

## New proteomics research promises to revolutionize biomedical discovery

*Montréal, July 19 2007* - Human cells function through the concerted action of thousands of proteins that control their growth and differentiation. Yet, the specific function of most human proteins remains either unknown or poorly characterized. Diseases being often due to aberrations in the function of key cellular proteins, numerous large-scale research initiatives have been launched internationally to crack the function of all human proteins. In a research article that will be published in the July 20<sup>th</sup> issue of the journal *Molecular Cell*, a research team led by Dr. Benoit Coulombe from the Institut de recherches cliniques de Montréal (IRCM) describes a powerful proteomics approach that promises to have a profound impact on our current understanding of the human proteome and the function of its individual proteins.

"In this work, we have taken advantage of an intrinsic property of proteins in order to develop a method that we use to infer a putative function to many previously uncharacterized proteins", said Dr. Coulombe who is very excited by his team's achievement and the future prospects these efforts hold. The unique property of proteins, exploited by this Montreal research team, is the fact that proteins rarely work alone, but rather assemble with other proteins into complexes to concertedly exert their function. The strategy of the IRCM researchers was basically to identify the interaction partners of many proteins of well-known function, using sophisticated proteomics procedures and computational algorithms they developed. The initial guess of the scientists was that proteins interacting together are likely to be partners in the same biological pathway and, consequently, to serve the same (or related) function(s). By systematically identifying the interaction partners of 32 human proteins known to exert specific functions in gene transcription and RNA processing, the Coulombe team has defined an intricate network of 805 high-confidence interactions that connect together 436 different proteins. Among them, many proteins of previously unknown function can now be inferred putative functions based on their association. To confirm that physically interacting proteins are also functionally related, the researchers have selected a number of the previously uncharacterized proteins present in their network and conducted more detailed functional assays. "The specificity of our procedure to identify functionally relevant interaction partners is amazing", said Dr. Coulombe. "For example, we present in the *Molecular Cell* article the long-awaited discovery of a cellular enzyme that regulates the stability of small RNA molecules playing pivotal roles in cell function and regulation. The existence and importance of this enzyme was recognized for more than a decade, but it had been so far impossible to isolate it in the sea of proteins that make up human cells and further characterize it. We succeeded in finding the enzyme, which we named MePCE, as an interaction partner of another cellular protein it regulates". Many other important proteins have been uncovered in this analysis and their precise roles in cell function will be published in the coming months and years.

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Defining the maps of protein interactions that regulate cell growth, differentiation and disease progression is the overall goal of the Human Proteome Initiative (HuPI), a forward-looking project conducted in the Coulombe laboratory. Central to the HuPI project is its experimental platform, termed the "HuPI discovery engine", which ultimately generates maps of protein interaction networks. The Molecular Cell article reports on the first generation of this technology platform that is currently being improved by a multi-disciplinary team of scientists. "What is most important is to develop a highly reliable and efficient discovery pipeline that generates interaction maps that are both as complete and as accurate as possible". Dr. Coulombe likes to compare his HuPI discovery engine to the Google search engine for the Internet. Setting in place a method that generates useless information would be a waste of time and resources. Instead, Coulombe aims to deploy all energy and brain power to build a proteomics discovery pipeline that produces only relevant, useful information (as Google is also efficient to map useful links for a Web search, leaving out most irrelevant information). Given the success seen thus far, Dr. Coulombe may well be on the right road to achieve his long-term objective which is to build a publicly-available repertoire of molecular maps that represents the fingerprint of the physiological status of normal human cells and the signature of some disease conditions. "If this comprehensive repertoire of protein interaction networks, termed the Human Proteome, can assist scientists worldwide in identifying important new proteins that can be used to diagnose and/or eventually cure specific diseases, then I will have succeeded in doing what I set out to do", concluded Dr. Coulombe.

Reference: Célia Jeronimo, Diane Forget, Annie Bouchard, Qintong Li, Gordon Chua, Christian Poitras, Cynthia Thérien, Dominique Bergeron, Sylvie Bourassa, Jack Greenblatt, Benoit Chabot, Guy G. Poirier, Timothy R. Hughes, Mathieu Blanchette, David H. Price and Benoit Coulombe. (2007) Systematic analysis of the protein interaction network for the human transcription machinery reveals the identity of the 7SK capping enzyme. *Molecular Cell* 27, July 20<sup>th</sup>, 2007 issue.

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*Established in 1967, the IRCM ([www.ircm.qc.ca](http://www.ircm.qc.ca)) is recognized as one of the country's top-performing health research centres. It has a mandate to understand the causes and mechanisms of diseases in order to find diagnostic tools and means of prevention and treatment; to train a new generation of high-level scientists; and to contribute to Québec's socio-economic development by facilitating the commercial development of new discoveries. The IRCM has 37 research units and a staff of more than 450.*

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