



Another project brought to you by **GenomeCanada**

Montreal Network for Pharmaco-Proteomics and Structural Genomics

Status	Past
Competition	Competition I
Sector	Health
Genome Centre	Genome Quebec
Project Leaders	John Bergeron, Mirek Cygler, Michel Desjardins & Robert Kearney

Project Description

The first goal of the Human Genome Project is to obtain the complete DNA sequence of humans and many other organisms. The next step is to find out how this genetic information directs the biochemical and molecular reactions in the cell, and thus determines how living things function. This kind of research is called "functional genomics" and it seeks to uncover how genetic information coded in DNA directs all the workings of a living organism. One of the ways to do that is to study the proteins in a cell—what they do, how they interact with one another and where they reside in the cell. This is called "proteomics"; when applied to disease it is called "pharmaco-proteomics".

Proteomics is instrumental in the discovery of biomarkers, which can indicate the presence of a particular disease. But, unlike a genome, a proteome differs from cell to cell and constantly changes through its biochemical interactions with the genome and the environment. Mapping human proteins, their functions and interactions has proven enormously challenging for scientists.

To bring order to the chaos of proteomics, we first set up a world-leading facility to allow researchers to investigate the function and structure of genes and proteins that could be used to develop new drugs. The facility, Caprion is now setting the world standard in protein mapping, identification and characterization, and our research has yielded numerous major discoveries and a paradigm shift in the study of proteomics. This facility is also the headquarters for the International Human Proteome Organization (HUPO).

We combine two kinds of expert knowledge in our studies. First, we are skilled in the use of a technology called mass spectrometry, which is used to determine the many different kinds of protein that populate the cell. Second, we are experts in purifying and studying the various kinds of miniature machines that do specialized jobs inside cells. These can be thought of as miniature organs and hence are called "organelles". We combine these two areas by studying the protein make-up of certain kinds of organelles and relate our findings to cell function and disease.

We have identified the total protein make-up of several organelles. By taking into account the stochastic nature of tandem mass spectrometry in which proteins are smashed into fragments then reconstructed by computer programming, a protein microscope was developed. Here

proteins are quantitatively assigned to different compartments of the cell by proteomics. Thus far more than half a dozen such organelles have been visualized by this protein microscope leading to insight into their identity and function in health and disease. We have deposited this information in a public database called CellMap, which created a standardized way to design quantitative proteomics experiments. Co-investigators have also discovered and validated more novel proteins associated with a particular vesicle structure than the rest of the field combined. This has produced a large number of papers in highly prestigious journals. These are but a few highlights of our major discoveries.

As part of the Outreach effort, the project has been highlighted in frontiers in Biotech 15, iPOD broadcast 12, entitled "The era of shock and awe in proteomics" by John Bergeron <http://www.twit.tv/fib>.

The value of our work was recognized by an editorial in *Nature* ("Proteomics' new order"), which highlighted the importance of the Montreal-based HUPO headquarters and its support from the Canadian government. Ultimately, this groundbreaking research will lead to new biomarker discovery, including new targets for cancer and other diseases, providing a tangible benefit to Canadians and others.

Fast Facts

<i>Highlighted outcome:</i>	Numerous major scientific discoveries that have led to a paradigm shift in the study of proteins, which is instrumental for the discovery of biomarkers indicating the presence of disease; successful transfer of the world headquarters for the Human Proteome Organization (HUPO) from Ann Arbor, Michigan, to Montreal; a Genome Quebec proteomics platform was created through several of the personnel from this project
<i>Number of research personnel employed by the project:</i>	59
<i>Number of peer reviewed publications published:</i>	103
<i>Resources generated:</i>	Protein content of several organelles, deposited in a public database called CellMap
<i>Number of patents in process or obtained:</i>	7 pending and 1 patent
<i>Other resources generated:</i>	Protein content of several organelles, deposited in a public database called CellMap