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The Genome Scientist

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The William H. Foege Building Opens

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The Genome Scientist is published by the Department of Genome Sciences at the University of Washington. For more information, please visit our website: www.gs.washington.edu

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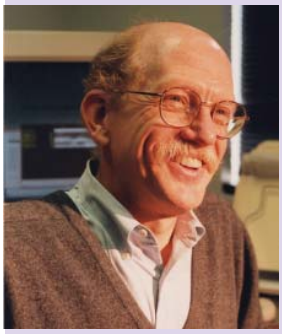
Notes From the Chair



Bob Waterston

The big news is that we have moved into the beautiful new Foege (pronounced fay-ghe) Building! Overlooking Portage Bay with views of the Olympics and Mount Rainier, the building brings the department together in state-of-the-art space with room to grow. Many thanks to the Gates Foundation, whose gift of $60 million made the building possible.

The building was dedicated last March, 2006, with a grand ceremony held in a tent just in front of the then unfinished building. Featuring dignitaries President Jimmy Carter, William H. Gates III and William H. Foege as speakers, the ceremony drew major University officials, including President Emmert and Dean Ramsey, and a crowd of several hundred into the tent, with an overflow crowd packing the auditorium. As luck would have it, rain was pouring down and wind was whipping the tent. Nonetheless all went well until just after President Carter introduced Bill Foege, when a sudden gust of wind literally lifted the tent a foot and half off the ground! Fortunately no one was injured, so with the guy wires now slack, the Secret Service detail led the President out of the tent, and the rest of us followed. The ceremony was moved to the auditorium, where only a small fraction of the original audience was privileged to hear Bill Foege's inspirational speech. (The full text is on our website at www.gs.washington.edu.) Weaving his own experiences in the fight to eradicate small pox with the struggles in global health today, he challenged all the occupants of the building - both present and future - to make a difference in the world. I think I speak for all when I say we gratefully accept the challenge.

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The Genome Scientist layout & design: Brian Giebel

questions / comments: bgiebel@u.washington.edu

New Faculty

John Stamatoyannopoulos, Assistant Professor

John Stamatoyannopoulos, M.D., joined Genome Sciences last fall from the Regulome Corporation, a privately held biopharmaceutical company where he had been Chief Scientific Officer. Dr. Stamatoyannopoulos commented that Genome Sciences "is in a class by itself with respect to the quality of the faculty and the breadth of their research interests. I am delighted to become a part of such a rich and dynamic environment."

Dr. Stamatoyannopoulos attended Stanford University where he graduated with degrees in Symbolic Systems, Biology, and Classics. He received his M.D. from the University of Washington School of Medicine and completed specialty (Internal Medicine) and subspecialty (Hematology/Oncology) training at Harvard Medical School institutions (Brigham and Women's Hospital, Dana Farber Cancer Institute, and Massachusetts General Hospital).

His research interests include analyzing gene regulation on a global scale, from regulatory elements encoded by the primary DNA sequence to nuclear architecture and ultimately the networks of genes and proteins that define the interface between the genome, the cell, and the organism. He states that "unraveling this puzzle will dramatically alter our ability to identify genetic variants that produce variation in both simple and complex phenotypic traits and contribute to or cause human disease."

John notes that he is "delighted to work with the many talented molecular and computational scientists in my lab; they are truly a great bunch, and have created a unique environment for genomic discovery and technology development." He is also extremely impressed with the quality of the Genome Sciences graduate students. His spouse, Lisa Strate M.D., M.P.H., is also a physician scientist and recently joined the UW Division of Gastroenterology, where she combines research in gastrointestinal bleeding and diverticular disease with patient care.

Faculty Honors

King Honored for Breast Cancer Research

Dr. Mary-Claire King, American Cancer Society Research Professor in Medicine and Genome Sciences, has received three awards for her pioneering work in breast cancer research:

The 2006 Dr. A.H. Heineken Prize for Medicine, one of six prizes for science, scholarship, and art, was presented in September during a special session of the Royal Netherlands Academy of Arts and Sciences.

The 2006 Weizmann Women & Science Award, given by the Weizmann Institute of Science in Israel, was presented in June at Rockefeller University. The Institute conducts interdisciplinary scientific research in technology, medicine and health, energy, agriculture, and the environment.

The American Cancer Society's Medal of Honor, the society's highest honor, is given annually to five Americans who have made outstanding contributions to fighting cancer.

Baker Elected to National Academy of Sciences

Dr. David Baker, Professor of Biochemistry and Adjunct Professor of Genome Sciences, has been elected to the National Academy of Sciences. Election to the Academy is considered one of the highest honors that can be accorded a U.S. scientist.

Dr. Baker's research is focused on the prediction and design of protein structures, protein folding and interactions between proteins. His election brings to 11 the total of GS primary and adjunct faculty who are members of the Academy.

Felsenstein Awarded Honorary Doctorate

Dr. Joseph Felsenstein, Professor of Genome Sciences and of Biology, was awarded an honorary Doctor of Science degree from the University of Edinburgh in Scotland. Dr. Felsenstein is well known for his research on evolution and population genetics.

