



A Canadian Human Proteome Project (CHPP)

Canada's leadership role in the Human Proteome Project

A Position paper initiated by discussion at the First Meeting of the CHPP Working Group, January 16-17, Holetown, Barbados

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The Human Proteome Project: International context

The Human Proteome Project (HPP) was launched in September 2010 at the Human Proteome Organization (HUPO) 9th Annual World Congress in Sydney, Australia. The HPP builds on the Human Genome Project by leveraging existing genomics information to identify, quantify and characterize the human proteome, which is thought to contain significantly over 20,000 protein coding genes.

The goals of the HPP are to map and characterize human proteins in their biological context, and develop innovative tools and reagents that the proteomics community can use to further their understanding in the field. For the HPP to be successful, it must inspire stakeholders, such as the medical and environmental communities, to engage and participate in the HPP through research, collaborations and applications.

The international proteomics community has conceived the HPP as a coordinated chromosome-centric project in order to guarantee ***completion of the human proteome within a defined timeframe***. While the disease-centric approach has led to the discovery of thousands of protein biomarkers, it may limit or altogether exclude the detection and characterization of low-abundance proteins or proteins of unknown function. It is thus conceivable that a complete proteome may never materialize even after integrating the results of many disease-centric studies. The chromosome-centric approach ensures the systematic study of all of the proteins encoded by a specific chromosome. This model facilitates a large-scale international project combining expertise from many different fields and communities. Using a wide range of complementary technology platforms, the HPP will provide a genome-wide human protein resource consisting of a proteome parts list, the protein distribution atlas, and maps of protein molecular pathways, interactions, and networks (HUPO Views, Molecular & Cellular Proteomics).

HUPO is now urging research funding agencies and the scientific community all around the world to contribute to the HPP by coordinating national initiatives and teams. To date, teams representing seven countries (Japan, China, Korea, USA, Russia, Sweden, and Iran) have responded to HUPO's call by committing to specific chromosomes.

A Canadian Human Proteome Project: Timing and opportunity

In Canada, the Canadian National Proteomics Network (CNP), which was established in 2008, is promoting a Canadian Human Proteomics Project (CHPP).



The concept of a CHPP was first introduced in October 2010 to Canadian and provincial funding sources, including the Canadian Institutes of Health Research, Genome Canada, Génome Québec, Genome BC, and the Ontario Genomics Institute. Funding agencies, led by Génome Québec, have expressed their interest in the project and asked the CNPN to prepare a well-defined initiative prior to any future discussion on funding opportunities. A CHPP Working Group, led by executive members of the CNPN, has recently been formed and consists of leading proteomics scientists and clinicians in Canada who expressed interest in CHPP.

The CHPP Working Group held its first meeting on January 16-17, 2011 in conjunction with the 7th Annual Proteomics Conference in Cell Biology in Holetown, Barbados. The two-day workshop aimed to develop potential projects for CHPP and to engage potential academic, clinical and industrial stakeholders.

Other participants in the meeting were international proteomics experts, key players, as well as interested participants of the Cell Biology Conference. **Dr. Pierre Legrain, Senior Vice-President of HUPO**, provided an update on the status of the HPP as well as an international perspective on the Canadian initiative. Dr. Legrain ***strongly urged the Working Group to leverage their current research and reputation in the proteomics field to coordinate a Canadian effort to participate in and contribute to the HPP.***

Subsequent presentations by Dr. Gary Kruppa, Vice-President Business Development at Bruker Daltonics, and Dr. Andreas Huhmer, Director for World-Wide Marketing at Thermo Fisher, further demonstrated the feasibility of early detection and prevention through their enthusiastic support of a CHPP. Both companies, as well as other industrial participants, expressed their excitement at the opportunity to participate as lead partners in the design, development, and commercialization of clinically relevant tools and technologies. ***Drs. Kruppa and Huhmer both see the direct benefits for industry as a result of CHPP through the creation of opportunities for clinical mass spectrometry and specialist positions within Canada to support a long-term business development in the diagnostic market.***

As a result of presentations by academic researchers, funding agencies, industries and the international proteomics community, several key strategies have been identified for CHPP that will support a comprehensive, integrated project with significant impact on healthcare in Canada. The CHPP should focus on the integration of clinical and basic science stakeholders to ensure effective and applicable solutions, as well as development of innovative technologies that not only strengthen Canada's position now, but also support the country's ability for future scientific contributions through international collaborations arising from the HPP.



In addition to the development of CHPP, Dr. Legrain stated that there is an urgent need for standardization across the field of proteomics to facilitate data exchange between projects, countries, and multiple technology platforms. To address this issue, the CHPP Working Group proposes to develop a set of guidelines and quality-control standards, which will be relevant to all HPP-related research. This initiative will include reagents, tools, and protocols that ensure the highest-quality research, data interpretation and inter-project communication across multiple technology platforms.

Dr. Legrain is enthusiastic about Canadian scientists being well-positioned to make such a significant contribution to the field of proteomics based on acknowledged technological expertise, interdisciplinary networks, and a successful track record in managing large-scale genomics/proteomics and infrastructure projects. Furthermore, Dr. Legrain is confident that Canadian contributions will set the foundation for further HPP projects at an international level of quality and scope.

The CHPP: Our chromosome-based strategy

The CHPP Working Group has thus far identified two potential human chromosome-based initiatives: one based on chromosome 6, and a second based on chromosome 21. These chromosomes contain many genes and proteins that are involved in the development of a broad range of diseases that have a significant impact on Canadians and our healthcare system. These diseases include neurological disorders (multiple sclerosis, Parkinson's disease and schizophrenia), childhood diseases (juvenile diabetes and Down's Syndrome), and age-related diseases (Alzheimer's, cardiovascular disease, arthritis and cancer).

