MedicalXpress

Discovery of new gene mutation in schizophrenia offers target for drug therapies

February 23 2011

In a major advance for schizophrenia research, an international team of scientists led by the University of California, San Diego School of Medicine and involving Trinity College Dublin researchers has identified a gene mutation strongly linked to schizophrenia that may be an important new target for the development of drug therapies. The findings are just published in the online issue of the journal *Nature*.

Schizophrenia is a chronic, severe and disabling brain disorder, with symptoms that include hallucinations, delusions and thought disorder. Schizophrenia is believed to be caused by environmental and genetic factors, most notably the latter: the illness occurs in 1% of the general population, or 10 % of people who have a first-degree relative with the disorder, such as a parent or sibling. Current therapies are only partially effective with little progress being made in identifying effective new treatments over several decades.

In the last three years researchers have discovered that rare mutations at many locations in the human genome resulted in significantly higher risk of schizophrenia. These mutations consisted of copy number variants or CNVs –a type of genetic variation in which the number of copies of a gene differs between individuals. The findings were the first conclusive evidence that rare mutations can cause schizophrenia, but this did not identify the specific genes involved.

Professor Aiden Corvin of the Psychosis Research Group at Trinity College Dublin, funded by Science Foundation Ireland and the Wellcome Trust, and an author on this paper, describes that the latest study goes substantially further.

Researchers scanned for CNVs in the genomes of 8,290 individuals with diagnosed cases of schizophrenia and 7,431 healthy controls. The study confirmed CNVs identified in earlier studies, but uncovered an important new finding: duplications at the tip of chromosome 7q were detected in individuals with schizophrenia at a rate 14 times higher than in healthy individuals. These duplications impact a gene coding for the brain receptor VIPR2.

Formally known as the Vasoactive Intestinal Peptide Receptor 2, VIPR2 is expressed in the nervous system, including in the brain, blood vessels and gastrointestinal tract. Previous studies have shown that VIPR2 helps to regulate the formation and activity of neurons in the brain. In mice, VIPR2 also has been found to play important roles in behavioral processes, including learning and timing of daily activity. The study next measured expression of the VIPR2 gene in blood cells from patients, they found that individuals with mutations had greater expression of VIPR2 and greater activity of the receptor.

"This suggests that the mutations increase signaling in the Vasoactive Intestinal Peptide pathway," says Professor Corvin. "We know that this activity can be modulated by synthetic peptides (compounds where amino acids are linked together) and the next step is to see if these compounds have a therapeutic effect in mice or in cultured human cells that carry the VIPR2 gene mutation."

Provided by Trinity College Dublin