grew 22 percent as R&D spending rose 6.6 percent and profits fell by 4 percent. Sales in the firm's measurement and control segment increased 4 percent to $172 million from $166 million.

Meanwhile, **Waters** announced that sales for the first quarter increased 8.2 percent atop rising R&D spending and a narrowed profit. The company credited in particular growth in Asia and the Acquity UPLC chromatography technology for its performance, which Waters characterized as "above our projections."

Sigma reported that sales were up 10.8 percent, R&D costs grew 8.3 percent, and net income fell 10 percent during the first quarter of this year.

Russia's **Ministry of Health and Social Development** has approved as medical devices **Bruker Daltonics**' entire MALDI-TOF product line, including Bruker's microflex, autoflex TOF or TOF/TOF, and ultraflex TOF/TOF mass spectrometers, as well as its ClinProRobot sample preparation platform.

NIH gave a five-year, $13.3 million grant to researchers from **Carnegie Mellon University** and the **University of Pittsburgh** to establish a National Technology Center for Networks and Pathways. The center will focus on developing fluorescent probe and imaging technologies to investigate regulatory pathways and networks in real time in living cells.

DNAVision has become a service provider for **Eppendorf**'s DualChip microarrays, which makes DNAVision the first European lab to provide services for low- to medium-density microarray testing.

The **International Standards Organization** has awarded **Geneservice**'s facilities its ISO 9001:2000 certification for functional genomic products and the conduct of contract research for academic and commercial customers. The Cambridge, UK-based company offers genotyping and gene expression services.

CombiMatrix Molecular Diagnostics has begun shipping its first diagnostic microarray product, a chip developed with **Array Genomics** that uses array CGH to detect copy number variations associated with both chromosome imbalances and imbalances linked to more than 40 defined genetic diseases and syndromes.

Scienion has launched the sciProclimate One climate chamber — which was developed by **Ribocon**, a **Max Planck Institute for Marine Microbiology** spin-off — that the company claims can provide constant temperature and humidity during the binding of capture molecules onto microarray substrates in the microarray production process.

Eurogentec has obtained a license for **Oxford Gene Technology**'s Southern array patents, which are the fundamental IP covering the manufacture, use, and marketing of oligonucleotide microarrays.

Array Diagnostic Development Heats Up

Now in its ninth month, Baylor College of Medicine's Prenatal Chromosomal Microarray Analysis service — the first of its kind — is just beginning to gain momentum, according to Arthur Beaudet, director of Baylor's cytogenetics lab.

Beaudet, who also chairs Baylor's Department of Molecular and Human Genetics, says that demand so far has been "relatively minimal, [but] it's just starting to increase. I think we are doing something between two to four [analyses] per week right now."

Baylor's service makes use of array comparative genomic hybridization using bacterial artificial chromosomes to interrogate a sample of amniotic fluid for more than 65 genetic disorders. While many in the field agree that array CGH is well-suited for prenatal screening, some of Baylor's commercial rivals believe its service is too much, too soon.

According to Mansoor Mohammed, CSO and executive vice president of CombiMatrix Molecular Diagnostics, "prenatal testing is an injustice to the rest of the [array CGH] community."

CMDX has its own plans to offer a diagnostic service using array CGH, and will begin screening samples for constitutional changes in adult patients with mental retardation later this month. However, Mohammed previously said that there is not enough data available to support comprehensive array CGH-based prenatal testing.

"More genotype-phenotype associations need to be [made] before [array CGH] can be used in the prenatal arena," Mohammed says. He adds that it is too soon to begin using an emerging technology like array CGH to counsel patients who could decide to terminate a pregnancy based on the analysis.

Others have voiced concern over Baylor's CMA service, and the issue prompted a *Nature* editorial on the topic in the Dec. 8, 2005 issue of the journal. The editorial used Baylor's case to specifically call for an increased regulatory presence in the area of microarray-based diagnostics.

— Justin Petrone

DATAPOINT

$20,000

CombiMatrix received $1.9 million from the US Army Research Office to develop a mini microarray reader for biodefense applications. Robin Liu, the PI on the contract, aims to develop a rugged, toaster-sized reader that costs only $20,000.

PATENT WATCH

US Patent 7,033,757. **Mutation scanning array, and methods of use thereof**. Inventor: Gerassimos Makrigiorgos. Assignee: Dana-Farber Cancer Institute. Issued: April 25, 2006.

