Gene duplication detected in depression

December 1 2010

A large genetic study of people with major depression has found that a duplicated region of DNA on chromosome 5 predisposes people to the disorder. The gene involved plays an important role in the development of nerve cells, adding to evidence that disruptions in neurotransmission networks form a biological basis for depression.

"The copy number variations we discovered were exclusive to people with depression, and were located in a gene region important in signaling among brain cells," said study leader Hakon Hakonarson, M.D., Ph.D., director of the Center for Applied Genomics at The Children's Hospital of Philadelphia. "This finding extends work by other researchers suggesting that disruptions in neurotransmitter networks in the brain are an underlying cause of major depressive disorders."

The study appears online today in *Public Library of Science One* (PLoS One).

The current research is the first large-scale genome-wide study of copy number variation (CNV) in major depressive disorder (MDD), a major psychiatric and behavioral disorder affecting an estimated 16 percent of the U.S. population. CNVs are deletions or duplications of segments of DNA. While a specific CNV is relatively rare in a population, it often exerts a strong effect on an individual who harbors the CNV in their genes.

Hakonarson's group conducted a whole-genome scan of DNA from 1,693 patients with MDD, mainly from a European database, and from

4,506 control subjects.

The researchers identified 12 CNVs exclusive to MDD cases. Their most notable finding was a large duplication of DNA segments on chromosome 5q35.1, a CNV shared by five unrelated patients and not observed in healthy controls. Residing at that location is the gene SLIT3, which is involved in axon development. The axon is the portion of a neuron that carries nerve impulses away from the cell body.

Hakonarson added that he plans follow-up studies with more refined sequencing technology, in which he expects to identify many more CNVs and possibly other types of mutations in the SLIT3 gene, as well as in other functionally related genes that may predispose to depression. Further studies may also reveal how strongly CNVs at SLIT3 and other related genes contribute to the risk of depression.

"Clinical applications for our discoveries are still in the future, but it may be possible at some point to incorporate these findings into personalized medicine," Hakonarson said. "Identifying causative genes may suggest future targets for drug development, and may also help us predict a person's future risk of developing depression," he added.

More information: "Duplication of the SLIT3 Locus on 5q35.1 Predisposes to Major Depressive Disorder," *PLoS One*, published online Dec. 1, 2010.

Provided by Children's Hospital of Philadelphia