

Genome

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Issue 4

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DUKE Institute For Genome Sciences & Policy

Center for Genomic Medicine is Born

Called "Logical Missing Piece"

In December, the Duke Institute for Genome Sciences & Policy (IGSP) announced the formation of the Center for Genomic Medicine (CGM). The CGM, which joins the other key research centers housed within the IGSP, will focus on the translation of genome sciences into clinical practice. When asked about the impetus for the creation of the CGM, IGSP Director Hunt Willard says simply, "It represents the finish line. If we're actually going to do genomic medicine, we're going to have to do it in the clinic. Neither we nor anyone else has had in place a unit specifically designed to examine both the science and policy issues relevant to translating scientific findings from the genome arena into a standard of clinical care. To me, this Center is the most logical missing piece of the IGSP and it's long overdue."

Willard cites two relationships as being key to the success of the CGM. The first involves the Center for Genome Technology, where the goal will be to take new developments in genome technology and, once they've achieved scientific muster, hand them off to the CGM where physicians and physician-investigators can determine how best to integrate those innovations into clinical medicine.

The second will be within the Duke University Health System and its ongoing efforts to develop a master plan for personalized medicine. Willard notes that personalized medicine involves a variety of issues ranging from lifestyle choices to "hardwired" factors relevant to personal health care decisions. "Genomic medicine is a critical part of that," he notes. "And while we've been



involved in various aspects of the discussions and the planning, we've lacked the sort of focus that comes with having a dedicated unit with a particular faculty champion directing those efforts."

Chancellor for Health Affairs Ralph Snyderman, Duke's most vocal and visible proponent of personalized health care, sees the CGM as an important part of the university's mission to reshape clinical medicine. "The Center for Genomic Medicine will play an important role in the transformation of health care, the development of personalized medicine and individual health planning. The relationship of both the IGSP and the CGM to Duke Health will enhance the value and impact of all three entities."

Center is Born (continued on pg 3) >

2003: The Genome Year in Review

We have to be honest with ourselves. When it comes to genome sciences and policy, the answer to the rhetorical question “Are We There Yet?” is still usually “No”. And yet, as we look over the past year’s genome-related headlines, we can’t help but be struck both by their breadth (from the serious to the frivolous) and by their reach (from the corporate to the academic to the public to the regulatory). We may not be “there” yet, but it’s clear that the Genome Revolution is underway in earnest. Without further adieu, here, in reverse chronological order, are *GenomeLIFE*’s entirely subjective Top Ten Genome Stories of 2003:

10 Draft of chimp genetic map published (*LA Times*, December 11)—What makes us human? Focusing in on the 1.2% of the genome where our genes differ from chimpanzees will surely yield some insights.

9 Genomics-derived drug for cardiovascular disease to advance to phase 3 clinical trials (*Dow Jones Newswires*, December 5)—What’s remarkable about this story is that it’s a story at all. In the mid-1990s, Wall Street was genuflecting at the feet of genomics only to shun the entire sector by the end of the decade. Now, judging by the NASDAQ’s recent run-up, boundless optimism has returned. But keep in mind that this drug for treating atherosclerosis and developed by Human Genome Sciences has its origins in a pact the company made with GlaxoSmithKline in 1993! The pipeline is indeed a long one.

8 Researchers find first heart attack gene (*AP*, November 27)—Eric Topol and his colleagues at The Cleveland Clinic found what many did not believe existed: a single gene that, when mutated, pretty much guarantees a heart attack sooner or later. While much of the genetics community is focused on finding many genes that contribute to the risk of developing common diseases, this is a powerful reminder that sometimes one is enough.

7 Open-source model challenges traditional biomedical research (*Wall Street Journal*, October 24)—This is exactly the kind of out-of-the-box thinking that energizes us here at Duke. Is it possible that open, interdisciplinary, collaborative research not only doesn’t hinder commercialization but may actually enhance it? Stay tuned.