Eichler, Green, Hall, & Wakimoto Named Fellows of the American Association for the Advancement of Science

Drs. Evan Eichler, Philip Green, Benjamin Hall, and Barbara Wakimoto were recently named fellows of the American Association for the Advancement of Science.

The American Association for the Advancement of Science is an international non-profit organization dedicated to advancing science around the world by serving as an educator, leader, spokesperson and professional association.

Evan Eichler

Phil Green

Ben Hall

Barbara Wakimoto

Foege Building

The William H. Foege Building Opens

The Department of Genome Sciences has moved into the new William H. Foege Building, named for the UW School of Medicine graduate and epidemiologist best known for leading the successful effort to eradicate smallpox.

Southwest corner viewed from Boat St.

Shared with the Department of Bioengineering, this $150 million, 265,000 square ft state of the art research facility was funded by a record $60 million donation from The Bill and Melinda Gates Foundation, along with $12 million from the federal government, $10 million from the Whitaker Foundation, and other generous donations from private sources.

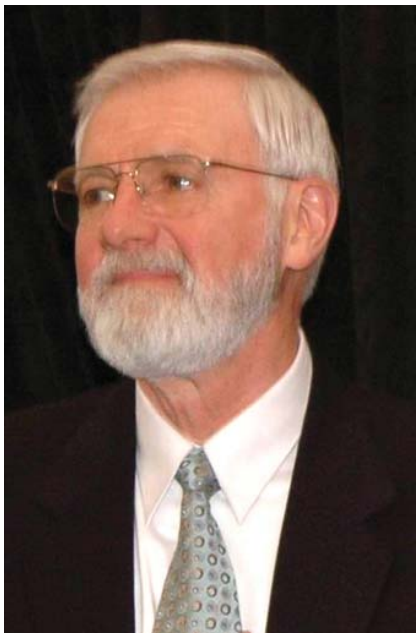
The building dedication in March 2006 brought together several notable figures in global health, among them former President Jimmy Carter, Microsoft co-founder Bill Gates, and building namesake Dr. William Foege (an excerpt from Dr. Foege's remarks is on the following page).

The building is uniquely designed to foster collaboration. Experimental laboratories are housed side-by-side with computational research groups, without separating walls, providing flexibility while encouraging conversation and collaboration. Colleagues in the Department of Bioengineering are just a short walk away in the north half of the building, and a 200 seat auditorium, along with several smaller conference rooms, provides much needed space for seminars, meetings, and classes. As one might expect, the Foege Building has a state of the art information technology infrastructure. The building is equipped with Gigabit Ethernet to every desktop and Gigabit uplinks to the UW campus network. Secured wireless networking is available throughout the building. The Genome Sciences Data Center has enough space, cooling, and power to support a computer cluster in excess of a thousand nodes.

The view looking south from the Vista Cafe in the Foege Building.

Foege Building

An Excerpt from Dr. Foege's Building Dedication Remarks



Dr. William Foege

"The gift is more than buildings. It is a gift from the Gates family for scientists to use their imaginations…to harness intellect and art and passion…to explore what has never been seen before, thought about before, available before. There is the challenge. It will require a building of learners. Eric Hofer said 'it is the learners who inherit the future. The learned usually find themselves equipped to live in a world that no longer exists.'

"In 1872, Stephen Smith, at 49 years of age, helped to form the American Public Health Association. For the 50th anniversary he was invited back to speak and at age 99 he walked to the lectern and spoke on 'The future of Public Health.' In these buildings are planted the seeds for the future of global health. The buildings, the equipment, the budget…are on loan… first to you and then to others.

"For me it was worth a 70 year journey to see this moment…but I hope I return for the 30th anniversary to say a few words about the future.

"Fast forward one hundred years. As the centennial of these buildings is celebrated, a speaker will reflect on the history of global health, and that speaker will talk about the impact of the buildings. The speaker will talk about an auspicious start, with President Carter sending us forth to change the world. The speaker will talk about the Gates family and will speak directly to their children (and I do mean their children because they will have a significant chance of living beyond a hundred) and their grandchildren .... rejoicing that they insisted that medical knowledge is not a gift to be hoarded, but to be shared, and the speaker will recount the origins of this grand adventure that married basic science to the liberation of global health."

The complete transcript of Dr. Foege's remarks is available at http://www.gs.washington.edu/news/building/foege_remarks.htm

Among those in attendance at the Foege Building dedication: UW President Mark Emmert, Microsoft co-founder Bill Gates, UW Regent and community leader William Gates Sr, and former President Jimmy Carter.

Research Highlights

Single-stranded DNA Used to Map Origins of Chromosomal Replication in Yeast

Wenyi Feng

A February 2006 Nature Cell Biology article describes a new technique, developed by Dr. Wenyi Feng in the laboratory of Drs. M. "Raghu" Raghuraman and Bonita Brewer, for identifying yeast origins of chromosome replication on a genomic scale. Chromosomal DNA replication is one of the most fundamental processes of life—before a cell divides it must first faithfully duplicate each of its chromosomes so that each of the "daughter" cells gets one copy of each chromosome that was present in the original cell. This process is tightly controlled and begins at particular locations in the genome called origins of replication. The basic mechanisms underlying how origins initiate DNA synthesis are largely conserved between organisms as far-flung as yeast and humans, but as yet there is much that we do not understand about what makes particular DNA sequences act as origins, how they are regulated in response to environmental or other stresses, or how their organization in the genome affects genome stability. Mapping origin locations is therefore an essential first step in understanding their makeup and the details of their regulation.

