NC STATE UNIVERSITY Bioinformatics Research Center

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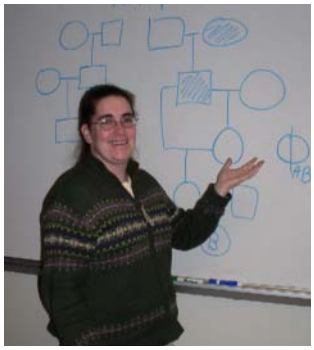
Chronic Pain Study Reveals Genetic Link



Dr. Amy D. Anderson, a BRC post-doc, collaborates with researchers at UNC in studying the genetics of pain while pursuing her own research in estimating relationships using genetic markers and population genetic theory.

"Working with Amy completely changed my perception of statistics as a dry science."
Luda Diatchenko,
UNC School of Dentistry

Dr. Amy D. Anderson, a postdoctoral researcher at the Bioinformatics Research Center, is applying her statistical savvy to help determine if our genes hold keys to developing new treatments for chronic pain sufferers.

Since August, Anderson has been collaborating with Dr. Luda Diatchenko and Dr. William Maixner of UNC-Chapel Hill's Comprehensive Center for Inflammatory Disorders to study the genetic basis for individual variation in pain perception and the development of temporomandibular joint disorder (TMD).

TMD is a painful condition of the jaw joint and muscles, often accompanied by heightened sensitivity to pain at other body sites. Diatchenko's research explores how genetic and physiological, psychological, and behavioral factors may combine to cause TMD, using data she collected from about 200 women. During three years of monitoring, 15 of the women developed TMD.

Anderson is evaluating data on variants of a human gene that code for a particular hormone receptor. One variant, the most common in the human population, seems to be protective against developing TMD. Only one of the women with TMD carried this variant. Anderson's analysis confirmed that this finding was statistically significant. Anderson has also found significant associations between the gene variants and several psychological factors, such as depression, anxiety, expressions of anger, and somatization.

"Luda is great at developing hypotheses that might explain the data," said Anderson. "My job is to determine if the patterns we think we see in the data are likely to have resulted by chance or might have some biological significance."

"Working with Amy completely changed my perception of statistics as a dry science," said Diatchenko. "In Amy's hands, endless columns of numbers were converted into meaningful and potent explanations of why people feel and deal with pain differently."

Trained in mathematics, Anderson earned her Ph.D. in statistical genetics at the University of Washington, where she worked on mapping genes in pedigrees. Now she is exploring how to estimate relationships using marker data and taking population structure into account. This work has applications in gene mapping, forensics, and conservation genetics.

From the Director

We are very pleased to welcome Dr. Eric Stone of Stanford University to the BRC faculty in the fall.

We also thank our industry partners who met with our great group of graduate student applicants in February.

This spring the BRC extends a warm welcome to new faculty member Dr. Eric Stone, who joins us in the fall, and to a new group of outstanding applicants, who we also hope to see here in the fall.

Dr. Stone will join the Department of Statistics, with an appointment to the bioinformatics graduate program. Stone, who received his Ph.D. in statistics at Stanford in 2004, is currently a post-doctoral research associate at Stanford's Department of Pathology and Genetics. His research is in statistical methods for interpreting genomic data. A number of our readers will remember his seminar in February on the robustness of the phylogenetic comparative method. Dr. Stone's office will be at the BRC, and we look forward to his arrival.

In February we also hosted 12 prospective bioinformatics students, all with outstanding academic credentials and all of whom we hope to see here in August.

A special thanks goes to our industry partners at EPA, BD Technologies, GSK, and Athenix Corp. who took time to visit with the applicants and describe potential graduate student research opportunities. Our relationships with Triangle-area industries through the Graduate in Training program are a vital part of our education program and an important feature in attracting the best students to NC State. Thanks, too, to Bryon Sosinski for the tour of the Genome Research Lab and to Christine Duarte and other graduate students who helped welcome the applicants at lunch and dinner.

Bruce Weir

Grad Student Finds Digital Signals of RNA Interactions

In research that could help biologists efficiently produce human proteins in bacteria, grad student Josh Starmer is using digital signal processing techniques to analyze how messenger RNA (mRNA) is translated correctly into the chains of amino acids that comprise proteins.

"E. coli are already used to make human insulin for treatment of diabetes, but the mRNA translation process is hit or miss. We would like to remove the 'miss.'"
Josh Starmer
Bioinformatics Grad Student

Starmer works with Computer Science Professor Don Bitzer's protein translation group. The group is interested in how ribosomes (RNA-rich particles involved in protein synthesis) consistently "read" three nucleotides at a time on the mRNA chain. Each three-nucleotide series codes for one of the 20 amino acids that make up proteins. "Frame-shift" errors – reading two or four bases instead of three – result in defective proteins.