6 In 95-0 vote, Senate passes bill barring genetic discrimination (*Wall Street Journal*, October 15)—Once in a while our elected representatives do the right thing. Sorry, insurance industry. Will the House of Representatives follow suit?

5 Every baby’s DNA may be stored for future health care (*The Independent [UK]*, June 25)—The British Government has asked its watchdog commission on DNA technology to consider the case for screening every baby at birth and storing his/her genetic profile for future use in tailoring health care according to individuals’ needs and their genes. If we are serious about personalized health-care in this country, we will have to confront this same issue, preferably sooner rather than later.

4 Genome Project completed (*Washington Post*, April 15)—A strange feeling is coming over us. We’re being transported back to the year 2001 and Francis Collins and Craig Venter are telling us that the human genome sequence has been completed (again) and this time they really mean it. Whoa, dudes. This is like déjà vu all over again. Can we do this every year?

3 Canadian scientists find code for SARS virus (*Washington Post*, April 14)—If there is a better example of how the genome sciences can contribute to the public health during an acute crisis, we’re not aware of it. Less than two months after the virus was identified, its sequence was freely available on the Internet. O Canada!

2 Ashcroft wants \$1B for DNA testing (*AP*, March 12)—There may be no bigger influence on our criminal justice system and no more tangible social consequence from the genome sciences to date. As lawyer, novelist and recent author of a nonfiction book on the death penalty Scott Turow observes, “DNA has been a revelation.”

1 Beer belly ‘gene’ found (*BBC*, January 8)—The genome year got off to a bang with this story about a gene that predisposes to huge increases in pounds and inches in older men. The only shock is that the culprit is not on the Y chromosome...

Who knows what 2004 will bring? We can hardly wait. ▶

The Editors of *GenomeLIFE*

Center is Born *(continued)*

Duke Comprehensive Cancer Center Director Kim Lyerly is hopeful that cancer can serve as a proving ground for personalized medicine and that the CGM will be a major part of that effort. "Cancer is [primarily] the result of genomic instability. So what we do is at the heart of what the CGM is all about. The hope is that we can extend the link from [full-blown cancer] to cancer susceptibility and that that link becomes a fundamental building block for prospective medicine and personalized health care."

Given the pervasiveness of genomics efforts nationally and internationally, it might be fair to ask how well Duke is positioned to bring about the union of genome science and clinical medicine. Willard notes that several institutions are pursuing so-called 'genetic medicine'. But he sees a clear distinction between *genetic* medicine as it's practiced currently and Duke's vision of *genomic* medicine. In his view, genomic medicine, like all good clinical medicine, considers the whole patient. Genetic medicine, on the other hand, is more apt to look at one gene at a time. "Genomic medicine really represents a data-intensive gestalt approach, as opposed to genetic medicine, which is the equivalent of, say, just looking at one aspect of a patient's record. To me genomic medicine represents not just a word change, but a fundamental shift in perspective. One needs both, of course, and Duke will now be able to do both."

"Genomic medicine represents a data-intensive gestalt approach, as opposed to genetic medicine, which is the equivalent of just looking at one aspect of a patient's record. To me, it represents not just a word change, but a fundamental shift in perspective."

When asked to comment on the creation of the CGM, Duke Medical Center thought-leaders sound notes of enthusiasm. Lyerly says that he looks forward to the Cancer Center collaborating with the CGM and, echoing Snyderman, finding ways of extracting the maximum value from both enterprises. Chair of Medicine Pascal Goldschmidt believes applications of genomic medicine to patient care at Duke will occur within the next five years. Together with other key units throughout the Medical Center, the CGM, he says, represents "...a unique opportunity for the patients who entrust us with their care, for the physicians who treat them, and for the trainees who come to Duke to become the new leaders of medicine."



