

The Genome Scientist

University of Washington Department of Genome Sciences Newsletter/Volume 1, Number 1/Fall 2002

Robert H. Waterston, M.D., Ph.D. to Chair the Department of Genome Sciences

Dr. Robert H. Waterston will chair the recently formed Department of Genome Sciences and will hold the endowed William H. Gates III Chair in Biomedical Sciences. An innovator in genome research, Dr Waterston will lead the Department in exciting new areas.

The goals of the Department are well matched to those of Dr. Waterston: bring together model organism biologists, computational biologists, and technology developers to speed the analysis needed to interpret the genome. "It's a magnificent opportunity," said Dr. Waterston. "They have marshaled the resources to make this a very strong program." Stan Fields, Acting Chair, said, "We are tremendously excited...we will be able to hire new faculty and move into new areas of biology."

At 58, Bob Waterston is internationally recognized as a leader in genome sequencing and the International Human Genome Project. His awards include the 2002 International Gairdner Award for outstanding achievement in biomedical research (see page 8), election to the National Academy of Sciences, the 2000 George W. Beadle Medal, the first Dan David Prize, and the Alfred P. Sloan Award.

Dr. Waterston's achievements in genome research began early on in his career. In the mid-80's, together with John Sulston of the Sanger Centre, he proposed one of the largest scientific ventures ever attempted: the sequence of *Caenorhabditis elegans*, "the worm." In the face of scientific skepticism Dr. Waterston forged ahead, creating the Genome Sequencing Center in St. Louis, administering and winning governmental support, and in 1998 completing the first genome of a cellular animal. This remarkable achievement became inextricably linked to other genome sequencing projects, including the human genome. "Bob is one of those people who has succeeded at everything he has undertaken," said Dr. Maynard Olson. *Continued on next page*



Willie Swanson, New Assistant Professor Working on Reproductive Proteins

Willie J. Swanson, Ph.D., moved recently to our department from the University of California, Riverside because he believes that the opportunities here at the University of Washington and in Seattle are extraordinary for his interests. "Seattle is a great place," Dr. Swanson commented, "there are many people to interact with here at the University."



Dr. Swanson has already had a major impact in the field of molecular evolution and has contributed to the understanding of the protein-protein interactions that mediate fertilization. His work combines an array of disciplines and techniques: genomics, bioinformatics, biochemistry, molecular biology and population/evolution analysis at the DNA and protein level, which complement the scientific research under way in the department. *Continued on next page*

William Noble, New Assistant Professor in Computational Biology

William Stafford Noble, Ph.D., joins the Genome Sciences faculty from Columbia University, where he held the position of Assistant Professor in the Department of Computer Science and the Columbia Genome Center. Commenting on his appointment, Dr. Noble noted that, "the University has one of the best computer science departments in the world, plus computational biology and genomics have a very strong community here in Seattle."

Dr. Noble has established himself as a leader in basic research problems for his applications of learning techniques such as hidden Markov models and support vector machines to problems in functional genomics. His use of artificial intelligence techniques in molecular biology and genomics is interdisciplinary and fits well into Genome Sciences. *Continued on next page*



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"He is a patient, effective leader who sets a high scientific standard and is good at encouraging the people around him to set and achieve ambitious goals," Olson continued.

Bob Waterston's leadership and contributions to the International Human Genome Project are many. His lab group constructed the physical map that was the framework of the entire sequencing effort for the human genome and ultimately contributed 20% of the entire sequence. He put together strong collaborations and led a federally funded consortium of researchers who completed a working draft of the human genome in June of 2000. He wrote at that time, "Although comparative sequencing with other genomes will be needed to further explain the human sequence...these initial views on the genome provide some fascinating insights."

One of Dr. Waterston's most significant achievements may well be his commitment to the public distribution of scientific knowledge. Through his insistence and that of colleagues, the release of sequence data into public databases became a condition of the human genome project. This idea of shared access has continued with other genome projects and will likely continue to accelerate scientific progress. "Bob Waterston is certain to further cement the UW's growing reputation as the epicenter of one of the most exciting fields of biomedical inquiry today," stated Dr. Paul Ramsey, Vice President for Medical Affairs and Dean of the School of Medicine.

Dr. Waterston commented at the announcement of his appointment, "I am delighted to join the University of Washington as the Chair of the new Department of Genome Sciences. This is an exciting time in genome sciences, and the combination of the department, the University and the community offers a special opportunity to shape the direction of this important field. I am honored to be given this chance and look forward to the challenge."

Dr. Waterston is expected to begin his appointment January 2003. He earned his bachelor's degree in engineering from Princeton University and received both a medical degree and a doctorate in 1972 from the University of Chicago. He joined the Washington University faculty in 1976 where he has directed Washington's Genome Sequencing Center, held the chair in the Department of Genetics and is the James S. McDonnell Professor of Genetics.

