

Genome

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DUKE Institute For Genome Sciences & Policy

A Prescription for Success

Putting Pharmacogenetics into Practice

"The question is," says Chair of Community and Family Medicine Lloyd Michener, "when will all of this start becoming real?"

"This" is pharmacogenetics, the science of using patients' genetic data to inform the way drugs are prescribed. For decades, scientists have known that two people may take the same dose of the same drug and exhibit dramatically different responses. Moreover, they have known that a significant amount of difference in those responses can be attributed to variation in our genomes. The thinking among many clinicians and genome scientists is that if we can figure out which people respond best to which drugs based on their DNA, we can avoid many of the 100,000 or more serious adverse drug reactions that occur every year while improving both dosing and the overall quality of care.

Clinical Thinking

Michener's concern, he says, is exacerbated by the gap between our growing knowledge base and the time needed to incorporate that knowledge into real-world medical practice. "We're learning more about diseases and more about genetics. We have to put it all together and figure out how to deliver care to a diverse and aging patient population that has different diseases, different propensities for disease, and different preferences."

In an effort to close that gap, Michener and his staff at the Pickens Clinic on Erwin Road have teamed up with two IGSP Centers charged with translating academic concepts in genomics into workable clinical models. Geoff Ginsburg, Director of the IGSP Center for Genomic Medicine, and David



Goldstein, Director of the IGSP Center for Population Genomics & Pharmacogenetics, contend that if we want to know how—or even whether—to integrate pharmacogenetics into clinical practice, we need to start at the beginning. And that means understanding how drugs are prescribed right now and whether any indirect connections to patients' genotypes can already be made. To do that, the Duke team is conducting an observational study at Pickens and examining if particular gene variants can be correlated with particular medications doctors opt to use in their patients.

Pharmacogenetics (continued on pg 3) >



Message from the Director

Who wants to look under the hood of your genome and what do they want to know?

We have no idea how the battle over genetic privacy will play out. But I suspect that years from now, we will look back upon October 2005 as a pivotal time.

First, IBM, the largest technology company in the world, took the preemptive and unprecedented step of vowing never to use genetic information in its hiring practices or in determining health benefits for its 300,000 employees. Clearly, given its extensive involvement in computational research, including in genomics, IBM has a vested interest in setting itself up on the right side of the genetic discrimination issue. But whatever its motives, the company should be applauded.

Two weeks after IBM's announcement, Wal-Mart unwittingly betrayed a more jaundiced view of its workforce. In a memo leaked to *The New York Times*, a Wal-Mart executive mused about ways to cut benefit costs, including discouraging unhealthy job applicants, cutting employer 401(k) contributions and reducing company-paid life insurance to \$12,000. Given the company's willingness to contemplate such draconian measures toward a labor force whose average wage is roughly \$17,500 per year (and 55 percent of whom are not covered by company insurance), it's hard to imagine Wal-Mart ever stepping up to the plate against genetic discrimination the way its Fortune-500 compatriot IBM did.

What might tempt Wal-Mart to look at genetics as a way of reducing health expenses? You don't get to be a \$200-billion company by ignoring the bottom line. And increasingly, the cost of benefits is eating into corporate profits. One can imagine the reaction from some shareholders if Wal-Mart were to announce that it would never consider pre-existing genetic conditions in making hiring decisions.

Some (including more than a few members of the House of Representatives) have argued that all this concern about genetic privacy is a tempest in a teapot and that there is no need for federal legislation banning genetic discrimination and ensuring privacy of genetic or genomic information. The fact is, they say,

there are very few cases of genetic discrimination on record, and some 33 states already have at least some laws protecting citizens against it on the books. Moreover, the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) prohibits almost all employers from considering genetic risk factors as preexisting conditions or from selectively choosing what conditions they will or won't cover ("medical underwriting"). Nonetheless, hopes run high in some quarters that the House will at least agree to consider a version of the Genetic Non-Discrimination Act that passed the Senate earlier this year by a vote of 98-0.

