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CANADIAN GENETIC DISEASES NETWORK

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A FIRST IN HUNTINGTON DISEASE RESEARCH: Scientists discover new functions of the HD gene

Canadian Genetic Diseases Network, Vancouver, Canada - June 1, 1995:
A group of researchers led by Dr. Michael Hayden, Scientific Director of the Canadian Genetic Diseases Network, has produced the first-ever mouse with a defect in the Huntington disease gene. These findings add important novel insights into the role the HD gene plays in causing the disease.

The research results are published in the June 2, 1995 issue of the scientific journal *Cell*. The paper describes Dr. Hayden's approach to understanding the functions of the HD gene by producing a "knock out" mouse where specific parts of the gene are deleted in every cell.

Since the discovery in 1993 of the genetic defect which causes Huntington disease, research teams around the world have been attempting to unlock the sequence of events which results in deterioration of brain cells, severe behavioral disturbance, involuntary movements, and eventual death in individuals who inherit DNA changes in the HD gene. How the gene causes the disease remains unknown. Mice models of disease are used to understand the disease process and to devise and test possible therapies.

Dr. Jamal Nasir, a principal scientist in the team, believes this new information indicates that an entirely new area in the brain may play a crucial role in the pathology of the disease. Said Dr. Nasir "This specific region of the brain has generally been overlooked by scientists for many years, so our new discovery about the functioning of the gene has raised the exciting possibility that this new area of the brain is very important in the development of Huntington disease".

Last year Hayden's team identified the HD gene in the mouse and, until now, has been working non-stop to create mice with changes in the HD gene. Noted Dr. Nasir, "The mice carrying one specific HD defect have problems switching behavioural strategies and are hyperactive. Their brains also show cellular damage in particular areas not usually studied in Huntington disease". He added that, in addition, mice with two changes in the HD gene die early in development, thus clearly demonstrating that this gene plays a crucial role in growth and development.

Dr. Anthony G. Phillips, Head of the Department of Psychology and a member of the UBC research team observed "these findings not only add to our understanding of Huntington disease, but also show that the complex relationship between brain and behaviour is open to genetic analysis".

The team's latest findings mean that the new HD mouse can be used to test a wide variety of existing drugs along with drugs under development to assess the impact of possible therapies. Commented Dr. Hayden, "This is another step forward in a greater understanding of Huntington disease. We are hopeful that future studies will make it possible to identify approaches to treatment for people afflicted with this disease".

Huntington disease is a devastating inherited neurological condition which usually starts in mid-life and leads to death after progressive deterioration of brain cells and brain function over 10-15 years.

Dr. Hayden's milestone research was supported through the funding and core technology facilities of the Canadian Genetic Diseases Network, one of Canada's Federal Centres of Excellence networks. This work was performed at the University of British Columbia in collaboration with faculty in six departments, four affiliated with the Faculty of Medicine. The newly established Centre for Molecular Medicine and Therapeutics in Vancouver was also involved in some aspects of the work.

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