The Genome Scientist is published by the Department of Genome Sciences.

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Willie Swanson, continued from page 1

Dr. Swanson was the first to clone a female receptor protein involved in species-specific mediation of fertilization, a protein known as the VERL protein. He identified a new group of *Drosophila* genes that are likely to encode critical players in reproduction, proteins transferred from the male that have striking influences on female reproductive physiology and behavior. His definition of a rapidly evolving sperm protein from abalone, along with the identification and evolutionary studies of its egg receptor, were the first studies of a receptor/ligand pair and its evolution.

Dr. Swanson's immediate goals are to get his lab operational and to recruit a strong team of scientists from the fields of computational biology and traditional genetics. Dr. Swanson indicated that he intends to pursue integrated approaches to further study sperm/egg interactions in abalone, mammalian species and *Drosophila*.

The Department welcomes Dr. Swanson, his wife Jennifer Calkins and young son Devlin, who arrived in Seattle in August, when Dr. Swanson began his appointment as Assistant Professor of Genomes Sciences.

William Noble, continued from page 1

A successful researcher and educator, Dr. Noble's work has been recognized through several awards, including a Pharmaceutical Research and Manufacturers of America Foundation Faculty Development Award in Bioinformatics, a National Science Foundation CAREER Award, and an Alfred P. Sloan Foundation Fellowship. Dr. Noble indicated his first priority here at the University will be to build a strong and cohesive team.

The Department welcomes Dr. Noble and his wife Nan Noble. Dr. Noble began his appointment as Assistant Professor of Genome Sciences in July.

FOCUS ON STUDENTS

Genome Sciences 2002 Incoming Class:

Nathaniel Clark, University of Texas, Austin
Lazar Dimitrov, Dartmouth College
Chung-Ying Huang, National Taiwan University
Lisa Kim, transfer from UW Quantitative Ecology and Resource Management Program
Charla Lambert, University of Washington
Tobias Mann, University of Washington
Mariko Sasaki, exchange student, Osaka Univ, Japan
Sara Selgrade, Middlebury College

Congratulations to 2001-2002 Graduates:

Bill Buaas, Ph.D. Sonia Hunt, Ph.D.
Christina Buchanan, Ph.D. Karen James, Ph.D.
Larry Gallagher, Ph.D. Heather Mefford, Ph.D.
Flaviano Giorgini, Ph.D.



Stan Fields, Acting Chair

Notes from the Acting Chair

As the year 2000 began, the future looked uncertain for the departments of Genetics (in the College of Arts and Sciences) and Molecular Biotechnology (in the School of Medicine). Chair positions in both departments were open. Genetics sorely needed to recruit young faculty and to renovate its facilities. Molecular Biotechnology was down to three core faculty and had barely the critical mass to keep its programs running. Beyond their differing University affiliations, the two departments had distinct cultures, styles of doing science, administrative structures, graduate programs, and responsibilities for undergraduate teaching. In spite of the clear challenges in joining such disparate groups, the two faculties elected to merge into a single department.

As the summer of 2002 began, Paul Ramsey, Dean of the School of Medicine, announced that Bob Waterston, director of the Genome Center and chair of Genetics at Washington University in St. Louis, had accepted his offer to come here to head the Department of Genome Sciences. The prospects for a new building on campus to house the department looked bright. Genome Sciences had just completed the recruitment of two junior faculty, had put together an innovative graduate program that combined the

traditions of the programs in Genetics and Molecular Biotechnology, and had created two relevant undergraduate courses. The Department had sponsored a successful symposium on “Genetic Variation in Disease and Development” and begun the planning for another, and had hosted an impressive seminar series over the past year. The administrative wrinkles of merging two office staffs and bringing Arts and Sciences faculty into the School of Medicine had been largely smoothed out. An eventful year and a half, to say the least. That the future of Genome Sciences now sparkles so brightly is a testament to the determined efforts of so many in the Department, to the cooperation of deans and administrators across two schools as well as in the Provost’s and President’s offices, and to the compelling vision of where biology is heading.

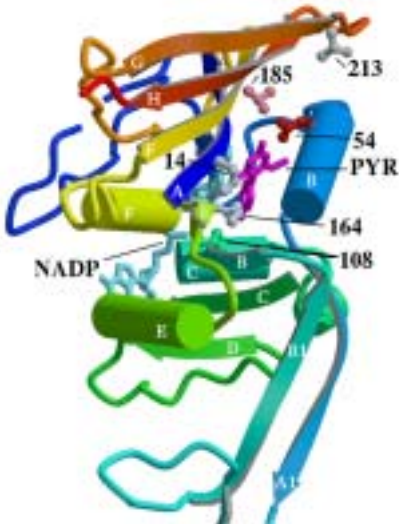
With a draft of the human genome sequence completed and the sequences in hand or in progress for literally hundreds of pathogens, of model organisms such as yeast, the nematode worm, and the fruitfly, and of other creatures, biology is at a turning point. Computational sciences have moved into a key position within the discipline, with the increasing accumulation of many types of large data sets accelerating this trend. There is an urgent need for new genomic and proteomic tools to analyze the thousands of RNAs and proteins predicted by the sequence data. Human genetics is poised to identify the basis of complex diseases, to begin to understand the consequences of the variation between individuals, and to work hand in hand with model organism biologists to interpret the complexity of biological processes. And the Department of Genome Sciences is positioned to become a central player in these efforts.

