



CIHR IRSC
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Genetics

The CIHR Institute

CIHR's Institute of Genetics supports research on the human and other genomes and on all aspects of genetics, basic biochemistry and cell biology. New advances in genetics and genomics, and in the understanding of how cells work, pose challenges to our healthcare system and often raise complex ethical, legal and social issues. The Institute is addressing these challenges to develop solutions that benefit Canadians.

About CIHR

The Canadian Institutes of Health Research (CIHR) is the Government of Canada's agency for health research. CIHR's mission is to create new scientific knowledge and to catalyze its translation into improved health, more effective health services and products, and a strengthened Canadian healthcare system. Composed of 13 Institutes, CIHR provides leadership and support to more than 10,000 health researchers and trainees across Canada.

The Canadian Institutes of Health Research (CIHR) is the Government of Canada's agency for health research. Through CIHR, the Government of Canada invested approximately \$189.9 million in 2005-06 across Canada in research on genetics.

The Facts

- The human genome is made up of 3 billion (3,000,000,000) bases of DNA, split into 24 chromosomes.
- This information...
 - would fill two hundred 500-page telephone directories;
 - would take a century to recite, if recited at the rate of one letter per second, 24 hours a day.
- The human genome contains about 20,000-25,000 genes.
- Genes contain instructions on how to make proteins which are responsible for carrying out all of the cell functions (examples – facilitating chemical reactions, controlling growth and transporting substances through the body).
- Many diseases stem from problems associated with proteins (examples – too many proteins produced, too few proteins, the protein is the wrong shape or “misfolded”).
- The proteome is the complete set of proteins produced by the genome at any one time, approximately 60,000.
- Proteomics is the study of proteins – what proteins look like (structure), interactions between proteins and the types of proteins expressed in different samples, such as healthy vs. diseased tissues.
- Currently, more than 900 genetic tests are available from testing laboratories.
- Between humans, our DNA differs by only 0.1%, or 1 in 1000 bases (letters).

Research Unlocking the Mysteries of the Genetic Code

- Dr. Jack Greenblatt of the University of Toronto has recorded the most comprehensive and reliable map of protein interactions in a living organism to date. His work, conducted with Dr. Andrew Emili, used sophisticated proteomic techniques to identify close to 4,000 proteins and 550 protein complexes involved in 7,123 protein-protein interactions in yeast cells. Disease results when these complexes and interactions go awry. The structure of proteins and their interactions in yeast cells are virtually identical to those in humans.
- Human organ transplants have to be completed at lightning-fast speed to make sure organs are fresh. An antifreeze protein in snow fleas, discovered by Drs. Laurie Brown and Peter Davies from Queen's University, may help extend the window, creating the possibility of more successful transplantations. With the new protein, organs could be safely stored at below the freezing point, preserving them for longer periods of time.
- To date, more than 1,000 genes have been identified for rare, highly heritable diseases, diseases that can be triggered by variation in only one gene. But many more common disorders are thought to be the result of numerous DNA variants acting together in response to environmental factors. In these cases, it is much more difficult to pinpoint the genetic source of disease, because of both the difficulty of tracking all the possible variations involved and understanding the relationship between these variations and between the variations and environmental factors. An international research group known as the International HapMap Consortium has created the world's first database containing information on more than one million instances of genetic variation and gives information on how these variations are linked. CIHR-supported researcher Dr. Tom Hudson of McGill University was the lead Canadian researcher on the study. The findings open major new possibilities in the search for causes of disease.