And yet October also showed us some cracks in the façade. On October 4, the Chicago Bulls traded one of its star players, Eddy Curry, after he refused to take a DNA test to determine whether he carried a mutation that would predispose him to sudden death from cardiomyopathy, an excessive thickening of the heart muscle. Bulls General Manager John Paxson maintained that, in demanding the DNA test, his number one concern was for Curry's health. Given that Curry was already known to have an irregular heartbeat, can we really begrudge the Bulls for wanting a more complete picture of its player's risk? Ironically, barely two weeks after the Curry dustup, Atlanta Hawks center Jason Collier died at home after experiencing difficulty breathing. An autopsy revealed an enlarged heart possibly due to cardiomyopathy.

As the price of genome technology drops, the number of employer-employee conflicts over genetic privacy, as in the Bulls versus Curry, will only increase. Right now to sequence a human genome from the first base to the last costs about \$2 million. Not cheap to you or me, but a far cry from the several billion dollars we spent the first time around. The goal, of course, is to reduce the cost by another three orders of magnitude: the \$1000 genome. In genome sciences circles, the figure has become a mantra and a Holy Grail of sorts. NIH has vowed that it can be achieved within ten years. More than a few companies have bet their business plans on much faster developments.

So what happens then? What if, a decade from now, a large company (or its insurer) needs to spend just \$1000 per employee in order to uncover every genetic flaw in its workforce? What would Wal-Mart do then?

Heck, what would Duke do then? Would we begrudge Coach K wanting to prescreen his players' genomes for heart defects, if only to protect their well-being? Can we imagine a scenario under which the genome sequences of everyone else in the Duke community were encoded on our DukeCards and used to assign each of us to a benefit category? Or would Duke consider going the way of IBM and "just say no"?

There are no easy answers. But if American institutions—from the board room to the hardwood—are contemplating these issues, then perhaps it's time for Duke to do the same. ▶

Huntington F. Willard, Director

Pharmacogenetics (continued)

"The idea," says Goldstein, "is [to find out] if, in this normal clinical setting, the choices that are made by the physicians as to what medicines to use are [indirectly] influenced by the genetic makeup of the patients. If so, then that strongly suggests that using genetic information would be useful to guide treatment choices."

The Duke team has chosen to study hypertension, asthma and high cholesterol. Why those three? "They are common disorders in our population," says Ginsburg. "Plus, we believe the genetic variants in them that could affect drug efficacy and potential side effects are well known."

The investigators plan to enroll 400 newly diagnosed patients in each category just as they are starting pharmacological treatment. Once they give their consent, patients will be asked for blood samples for DNA, biomarker and various other laboratory tests. As the study progresses, doctors at Pickens will monitor patients' dosages, compliance, side effects, and how well the medications appear to be working. After one year of treatment, subjects' DNA will be analyzed to see if genetics can be used to predict both positive and negative responses to patients' drug regimens.



The Pickens Clinic on Erwin Road

Industry: Getting Beyond the Hype

Over the last few years, pharmacogenetics has been the subject of extensive media coverage; a recent internet search on the subject retrieved nearly two million hits. A report issued this fall by the United Kingdom's national academy of science lamented media hype over pharmacogenetics and complained that the field has been saddled with unrealistic expectations.

While acknowledging that the media may have jumped the gun, some scholars within the IGSP think pharmacogenetics is inevitable. Senior Policy Analyst and close observer of pharmacogenetics Susanne Haga, for one, believes the science has come too far for companies to ignore genetics or other biomarkers in assessing a drug's safety and efficacy. In addition, she thinks the recent guidance issued by the US Food and Drug Administration regarding when and how to include pharmacogenetic data when submitting applications for new drug approvals represents a watershed.

"It's a whole new ballgame," she says. "The fact that [FDA administrators have] recognized the importance of pharmacogenomics says a lot. They now have an office dedicated to pharmacogenomics—it really puts their money where their mouth is. At the same time, they also recognize the relative immaturity of the field."