The Center for Interdisciplinary Engineering, Medicine and Applied Sciences building, the likely home of the Center for Genomic Medicine

Willard also sees the CGM as being distinctive in its embrace of what he calls the "non-lab bench" elements of health care. The CGM, he says, will involve a broad range of experts, including health care analysts, health care economists and health policy specialists. Willard believes that for the CGM to succeed, it will be absolutely essential to involve people with experience in developing and delivering clinical programs within the context of a larger health system. Kevin Schulman, Director of the Center for Clinical and Genetic Economics at the Fuqua School and the Duke Clinical Research Institute, notes that Duke already possesses strengths in many aspects of institutional health care delivery. "The challenge for the new Center," he says, "will be in the systems part, i.e., bringing the total concept to individual patients."

Clearly, the next step for the CGM is to find a Director. Willard has several criteria in mind. "We want someone who is open to developing something outside of the box, which is what we're trying to do all across the IGSP. This hasn't been done before; thus, by definition, there's no blueprint out there to copy. My gut instinct is that there may be some interesting candidates on the for-profit side, as well as those in academic medicine. If someone from the private sector can bring in expertise in economic planning and business modeling and marry that with the strong science and academic medicine traditions we have here at Duke, then he or she may be a perfect fit. We'll see. We're going to look as broadly as we need to in order to find the right person. In combination with Duke University Health System, this will be an opportunity for real leadership." ▶

In the next issue of **GenomeLIFE:**

Environmental Genomics: Not Waiting to Exhale

FOCUS Program on Genome Sciences & Policy

*Profile on Maria Sippola-Thiele, PhD,
Assistant Dean of Business Development*

Biomedical Engineering Recruitment in Genome Science

Duke Delivers the Genome to Undergrads

...with a Little Help from HHMI

In a recent article in *Genomics & Proteomics*, Princeton geneticist David Botstein likened undergraduate biology education to “hazing,” lamenting that the current model for educating freshman interested in the life sciences is, “learn this now, it’ll be good for you later.” The problem with that model, of course, is that it tends to diminish rather than promote excitement for the life sciences among matriculating college students. Thus, according to this line of thinking, the field tends to become nothing more than a four-year means to an end for those interested in medical school or postgraduate training.

Duke Life Sciences Transformed

In an effort to combat the “learn this now” approach and its consequences, last year the Howard Hughes Medical Institute (HHMI) awarded \$80 million to research universities and gave them a mandate to “...address the challenges of a rapidly changing and increasingly interdisciplinary science.” As part of that mandate, HHMI expects that awardees—including Duke—will use the funds to bring emerging scientific disciplines such as genomics into the undergraduate curriculum. The \$1.8 million awarded to Duke in 2002 to fund the Making Meaning of Genomic Information Program represents the University’s fourth consecutive five-year grant from HHMI focused on education in the biological sciences. Trinity College Dean Robert Thompson believes that it is difficult to

overestimate what those grants have done by way of transforming how the life sciences are studied and taught at Duke. “Howard Hughes’ presence in facilitating life sciences research and education here in both the Medical Center, as well as in Arts and Sciences, has been enormous,” he says.

In addition to a variety of courses, seminars and capstone experiences, the Making Meaning Program features funded research scholarships and fellowships (see below). Both the Howard Hughes Research Fellows Program (first-year students) and the Summer Scholars Program (sophomores and juniors) offer eight-week mentorships with stipends of \$3300. Details are available on the Duke Howard Hughes Undergraduate Programs web site (<http://www.aas.duke.edu/trinity/hhughes/introduction/#overview>).

Although a substantial part of HHMI’s mission is to transform life sciences classroom learning, for Thompson, classroom education is only one part of the equation. What is at least as important is real-world laboratory experience. In this realm, too, he is grateful to HHMI for recognizing the necessity of getting undergrads into laboratories. “This program offers unparalleled opportunities for our undergraduates to be nurtured in their discovery of investigative work. It is those mentored types of experiences that make all the difference in their own learning while they’re here. Moreover, they are also the best preparation for moving on to graduate programs.”