- Protein phosphorylation is one of the key tools that organisms use to regulate and control many basic cellular processes. Other proteins involved in these processes, such as enzymes and receptors, are turned on or off as a result of phosphorylation. Three CIHR-funded researchers have helped put together the first-ever phosphorylation map for yeast, charting 4,000 phosphorylation events involving 1,325 proteins. Information from this map can be applied to humans and may open the door to new drug therapies for diseases such as cancer, diabetes and AIDS. Dr. Michael Snyder of Yale University and a member of CIHR's Institute of Genetics Advisory Board, led an international research team that included CIHR-funded researchers Drs. Brenda Andrews, Richelle Sopko, and Michael Tyers, from the University of Toronto.
- Is genetic testing changing the way the medical system and patients view and interpret disease? This is among the questions being posed by Dr. Fiona Miller at McMaster University as part of research into the impact of genetics research on the medical system. Traditional diagnosis is based on observation and tests. Early results suggest that genetic testing, which is still not that widespread, is being treated as just one of a number of diagnostic tools, not the definitive tool and, therefore, not changing the diagnostic landscape radically. The future use of DNA microarrays, however, may change this perspective. Microarrays can simultaneously test for numerous conditions, resulting in diagnoses that doctors may never have considered and possible surprises for both patients and doctors.

In the Pipeline... From Genes to Genomic Medicine

Each day we learn more about the genetic factors involved in the development of organisms, addressing key questions such as: how do cells know what to become? How do organs and tissues develop? What guides the development of key functions such as the ability to reproduce or the ability to transmit and respond to electrical signals being sent to the brain? Despite an increasing genetic understanding of these subjects, the impact on medical practice to date has been limited.

The From Genes to Genomic Medicine Initiative is a strategic research priority theme of CIHR's Institute of Genetics. One of the goals of the initiative is to address the increasing need to translate scientific advances in our understanding of basic developmental processes, genetics and genomics into medical practice. Five different research projects have received funding as part of this initiative, involving research teams from Montreal, Toronto and Vancouver. One such project, led by Drs. Peter Lansdorp and Richard Humphries, is studying blood-forming stem cells needed for the daily replacement of short-lived mature blood cells. The researchers are studying the role of an enzyme thought to be essential to the self-renewal process. The hope is to ultimately produce a therapy to help the body compensate in cases where a deficiency in this enzyme is preventing adequate replacement of blood cells.

The Researchers... Dr. Frédéric Charron – Helping to Mend Damaged Spinal Cords

Dr. Frédéric Charron, a CIHR-supported researcher at the Institut de recherches cliniques de Montréal, doesn't doubt for a moment the ingenuity of nature, its ability to create complex tools and its habitual reuse of these tools for different tasks. He relies on these qualities in pursuing research that, one day, may lead to new and novel ways of repairing the damage caused by spinal cord injuries.

So it was that, during post-doctoral studies at Stanford University, Dr. Charron, 2005 winner of the Peter Lougheed/CIHR New Investigator Award, came to work with a molecule named after a videogame character – Sonic Hedgehog (Shh).

This research helped define a new role for Shh, helping guide the growth of axons, long fibers that carry electrical nerve impulses from one neuron to another.

"It's far easier for nature to evolve or adapt something for another task, rather than developing completely novel guidance cues, plus new receptors for those cues plus new signalling pathways to be able to carry this information," Dr. Charron notes.

Axons need to know where to go and this is an epic journey. In humans, axons can grow to one metre in length as they migrate up the spinal cord to the brain, where they form connections. All the while, the presence of Shh, like some artificial light source, helps attract and guide the growing axon. Dr. Charron explains that this journey is broken up into a number of steps.

"The system doesn't try to go the whole distance at once. It moves from A to B, then from B to C, and so on. Each of these steps is what we call a choice point. At each choice point, the system resets itself and becomes responsive to a new molecule to attract the axon," he notes.

Information such as this is critical in helping understand what it will take to repair spinal cord injuries. For example, once a person reaches adulthood, the guidance cue molecules are no longer effective because other molecules are working to maintain the now mature nervous system.

"We hope that we can reproduce the normal steps that occur when the spinal cord is being developed and encourage therapies. It's not enough just to make spinal cord axons regrow; just like electrical wires, they also need to know where to go and to reconnect correctly," Dr. Charron comments.

"For my research, genetics is a fundamental tool for dissecting and understanding how molecular mechanisms work."