Because replication initiates by first separating the two strands of the DNA double helix at replication origins, the researchers equated single-stranded DNA (ssDNA) formation with origins of replication. Working with Baker's yeast and using a combination of chemical and genetic manipulations, the researchers were able to "pause" replication at every origin immediately after it had just begun, thereby exposing ssDNA around each origin in the genome. Then, exploiting unique properties of ssDNA that distinguish it from standard double-stranded DNA, they labeled the exposed ssDNA regions in the genome with a fluorescent tag

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Sequence Variation and Natural Selection

The genomes of modern human beings have been shaped by our evolutionary past. Important historical events, such as increases or decreases in population size or the spread of an advantageous mutation by natural selection, leave "signatures" in patterns of DNA sequence variation. Careful analyses of these signatures are beginning to provide exciting insights into human evolutionary history.

In an article in *Human Molecular Genetics*, Dr. Joshua Akey and colleagues performed a meticulous evolutionary analysis of a gene called *TRPV6*. This gene encodes a protein that allows dietary calcium to be absorbed into the small intestine. Dr. Akey and colleagues found that patterns of genetic variation at *TRPV6* have been influenced by strong selection in non-African populations. In addition, they narrowed down the likely targets of selection to three changes in the DNA sequence that result in amino acid changes in the protein product of *TRPV6*. These results suggest that as modern humans migrated out of Africa into new environments approximately 50,000 years ago, a change in calcium requirements, perhaps related to shifting diets or skin pigmentation levels, shaped the evolution of *TRPV6*. Ongoing work is focusing on better understanding the exact selective pressure and correlating patterns of *TRPV6* genetic variation with phenotypic variation and disease susceptibility, such as risk of developing osteoporosis.

Akey JM, *et al*. (2006). *TRPV6* exhibits unusual patterns of polymorphism and divergence in worldwide populations. *Human Molecular Genetics* **15**: 2106-2113.

Research Highlights

Novel Drugs Target Two Malaria Parasites

Sonia Hunt

Plasmodium falciparum and *Plasmodium vivax* are parasites responsible for the majority of malaria cases in humans. Both species have evolved resistance to antimalarial drugs called antifolates. In particular, four point mutations within the dihydrofolate reductase (*DHFR*) gene, the main target of antifolates, cause high-level resistance to an antifolate drug called pyrimethamine. Because *P. falciparum* and *P. vivax* often coexist in a single infected host, drugs are urgently needed that are effective against the DHFR enzymes carrying these mutations in both parasite species.

A new antifolate drug named WR99210 was developed recently by a consortium that includes Jacobus Pharmaceutical, Inc. in Princeton, New Jersey, and the Walter Reed Army Institute of Research in Silver Spring, Maryland. The drug and its related compounds inhibit both species of malaria parasites even when the parasites carry the highly resistant, quadruple-mutant allele of *DHFR*. In a December 2005 paper published in *Molecular and Biochemical Parasitology*, the laboratory of Dr. Carol Hopkins Sibley tested WR99210 and related compounds for efficacy against the quadruple-mutant DHFR protein from *P. falciparum* and *P. vivax*. The assays indicated the importance of a 3-carbon linker and a flexible oxygen bridge in the compound. Chemists at Jacobus Pharmaceutical then designed additional WR99210 analogs with these chemical characteristics and Dr. Sonia Hunt (pictured) tested them against quadruple-mutant DHFR from both *P. falciparum* and *P. vivax*.

Against the *P. falciparum* quadruple-mutant DHFR, three of the twelve compounds showed a 6-7-fold increase in potency when compared to the WR99210 parent compound; the remainder were equivalent or less potent. Against the *P. vivax* mutant DHFR, several analogs showed efficacy equivalent to the parent compound. Computer modeling in collaboration with Dr. Gabriele Varani's group in the University of Washington Chemistry Department was also employed to examine the biochemical properties of the compounds against the *P. falciparum* DHFR enzyme. From these data, Dr. Sibley's laboratory chose the 2-chloro-4-trifluoromethoxy analog of WR99210 for further development as a malaria drug. Currently, the consortium is planning the first human trials of the drug in collaboration with colleagues from Australia and Thailand.

Hunt SY, *et al*. (2005). Identification of the optimal third generation antifolate against *P. falciparum* and *P. vivax*. *Molecular and Biochemical Parasitology* **144**: 198-205.

Single-stranded DNA Used to Map Origins of Chromosomal Replication in Yeast, *continued from page 6*

and thereby were able to identify the locations of replication origins across the genome. As an added bonus, they were then able to apply the same technique to identify replication origins in a different species of yeast. Taken together, these results hold out the prospect of being able to map origins of replication on a genome-wide scale in other organisms including humans.

Feng W, et al. (2006). Genomic mapping of single-stranded DNA in hydroxyurea-challenged yeasts identifies origins of replication. *Nature Cell Biology* 8(2): 148-155.