Trinity Junior Spreads the Research Gospel

‘Genomic Information’ Program Immerses Student in Lab Life

At the tender age of 20, Emily Heikamp is already a veteran of laboratory research, having toiled in labs every summer since the age of 16. Thus, the fact that she was chosen to be a Howard Hughes Research Fellow as part of the Making Meaning of Genomic Information Program during the summer of 2002 seemed quite natural. “I saw an ad in The Chronicle and immediately knew it was something that I wanted to do,” says Heikamp. “Getting involved in research here can be somewhat intimidating

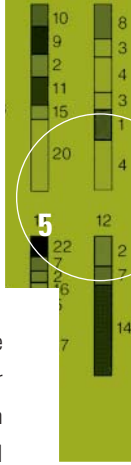
for a freshman. The Making Meaning Program made it possible for me to focus on research for eight weeks at Duke, providing a much more intensive experience than I could have received in the lab during the academic year.”

Heikamp worked in the lab of James B. Duke Professor of Immunology Garnett Kelsoe on the genomic mechanisms of recombination that give rise to the dizzying array of antigen receptor molecules residing on cells in the humoral immune system. “I learned more about

molecular biology techniques and basic immunology than I had in my undergraduate coursework at Duke thus far,” she says. She was particularly gratified by the opportunity to present her work in a public forum or two; in this case, at a research symposium for all of the summer research scholars and at a national conference at the University of Maryland in October 2002.

Other benefits from the program have also accrued. Heikamp will be included as a co-author on a paper to be published by Kelsoe’s group. In addition, she was eligible for funding in 2003 to continue her research with a





Connecting Undergrads Through Genomics

But why genome sciences in particular and why now? Thompson believes that it is essential for Duke to be able to use its resources to “catch the wave” and be in a position to “capture and download” that wave for undergraduates. Duke’s previous HHMI grant focused on neurocognition, a field that was taking root nationwide and emerging at Duke in the burgeoning interdisciplinary Center for Cognitive Neuroscience. “In 2002,” says Thompson, “the challenge was: what’s the next wave that is transforming biological sciences? And how can we make sure we have an undergraduate connection to that? Well, everybody could see that it was genomics. We wanted to make sure that undergraduates were able to connect to it.”

Thompson takes pains to point out that the genome sciences offer a perfect vehicle through which to achieve Duke’s goals of a liberal education within the larger structure of a research university. “We think about the hallmarks of a Duke education as 1) the ability to bring meaning to information, and 2) to discern among competing claims based on a thorough understanding of the basis of those claims. Our students should understand how knowledge is generated, how it’s organized, how it’s accessed, and how it’s applied to pressing human problems. Put those things together and that’s what drives our connection to genomics made manifest with the Making Meaning Program. How do we literally make meaning out of all of these Cs and Gs? How do we do that from a scientific standpoint and how do we do that from a social/policy standpoint as well?” He cites the IGSP as the most obvious mechanism.

Focus on FOCUS

Looking beyond the HHMI program, Thompson is most excited about the prospect of a FOCUS Program devoted to the genome. The FOCUS (First-year Opportunity for Comprehensive Unified Study) Program is an intensive program offered only in the fall semester of the freshman year. Characterized by small class sizes and interdisciplinary approaches, FOCUS allows students and faculty to explore areas of rapidly evolving knowledge, artistic ideals, and acute social and political concerns. Genomics, says Thompson, is a perfect choice for a FOCUS theme, given its intrinsically interdisciplinary nature and Duke’s unique blend of faculty with an interest in the subject from such a broad range of perspectives, including the humanities, the social sciences and the natural sciences. (Look for detailed coverage of the FOCUS Program on Genome Sciences & Policy in the next issue of *GenomeLIFE*.)

