

CANADIAN GENETIC DISEASES NETWORK

Genetic Instability in family of Neurological Disorders**Canadian Genetic Diseases Network (CGDN) scientist leads team in identifying DNA flanking region as trigger for genetic instability in family of neurological disorders**

TORONTO - April 22, 2002 — Scientists at The Hospital for Sick Children (HSC) and the University of Toronto have shown that the DNA flanking region in a family of neurological disorders is triggering the genetic mutation that underlies these diseases. The discovery is reported in the May issue of the scientific journal *Nature Genetics* by Dr. Christopher Pearson, a CGDN scholar and senior scientist on the research. (Reference AOP at <http://www.nature.com/ng/>).

Trinucleotide repeat disorders are neuromuscular, neurological or neurodegenerative in nature and include myotonic dystrophy (a form of muscular dystrophy), Huntington disease, and Fragile X syndrome (the most common form of inherited mental retardation). In these disorders, a disease state is caused when too many of the triplet DNA sequences within the gene are repeated. This mutation affects either gene expression or produces irregular proteins. The age of onset and severity of the disease are also associated with the number of triplet repeats. This type of genetic problem, known as an expansion mutation, was identified only a decade ago and is now known to be the cause of at least 15 diseases.

The genetic information gathered from affected families over the years had led researchers to believe that there was something in the flanking region (in the DNA sequence surrounding the triplet) that was causing the DNA triplets to repeat too many times.

“We have proven for the first time that there is something in the flanking DNA sequence that is triggering the genetic instability. These flanking regions effectively drive the mutation. Such flanking regions are a possible new therapeutic target for treating, or preventing, the trinucleotide repeat disorders,” said Dr. Christopher Pearson, the study’s principal investigator who is a scientist in Genetics and Genomic Biology in the HSC Research Institute, an assistant professor of Molecular and Medical Genetics at the University of Toronto, and a CGDN member.

This research group has also developed a technique (an assay) that allows the DNA expansion to be reconstituted in a test tube (published in the April 19 issue of the Journal of Biological Chemistry). This is the first assay that will allow researchers to study this type of genetic mutation using human cells, and at a much quicker rate than previously possible.

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