"If we can determine how a ribosome stays in frame, we will be a step closer to understanding how to translate foreign genes accurately in transgenic organisms to produce proteins for therapeutic purposes," said Starmer. "For example, E. coli are already used to make human insulin for treatment of diabetes, but the mRNA translation process is hit or miss. We would like to remove the 'miss.'"

Using software that simulates interactions between ribosomal RNA and mRNA, Bitzer's group identified a putative "synchronization signal" in the simulated data.

To see if the signal has biological importance, Starmer is now testing his hypothesis that organisms that live at high temperatures should posses a strong signal, relative to organisms that live at low temperatures, as a means of overcoming the increased "noise" in the process introduced by heat. Starmer's analysis of binding energies between mRNA and ribosome in two bacteria that live at 37 C and two that live at 60 C or more seems to support his hypothesis.

"I like trying to figure out exactly how this works. This type of research brings out the Erector-Set builder in me," said Starmer.

After earning degrees in music composition and computer science at Oberlin, Starmer began sitting in on biology lectures at the College of Charleston (SC). "There I discovered that I could combine my computer programming skills with my fascination for biology," he said. "Dr. Rob Dillon at the College gave a glowing endorsement of the statistical genetics program at NC State. That, and the lively music scene in Raleigh [Starmer plays electric cello with two bands], made the bioinformatics program here an obvious choice for me."

Chinese Dumpling Party Rings in Year of the Rooster

Nearly 30 BRC grad students and friends gathered to enjoy Chinese dumplings and other specialties at the annual Chinese New Year party, held February 6 at the home of Christine Duarte. The Year of the Rooster officially began with the new moon on February 9. In China (but, alas, not at the BRC) the celebration lasts until the full moon 15 days later.

Some of the Chinese students put up traditional characters of greeting on the doorway to welcome guests and wish them a happy new year.

The party's centerpiece is preparing (and eating) the small meat dumplings that are the traditional New Year's food of Northern China. The dumplings are universally enjoyed, however, as all the BRC's students can attest.

"We had a ton of food," said Duarte. At least a dozen different traditional Chinese dishes shared the table with the dumplings, as well as a few American standards (after all, it was also Superbowl Sunday).

Celebrating the 2005 Chinese New Year (from left to right, both photos): Frank and Andrea Mannino, Christine Duarte, and Errol Strain; Li Li, Chuanhua Xing (from ECE), and Sihui Zhao.

Deer DNA Analysis Leads to Murder Charge

In the country's first criminal investigation using deer DNA, forensic analyses by the BRC's Dr. Christopher J. Basten led to an arrest in a 7-year-old Pennsylvania murder case.

Forensic analysis of deer DNA by Dr. Christoper J. Basten of the BRC led to an arrest in a seven-year-old murder case in Uniontown, PA, in which the suspect was charged with deliberately shooting and killing a hunter in 1997 and taking the hunter's deer home with him. It was the country's first criminal investigation involving deer DNA.

Basten, a statistical geneticist and forensic expert, analyzed DNA profiles from samples collected at the crime scene and from venison steaks found some months later in the suspect's freezer. The DNA matched at each genetic region in the profiles. Using DNA profiles from 24 local deer collected for the purpose and from a larger database compiled by wildlife researchers in Mississippi, Basten determined that the observed match between the crime scene samples and frozen steaks was 47,000 times more likely if the samples came from the same deer rather than from two unrelated deer, and 1,700 times more likely if the samples came from the same deer than from two full siblings. Basten's report was completed last September. The Associated Press reported the subsequent arrest on October 29, 2004.

Said Basten about the unusual case, "It's all just data to me."

More Secrets (of Plants) Revealed

Basten's DNA analyses have also supported discoveries that will help shape the future of genetic research in flowering plants and in forestry.

He has helped Swiss scientists map nine genes that seem to account for most of the physical differences (e.g., blossom shape and nectar composition) in flowers of two petunia species, one pollinated by hawkmoth, the other by bees. This research should yield the first robust model for studying the genetics and evolution of insect-mediated pollination systems in flowering plants (see J. Stuurman et al. in Recent Publications).

Basten has also collaborated with researchers at NC State's Forest Biotechnology Group who are studying the genetic regulation of growth rate and wood density in eucalyptus. Basten wrote a computer program to automate the analysis of microarray data representing the expression of more than 2600 genes in 91 hybrid trees and correlate the data to genotype of the parental lines. The researchers were able to identify the chromosomal locations of more than 40 percent of the genes expressed on the microarrays, thus narrowing the search for genes that regulate these economically important traits in trees (see M. Kirst et al. in Recent Publications).

