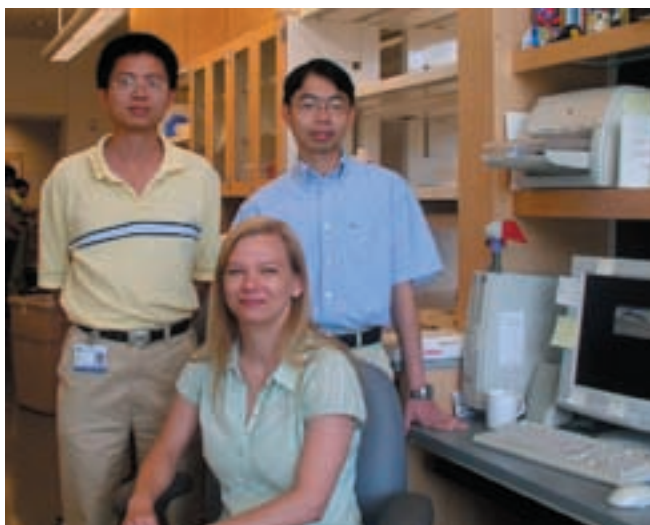


## Interns Probe Genetics of Autism, Alzheimer's Disease

As grad student interns at Duke University's Center for Human Genetics (CHG), NC State bioinformatics students Hao Mei and Ren-Hua Chung are helping create better tools for exploring the genetics of complex human diseases.

Hao Mei has helped develop new software, called EMDR 1.90 (for "extended multiple dimensionality reduction"), for identifying multiple gene interactions in autism and other diseases. The new program is able to identify genetic patterns (combinations of several gene locations) that appear to be associated with the disease even if each gene location analyzed alone does not.



Graduate student interns Hao Mei (left) and Ren-Hua Chung (right) with Dr. Eden Martin at the Duke University Center for Human Genetics.

Working under the direction of Dr. Allison Ashley-Koch and Dr. Eden Martin (Ph.D. 1997 NC State), Mei incorporated advanced test statistics and analytical methods into the program and designed efficient data structures and algorithms to optimize memory utilization and improve program efficiency.

When applied to the autism data, EMDR was able to detect interactions among three gamma aminobutyric acid (GABA) receptor subunit genes on chromosome 15. Mei is co-author on two papers that are accepted for publication and a third that is submitted. A new

project, MDR-Phenomics, aims to integrate clinical phenotype information with the genetic analyses.

More than 20 people from different fields – clinical medicine, biology, statistics, and computer science – attend weekly meetings on the autism project. "I am honored to be working with a diverse team and participating in several challenging projects that will be components of my Ph.D. thesis," Mei said. Prior to coming to NC State, Mei earned a degree in medicine from China Medical University in the People's Republic of China and an M.S. in biomedical informatics from the University of Washington.

Ren-Hua Chung, who trained as a computer scientist in Taiwan and at the University of California at Davis, is busy on two projects at CHG. As a data analyst on the Alzheimer's disease project, he checks for genotyping errors in family data using tools such as pedigree consistency and Hardy-Weinberg assumption testing. Then he performs linkage and association analyses using various software packages.

"We are excited to have found significant association of several genes and gene variants with Alzheimer's disease," said Chung, who is co-author on a paper to appear in the *Journal of Medical Genetics* and two conference presentations related to the project.

Chung also works with Eden Martin in developing statistical methods for family-based association analyses (finding genes associated with a trait such as a complex disease). Currently they are studying association in the presence of linkage (APL), which Chung implemented as a computer program.

"APL can handle missing parental genotypes and it works correctly even when the disease loci and the markers being tested are linked on the chromosome," said Chung. Scientists at CHG have used the APL program to help find a gene variant that is a major risk factor for age-related macular degeneration (Haines JL, et al. *Science*, April 15, 2005).

"The abundance of data at CHG is a great asset for exploring disease-causing genes," said Chung.

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## New Faces at the BRC

The BRC extends a warm welcome to post-doctoral research associate Dr. Asger Hobolth, from the Bioinformatics Research Centre at the University of Aarhus. Asger has joined Jeff Thorne's research group to work on developing statistical measures of the interaction of phenotype and genotype.

Post-doctoral fellows Dr. Augusto Garcia and Dr. Luciana Carlini-Garcia of Brazil have been working with Zhao-Bang Zeng since last fall on QTL mapping

and developing multi-QTL analytical methods to explore and compare the genetic basis of hybrid vigor of yields in maize and rice.

Dr. Diane Byers, on sabbatical from Illinois State University, is also working with Zhao-Bang on environmental effects on QTL expression in *Arabidopsis*. She returns to Illinois in late August.

It is a pleasure to have these talented scientists at the BRC.