

Web Activity

Canadian Achievers: Researchers in Human Genetic Disorders

Huntington's Chorea

Huntington's chorea, an incurable brain disorder, typically strikes people in the prime of life, setting them on an irreversible course of debilitating mental breakdown and eventual death. Victims have been described as being trapped inside their own bodies, unable to communicate. In 1993, Dr. Michael Hayden of the University of British Columbia led a team that isolated the gene responsible for Huntington's chorea. As a result, doctors can now use a simple DNA test to screen people with a family history of the disease and, with 98% accuracy, warn potential sufferers, or parents who might pass on the disorder.

Using another technique, known as animal modelling, laboratory mice are genetically manipulated to behave like people with Huntington's. They are then studied to find out how and why the disorder causes brain cells to die prematurely. The ultimate goal is to develop treatments to alleviate the effects of this fatal condition.

Cystic Fibrosis

Cystic fibrosis is an inherited disorder associated with a single gene, which produces a protein known as CFTR (cystic fibrosis transmembrane conductance regulator). Those who suffer from cystic fibrosis must inherit two defective alleles, one from each parent. Since approximately 1 in every 25 people of European ancestry carries the defective gene, cystic fibrosis is the most common recessive genetic disorder within this population. Families in Ontario who had more than one child suffering from cystic fibrosis provided most of the samples required for the laboratory research into locating the gene. The Hospital for Sick Children in Toronto is a leading centre for research into this disorder. Led by Dr. Lap-Chee Tsui, a team working at this hospital identified the gene in 1989. This group has mapped two modifier genes in animals that alter the severity of cystic fibrosis. The team continues to investigate the impact that these modifier genes can have on the treatment of this disorder.



Figure 2
Dr. Lap-Chee Tsui

Dr. Christine Bear of the University of Toronto, using a cystic fibrosis mouse model, has demonstrated that it is possible to correct the basic defect by delivering a normal version of the CFTR protein. Her team is working to develop a method of providing the protein therapy that would be able to correct the defect.

The field of genetics is also extending beyond the research laboratory and into daily medical practice. Dr. Judith Hall (**Figure 2**), head of pediatrics at the University of British Columbia (1999–2000) is a clinical geneticist with considerable experience dealing with families affected by genetic disorders such as cystic fibrosis. Communicating the genetic reasons for a disease to children and their families is both challenging and rewarding for Dr. Hall. Genetic research is advancing every day in finding ways to treat or prevent disorders.



Figure 2
Dr. Judith Hall

Muscular Dystrophy

Muscular dystrophy is the name given to a group of genetic disorders that cause the weakening and deterioration of muscles. Some forms of muscular dystrophy result from defects on autosomal chromosomes and may occur in both males and females. Other forms are sex-linked and affect males. The rare form known as Emery-Dreifuss muscular dystrophy occurs in males as a result of a recessive X-linked gene. However, even female carriers, who have the normal dominant allele in addition to the recessive defective allele, can exhibit some mild symptoms.

Much of the research on muscular dystrophies has occurred in Canada. Dr. Ron Worton and his colleagues at the Ontario Hospital for Sick Children opened a new era in research and treatment for this group of disorders when they located the gene responsible for Duchenne muscular dystrophy in 1987. This is a sexlinked form that begins to affect boys between ages two and six. They suffer progressive damage beginning in the muscles of the pelvis, upper arms, and legs. The calf muscles enlarge because the enzyme creatinine kinase leaks out from the muscles causing them to swell. Most boys with Duchenne are confined to a wheelchair by age 12.

There are other forms of muscular dystrophy that affect males and females equally, since the defective genes are carried on the autosomes. Some forms are due to recessive alleles and others are caused by dominant alleles.

Canadian researchers who have identified genes for muscular dystrophy and related disorders are summarized in **Table 1**.

Table 1: Researchers of Some Genetic Disorders

Disorder	Year	Institution	Researchers
Duchenne muscular dystrophy (sex-linked, affecting males)	1987	Ontario Hospital for Sick Children	Dr. Ron Worton
amyotrophic lateral sclerosis (Lou Gehrig's disease)	1993	Montreal General Hospital	Dr. Denise Figlewicz Dr. Guy Rouleau
spinal muscular atrophy (SMA)	1995	Ontario Research Institute, Ottawa	Dr. Alex MacKenzie
oculopharyngeal muscular dystrophy (autosomal dominant)	1997	McGill University, Montreal	Dr. Guy Rouleau
autosomal spastic ataxia	2000	Montreal General Hospital/ Saint-Justine Hospital	Andrea Richter Dr. Serge Melancon Dr. Thomas Hudson