According to the abstract, the method described in this patent is directed to using a mutation scanning array to identify mismatches or polymorphisms in multiple genes or the same gene in multiple individuals. The array can be a chip or a microsphere and has elements containing immobilized oligonucleotides that collectively span at least 10 different whole genes.

US Patent 7,025,935. **Apparatus and methods for reformatting liquid samples**. Inventor: Aaron Jones and Brett Ellman. Assignee: Illumina. Issued: April 11, 2006.

This invention describes a compact and efficient format for liquid handling, which does not require active automation for transferring samples and which can be used to transfer fluid samples in the absence of an externally applied force. An apparatus or method of the invention can be used for reformatting samples when the array of source sample locations differs in shape or orientation from the array of destination sample locations.

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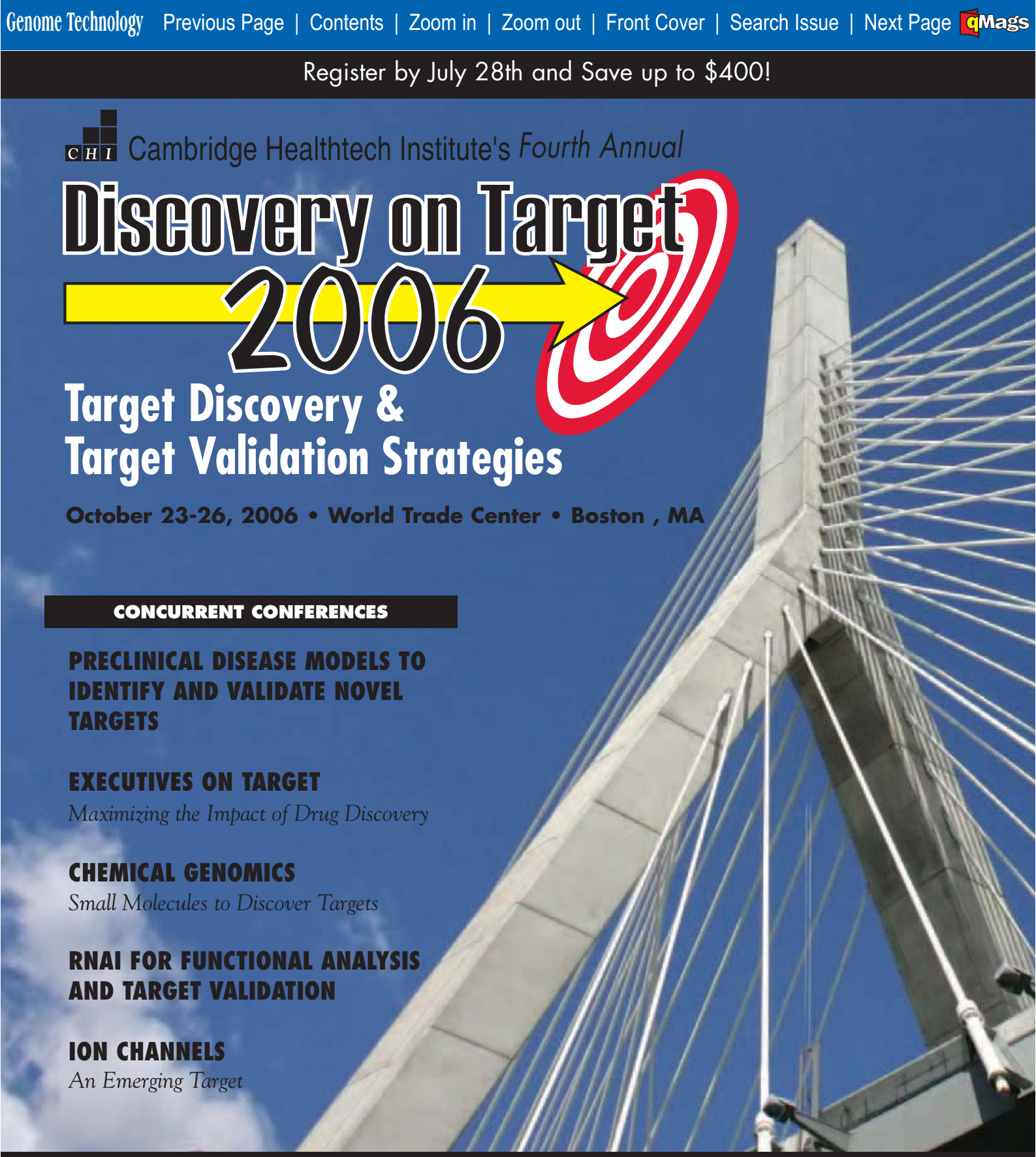