While few would dispute the importance of cultivating an undergraduate curriculum in genome sciences and policy, Thompson recognizes that it is not sufficient to merely create classroom and lab opportunities without any sort of gauge for success. The best measure, he believes, is simply to track the proportion of undergraduates who have at least “tasted” research by the end of their time at Duke. By this yardstick, programs like Making Meaning have begun to make their impact. Among the class of 2001, for example, 13% completed some sort of research project. By contrast, 29% of last year’s graduating class finished a research project. “I’d like for research to be normative of the Duke experience,” says Thompson. “I know that it will never be 100%, but I want it to be the norm. And we’re getting closer.” ▶

collaborator of Kelsoe’s at Cambridge University in Cambridge, England. More important for Heikamp, though, was the Genomic Information experience itself. “I feel that I now have invaluable mentors in Dr. Kelsoe and the graduate students in his lab.”

If there were any doubts about Heikamp’s commitment to the research enterprise, she erased those last November when she organized—along with Associate Dean of Trinity College Mary Nijhout—the first Triangle Undergraduate Research Symposium, which featured presentations of scholarly work by students at Duke and four other regional univer-

sities. At the University of Maryland conference she attended, it occurred to her that Duke should have a similar event along with other major institutions in the Triangle. “In fact,” she notes, “Duke, UNC-Chapel Hill, and NC State all hold research symposia in the spring, but only their own undergraduates are invited to participate. The Triangle Undergraduate Research Symposium is an opportunity for collaboration among regional institutions, and the fall timing of the event gives students who participate in summer programs a chance to present their work during the academic year.”

Where will Heikamp next apply her genome



Emily Heikamp

analysis skills? “I am not sure of my plans for next summer, but it will be difficult to top my experience at Cambridge. My long-term career goals definitely involve research at an academic institution.” ▶

Reflections on Race and the Genome

James Seeks to Understand Skin Color in Light of Biology, Society and Environment

Sociologist Wilmot James spoke at the Sanford Institute of Public Policy recently on “The Evolution of Skin Color Variation and the End—Finally—of Race.” James, who was introduced by Center for Genome Ethics, Law and Policy Director Robert Cook-Deegan, is Executive Director of the Human Sciences Research Council based in Cape Town, South Africa. He is also a member of the board and Chairman of the Education, Media, Arts and Culture Global Portfolio of the Ford Foundation of New York. James is active in the Africa Genome Initiative, a loose affiliation of persons and institutions interested in exploring the meaning of the Human Genome Project for Africa. The Initiative advocates for application of genomic information to African health, studies of human history and the cultivation of the biotechnology industry on the African continent.

Skin Modification In The Extreme

James began his talk by exploring some of the extremes to which humans go to modify their own skin color. He cited the multibillion-dollar skin-lightening industry, which is devoted to creams, soaps and lotions designed to lighten the complexion. James noted that some of these formulas are toxic due to the presence of bleach, hydrogen peroxide and/or mercury; consequently, many have been banned in South Africa and elsewhere. Nevertheless, said James, demand for these products has persisted and led to “massive smuggling” of illicit skin-lighteners into South Africa. By way of contrast, James noted that tanning—or skin-darkening—represented a \$300-million market in the United Kingdom in 2003 and that growth in the tanning industry has taken place despite dermatologists’ repeated warnings about the dangers of excessive exposure to ultraviolet (UV) radiation, including carcinoma, melanoma and other diseases. Clearly, James observed, human beings are



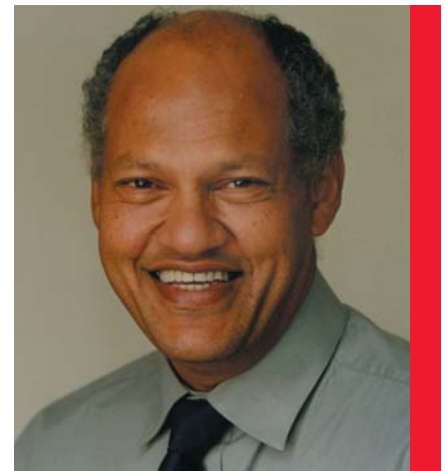
willing to invest substantial time and money in the color of their skin for reasons of health, vanity and, in light of data showing that fairer-skinned partners may be more successful at obtaining mates, sexual selection.