The history of how Genetics and Molecular Biotechnology became Genome Sciences – in my mind at least – is now largely a blur of the countless meetings among all the individuals involved that were required to make the department a reality. Throughout this process, there was enormous patience and good will that can be illustrated perhaps by a single milestone: the creation of a name for the department. Initially, we tried out almost every dyad or triad of Genetics and Molecular Biotechnology and Computational Biology and Genomics and Molecular Technologies and Genome Biology and Genome Technologies and . . . you get the idea. All had the disadvantages of sounding cumbersome and seeming to represent an uneasy melding of two unwilling participants. Over the course of many email ballots and accompanying commentaries (including Jon Gallant’s short list of DNA Studies, Biological Engineering, Botany and Bulgarian), we came to realize that the simple phrase Genome Sciences best embodied our aspirations. Yet giving up names that stood for distinguished histories at the University of Washington was not an easy parting.

As my tenure as acting chair comes to an end, encompassing to me both an official year in the position as well as a previous year that had me first as designated chair of Genetics and then designated acting chair of Genome Sciences and finally acting chair of Genome Sciences, I want to thank the faculty, graduate students, postdocs and staff for their forbearance as we worked through so many educational, administrative and financial issues. Most especially, I am grateful to Breck Byers and Maynard Olson, my fellow acting chairs over this period, for their sage advice; and to David Hodge and Paul Ramsey, who displayed first the vision to take a bold step and then the commitment to ensure it a spectacular future.

Research Highlights

Analyzing Drug Resistance of Tanzania Malaria with a Yeast Assay



Structure of DHFR

Plasmodium falciparum is a parasite that causes the most deadly human malaria. There is currently no vaccine and about 500 million people suffer from malaria each year. Inhibitors of dihydrofolate reductase (DHFR) have been a mainstay of chemotherapy, but point mutations in the *dhfr* gene have rapidly diminished the clinical effectiveness of pyrimethamine, the major antifolate treatment. As more countries use pyrimethamine, surveillance for *dhfr* mutations has been initiated in Africa. The standard molecular analysis uses PCR amplification specific to the *dhfr* mutations associated with drug resistance, which can miss rare alleles.

The laboratory of Dr. Carol Sibley has developed a simple yeast-based system that can identify point mutations in the *P. falciparum dhfr* gene even if they are rare. In work in press in *Transactions of The Royal Society of Tropical Medicine and Hygiene*, they have used this system to screen patient samples from Tanzania. Each patient sample had multiple haploid parasites, so all of the *P. falciparum dhfr* sequences in the sample were amplified by the PCR. The whole population of *P. falciparum dhfr* linear molecules was then transformed into DHFR-deficient yeast such that each transformed yeast colony carried only one *dhfr* sequence. *dhfr* alleles that encode highly resistant enzymes can be detected by replica plating onto plates that contain high levels of pyrimethamine, and then sequenced. With this

approach, even rare drug-resistant alleles can be easily detected.