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UPCOMING EVENTS

Calendar of Meetings, Deadlines & Workshops

CONFERENCES

DATE	CONFERENCE	ORGANIZER	LOCATION	CATEGORY
JUNE				
Jun 2-6	42nd ASCO Annual Meeting	ASCO	Atlanta	Cancer
Jun 7-9	Bangalore Bio 2006		Bangalore	General
Jun 8-9	CAMDA 2006	CAMDA	North Carolina	Arrays
Jun 13-15	DDT China	IBC Life Sciences	Shanghai, China	Pharma
Jun 15-16	Structure-Based Drug Design	CHI	Boston	Pharma
Jun 18-22	Drug Information Association 42nd Annual Meeting	DIA	Philadelphia	Pharma
Jun 19-21	Beyond Genome	CHI	San Francisco	Genomics
JULY				
Jul 9-21	Quantitative Approaches to Gene	UCSD Regulatory Systems	UCSD	Systems biology
Jul 12-14	3rd Joint BSPR/EBI Proteomics Meeting	British Society for Proteome Research	Hinxton, UK	Proteomics
Jul 12-14	Conference on Systems Biology of Mammalian Cells		Heidelberg, Germany	Systems biology
Jul 17-18	Systems Biology, Toxicogenomics, and Drug Discovery	Medical College of Wisconsin, PhysioGenix	Milwaukee, WI	Systems biology
Jul 20-23	First International Conference on Computational Systems Biology	Fudan University	Shanghai, China	Systems biology
AUGUST				
Aug 5-9	20th Annual Symposium of the Protein Society	Protein Society	San Diego	Proteomics
Aug 6-10	11th International Congress of Human Genetics	Internat. Fed. of Human Genetics Societies	Brisbane, Australia	Genetics
Aug 6-10	ISMB 2006	ISCB	Fortaleza, Brazil	Bioinformatics
Aug 7-10	Drug Discovery Technology World Congress	IBC	Boston	Drug discovery
Aug 14-18	Computational Systems Bioinformatics Conference	Life Sciences Society	Stanford, CA	Bioinformatics
SEPTEMBER				
Sep 10-14	5th European Conference on Computational Biology 2006	Diesenhaus-Unitours	Eilat, Israel	Bioinformatics
Sep 14-16	HGV2006: Human Genome Variation and Complex Genome Analysis		Hong Kong	Genomics
Sep 17-21	Society for Biomolecular Sciences	SBS	Seattle	Screening
Sep 25-28	Chips to Hits	IBC Life Sciences	Boston	Microarrays
Sep 27-Oct 1	Genome Informatics		Hinxton, UK	Bioinformatics
Sep 28-29	RNAi Europe		Prague	RNAi
Sep 29-Oct 2	3rd Biologie Prospective Santorini Conference 2006	Biologie Prospective	Santorini, Greece	
OCTOBER				
Oct 8-12	International Conference of Immunogenomics and Immunomics	Diamond Congress	Budapest, Hungary	Genomics
Oct 8-13	Pathways, Networks and Systems 4		Mykonos, Greece	Pathways
Oct 9-13	International Conference for Systems Biology		Yokohama, Japan	Systems biology
Oct 10-14	ASHG 2006	ASHG	New Orleans	Genomics
Oct 14-18	Neuroscience 2006 Annual Meeting	Society for Neuroscience	Atlanta	General
Oct 16-19	GSAC 2006: Genomes, Medicine, and the Environment	Venter Institute	Hilton Head, SC	Genomics
Oct 28-Nov 1	HUPO 5th Annual World Congress	HUPO	Long Beach, CA	Proteomics
NOVEMBER				
Nov 13-14	4th Symposium on the Functional Genomics of Critical Illness and Injury	NIH	Bethesda, MD	Genomics
Nov 15-18	Pharmacogenomics	CSHL	Cold Spring Harbor, NY	Genomics

DEADLINES

June 8 — Poster submission deadline for the **5th European Conference on Computational Biology 2006**. Software demo proposals are also due on this date.

