

Genetic Association Information Network Announces Genotyping Award for UCSD Researcher

Whole Genome Association Study to Focus on Bi-Polar Disorder

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The genetics of bipolar disease will be one of six areas of focus supported by a new initiative called the Genetic Association Information Network (GAIN), announced by the Foundation for the National Institutes of Health (FNIH). John Rice Kelsoe, M.D., professor of psychiatry at the University of California, San Diego (UCSD) School of Medicine will lead the "Whole Genome Association Study of Bipolar Disorder," developed from his on-going genetic studies conducted at UCSD.

Kelsoe is director of the UCSD Laboratory of Psychiatric Genomics where he leads research as part of an 11-site consortium funded by the National Institute of Mental Health to collect DNA samples from 5,500 patients with bipolar disorder for genetic mapping studies. The genetic library they compile will be compared with genetic information from normal, healthy volunteers in an effort to identify genetic abnormalities that might contribute to bipolar disease.

"It is well-established that genes play a prominent role in many major psychiatric disorders," said Kelsoe. "By identifying these genes, it is hoped that the basic mechanisms for these disorders will be better understood, and that new methods of treatment might be developed."

As part of the GAIN project, 1,000 patients with bipolar disorder as well as 1,000 matching control subjects will be genotyped at more than 500,000 DNA markers covering the genome. The resulting data will be made immediately available to the scientific community in order to foster gene and pathway discovery.

GAIN was established to identify the genetic contributions to common illnesses that affect the public health, such as depression and diabetes. Using biological samples already collected in earlier clinical studies, GAIN will comprehensively evaluate the subtle differences between the genomes of approximately 1,000 to 2000 normal, healthy volunteers and the genomes of 1,000 to 2000 patients with the condition being studied. Identifying genetic differences between the two groups will speed up the development of new methods to prevent, diagnose, treat and even cure common conditions.

The Genetic Association Information Network is a unique public-private partnership involving the National Institutes of Health (NIH), Pfizer, Inc., of New York City, Affymetrix, Inc., of Santa Clara, CA, and the FNIH, as well as Perlegen Sciences, Inc., of Mountain View, CA., Abbott, of Abbott Park, IL, and the Broad Institute of Massachusetts Institute of Technology and Harvard University. GAIN was established in February, 2006 to help find the genetic causes of common diseases by conducting large-scale genomic studies and making their results broadly available to researchers worldwide. Private donors have contributed approximately \$26 million to the project in order to stimulate rapid progress in this field.

The FNIH Board of Directors selected the first six studies after rigorous peer, technical and ethical reviews and at the recommendation of the GAIN Steering Committee, comprised of twenty-one distinguished scientific leaders

from government, academia, and industry. The other five studies selected, with their principal investigators and affiliated medical institutions, are:

Goncalo Abecasis, Ph.D., University of Michigan School of Public Health, Ann Arbor, MI, "Collaborative Association Study of Psoriasis."

Stephen V. Faraone, Ph.D., Research Foundation of the State University of New York (Upstate Medical University), Syracuse, NY, "International Multi-Center ADHD Genetics Project."

Pablo V. Gejman, M.D., Center for Psychiatric Genetics, Evanston Northwestern Healthcare Research Institute, and Feinberg School of Medicine, Northwestern University Evanston, IL, "Genome-Wide Association Study of Schizophrenia."

Patrick Francis Sullivan, M.D., The University of North Carolina at Chapel Hill, "Major Depression: Stage 1 Genome-wide Association in Population-Based Samples." (samples collected as part of the Netherlands Study of Depression and Anxiety and the Netherlands Twin Registry at the Vrije Universiteit (VU), Amsterdam, and the VU Medical Center.)

James Heber Warram, M.D., Joslin Diabetes Center, Boston, MA, "Search for Susceptibility Genes for Diabetic Nephropathy in Type 1 Diabetes."

The studies were chosen out of nearly three dozen applicants during a rigorous five-month selection process. A unique feature was the involvement of a Technical Analysis Group (TAG) that provided a secondary level of evaluation beyond the peer review of written applications. The TAG, which consisted of experts in genetics, epidemiology, bioethics, and data analysis, pre-tested the DNA in study samples, analyzed multiple informed consents, checked case/control matching, and carefully evaluated the study populations of the top-ranked applications that passed peer review.

"GAIN is a critical first step in identifying the genetic factors that influence disease susceptibility and health, and it is essential to choose studies that offer the best possible potential to find these factors in common diseases," said Francis S. Collins, M.D., Ph.D., director of the National Human Genome Research Institute at NIH and chairman of the GAIN Steering Committee.

GAIN will pay for analyzing approximately 18,000 samples across the six diseases, using genotyping services provided by Perlegen Sciences (in partnership with Pfizer) and the Broad Institute (in partnership with Affymetrix) over the next four to eight months. Genotyping uses standardized laboratory procedures to identify genetic variations between individuals. By comparing the frequency of genetic variants across all of the chromosomes in both affected and unaffected persons, researchers can pinpoint hereditary factors that contribute to illness.

As DNA samples from each study are genotyped, the results will be made broadly available to the research community in keeping with the principles pioneered by the Human Genome Project. A portion of the \$5 million provided by Pfizer to pay for the overhead of the GAIN project will support development of the GAIN database by The National Center for Biotechnology Information (NCBI), a part of the National Library of Medicine at NIH.

In addition to free genotyping of their samples, the primary investigators for each of the chosen studies and their institutions will receive additional grants from NIH to support analysis of the new genetic data.

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