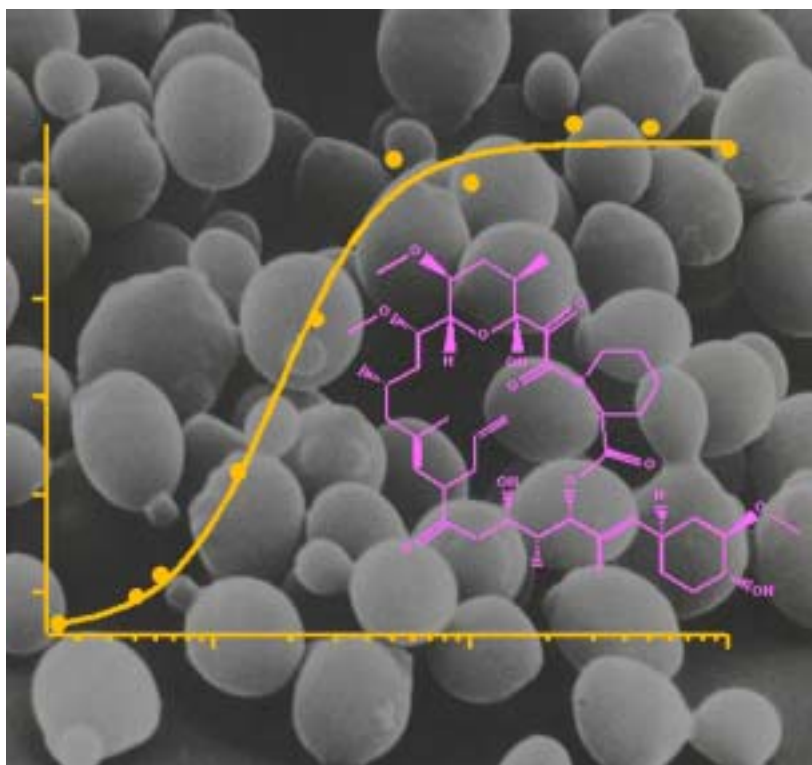
This study showed first, that all isolates contained alleles of *dhfr* that encode highly pyrimethamine-resistant enzymes. Second, 3 of the 6 patient isolates contained the isoleucine to leucine change at amino acid 164 that is associated with pyrimethamine-sulfadoxine treatment failure in Southeast Asia. This is the first report of these highly resistant alleles of *dhfr* in Africa, and it is an important wake up call. The Sibley laboratory is currently analyzing parasite samples from other locations with methods of comparable sensitivity to understand the prevailing situation and to begin to determine the factors most important for rapid selection of drug resistance.

Hitchhiking or Selection in the Human Genome?

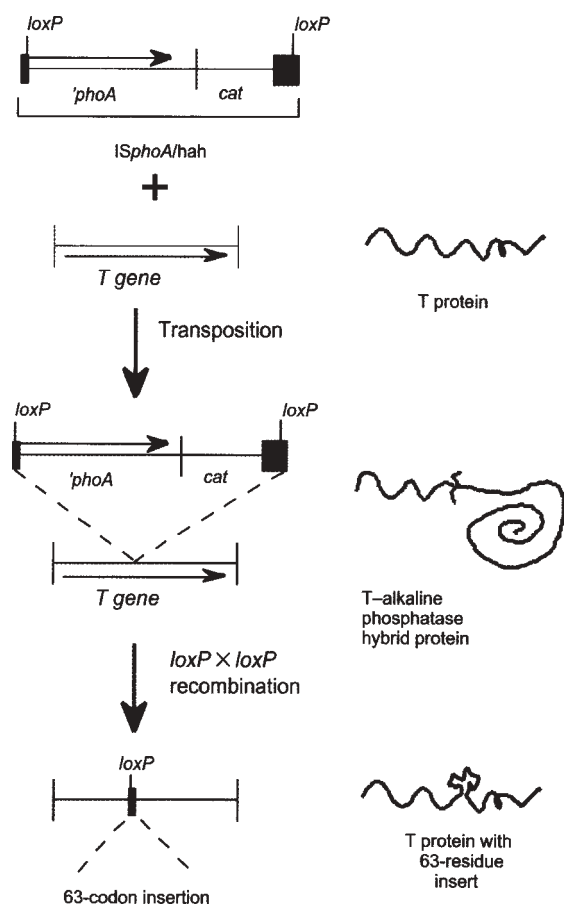
ApoAII is a major component of high-density lipoprotein (HDL) particles and plays an important role in human lipid metabolism. Recent data suggest that there is a relationship between the production of ApoAII and the distribution of another apolipoprotein, ApoAI, in HDL particles. Importantly, HDL particles containing only ApoAI have anti-atherogenic activities, and changes in the distribution of ApoAI among HDL subclasses by ApoAII could promote atherosclerosis and increase risk for cardiovascular disease in humans. Transcription of the ApoAII gene occurs primarily in liver and is controlled by a complex array of regulatory elements located -911 to +29 base pairs relative to the cap site. Based on the potential significance of ApoAII production in promoting atherosclerosis, Debbie Nickerson's laboratory, together with collaborators at Pennsylvania State University, Helsinki and the University of Texas, undertook a comprehensive analysis of sequence variation in this gene (Fullerton *et al.* (2002) *Human Genetics* 111:75-87). Genetic variation in ApoAII was surveyed in three different populations: African-Americans from Jackson, MS (USA), Europeans from North Karelia (Finland) and European-Americans from Rochester, MN (USA), all being followed for differences in cardiovascular disease risk in large-scale epidemiological studies. Fifteen polymorphisms in and around the ApoAII were detected and the pattern of nucleotide and haplotype diversity characterized. The investigations showed significantly lower genotype and haplotype diversity in the African-American samples. Exactly what caused the observed deficit in ApoAII variation in the Jackson sample is unclear. However, a similar pattern of reduced diversity in an African sample is seen at the Duffy locus, a gene with known effects from natural selection. In ApoAII, these studies suggest that polymorphic sites at the 5'-most region of the gene may be the focus of selective effects, which is significant since one of the most 5' polymorphic sites falls directly in a key transcription factor binding site. Alternatively, polymorphic sites further upstream to the ApoAII gene could also be responsible for these observations and may be related to extended effects of the Duffy locus, which is 5' to ApoAII on chromosome 1. In populations of African origin, the Duffy locus is nearly monomorphic, and it is possible that genetic hitchhiking with one or more of the selected alleles could in part explain the reduced variation in ApoAII. Additional analysis of this region is under way to further explore the origins of these differences in human populations. These findings also suggest that substantial differences in cardiovascular disease risk could exist among human populations based on these genetic differences, and this question is under investigation as well.