Research Highlights

Testosterone's Role in Sperm Cell Development

Jing Meng

Sex hormones are crucial for fertility. For example, the hormone testosterone is essential for normal development of sperm cells in the male. However, the reason this testosterone requirement is not known. The laboratory of Dr. Robert Braun has been analyzing the role of testosterone in the developmental process. In a November 2005 paper published in the *Proceedings of the National Academy of Sciences*, they used a mouse model to investigate how testosterone influences the formation of the blood-testis barrier. This barrier keeps cells in the developing testes separate from the bloodstream.

By analyzing a mouse mutant in which the gene for the testosterone receptor has been eliminated, Dr. Braun and colleagues showed that a molecule whose presence they could detect by fluorescence was able to cross over from the bloodstream to the location where sperm cells are developing. However, in a mouse with a normal receptor, this movement does not occur. Thus, testosterone regulates the environment in which the sperm cells develop, and protects them from the immune system. In more recent studies, Dr. Braun's laboratory has shown that in the mutant mice, an autoimmune response is generated to antigens that are expressed in developing sperm cells. This response is consistent with developmental timing, in which the immune system forms shortly after birth but germ cells not until the time of puberty. These data argue that the role of the blood-testis barrier is to protect the developing sperm cells from the body's own immune system.

Meng JRW, *et al*. (2005). Androgens regulate the permeability of the blood-testis barrier. *Proceedings of the National Academy of Sciences USA* **102**: 16696-16700.

Genetic Basis of Pesticide Sensitivity

Chronic, low-dose exposure to organophosphate pesticides is known to affect human development, especially development of the nervous system. Newborns can be particularly sensitive to the effects of organophosphates because they have decreased levels of an enzyme called paraoxonase, encoded by the gene *PON1*. This enzyme is responsible for detoxifying organophosphates. The *PON1* gene can specify either of two forms of the enzyme, defined by the amino acid glutamine or arginine at position 192 in the protein. The ability to detoxify the pesticide chlorpyrifos increases with the number of arginine alleles present, such that people with both copies having arginine have increased activity over those with one copy having arginine and one glutamine, and those with both copies having glutamine have the least activity. There is also an interaction between enzyme levels and alleles; the level of paraoxonase is important to ascertain when determining resistance to chlorpyrifos exposure.

In a March 2006 paper published in *Pharmacogenetics and Genomics*, the laboratory of Dr. Clement Furlong sought to predict the organophosphate sensitivity of mothers and newborns who are at high risk for exposure to organophosphate pesticides. They assayed the enzyme level in the blood from a cohort of mothers and their newborns from the agricultural Salinas Valley region of California. All mothers were Latina by ethnicity, 42% held agricultural jobs, and 82% had agricultural workers living in their households during pregnancy. Protein levels of the enzyme varied widely among the subjects, with a 65-fold production difference between the highest-expressing mother and lowest-expressing baby. Overall, there was an average 4-fold

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Research Highlights

Genome Hotspot Research Uncovers Causes of Mental Retardation

Andrew Sharp

Research on the human genome's hotspots has uncovered several causes of mental retardation. The study, led by Dr. Evan Eichler, associate professor of genome sciences and investigator with the Howard Hughes Medical Institute, was published in the August 2006 edition of the journal *Nature Genetics*. Eichler and his colleagues studied nearly 300 children with mental retardation and identified abnormal genetic events on the patients' genomes. They used high-resolution genome microarrays, or "gene chips," from NimbleGen Systems in Madison, Wisc., to pinpoint the location of an abnormal event on each patient's genome.

Eichler and his colleagues, including Dr. Andrew Sharp, senior fellow and Rosetta Fellow at the UW, hypothesized that genomic disorders may stem from genome "hotspots," or areas of instability on the genome where sections of DNA may be duplicated, deleted, or reversed. They found several such areas in this study, suggesting that these genome hotspots are connected to some types of mental retardation. One of those events, a large deletion of genomic material on chromosome 17, was found in several of the children in the study. It has characteristic facial, behavioral, and other physical features, such as fair hair and blue eyes, which may help physicians in identifying similar syndromes. According to current data on its prevalence, this deletion may be responsible for about 1 percent of all types of mental retardation. Dr. Eichler's results should spur further analysis of structural variation in the human genome, leading to a better understanding of the molecular basis for disorders caused by genomic rearrangements.

Sharp AJ, *et al*. (2006). Discovery of previously unidentified genomic disorders from the duplication architecture of the human genome. *Nature Genetics* **38**: 1038-1042.

Genetic Basis of Pesticide Sensitivity, *continued from page 8*

production difference between mothers and infants. The Furlong laboratory suggests that a 130- to 163-fold range of sensitivity to chlorpyrifos may exist between the most and least sensitive subjects, once both protein levels and *PON1* genotypes are considered. These data support that idea that tests of both protein levels and functional genotypes must be used when making predictions about the pesticide sensitivity of individuals.

Furlong CE, *et al*. (2006). *PON1* status of farmworker mothers and children as a predictor of organophosphate sensitivity. *Pharmacogenetics and Genomics* **16**: 183-190.

