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A Gene for Depression Localized

Reports new study in Biological Psychiatry

Philadelphia, PA, January 4, 2012 – Psychiatric disorders can be described on many levels, the most traditional of which are subjective descriptions of the experience of being depressed and the use of rating scales that quantify depressive symptoms. Over the past two decades, research has developed other strategies for describing the biological underpinnings of depression, including volumetric brain measurements using magnetic resonance imaging (MRI) and the patterns of gene expression in white blood cells.

During this period, a great deal of research has attempted to characterize the genes that cause depression as reflected in rating scales of mood states, alterations in brain structure and function as measured by MRI, and gene expression patterns in post-mortem brain tissue from people who had depression.

So what would happen if one tried to find the gene or genes that explained the “whole picture” by combining all of the different types of information that one could collect? This is exactly what was attempted by Dr. David Glahn, of Yale University and Hartford Hospital's Institute of Living, and his colleagues.

“They have provided a very exciting strategy for uniting the various types of data that we collect in clinical research in studies attempting to identify risk genes,” said Dr. John Krystal, Editor of *Biological Psychiatry*.

Their work localized a gene, called *RNF123*, which may play a role in major depression.

They set out with two clear goals: to describe a new method for ranking measures of brain structure and function on their genetic ‘importance’ for an illness, and then to localize a candidate gene for major depression.

“We were trying to come up with a way that could generally be used to link biological measurements to (psychiatric) disease risk,” said Dr. John Blangero, director of the AT&T Genomics Computing Center at the Texas Biomedical Research Institute. “And in our first application of this, in relation to major depressive disorder, we’ve actually come up with something quite exciting.”

While *RNF123* hasn't previously been linked to depression, it has been shown to affect a part of the brain called the hippocampus, which is altered in people with major depression.

“We assume that the biological measures are closer mechanistically to the underlying disease processes in the brain. Yet, ultimately we are interested in the subjective experiences and functional impairment associated with mental illness,” added Krystal. “The approach employed in this study may help to make use of all of this information, hopefully increasing our ability to identify genes that cause depression or might be targeted for its treatment.”

Glahn said: “We still have more work before we truly believe this is a home-run gene, but we've got a really good candidate. Even that has been tough to do in depression.”

The article is “High Dimensional Endophenotype Ranking in the Search for Major Depression Risk Genes” by David C. Glahn, Joanne E. Curran, Anderson M. Winkler, Melanie A. Carless, Jack W. Kent Jr., Jac C. Charlesworth, Matthew P. Johnson, Harald H.H. Göring, Shelley A. Cole, Thomas D. Dyer, Eric K. Moses, Rene L. Olvera, Peter Kochunov, Ravi Duggirala, Peter T. Fox, Laura Almasy, John and Blangero (doi: 10.1016/j.biopsych.2011.08.022). The article appears in *Biological Psychiatry*, Volume 71, Issue 1 (January 1, 2012), published by Elsevier.

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Notes for editors

Full text of the article is available to credentialed journalists upon request; contact Sacha Boucherie at +31 20 485 3564 or s.boucherie@elsevier.com, or Rhiannon Bugno at +1 214 648 0880 or Biol.Psych@utsouthwestern.edu. Journalists wishing to interview the authors may contact David Glahn, Ph.D., at 860-545-7700, ext 7552 or david.glahn@yale.edu.

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The journal publishes novel results of original research which represent an important new lead or significant impact on the field, particularly those addressing genetic and environmental risk factors, neural circuitry and neurochemistry, and important new therapeutic approaches. Reviews and commentaries that focus on topics of current research and interest are also encouraged.

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