A Yeast Sensor of Ligand Binding

The identification of small molecule drugs that inhibit cellular proteins and pathways is a major challenge in drug discovery. While there are many different methods to identify molecules that bind an interesting target protein, these methods can be expensive, require complex chemical modifications, or require that an enzymatic activity be easily monitored *in vitro*. In the interest of generating a simple, inexpensive, yeast-based screen for assaying small-molecule binding *in vivo*, Dr. Chandra Tucker, working in the laboratory of Dr. Stan Fields, generated a novel cell-based biosensor that reports the binding of small molecule ligands to proteins by using a yeast growth assay, as described in *Nature Biotechnology* 19:1042-1046 (2001). The biosensor is a chimeric molecule containing a ligand-binding domain or protein that is inserted in a loop region of the essential metabolic protein dihydrofolate reductase (DHFR). The yeast lack endogenous DHFR, such that growth of the yeast is dependent on activity of the chimeric protein, which results in a temperature-sensitive phenotype. The assay is based on the premise that a ligand binding to its target may cause a subtle change in conformation or stability of the chimeric DHFR protein, resulting in an alteration in DHFR activity and a change in temperature sensitivity of the yeast. This work demonstrated that biosensors could be developed that detect either the presence of various estrogen compounds or the immunosuppressant FK506.



A growth curve showing the effect of increasing concentrations of FK506 (structure inset) on yeast cells containing the FK506 sensor.



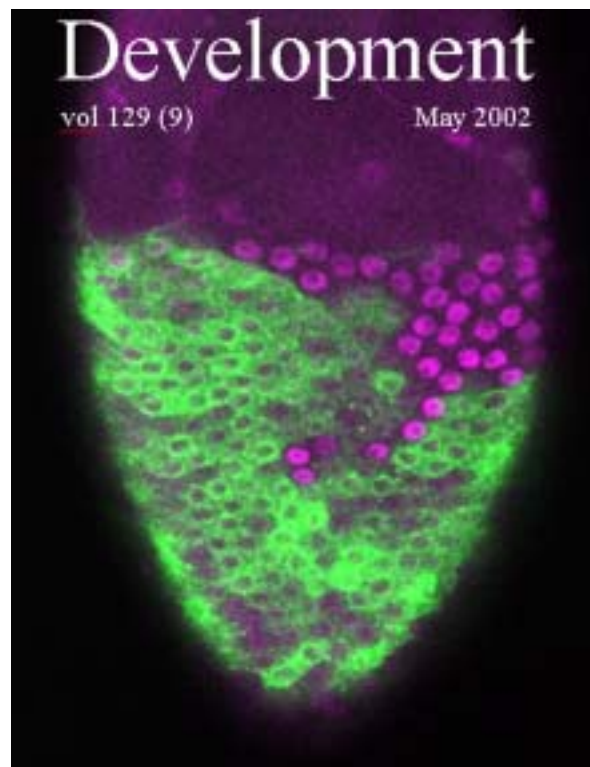
Genome-Wide Tagging of Bacterial Proteins

Jeannie Bailey and Dr. Colin Manoil designed a genetic internal tagging procedure selective for membrane and secreted proteins in Gram-negative bacteria such as *Escherichia coli* and *Pseudomonas aeruginosa*. The technique, published in *Nature Biotechnology* 20:839-842 (2002), is based on a broad host range transposon which may be used to generate both alkaline phosphatase gene fusions and short in-frame insertions in the genome. The in-frame insertion generated encodes an epitope and a hexahistidine sequence, permitting sensitive detection and metal affinity purification of tagged proteins. For each gene targeted, it is thus possible to monitor the disruption phenotype (using the transposon insertion), the gene's transcription and translation (using the AP reporter activity), and the behavior of the unfused protein (using the internal tag). Studies of a sequence-defined collection of *Escherichia coli* strains generated using the transposon showed that the synthesis and subcellular localization of tagged proteins could be readily monitored.

Function of *ISphoA/hah*. The insertion of *ISphoA/hah* into a target gene encoding an exported protein can generate an active gene fusion that may be converted into a 63-codon insertion by *loxP* recombination.