June 16 — Full proposals are due in response to NSF solicitation 06-555, **Plant Genome Comparative Sequencing Program**.

June 15 — Closing date to get applications in for the USDA's **Animal Genome National Research Initiative**, also known by the catchy handle USDA-GRANTS-101705-001.

June 21 — Applications due for NHGRI's research initiative on the **Identification of All Functional Elements in Selected Model Organism Genomes**, RFA-HG-06-006. Between six and 12 awards will be made under this RFA, which will be funded with $16.5 million dollars.

June 21 — Both letters of intent and applications are due at NHGRI for RFA-HG-06-007, **A Data Coordination Center for the Model Organism ENCODE Project (modENCODE)**. A total of $1.5 million dollars per year in total costs for three years is to be awarded through this RFA.

June 23 — Applications are due for RFA-RM-06-007, **Nanomedicine Development Centers** by the NIH Nanomedicine Roadmap program. Each multidisciplinary center will join a network of four NDCs that were awarded in fiscal year 2005.

June 24 — Applications due in response to PAR-06-088, **Innovations in Biomedical Computational Science and Technology SBIR Initiative**. The NIH asks that projects "span the interface of biomedical research and biomedical computational science and technology."

June 26 — Poster presentation abstract submission deadline for the **Society for Biomolecular Science's 12th Annual Conference and Exhibition**.

June 27 — Registration begins for the **232nd National Meeting of the American Chemical Society**.

June 30 — Early registration due for the **International Conference of Immunogenomics and Immunomics**.

July 1 — **HUPO 5th Annual World Congress** abstract submission deadline.

July 1 — Final deadline to submit abstracts for the poster session at the **7th International Conference on Systems Biology**. Topics include systems biology for medicine, systems biology of basic biological processes, and expanding fronts in systems biology.

July 11 — Applications are due in response to NSF's program solicitation 05-0577, **Biological Databases and Informatics**. The program encourages research on new methods, data structure, metadatabase architectures, algorithms, ontologies, and related sofware tools for biology.

July 12 — Full proposal target date for PD 04-1114, **Cellular Systems Cluster**. This NSF program focuses on the structure, function, and regulation of plant, animal, and microbial cells, and their interactions with the environment and with one another. Research using multidisciplinary approaches, computation and modeling, and approaches that exploit genomic information is encouraged.

July 15 — Young Investigator Award Competition deadline for **HUPO 5th Annual World Congress**.

BLUNT END

The Lighter Side of Life Sciences

Sudoku for Scientists

Here at *Genome Technology*, we're big fans of the "if you can't beat 'em, join 'em" philosophy. We tried waiting out the Sudoku craze — it has to go away at some point, right? — but finally we broke down and embraced the grid fad. Here's our version of Sudoku, with a genome twist: instead of the numbers 1 through 9, we use letters. When completed, one line of the puzzle will spell a name or term common in this field.

In case you haven't gotten hooked yourself, the rules are simple: each row, column, and bold-outlined box must contain all of the letters with no repeats. Good luck!

Puzzle #1 uses these letters: C G I N O T

		T	N		
N					T
	T			N	
	O			I	
G					O
		O	G		

Puzzle #2 uses these letters: A E G N R S

E	N			G	A
A					G
S					R
N	A			S	E

Puzzle #3 uses these letters: A J I M N O S T W

			W			S	O	
N							J	
		T			J	I		A
T	W	N				M	A	
		S		N	W			I
	A				S			
	T				N			O
S			T					M
A	M			O		N	W	T

Answers will appear under the Blunt End section on www.genome-technology.com

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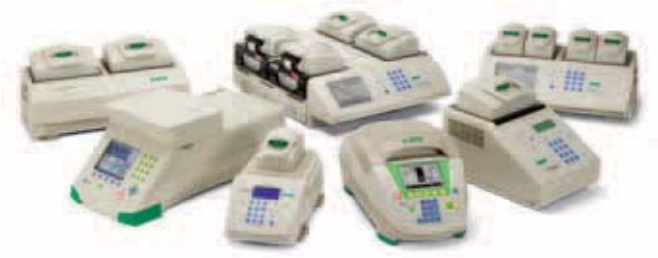

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