Support Genome Sciences

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Graduate Student News

Certain Awarded Graduate School Medal

Laura Certain and fellow grad Jon Ulmer greet former president Jimmy Carter during the Foege Building dedication.

Genome Sciences graduate student and Sibley Lab member Laura Certain, who studies the genetics of drug resistance in malaria, was one of two UW students awarded the 2006 Graduate School Medal, a $10,000 fellowship awarded to a Ph.D. student who displays an exemplary commitment to both the University and its larger community. The Graduate School Medal recognizes the "scholar-citizen" whose academic expertise and social awareness are integrated in a way that demonstrates active civic engagement and a capacity to promote political, cultural and social change.

A student in the UW's M.D. / Ph.D. program, Laura has traveled to Mali and Kenya to conduct research and has been a leader in the UW community in promoting awareness of international health and social justice. She was a co-founder of a medical student organization, The International Health Group, and helped initiate a popular course, Advanced Topics in Global Health. Laura also took the lead in organizing the 3rd annual Western Regional Conference on International Health, "Politics, Social Justice and Global Health". This 3-day conference, featuring keynote speaker Mirta Roses Periago, the Director of the Pan American Health Organization, and U.S. Representative Jim McDermott, attracted 700 attendees from all over the region.

Emerson & Findlay Awarded Hurd Fellowships

Two Genome Sciences graduate students have recently been selected for the UW School of Medicine's Hurd Fellowship. This award, for demonstrating excellence in the area of Biochemistry, is given to one first year Ph.D. student each year selected from throughout the School of Medicine and provides full funding for one year. Ryan Emerson was awarded the fellowship for the 2006-2007 academic year. Geoff Findlay was the recipient for the 2005-2006 academic year.

Salipante Awarded NRSA Fellowship

Genome Sciences / MSTP student Steve Salipante was awarded an individual predoctoral fellowship of $60,000 over four years for his research on "Phylogenetic Fate Mapping: Following Cellular Lineages in Embryogenesis and Aging".

2006 Incoming Class

Lisa Beutler, UW Medical Scientist Training Program

Daniel Blick, University of Texas

Nick Coley, UW Medical Scientist Training Program

Sara Di Rienzi, Bryn Mawr College

Ryan Emerson, University of Washington

Chris Murphy, Washington University

Kevin Roach, University of Washington

Alan Rubin, Pacific University

Oliver Serang, North Carolina State University

Kyle Siebenthall, Cornell University

Graduate Student News

Congratulations to 2005 - 2006 Graduates!

Daehyun Baek (Ph.D. in Bioengineering)
"Characterization of Evolutionarily Conserved Mammalian Alternative Splicing and Alternative Promoters"

Tushar Bhangale (Ph.D. in Bioengineering)
"Small Insertion-Deletion Polymorphisms in the Human Genome: Characterization and Automation of Detection by Resequencing"

Kerry Bubb (Ph.D. in Genetics)
"The Role of Balancing Selection in Maintenance of Natural Genetic Variation"

Lindsey Dubb (Ph.D. in Genetics)
"A Likelihood Model of Gene Family Evolution"

Stephen Eacker (Ph.D. in Genetics)
"Effects of androgen receptor mutations on murine testicular function and development"

Laura Flinn (Ph.D. in Mol & Cell Biology)
"Genomic Analysis of a Human Interferon-inducible Gene Family and Systemic Lupus Erythematosus"

Megan Fluegel (Ph.D. in Mol & Cell Biology)
"Establishment of a Drosophila model to study the role of NPC1a in sterol biology"

Kavita Garg (Ph.D. in Molecular Biotechnology)
"Genome-Wide Comparison of Alternative and Constitutive Splice Sites Conserved Between Human and Mouse"

Elena Linardopoulou (Ph.D. in Bioengineering)
"Structure, function and evolution of human subtelomeres"

Rachel Mackelprang (Ph.D. in Genetics)
"Evolutionary analysis of the T cell receptor using a sequence based approach"

Trey Powers (Ph.D. in Mol & Cell Biology)
"Reduced signaling through the evolutionarily conserved TOR pathway extends life span in *S. cerevisiae*"

Ed Ramos (Ph.D. in Molecular Biotechnology)
"Tools for studying gross nuclear organization, dynamics and epigenetic modifications of chromosomes"

Eric Smith (Ph.D. in Molec & Cell Biology)
"Genetic Adaptation by *Pseudomonas aeruginosa* during Chronic Cystic Fibrosis Infections, and Genetic Variation between Strains of *P. aeruginosa*"

Iyarit Thaipisuttikul (Ph.D. in Genetics)
"A mutant hunt in the genomic era: comprehensive identification of *Pseudomonas aeruginosa* anaerobic growth functions"

Jeanna Wheeler (Ph.D. in Genetics)
"Genetic Analysis of Rhythmic Behavior in *C. elegans*"

West side of the W. H. Foege Building viewed from 15th Ave.

Graduate Student News

Student Publications

Carlos Araya:
Boyle TJ, Bao Z, Murray JI, Araya CL, Waterston RH. AceTree: a tool for visual analysis of *Caenorhabditis elegans* embryogenesis. BMC Bioinformatics. 2006; 7: 275. published online before print June 1, 2006.