Mosaic analyses reveal the function of *Drosophila* Ras

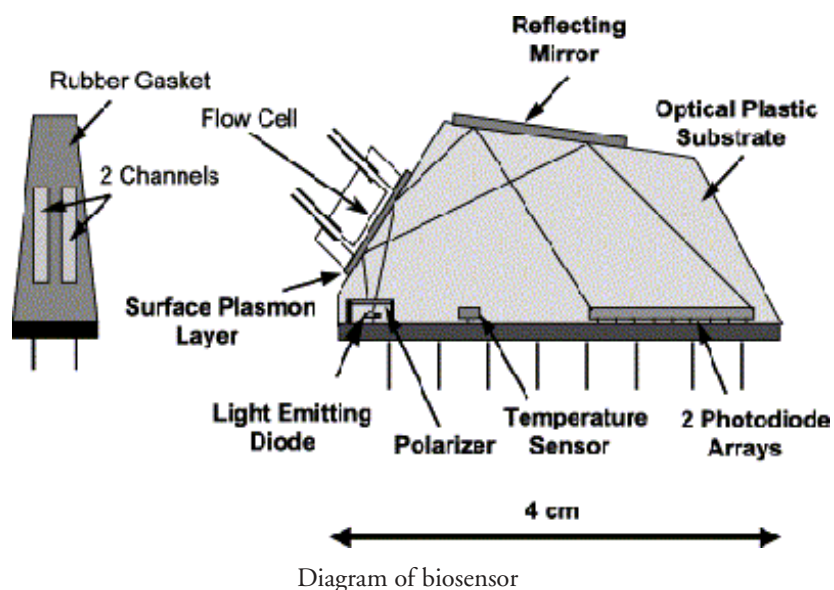
Ras is a well-known oncogene that is mutated in 70% of tumors. In normal tissue, Ras acts as part of a signaling cascade that regulates the growth and division of cells. During development, the Ras pathway also functions in determining cell fates. Karen James, working in Dr. Celeste Berg's laboratory, examined the function of Ras in a signaling cascade that establishes the dorsal/ventral polarity of the *Drosophila* egg, embryo, and eventually, of the adult fly. During oogenesis, signals from the oocyte to a surrounding layer of follicle cells act through Ras to pattern the follicle cells and create the proper ventral information needed by the developing embryo. When Ras function was removed in a subset of follicle cells, two surprising results occurred, as published in *Development* 129:2209-2222 (2002). First, when a small number of cells lacked Ras, later developmental processes could be modified to rescue the mutant eggs. Wild-type larvae hatched! This result shows that for such an important event as establishing the basic body plan of the animal, nature has evolved powerful methods to compensate for defects and ensure that development proceeds correctly. Second, when large numbers of follicle cells lacked Ras, these cells failed to move correctly. Although other Ras-like proteins are known to regulate the cell shape changes involved in cell migration, a role for the Ras oncogene in this process is new. Thus, two novel developmental roles for Ras function were discovered.



Follicle cells in green are wild type for Ras while cells that lack green also lack Ras. The Ras-minus cells misexpress a gene, pipe (magenta nuclei), that specifies ventral information in the embryo.

Genetic Variability in Paraoxonase; Development of Biosensor Systems

Dr. Clem Furlong's laboratory has been analyzing the genetic variability of a serum protein associated with the HDL or "good cholesterol" particles. The HDL-associated protein was named paraoxonase (PON1) because of its ability to hydrolyze the toxic metabolite of the insecticide parathion. The work in Dr. Furlong's laboratory has shown that this protein is important in protecting against poisoning by diazinon and chlorpyrifos, but surprisingly not parathion. Genetic and developmentally determined differences in levels and sequence of this protein affect sensitivity to diazinon and chlorpyrifos exposures as described, for example, in *Pharmacogenomics* 3:341 (2002). Efforts are also aimed at genetically modifying this protein so that it can be used to treat individuals exposed to other toxic organophosphate compounds. The other important normal physiological role of PON1 is to metabolize oxidized lipids that are involved in the initiation of vascular disease. A collaboration with Dr. Gail Jarvik has found that individuals with low PON1 levels have an increased risk for carotid artery disease (*Atherosclerosis, Thrombosis, and Vascular Biology* 20:2441-2447 (2000)).



Dr. Furlong has also been developing biosensors that have a wide range of applications from basic research to detection of agents of bioterrorism, in collaborations with the laboratory of Dr. Sinclair Yee in Electrical Engineering and researchers at Texas Instruments. This effort is aimed at the development of biosensor systems that have use as general instruments for the research laboratory and also for detecting agents of bioterrorism. These surface plasmon resonance based biosensors are capable of detecting proteins at subnanomolar levels in complex media such as seawater or plasma. They are also useful for detecting specific viruses or microbes, as described in *Biosensors and Bioelectronics* 17:573-584 (2002).

