Schizophrenia Cases Linked to Random, Not Inherited, Mutations

By Rob Waters

May 30 (Bloomberg) -- **Schizophrenia** researchers are a step closer to identifying some of the triggers of the disabling mental disorder that has no known genetic cause.

Many cases of the disease occur spontaneously when copies of genes are duplicated or deleted in a random process that isn't inherited from parents, said a report published today in the journal **Nature Genetics**.

The study, like several recent reports on autism, paints a picture of a complex mental disorder that may be caused by many different genetic flaws, varying from one person to the next. The findings help explain why schizophrenia continues to occur in about 1 percent of the population, as it has for many years, even though people with the condition have a low birthrate.

``Why would you continue to see the disease if people don't have children?'' said **Maria Karayiorgou**, the Columbia University psychiatrist who led the study. ``It makes sense because you have to have a mechanism where unaffected parents would have affected offspring.''

About 60 percent of people with schizophrenia have no close relatives with the disease and researchers have been trying for years to figure out why they develop the condition, Karayiorgou said in a telephone interview yesterday. While the other 40 percent have a family history of the condition, scientists haven't identified which shared genes, if any, are to blame, she said.

The schizophrenia analysis and the autism reports were made possible by the mapping of the human genome and the introduction of computer technology that can rapidly compare large volumes of DNA from different people and detect missing or extra pieces of chromosomes.

**South Africa**

Karayiorgou collaborated with researchers at Weskoppies Hospital in Pretoria, South Africa, who recruited 152 people with schizophrenia whose parents never had the disease. They compared the DNA of the children and their parents using the new gene-scanning technology and found that about 10 percent of the younger group had extra or missing copies of genes in sections of their chromosomes. These glitches, known to scientists as copy number variants, weren't found in the parents' DNA.

The people recruited into the study were **Afrikaners** descended from the group of Dutch emigrants who settled in South Africa in the 17th century. The researchers chose this group to study because of their genetic similarity, Karayiorgou said.

The study provides little immediate help to patients who suffer from a condition that causes hallucinations and disrupts their ability to think clearly and who desperately need better treatments. The vast majority of schizophrenics in this country take antipsychotic medications, which helps control their behavior while causing serious side effects including weight gain, diabetes and movement abnormalities.

**Greater Understanding**

What the new findings provide is deeper insight into the workings of a poorly understood condition and an initial
list of genes that may trigger the disease, Karayiorgou said. As this list expands and researchers learn more about how different genes may act together in triggering the disease, doctors may get new ideas about therapies.

``The hope,'' Karayiorgou said, ``is that we'll look at all the genes implicated carefully and give better judgment about what treatments to use and what outcome is likely.''

More immediately, the findings could lead to better ways of diagnosing schizophrenia by looking for aberrant genes.

To contact the reporter on this story: Rob Waters in San Francisco at rwaters5@bloomberg.net.

Last Updated: May 30, 2008 13:00 EDT