Pat Deverka, Genome Ethics, Law & Policy Wyngaarden Fellow, agrees that the FDA's guidance will encourage industry to conduct more studies, but thinks the field has yet to experience a tipping point. "There hasn't been anything in the marketplace [so far] that's demanded a policy solution."

Both Haga and Deverka see the poster child for pharmacogenetics as Herceptin, a chemotherapeutic treatment for metastatic breast cancer. Patients whose tumors overexpress a particular genetic marker (*HER2/neu*) are more likely to respond to Herceptin with limited side effects than those without overexpression of *HER2/neu*. Testing for the marker is now a routine part of breast cancer care. A recent report in *The New England Journal of Medicine* hailed the effects of the drug in those patients who overexpress *HER2/neu* as "simply stunning."

Deverka believes the lesson from Herceptin may be that oncology is among the best places to look for further opportunities in pharmacogenetics. "People still die from the wrong [cancer] treatments," she says. "And many of these new breakthrough products like Herceptin are biotech products that are very expensive—so there's an economic incentive to [do pharmacogenetic testing]."

Data Please

Rare successes like Herceptin notwithstanding, Goldstein believes the slow uptake of pharmacogenetics is largely due to "...our complete ignorance. There just aren't sufficient data right now to guide treatment choices by genotype," he says. "Lots of genetic studies have been done, but too often they've been done in idealized settings [rather than] real clinical contexts with all of their complexity."

Michener thinks the sooner that complexity can be addressed, the better off his patients will be. "Right now," he says, "it takes us probably two to three months to get a depressed patient on appropriate antidepressants. Hypertensives take even longer. We go through a very slow and painful process of finding the right drugs and the right dosages."

From Drug Response to Community Response

The prospect of identifying appropriate medications for each patient is an easy sell to his staff, says Michener. The patients seen by his department, on the other hand—largely African-American and from Durham's lower economic strata—will probably need to be convinced. Michener believes that their reticence is understandable and stems from the Tuskegee syphilis experiments, where, over a 40-year period ending in 1972, 400 black men with late-stage syphilis were used for medical experiments. The legacy of Tuskegee, he says, is a lack of trust in academic institutions and in medical research in general.

"[Our patients are] not going to give us carte blanche and assume we have their best interests at heart. We're going to have to talk it through, make it clear this is optional and that at every point in the process they are in control of what treatments they get. This [study] will test the trust we've spent decades trying to build." ▀

Faculty Profile: Brian Chadwick, PhD

Brian Chadwick came to Duke in 2003 and was appointed an IGSP Scholar this July. In September, he joined the Department of Cell Biology as an Assistant Research Professor.

Chadwick did his doctoral work at the Imperial Cancer Research Fund and was awarded a PhD in Molecular Genetics from University College

London in 1997. Subsequently, as a Research Fellow at Harvard Medical School under the supervision of Jim Gusella and Susan Slaugenhaupt, Chadwick worked on mapping disease genes on human chromosome 9.

From the time he moved to Case Western Reserve University in 1999, Chadwick's focus has been on X chromosome inactivation—the mechanism whereby, just before implantation of

the embryo, expression of most of the genes on one of the two X chromosomes in females is turned off. "X-inactivation is the mammalian dosage compensation mechanism," he explains. "It's nature's way of ensuring that females, like males, have no more than the appropriate number of X-linked genes active in each of their cells."

Chadwick is particularly interested in how X inactivation persists through repeated cell divisions and how the inactive X gets packaged into transcriptionally inactive material called heterochromatin. During his post-doctoral training, Chadwick discovered that inactive X chromosomes are characterized by at least two types of heterochromatin. A major focus of his current research involves trying to elucidate the spatial organization of the different types of heterochromatin along the inactive X.