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Genome Sciences Symposium on Genetic Variation

On May 29th, 2002, the Department of Genome Sciences hosted a symposium entitled “Genetic Variation in Disease and Development.” Development and disease are subject to complex genetic control, involving many genes that directly regulate or modify the primary phenotype. Identifying these genes has traditionally involved forward genetic screens in model organisms, or positional cloning of human disease genes. More recently, sophisticated enhancer and suppressor screens, altered patterns of gene expression detected by microarray analyses, and association studies in humans, made possible in part with the sequencing of the human genome, have broadened the geneticist’s net for finding interesting and important genes.

Dr. Paul Ramsey, Dean of the School of Medicine, opened the symposium by expressing his enthusiasm for the new Department of Genome Sciences. He remarked that these are exciting times for the new Department and the University of Washington, and he wished the Department great success at developing strong programs in computational biology and technology development.

Dr. Cynthia Kenyon from the University of California at San Francisco spoke on the genes and cells that regulate lifespan in nematodes. Using classical genetic approaches, her laboratory has identified several genes that increase the lifespan of worms. She described the conservation of many of the genes across species and speculated that some of these genes may also influence lifespan in mammals.

Dr. Bradley Merrill from the University of Chicago described recent advances in understanding the biogenesis and maintenance of skin. Key conserved genes regulate cell fate decisions necessary for directing the skin stem cell to assume the many types of cells that collaborate to confer the functional and protective properties of skin. Dr. Merrill also described how careful phenotypic analysis of genetically engineered mice, and a thorough review of the medical literature, can occasionally lead to the identification of genes involved in human skin pathologies.

Complex traits in mice are often studied using various strains of inbred mice that investigators have established through many years of selective breeding and phenotyping. Dr. Joseph Nadeau from Case Western Reserve University, in his talk, “Building Hearts, Getting Fat, and Breaking Bones: Computational Analysis of Component Traits in Genetically Randomized Populations,” described how modern phenotyping of complex traits in recombinant inbred and chromosome substitution mouse lines can be used to identify genes with major and minor effects on complex traits. He described the power of chromosome substitution strains, lines of mice with single intact chromosomes from different inbred mice, for rapid testing of candidate modifier loci identified in more traditional genetic mapping experiments involving two different inbred lines of mice that show variation in phenotype.

Dr. Leena Peltonen from the University of California at Los Angeles discussed methods and successes of tracking rare and common disease genes using isolated human populations. She informed the audience of the many successes of identifying genes associated with monogenic diseases. Dr. Peltonen remarked that ethical concerns associated with genotyping individual humans should not be of serious concern as all of us are certain to carry many recessive disease-causing alleles. She also reminded the audience that humans who are lactose intolerant are actually more common, and are therefore the wild-type, than individuals who are milk drinkers.

Dr. Leonid Kruglyak from the Howard Hughes Medical Institute and Fred Hutchinson Cancer Research Center discussed what it would take to carry out whole-genome disease association studies in humans. Dr. Kruglyak presented a realistic, and somewhat daunting overview, of how many small nucleotide polymorphisms, SNPs, are required for large scale mapping of complex traits. The identification of usable SNPs in the human population is likely to be the easy part. Required are new high throughput methods for genotyping hundreds of thousands of SNPs in the DNA from single humans.

Dr. George Weinstock from the Baylor College of Medicine presented a talk entitled “Genomania from Microbes to Mammals.” He highlighted the remarkable productivity of the various genome centers, which have sequenced the human, fly, worm, mouse, and more than 150 microbial genomes. Comparative genome analysis has revealed the functional clustering of families of genes and insights in the evolution of chromosome architecture.

The symposium ended with a provocative talk, “An Ape Perspective on Human Uniqueness” by Dr. Svante Pääbo from the Max Planck Institute of Evolutionary Anthropology. Dr. Pääbo described comparative gene expression patterns in different regions of the brain between humans and various non-human primates. He suggested that changes in gene expression patterns, as opposed to changes in gene number and function, might play a major role in the many behavioral and morphological differences between humans and chimps.

Planning is under way for the 2nd Genome Sciences symposium, which will be held on May 14th, 2003, on the topic of Human/Mouse: Comparative Biology. Everyone is welcome to attend what looks to be another outstanding symposium.

Philip Green, Maynard Olson, and Robert Waterston Win Gairdner Awards

Dr. Philip Green, Dr. Maynard Olson and Dr. Robert Waterston are three of eight scientists honored by the Gairdner Foundation for their major original and pioneering contributions, both fundamental and applied, to our understanding of mammalian and other genomes.

Maynard Olson is honored as an early architect for his original concepts as well as technological and experimental innovations critical to the sequencing of mammalian genomes. “Dr. Olson played a central role in laying the conceptual and technical foundations for the Human Genome Project,” the Foundation stated. “He established the paradigm and the technologies for the physical mapping of complex genomes.”