Shameek Biswas:
Biswas S, Akey JM. Genomic insights into positive selection. Trends Genet. 2006 Aug;22(8):437-46. Epub 2006 Jun 30.

Max Boeck:
Feng W, Collingwood D, Boeck ME, Fox LA, Alvino GM, Fangman WL, Raghuraman MK, Brewer BJ..Genomic mapping of single-stranded DNA in hydroxyurea-challenged yeasts identifies origins of replication. Nat Cell Biol. 2006 Feb;8(2):148-55. Epub 2006 Jan 22.

Laura Certain:
Certain LK, Sibley CH. Plasmodium falciparum: A novel method for analyzing haplotypes in mixed infections. Experimental Parasitology. 2007 Mar;115(3):233-41.

Nathan Clark:
Clark NL, Aagaard JE, Swanson WJ. Evolution of reproductive proteins from animals and plants. Reproduction. 2006, 131, 11-22.

Panhuis TM, Clark NL, Swanson WJ. Rapid evolution of reproductive proteins in abalone and *Drosophila*. Philosophical Transactions of the Royal Society B-Biological Sciences 361, 261-268, 2006.

Cindy Desmarais:
Miller JP, Lo RS, Ben-Hur A, Desmarais C, Stagljar I, Noble WS, Fields S. Large-scale identification of yeast integral membrane protein interactions. Proc Natl Acad Sci U S A. 2006, 102:12123-8

Diane Dickel:
Dickel DE, Veenstra-VanderWeele J, Cox NJ, Wu X, Fischer DJ, Van Etten-Lee M, Himle JA, Leventhal BL, Cook EH Jr, Hanna GL. Association testing of the positional and functional candidate gene SLC1A1/EAAC1 in early-onset obsessive-compulsive disorder. Arch Gen Psychiatry. 2006 Jul;63(7):778-85.

Joanna Kelley:
Kelley JL, Madeoy J, Calhoun J, Swanson WJ, Akey J. Genomic signatures of positive selection in humans and the limits of outlier approaches. Genome Research. 2006, 16(8):980-9.

Aaron Klammer:
Klammer AA, MacCoss MJ. Effects of modified digestion schemes on the identification of proteins from complex mixtures. J Proteome Res. 2006 Mar;5(3):695-700.

Blackler AR, Klammer AA, MacCoss MJ, Wu CC. Quantitative comparison of proteomic data quality between a 2D and 3D quadrupole ion trap. Anal Chem. 2006 Feb 15;78(4):1337-44.

Kristen Lewis:
Cupples C, Champagne J, Lewis K, Dyer R, Dawson Cruz T. Evaluation of the ABI Quantifiler Human DNA Quantification Kit: Optimization of Input DNA for STR Analysis by CE and Determination of a True Zero Value. submitted.

Coy K, Lewis K, Fulmer A, Hudson A, Dawson Cruz T. Obtaining typable DNA from bloodstains that serologically test negative. Journal of Forensic Identification. 2005, 55(5):633-643.

Rachel Mackelprang:
Mackelprang R., Livingston RJ, Eberle MA, Carlson CS, Yi Q, Akey JM, Nickerson DA. Sequence diversity, natural selection and linkage disequilibrium in the human T cell receptor alpha/delta locus. Hum. Genet. Epub 2006 Jan 20.

Tobias Mann:
Mann TP, Noble WS. Efficient identification of DNA binding partners in a sequence database. Bioinformatics (Proceedings of the Intelligent Systems for Mol Biology Conference), 22(14):e350-e358, 2006.

Graduate Student News

Student Publications

James Ronald:
Ronald J, Akey JM. Genome-wide scans for loci under selection in humans. Hum Genomics. 2005, 2(2):113-125.

Ronald J, Brem RB, Whittle J, and Kruglyak L. Local regulatory variation in *Saccharomyces cerevisiae*. PLoS Genet. 2005, 1(2):e25.

Steve Salipante:
Salipante S, Horwitz M. Phylogenetic fate mapping. Proc Natl Acad Sci U S A. 2006 Apr 4;103(14):5448-53. Epub 2006 Mar 28.

Salipante, S.J, K.F. Benson, J. Luty, V. Hadavi, R. Kariminejad, M.H. Kariminejad, N. Rezaei, M.S. Horwitz. Double de Novo Mutations of ELA2 in Cyclic and Severe Congenital Neutropenia. submitted.

Matt Sandel:
Bao Z, Murray JI, Boyle T, Ooi SL, Sandel MJ, Waterston RH. Automated cell lineage tracing in *Caenorhabditis elegans*. Proc Natl Acad Sci U S A. 2006 Feb 21;103(8):2707-12.

Will Sheffler:
Sheffler W, Upfal E, Sedivy J, Noble WS. A Learned Comparative Expression Measure for Affymetrix GeneChip DNA Microarrays. Proc IEEE Comput Syst Bioinform Conf. 2005;144-54.