"I find X inactivation to be endlessly fascinating," he says. "But beyond the details of the process itself, my hope is that what we learn about heterochromatin and gene silencing on the inactive X will help us understand the more general process of cell differentiation. That's a place where the genome really impinges upon the biology of the cell." ▶

Brian Chadwick, PhD
Office: 4008 GSRB II
Phone: 684-2634
Email: brian.chadwick@duke.edu

Further Reading:

Chadwick BP, Willard HF. Multiple spatially distinct types of facultative heterochromatin on the human inactive X chromosome. *Proc Natl Acad Sci U S A*. 2004 101:17450-5.

The Way Things Used to Be

Hartemink Reconstructs Duplicated Genomes

Why would an organism duplicate its entire genome? Assistant Professor of Computer Science Alex Hartemink can think of at least one reason: if an organism can stably duplicate some or all of its chromosomes, he says, then one set becomes free to evolve new functions. "It presents a species with a tremendous opportunity for new evolutionary possibilities."

Research suggests that probably because of the asymmetric way their sex chromosomes are organized, higher animals do not appear to have duplicated their genomes much, if at all, over the course of evolutionary history. However, yeast experts agree that the evidence for genome duplication in their organism appears to be strong.

Getting Here from There

What Hartemink wanted to know is what the yeast genome looked like *before* its duplication event. To get at that question, he and former graduate student Peng Yin (now a postdoc at Caltech) set out to develop a computational method that might be able to reconstruct ancestral genomes. Their "genome halving" approach, which originated with a class project of Yin's, was described in a recent issue of *Bioinformatics* (21:869-79, 2005). Hartemink says the basic idea is akin to solving a puzzle in as few steps as possible.

"The general principle behind the algorithms is that the simplest explanation is best," he says. "We're asking, 'At least how many steps would be required to see what we see today?'"

Ancient Genes, Modern Functions

Why might one be interested in reconstructing those paths in the first place? "Part of our curiosity is simply archeological or historical," says Hartemink. "We would like to know what early versions of these organisms looked like. But as with any archeologist, it's not only because we're curious, but also because it allows us to ask new questions. For example, if we knew what the ancestral sequence was, we might learn things about the rate at which evolution is taking place in the duplicated genes. Or perhaps the presence or absence of certain genes in the ancestral genome can give us clues as to the environment in which these creatures were living at the time."

Assistant Professor of Molecular Genetics & Microbiology and fungal genomicist Fred Dietrich thinks reconstructing ancestral genomes is an intrinsically appealing notion for any genome scientist interested in understanding what contemporary genes do. "Of yeast's 6000 genes, we still don't know the function of 1400 or so," he says. "In humans, we still don't know what most of the genes do. So I think [genome halving] can help us understand something about basic biology. By understanding where these [duplicated] genes came from and their relationship to other genes, often we can learn something about their function." ▶



The Fantastic Plastic Brain

Recent Recruits Explore Synapses at the Genomic Level

A few years ago, a popular science book appeared with the title *Nature Via Nurture*. The central idea, as expressed by the title, was that genes did not act in a vacuum, but rather, they acted in concert with—and often in response to—the environment. Two recent arrivals to the Department of Neurobiology, Assistant Professors Anne West and Nicole Calakos, are showing that nowhere is this relationship between genes and environment more evident than in the brain.

Neuron to Neuron

The human brain is estimated to contain some 100 billion nerve cells, the neurons. Elaborate networks of neurons send and receive messages as electrical impulses between the body and the brain. These messages may contain sensory information such as heat or pain, or they may elicit muscle contractions. How do such messages, conveyed by chemical neurotransmitters like dopamine and serotonin, bridge the gaps between neurons? They use something called the synapse.

“Synapses are the connections between neurons,” says West. “They form a crucial site of information transfer—and transformation—in the brain. [Most] synapses form in the months after birth, at a time when the brain is beginning to be inundated by sensory signals from the outside world. You can observe that yourself if you watch a child grow—you can see how quickly she learns from the environment and changes her behavior with respect to it.”

It is that flurry of signals in the first year or so of life, says West, that causes proliferating neurons to fire and turns on a large number of genes, many of which play important roles at the synapses. “This kind of synaptic plasticity, in which the environment modifies the structure and function of synapses, is thought to be crucial for learning.”