Comprehensive understanding of the proteins encoded by these genes will have significant medical benefits, including improved capabilities for early detection and diagnosis, therapeutic development and monitoring, and personalized healthcare programs to reduce mortality, morbidity and costs. Characterization of the proteins encoded by chromosomes 6 and 21 could be a resource of immediate value to biologists, clinicians and industry. Chromosome 6 is the largest chromosome proposed for analysis to date. It contains regions of high gene density, including the genes for the major histocompatibility complex (MHC), which plays an important role in the immune system, bone marrow and organ transplantation, and immune-deficiency diseases. It is estimated that more than 50 different diseases are linked to chromosome 6. Trisomy of chromosome 21 defines Down's syndrome; many proteins encoded by this chromosome are linked to diseases, including



Alzheimer's disease. Of the 260 predicted protein-coding genes of this chromosome, only 148 have been characterized at the protein level in a few cell types.

A gene/protein-centric database is being proposed as an outcome of the HPP, sorted by chromosomes. The CHPP Working group is proposing to contribute towards this database via Canada's chromosome(s) by characterizing all encoded proteins, as well as their splice variants and isoforms in multiple cell types and body fluids. In addition, chromosome-specific reagents and assays will be created, which will be valuable commercial resources as tools for the research and clinical communities.

In addition to the previously identified initiatives based on chromosomes 6 and 21, the CHPP Working group expects that others groups and consortia will shortly show their interest in the CHPP and propose additional chromosome-based initiatives for consideration. To facilitate national collaborations and contributions, CNPN is holding a second CHPP meeting in Toronto on February 22. A third meeting is being planned for Vancouver in March/April. A final, concluding meeting will be held in conjunction with CNPN's 3rd Symposium: Proteomics in Human Health, May 8-11, 2011, in Banff, Alberta. An outcome of these series of meetings will be a white paper describing more fully the Canadian Human Proteome Project and proposed chromosome-based initiatives from the community.

Canada's Leadership role in the international HPP: When, How, Who, Why?

- Canada needs to engage immediately

To reiterate, HUPO is now urging the Canadian scientific community and research funding agencies to contribute to the HPP by coordinating national projects. To date, at least seven countries (Japan, China, Korea, USA, Russia, Sweden, and Iran) have already responded to HUPO's call by committing to specific chromosomes.

The scientific community around the country led by CNPN must leverage its current research and reputation in the proteomics field to coordinate a Canadian effort to participate in and contribute to the HPP and position Canada as a leader of this international initiative.

Canada has the capacity, experience and expertise in proteomics, genomics and the biomedical sciences to make a substantial contribution to the HPP. The speed at which the international community is advancing HPP demonstrates the urgency with which Canada must engage in national projects. Thus, the CHPP Working Group is formally requesting



that Canada's funding agencies and governments consider the nationwide benefits and future opportunities for Canada to take a leadership role in the international HPP.

- The CHPP proposal

It is our hope that the efforts of the CHPP Working Group will provide the framework upon which all funding agencies in Canada involved in proteomics, human health research and technology can build to invest in a national funding initiative dedicated to the launch of a pan-Canadian effort to participate in defining the human proteome.

All Canadian funding agencies and industries involved in proteomics and health research should contribute to a fund dedicated to a specific call for proposals for the CHPP. We are of the opinion that the best option for the selection of the CHPP should be determined by a dedicated call ***for proposals to be submitted to an international peer-review panel***. This competition may be led by Genome Canada in collaboration with the Genome Centres and all other funding agencies interested to contribute to this major international initiative.

We are confident that the CHPP will lead to better scientific understanding and breakthroughs that will have a significant and lasting impact on Canadian health. More importantly, the CHPP, as part of the international HPP, will stand the best chance in filling the gap between basic genomics research and healthcare, which has been identified as the major barrier today in translating research results into clinical practice.

- The CHPP: Benefits for Canada

The CHPP will leverage Canada's existing strengths in proteomics and the massive previous investments made by all governments in the field of human health research and technology. It will provide Canada with a leadership opportunity by supporting innovative technologies and research that will rapidly improve our understanding of human disease and ageing in an effort to advance current medical practices towards an approach that is predictive, personalized and sustainable.

The CHPP will also provide the proteomics community the opportunity to make strategic use of the infrastructures in which all funding agencies and federal and provincial governments have invested, including strategic networks, Genome Canada-funded platforms, Canada Foundation for Innovation-funded facilities, and Centres of Excellence.

Proteomics has already demonstrated its enormous potential. For example, research in the plasma proteome has led to the discovery of novel biomarkers for acute kidney and heart transplant rejection, which offer rapid, robust and cost-efficient assays for continuous monitoring and early therapy to prevent graft injury in organ transplantation, while



reducing the burden of invasive graft biopsy. Combined with the discovery of novel genomic biomarkers in these disorders, they offer critical insights into the mechanisms of disease and opportunity for the discovery of new therapeutic targets, which are critical steps in the evolution of personalized medicine.

Throughout the first CHPP meeting, the impact that genomics and medical advancements has had on patient healthcare was extensively demonstrated. However, it is now clear that ***proteomics is the crucial missing link between genetics, phenotypic information and patient treatment.*** With our current technologies, diagnosis today occurs at an advanced stage of disease, which typically results in poor prognosis for the patient and limits treatment options. From a clinical perspective, proteomics is an untapped field and has the potential to transform medicine, and render early detection and personalized medicine a reality.

Canada has everything required to become a major contributor to the HPP, and must engage now to be recognized as a world leader in the field.