James expanded upon this theme by looking at what he called the “social compulsion to whiteness,” which he sees as being especially pervasive in South Africa. He believes that there are strong cultural pressures in his country, particularly on young people, to find fair-skinned partners. Moreover, he noted that obsession with skin color is certainly not limited to South Africa, but can be found in South America as well. Such obsessions, said James, can often be detected through language. In Brazilian Portuguese, for example, James pointed out that there are 32 words designated for denoting gradations of skin color.

Why do these obsessions with skin color linger on? James believes that the answer is a combination of ignorance and an intrinsic human tendency to elevate oneself above others. He cited Harvard zoologist-geneticist Richard Lewontin, who views skin color through the combined prism of “the social, the environmental and the biological.”

Skin Color: A History

James then went on to explain why such dramatic differences in skin color exist. Referring to an October 2002 *Scientific American* article by Nina G. Jablonski and George Chaplin, he suggested that that the worldwide pattern of human skin color is the product of natural selection acting to regulate the effects of the sun’s UV radiation on key nutrients crucial to reproductive success at different latitudes. Thus, depending upon where our ancestors



Wilmot James
Executive Director of the Human Sciences
Research Council in Cape Town, South Africa

lived, human skin color may have evolved to be dark enough to prevent sunlight from destroying the nutrient folate but light enough to foster the production of vitamin D. James conjectured that if there were indeed natural selection pressures on skin color during human evolution, skin color may actually provide a clue as to when and why African populations migrated.

He concluded by citing a recent article by Stanford geneticist Gregory Barsh (*PLoS Biol.* October 2003), who wrote that there are two reasons for studying variation in human skin color. First, inadequate protection from sunlight has a major impact on human health. In Australia, for example, the lifetime cumulative incidence of skin cancer approaches 50%. Second, Barsh sees studies of variation in human skin color as an opportunity for scientists to learn more about subcellular organelles, better characterize the

relationship between genotype and phenotype, further investigate human origins, and understand how recent human evolution may have been shaped by natural selection.

Education Key For Change

For James, there is a third reason to understand the molecular basis of skin color: to combat racism and bigotry. In his view, such an understanding could also help to validate the potential of all human beings. By understanding skin color biology, James contended that science would have a chance to “redeem itself” for past abuses. The challenge, he noted, will be to get this information into school curricula and to do so in such a way that will capture the “breathtaking” nature of the story of human evolution. When asked by another audience member whether simply getting accurate information into the public domain would be sufficient to alter people’s attitudes given the long history of racism, James emphasized that education of the young will be critical. “I’m not sure how much we can do to alter the belief structures of adults. The key thing is to work with children.”

The Africa Genome Initiative

James was asked by GELP Fellow and genome diversity scholar Jenny Reardon to elaborate further on the mission of the Africa Genome Initiative. “The idea,” James responded, “is to try to answer the very tough questions about what the Human Genome Project means for Africa.” He noted that the most immediate benefits of the Project—improved diagnostics and medical care—will probably only affect a tiny segment of the African population. “Africa has much more fundamental problems than access to the genome,” he said. “HIV/AIDS, for example, and trying to get a functioning health care system in place. What the genome means for Africa more immediately is [its role] in the effort to reconstruct human history.” ▶

For more information on the Human Sciences Research Council, go to <http://www.hsrc.ac.za/>

Nevins Named Director of Center for Genome Technology

The IGSP’s Center for Genome Technology, which began operations four years ago, now has a permanent Director. Joseph Nevins, PhD, James B. Duke Professor of Genetics and a leading researcher in gene profiling of breast cancer, was appointed Director by IGSP Director Hunt Willard in December.