Looking for the Knockout Punch

One tool West is employing to study synaptic development is RNA interference (RNAi), the use of double-stranded RNA to block the expression of specific genes. West’s aim is to turn off or turn down those genes suspected to be involved in the formation, stabilization and/or elimination of synapses in order to understand what those genes do. According to her, traditional approaches to knocking out genes in mice thought to be involved in synaptic processes have had limited success, in part because synapses tend to grow like weeds.

“It’s been difficult to identify the molecules required for synapse formation, because it seems that no matter what [gene] you knock out, synapses still form.” The advantage of RNAi, she says, is that it is faster and cheaper than conventional knockouts and makes it possible to block expression of multiple genes.

In the Zone

While West concentrates on early postnatal development, Calakos’s focus is on proteins that mediate synaptic plasticity in the adult. Of particular interest to Calakos is a family of proteins (and the genes that encode them) called RIM that live in a specialized area of the synapse known as the presynaptic active zone.

“The presynaptic active zone is command central for neurotransmitter release,” explains Calakos. “RIM mediates several forms of presynaptic plasticity by altering the probability that neurotransmitter release will occur. We are studying the [connection] of this plasticity to learning and memory.”

The Healing Brains

In addition to doctorates in neuroscience, both West and Calakos have medical degrees and both see their work as being readily applicable to

clinical problems. West, for example, is trying to understand gene activity in the brain in the autism-like neurodevelopmental disorder Rett Syndrome.

Calakos is using mouse models to study synaptic function in Parkinson’s disease and the movement disorder dystonia. She is also collaborating with David Goldstein, Director of the IGSP’s Center for Population Genomics & Pharmacogenetics, on finding variants in synaptic plasticity genes that are associated with candidate diseases. She believes her involvement with Duke’s Center for Translational Neuroscience will allow her to integrate her basic research with her role as a clinician.

“My goal as a member of the Center for Translational Neuroscience is to bridge my experiences in the clinic to the questions we are studying in the lab,” she says. “For example, I hope to screen patient populations I identify in my clinical work.” ▶



Anne West and Nicole Calakos

The Crooked Path to Disease

Analyzing Molecular Pathways to Guide Treatment in Cancer

Despite declining death rates, recent data from the Centers for Disease Control and Prevention show that cancer remains the second leading cause of mortality in the US. What makes cancer such a tenacious and prolific killer in the face of the best efforts of biomedical science? Two decades' worth of research suggests that much of cancer's resilience lies in its genomic complexity. For example, we now know that tumors develop when multiple independent mutations accumulate in genes underlying cellular signaling pathways, thereby disrupting cells' ability to control their own growth.

In a recent paper in *Nature* (published online November 6), Joe Nevins, Director of the IGSP's Center for Applied Genomics & Technology, and his colleagues attempted to correlate changes in gene expression (the degree to which genes are turned off or on) with the complex biology of the various "broken pathways" seen in cancer. In doing so they have detected recurrent patterns—pathways made up of multiple underlying genes that appear to be consistently deregulated in certain types of tumors. Furthermore, they have found that dysregulation of specific pathways can be used to predict disease outcome and perhaps identify more effective therapies.

From Test Tube to Tumor

The Nevins team first wanted to prove that its approach could be used to distinguish normal cells from those expressing genomic signatures indicative of cancer. They created artificial cancer conditions by introducing a series of cancer-causing genes ("oncogenes") known to disrupt specific pathways into otherwise normal cells. By comparing gene expression patterns in those cells

"It's really the combinations of pathways that reveal both important biology and subgroups of patients with quite distinct clinical outcomes."