Phil Green’s award, in bioinformatics, honors his contributions to the development of the computational tools essential for sequencing of the human genome. The Foundation noted his development of a software package critical to the advance of DNA sequencing where success depended on combining a variety of algorithmic innovations with rigorous focus on the entire life cycle of the data – from laboratory instrument to Genbank submission. The Foundation further stated that he provided compelling early evidence for a dramatically reduced number of human genes.

Bob Waterston receives his award for major seminal contributions to the sequencing of human and other genomes. “One of the most exciting scientific accomplishments of our times was the publication in February, 2001, of the initial sequencing of the human genome,” the Foundation announced. Dr. Waterston was specifically recognized for his inspired leadership and commitment to the goal of determining the complete human DNA sequence.

The 2002 awards will present each scientist with \$30,000 for achievement in genomics research. The ceremony will be held October 24, 2002, in Toronto.

Leland Hartwell Wins Nobel Prize in Medicine

On December 10, 2001, Dr. Leland Hartwell was one of three laureates to receive the Nobel Prize in physiology or medicine. Dr. Hartwell, Director of the Fred Hutchinson Cancer Research Center and Professor of Genome Sciences, received the Nobel Prize for his discoveries of a specific class of genes that control the cell cycle. One of these genes was found to have a central role in controlling the initial step of each cell cycle. Lee Hartwell also introduced the concept of a “check-point,” a valuable aid to understanding the cell cycle. The findings in the cell cycle field are being applied to tumor diagnostics, as increased levels of these regulators are sometimes found in human tumors. The discoveries may lead to new principles for cancer therapy. Dr. Hartwell carried out this work as a member of the Department of Genetics. Together with Timothy Hunt of the Imperial Cancer Research Fund in Hertfordshire, England, and Paul Nurse of the Imperial Cancer Research Fund in London, Dr. Hartwell shared in the \$943,000 award.

Leroy Hood Wins Kyoto Prize

Dr. Leroy Hood, founding chair of the Department of Molecular Biotechnology, one of Genome Sciences’ progenitor departments, will receive the Inamori Foundation’s Kyoto Prize for “outstanding contributions to the life sciences through the development of automated instruments for the determination of protein and DNA sequences and their syntheses.” Dr. Hood’s award is in the fields of biotechnology and medical technology. “The development of many types of high-speed, automated instruments by Dr. Hood and other researchers has been a major driving force behind progress in genomic science studies,” the Foundation stated. The Kyoto Prize Presentation Ceremony will be held in Japan on November 10, 2002. Dr. Hood will receive a diploma, a Kyoto Prize Medal and prize money in the amount of 50 million yen. Dr. Hood is President and Director of the Institute for Systems Biology in Seattle.

Genome Sciences Upcoming Seminars and Events

Sept 23-25: 2002 Department Retreat

Oct 2: Chris Burge, MIT (with COMBI)

Oct 9: David Pollock, Louisiana State Univ (with COMBI)

Oct 16: Stephen Altschul, NCBI (with COMBI)

Oct 23: Richard Smith, Pacific Northwest Natl Lab

Oct 30: Richard Young, MIT

Nov 6: Andrew Feinberg, Johns Hopkins University

Nov 13: David Roos, University of Pennsylvania

Nov 20: David Allis, University of Virginia

Dec 4: Lincoln Stein, Cold Spring Harbor Lab (with COMBI)

Dec 11: Andy Clark, Cornell University (with COMBI)

Jan 8: Richard Mathies, University of California, Berkeley

Jan 15: Eric Green, NHGRI (with COMBI)

Jan 22: Lap-Chee Tsui, Children’s Hospital, Toronto

Jan 29: Peter Nelson, Fred Hutchinson Cancer Research Ctr

Feb 5: Joel Richter, University of Massachusetts

Feb 12: Bevin Engleward, MIT

Feb 19: George Church, Harvard University (with COMBI)

Feb 20: Ian Hickson, University of Oxford

Feb 26: Mel Feany, Harvard University

Mar 5: Richard Losick, Harvard University

Mar 12: Joanne Chory, Salk Institute

Apr 2: Terry Gaasterland, Rockefeller University

Apr 9: Phil Benfey, New York University

Apr 16: Randy Schekman, University of California, Berkeley

Apr 23: Robert Darnell, Rockefeller University

Apr 30: John Carlson, Yale University

May 7: Liz Blackburn, University of California, San Francisco

May 14: Genome Sciences Symposium “Human/Mouse: Comparative Biology”

May 21: Gabriel Guarneros, Centro de Investigacion y de Estudios Avanzados del IPN, Mexico City

May 28: Martin Yanofsky, University of California, San Diego

June 4: Deirdre Meldrum, University of Washington

Our website www.gs.washington.edu has all updated information on seminars, COMBI, Journal Club and other special events.