Jon Ulmer:
Sampathkumar P, Turley S, Ulmer JE, Rhie HG, Sibley CH, Hol WG. Structure of the Mycobacterium tuberculosis flavin dependent thymidylate synthase (MtbThyX) at 2.0A resolution. J Mol Biol. 2005 Oct 7;352(5):1091-104.

Troy Zerr:
Till BJ, Zerr T, Bowers E, Greene EA, Comai L, Henikoff S. High-throughput discovery of rare human nucleotide polymorphisms by Ecotilling. Nucleic Acids Res. 2006 Aug 7;34(13):e99.

Travel Awards

Nathan Clark was awarded travel funding for his presentation, "Combining Proteomic and Evolutionary Data: Insights into Mammalian Seminal Proteins" at the 2006 Society for Molecular Biology and Evolution conference in Tempe AZ.

Recent **Allan Wade Parker travel award winners** for best poster at the department retreat were **Lazar Dimitrov** in 2005; **Allyson McCormick** and postdoctoral fellow **Marissa Vignali** in 2006.

Ilona Holcomb was awarded a 2006 AACR-WICR Brigid G. Leventhal Scholar Award in Cancer Research to attend the 97th AACR Annual Meeting, in Washington, DC.

Joanna Kelley was awarded travel funding for her presentation, "Positive selection in primate tooth enamelin and evidence for human population specific adaptation" at the 2006 Society for Molecular Biology and Evolution conference in Tempe AZ.

Graduate Student News

Conference Presentations:

Laura Certain:
"Pilot study of sulfadoxine-pyrimethamine resistance using a novel method to analyze mixed infections." American Society of Tropical Medicine and Hygiene, 2005, Washington, DC.

"Minimum genetic diversity in resistant strains of *Plasmodium falciparum* from Kenya." 18th Annual Seattle Parasitology Conference, 2006, Seattle, WA.

Karen Chisholm:
"Genetic backgrounds susceptible to genomic deletions: Alu-mediated mutations of BRCA1 as a model." American Society of Human Genetics (ASHG) 55th Annual Meeting, Salt Lake City, Utah, 2005.

Nathan Clark:
"Combining Proteomic and Evolutionary Data: Insights into Mammalian Seminal Proteins". Society for Molecular Biology and Evolution. 2006, Tempe AZ.

"Female-male Co-evolution: Sexual Conflict at Abalone Fertilization." Genomics of the Life Aquatic. 2006, Friday Harbor Labs, WA.

Geoff Findlay:
"Positive Selection and Gene Duplication in Abalone Sperm Lysin." American Genetics Association's conference on "The Genetics of Speciation", 2006, Vancouver, BC.

Michael Hoopmann:
"Automated Detection of Unusual Isotope Distributions in Complex Mixtures: Application to the Identification of N-linked Glycosylation Sites of Proteins." American Society for Mass Spectrometry, 2006, Seattle WA.

Zhaoshi Jiang:
"Evolutionary reconstruction of segmental duplications reveals genomic cores of human gene innovation." 2006, Biology of Genomes, Cold Spring Harbor Labs

Joanna Kelley:
"Positive selection in primate tooth enamelin and evidence for human population specific adaptation." Invited Talk, Fitch Symposium, Society for Molecular Biology and Evolution, 2006 Tempe, AZ

"Positive selection in primate tooth enamelin and evidence for human population specific adaptation." Genome Sequence Variation, Keystone Symposia, 2006 Big Sky, MT

Kristen Lewis:
"Comparative Analysis of Human-Specific DNA Quantitation Techniques. " American Academy of Forensic Sciences, 2006 Annual Meeting, Seattle.

Tobias Mann:
"Efficient identification of DNA binding partners in a sequence database", 2006 Intelligent Systems for Molecular Biology conference, Fortaleza, Brazil

Steve Salipante:
"Phylogenetic Fate Mapping: Revealing the Body's own Family Tree." University of Colorado Annual MD/PhD Student Conference, July 2006.

East side of the W. H. Foege Building viewed from Health Sciences K-wing.

News & Notes

Sharp Wins ASHG Trainee Award

Dr. Andrew Sharp, a postdoctoral fellow in the Eichler Lab, won the 2006 American Society of Human Genetics Trainee Award (Postdoctoral Translational category) for his presentation, 'Discovery of novel recurrent genomic disorders from the duplication architecture of the human genome', at the 56th meeting of the ASHG in New Orleans.

Notes From The Chair, *continued from page 2*

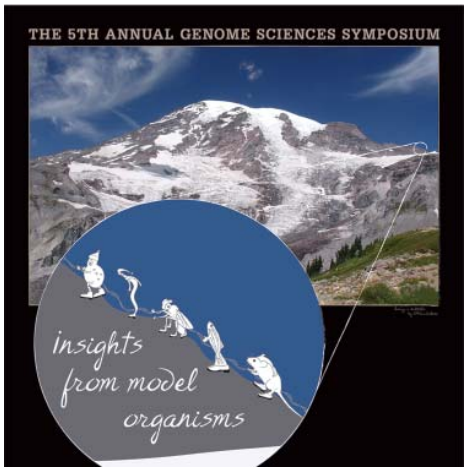
While dedicated in March, the building was unfortunately not ready for occupancy until late October. Over a period of a few weeks, each of the labs was moved, until we were all in by mid-December. The move went remarkably smoothly, thanks to our hard-working administrative and IT staff. There have been a few glitches, but these are being set right, and the building promises to be a great place for science. The space is designed to foster interactions through a variety of mechanisms. We've intermixed wet and dry labs and the various disciplines of the Department throughout the 5 floors of the building. The labs are open, connected by internal corridors running the length of the building. Each floor has a common space with marker boards (already well decorated with crosses and equations!), usually adjacent to our large open atrium in the center of the building. We also have conference rooms on every floor and a 200-seat auditorium for more formal gatherings and seminars.