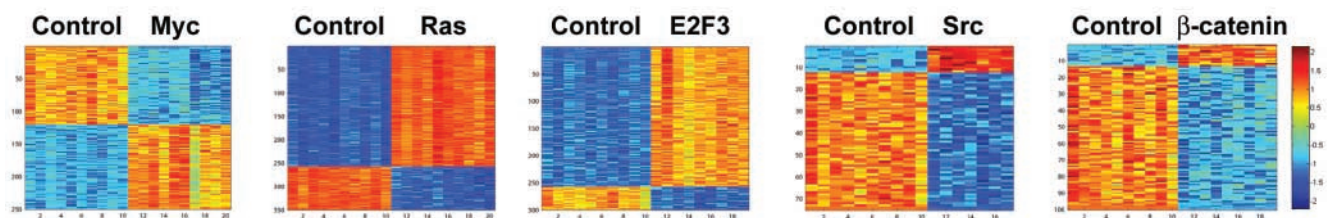
harboring oncogenes against patterns seen in normal cells, it became clear that each cellular signaling pathway is associated with a unique pattern of gene expression. Moreover, the gene expression signatures could be used to *predict* which cells carried the oncogenes and the associated deregulated pathways.

Having proved the validity of the approach in cells (and subsequently in mice), the IGSP team wondered whether the pathway approach would work in human tumors. Their first goal was to try to distinguish two types of lung cancer from each other: adenocarcinoma, which originates in the periphery of the lung, and squamous cell carcinoma, which forms in the central chest area. What they found was that the overwhelming majority of adenocarcinomas were predicted to be deregulated for the oncogene Ras, while only a tiny minority of squamous cell carcinomas exhibited Ras deregulation. The upshot, says Nevins, is that deregulation of the Ras pathway appears to be an important signature of adenocarcinomas.

Nevins notes that even more powerful insights can be gained by looking for patterns of multiple pathway deregulations in any given tumor. "It's really the combinations of pathways that reveal both important biology and subgroups of patients with quite distinct clinical outcomes."

Special Treatment

Nevins emphasizes that simply stratifying patients into different groups such as "high risk" and "low risk" is not enough. What he and his clinical collaborators want to know is whether gene expression signatures associated with deregulation of a particular pathway might also be used to predict sensitivity to drugs



Finding gene expression patterns in cells that predict deregulation of cancerous pathways. Each of the five images compares levels of gene expression between control cells and cells manipulated to express one of five oncogenes. Genes are displayed by row, cellular samples by column. The effects of each oncogene on overall gene expression are color-coded according to the scale at right; genes expressed at high levels are shown in red, those expressed at low levels are shown in blue.

that target that pathway. In a series of breast cancer cell lines, for example, they found that the gene expression signatures indicative of pathway deregulation did indeed predict whether the breast cancer cells would be sensitive to drugs targeting particular pathways. In other words, gene expression data should be able to tell an oncologist which pathways are deregulated in a patient and therefore which drugs have the best chance of success.

Of course, says Nevins, the true test for this idea will come not from cell lines but from actual cancer patients. To that end, the IGSP team is in the midst of setting up a clinical trial where the prospect of using pathway analysis to help later-stage lung cancer patients can be explored.

“To figure out how to use [therapeutic] agents in a truly targeted way, the classic place to start is in a patient population that has advanced disease,” says Assistant Professor of Medicine and medical oncologist Jennifer Garst, a lung cancer specialist and collaborator on the project. “Our plan is to obtain tissue from these patients, see where the dysregulated pathways are, design a targeted treatment for them and then use that targeted therapy.”

Anil Potti, a medical oncologist and research fellow in the Nevins lab, believes that, ultimately, multiple targeted therapies will be necessary. “I don’t think [advanced] lung cancer will ever be cured by one therapeutic agent. But if each agent can take care of, say, 10 or 20 percent [of the disease], then we can combine agents and start getting to a place where a much larger number of patients are getting adequate treatment. Suddenly it’s no longer just a blind shot where everyone gets the same surgery and the same chemotherapy.”

This Year’s Model?

Beyond lung cancer, the Duke team is applying the pathway approach to breast and ovarian cancer. In those cases, Nevins says the principle is the same. “Let’s say within a group of [ovarian cancer] patients we identify a subpopulation that’s really at high risk. Why sit around waiting for those people to have recurrences and then try to figure out what to do? Let’s be aggressive: predict pathway status and then try to find therapeutics that match the characteristics of the individual patient.”