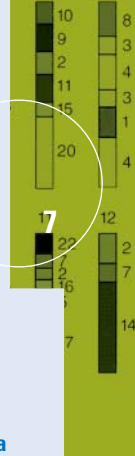
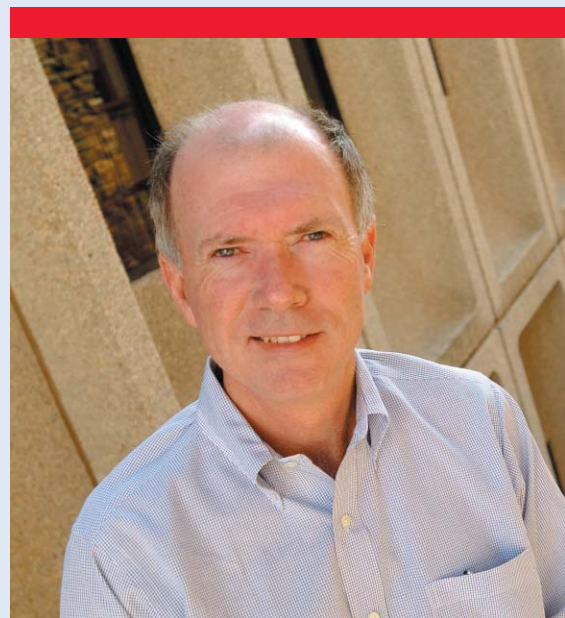
Nevins studies the genetic and genomic regulatory mechanisms that control cellular growth and the disruption of these mechanisms during tumor development. As highlighted in the October issue of *GenomeLIFE*, he makes use of DNA microarray technology to generate genome-scale gene expression profiles that predict the future course of breast, ovarian, and brain cancers. He had been the interim director of the Center for Genome Technology since its inception.

Willard feels that Nevins is perfect for the job. “Joe is a terrific geneticist with a deep appreciation of how to utilize genome technology to enhance a broad portfolio of both basic and clinical research. He also has a superb sense of academic duty and institutional loyalty. From our wide international search, it became very clear that he was ideal for the job. I’m thrilled that he agreed to take on this important task.”

Nevins received his Ph.D. in microbiology at Duke, where he studied viral gene regulation. He completed his postdoctoral studies as a Jane Coffin Childs Fellow at Rockefeller University, where he focused on the mechanisms of messenger RNA biogenesis, with James Darnell. He returned to Duke in 1987 as Professor of Microbiology and a Howard Hughes Medical Institute Investigator. Nevins was appointed Chair of the Department of Genetics in 1991 and continued as Chair of the merged Department of Molecular Genetics and Microbiology. He will step down as Chair in July to devote full effort to the Center for Genome Technology.

In his new role, Nevins will develop plans to catalyze use of genome technologies to enhance research across campus, both at the medical center and on the main campus. “There are terrific opportunities to build collaborations between the Center and programs in schools all around Duke, from the medical school to biology and chemistry and engineering,” he said. “I find it a great opportunity. All of the pieces are in place to further develop and apply genome technology to problems of very significant clinical and biological importance.” ▶

*Joseph Nevins, PhD, Director
IGSP Center for Genome Technology*



The Tuesday Series

A seminar series sponsored by the University

Program in Genetics and Genomics (UPGG)

and the Institute for Genome Sciences &

Policy. All seminars take place at 12:30 p.m.

in Room 147 of the Nanaline Duke building.

January

- 20 Ken Wolfe**, Dept. of Genetics,
Univ. of Dublin, Ireland
Gene Order Evolution and Birth of a
Metabolic Gene Cluster in Yeast
- 27 Dan McCollum**, *University of Massachusetts,*
TBA

February

- 3 Mark Johnston**, *Washington Univ., St. Louis*
Millions of Years of Evolution Reveal Functional
Features in the Yeast Genome
- 10 David Page**, *Whitehead and MIT*
Genes, Gender, and Germ Cells
- 17 Miriam Meisler**, *Univ. of Michigan*
SCNM1 Modifies the Severity of Neurological
Disease *via* Sodium Channel Splicing
- 24 Steve Henikoff**, *Fred Hutchinson Cancer Center*
TBA



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