Comparative Evolutionary Genomics Symposium, June 4

The first annual joint symposium on statistical genetics and evolutionary biology, sponsored by the new National Evolutionary Synthesis Center (NESCent; see story on page 4) and NCSU's Summer Institute in Statistical Genetics, will be held Saturday, June 4, 2005, on the NC State campus. The theme of the symposium is comparative evolutionary genomics.

The symposium features six noted researchers in the genetics of primates and humans, insects, fungi, grasses, and livestock. Speakers include Michel Georges of the University of Liege, Rytas Vilgalys and David Goldstein of Duke, Stephen Richards of Baylor College of Medicine, and Christina Grozinger of NCSU. Dr. Cliff Cunningham, the director of NESCent, will speak at the symposium dinner.

For more information, watch http://statgen.ncsu.edu/brcwebsite/summer_institute.php or www.nescent.org.

Recent Publications

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Weir BS, Hill WG, and Cardon LR. 2004. Allelic association patterns for a dense SNP map. Genetic Epidemiology 27:442-450.

NESCent to Synthesize Research in Biological Evolution

"NESCent will be a tremendous intellectual resource for the Triangle Area, as well as the national and international scientific communities."
Greg Gibson, NCSU Professor of Genetics and NESCent Associate Director of Outreach and Education

The new National Evolutionary Synthesis Center (NESCent) in Durham is pioneering the synthesis of the vast amounts of information on evolution being generated by researchers in biology, medicine, genomics, computation, and other fields. The center's goals are to facilitate collaborative research, accelerate productivity, and improve our ability to address important issues in health care, agriculture, conservation, and education.

To do this, a team of NESCent scientists will collaborate with hundreds of other researchers worldwide to develop new data management and software tools to coordinate, access, and analyze data in the various information databases being generated in different disciplines. These tools will open up new areas of collaborative research, help answer major questions in evolution, and foster synthesis of results among disciplines.

The center's education and outreach programs, led by Dr. Greg Gibson, professor of genetics at NC State, member of the BRC, and assistant director for life sciences for the North Carolina Agricultural Research Service, will communicate with policymakers, educators, and the public about advances in evolutionary knowledge and will assist with curriculum development.

Funded by a $15 million grant from the National Science Foundation and directed by Dr. Clifford Cunningham of Duke University, the center is a collaborative effort of Duke, UNC, and NC State.

"NESCent will be a tremendous intellectual resource for the Triangle Area, as well as for the national and international scientific communities," said Gibson. The BRC looks forward to participating in NESCent research and outreach activities.

2004 Ph.D. Grads Join Industry, Academia

Congratulations to the BRC's 2004 Ph.D. graduates, all of whom have have joined cutting-edge genomics research teams in industry and academia.

Sheng Feng (Statistics; advisor: Zeng) is assistant professor of biostatistics at Washington University School of Medicine, where he is pursuing research in microarray data analysis and linkage disequilibrium mapping.

Andrea Johnson (Genetics; advisor: Weir) is a biostatistician at Roche Molecular Systems in Alameda, CA, where she supports association testing of genetic markers with human disease phenotypes, using real-time PCR gene expression data.

Jian Li (Genetics; advisor: Zeng) is a post-doc at Cornell University, where he is working on association mapping of human cardiovascular disease genes.

Li Li (Bioinformatics; advisor: Weir) is principal scientist in GSK's Genetic Data Sciences group in Research Triangle Park. She first joined GSK as a student intern in 2003. Li works on methods of mapping genes for complex diseases such as Type II diabetes and asthma.

Elizabeth H. Scholl (Biomathematics; advisors: Thorne, Bird) is the senior bioinformatics analyst on NC State's Tobacco Genome Initiative project. She evaluates gene discovery trends across different sequencing strategies, characterizes repeat elements in the genome, and identifies target genes using data mining techniques.

Xiang Yu (Bioinformatics; advisors: Weir, Nielsen) is a biometrician in the clinical molecular profiling group at Merck & Co. in Rahway, NJ. His group performs pharmacogenomic and gene expression studies related to obesity, diabetes, asthma, atherosclerosis, and oncology.

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Director: Bruce Weir
weir@stat.ncsu.edu

Editor/Writer: Pat Westphal

Contributing Writer: Millie Maynor

Address correspondence and suggestions to the editor (pawestph@unity.ncsu.edu).

Bioinformatics Research Center
North Carolina State University
Campus Box 7566
Raleigh, NC 27695-7566

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