Andrea Bild, a postdoc in the Nevins lab and first author on the *Nature* paper, thinks pathway analysis represents a great opportunity for personalized medicine but expects that applying the method to breast cancer will require some tweaking. “Breast cancer is so diverse and so complex,” she says. “The patterns we see in those data are not as easily translatable as the lung and ovarian data. It’s going to take a more refined understanding of the dataset before we can make the same contribution [in breast cancer] that we can in the other two cancers.”

Potti is hopeful that any such challenges can be overcome. “There will always be disease-specific modifications,” he says. “For example, if we want to do this in brain tumors, we will probably need a different set of pathways, which we haven’t found yet. But in theory it should work. The important thing is that we keep trying to move it into patient care ASAP. Every day that goes by is a day lost to some patient.”

Faculty Profile:

Jingdong Tian, PhD

IGSP member and Assistant Professor of Biomedical Engineering Jingdong Tian came to Duke this fall. After completing his doctorate at SUNY Stony Brook in 1998, Tian moved to Harvard Medical School where he worked as postdoctoral fellow in Joan Ruderman’s lab and began to study cellular signaling and cell cycle regulation.

Remaining at Harvard, Tian moved to George Church’s lab in 2001 and turned his attention to synthetic systems biology and bioengineering. In his view, building synthetic genes, circuits and networks are potentially powerful tools for understanding cellular behavior.

“A sure way to learn how a clock works is by taking it apart and putting it back together again,” he says.

“Similarly, a good way to test genomic hypotheses is to design and build genetic systems—be they genes, genetic circuits, pathways, or even whole genomes—from scratch and see how they work.”

Currently, says Tian, there are limitations with that approach: gene synthesis is costly and slow. In an effort to lower those barriers, he spent much of his time in Church’s lab developing a new multiplex gene synthesis technology using programmable DNA microchips.

“This could be a starting point to dramatically reduce the cost and increase the speed of gene synthesis,” he says. “Our goal is to further improve the technology and make gene synthesis as easy and convenient as other molecular biology techniques such as the polymerase chain reaction. If we succeed, it would not only be useful for genome science research, but would also be of tremendous practical value for the pharmaceutical industry and for biomedical engineering.”



Jingdong Tian, PhD
Office: 1383 CIEMAS
Phone: 684-3494
Email: jtian@duke.edu

Further Reading:

Tian J, Gong H, Sheng N, Zhou X, Gulari E, Gao X, Church G. Accurate multiplex gene synthesis from programmable DNA microchips. *Nature*. 2004 432:1050-4.

Genomes@4

Not just another seminar series! The IGSP invites you to a biweekly series, "Genomes@4", held on Thursdays (at 4 o'clock naturally). This is an opportunity for all IGSP faculty, collaborators, students and any other interested parties at Duke to hear presentations and engage in discussions on various topics relevant to the genome sciences, ethics, and policy. Note new location: Bryan Research Auditorium, Room 103

November

- 17** **Pascal Goldschmidt, MD**, Chair, Department of Medicine; Genomics of Atherosclerosis

December

- 1** **James W. Vaupel, PhD**, Sanford Institute for Public Policy; Genetics and Genomics of Human Aging
- 15** **Winter Break**

IGSP Distinguished Lectures

All lectures take place at 3:00 in the Schiciano Auditorium in the F-CIEMAS building

- Friday, Nov. 18** Distinguished Lecturer **Arno Motulsky, MD, ScD**
"Impact of Genetics and Genomics on the Biomedical Sciences and Medicine"
- Thursday, Dec. 8** Distinguished Lecturer **Stephen O'Brien, PhD**
"Genetic Architecture of Complex Diseases: Lessons from AIDS"



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The Institute for Genome Sciences & Policy

Duke University
CIEMAS
101 Science Drive
Box 3382
Durham, NC 27708
www.genome.duke.edu

© 2005 Duke University
Durham, NC 27708 USA
919.684.8111