Another noteworthy event was the annual retreat at Sleeping Lady in September. Bill Foege was our keynote speaker, giving those who had missed his dedication speech a chance to hear him and providing Bill with a chance to learn more about the department. We of course welcomed our impressive new class of graduate students, heard from the faculty, perused the excellent posters and still had time to socialize. But what particularly impressed me this year was the evidence that the idea of bringing together scientists with interests in genomics but from various disciplines (genetics, both model organism and human, technology and computational biology) was working. A gratifying number of talks and posters presented work that was the result of collaborations between these different areas, producing exciting new results. You'll see some of this in other parts of the newsletter for yourself. Our move into the Foege Building will only increase this fruitful interaction.

The Department continues to thrive with energy and enthusiasm, as you'll see elsewhere in this newsletter. To learn more about what our Bioengineering neighbors in the new building are up to, we held a series of presentations from the faculty last fall. We hope our proximity will lead to new collaborations as genomics meets bioengineering. We welcomed John Stamatoyannopolis to the faculty in fall 2005; John Storey accepted a joint position (also in Biostatistics) in 2006. After a year's respite as we readied for the move we are recruiting again this year for several new positions. The candidates are superb, and competition will be intense; we expect nothing less. The NIH budget woes make it an intimidating time to begin a faculty career, but we hope to provide an environment where new faculty will thrive regardless. The opportunity for discovery is before us, and the excitement in the Department has never been greater. We hope you can find the time to come see us in our new home.

News & Notes

2006 Symposium: Insights from Model Organisms



Last year's symposium, held May 24 at the University of Washington, featured these speakers:

Barry Ganetzky, Ph.D., University of Wisconsin
"Temperature-sensitive paralytic mutants and gene discovery for neuronal function, development, and maintenance in Drosophila"

H. Robert Horvitz, Ph.D., Massachusetts Institute of Technology; HHMI
"The Genetic Control of Programmed Cell Death in C. elegans"

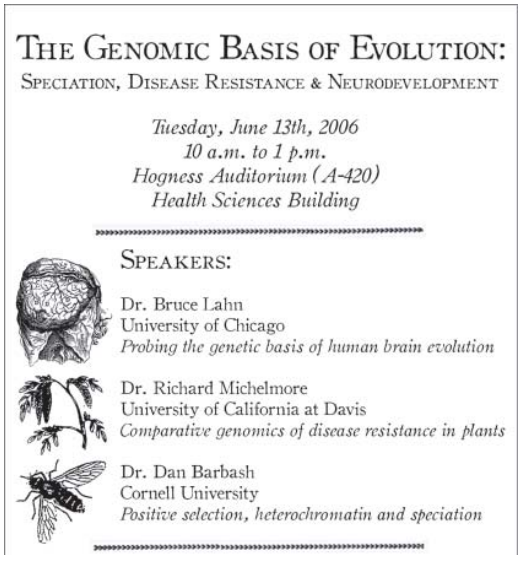
Simon John, Ph.D., The Jackson Laboratory; HHMI
"Glaucoma as a complex disease: Insights provided by mouse models"

Michael Marr, Ph.D., University of California, Berkeley
"Dynamic Interaction and Differential Requirement for Transcriptional Coactivator Complexes in Drosophila"

Gail Martin Ph.D., University of California, San Francisco
"FGF signaling in vertebrate organogenesis: the importance of getting it right"

Barbara Meyer, Ph.D., University of California, Berkeley; HHMI
"Sex and Death in C. elegans"

Pamela Silver, Ph.D., Harvard Medical School
"Discovery and Design of Nuclear Networks"


THE GENOMIC BASIS OF EVOLUTION:
SPECIATION, DISEASE RESISTANCE & NEURODEVELOPMENT

Tuesday, June 13th, 2006
10 a.m. to 1 p.m.
Hogness Auditorium (A-420)
Health Sciences Building

SPEAKERS:

Dr. Bruce Lahn
University of Chicago
Probing the genetic basis of human brain evolution

Dr. Richard Michelmore
University of California at Davis
Comparative genomics of disease resistance in plants

Dr. Dan Barbash
Cornell University
Positive selection, heterochromatin and speciation

2006 Genome Training Grant Symposium: The Genomic Basis of Evolution

The second annual GTG symposium, organized by trainees Diane Genereux and Jennifer Gogarten with assistance from other GTG trainees, featured these speakers:

Bruce Lahn, Ph.D., University of Chicago

Richard Michelmore, Ph.D., Univ of California, Davis

Dan Barbash, Ph.D., Cornell University