Researchers in Montréal and the US create model of key immune-system component

Model developed with the systems biology approach may lead to better understanding of infectious disease processes

Montréal, December 8, 2006 – Researchers at Université de Montréal, working with teams at Massachusetts General Hospital and Johns Hopkins University, have made a major breakthrough in understanding an essential aspect of the immune system.

For the first time, using a systems biology approach, they have developed a model that facilitates the study of the function of the phagosome. The phagosome is the organelle responsible for the destruction of infectious pathogens that cause such diseases as tuberculosis and salmonellosis, as well as pathogens that could be used in bioterrorism. The results of their study were published this week in the prestigious journal Nature.

Infectious diseases remain one of the main causes of death in the world, and the phenomenon of antibiotic resistant bacteria worsens the situation each year. Thanks to the model developed by teams led by Michel Desjardins of the Department of Pathology and Cellular Biology at Université de Montréal, Drs Lynda Stuart and Alan Ezekowitz at the Massachusetts General Hospital, a Harvard Medical School teaching hospital, and Dr Joel Bader of the Biomedical Engineering Laboratory at Johns Hopkins University, it will now be possible to better understand the complex interactions that govern the functioning of the phagosome. "We have taken a crucial step here," Prof. Desjardins explains. "We can now reach a better understanding of the molecular processes involved in infections by using a global approach based on proteomics and genomics.

This approach will expedite development of therapies and the production of new vaccines. The major investments made in recent years in proteomics research in Québec and Canada have enabled us to pool our resources and apply promising new approaches like systems biology." As Dr. Stuart explains, "Phagocytes are immune system cells that internalize, kill, and digest bacteria within an intracellular compartment called the phagosome, a major battleground in the host-pathogen conflict.

Despite its important role in our normal immune defense, the organization and functioning of the phagosome are poorly understood." By analyzing a cell line of phagocytes from the Drosophila fruit fly, a common biological model, the researchers identified more than 600 proteins that may be involved with the operation of the phagosome. They then constructed a detailed map of the interactions among these proteins and were able to identify previously unknown regulators of phagocytosis and potential molecular pathways of immune defense. "Phagocytosis is very similar in many organisms, so we are able to learn about this process by studying it in simpler organisms, such as Drosophila," Dr. Stuart continues. "By combining classic cell biology with the newer approaches of proteomics, functional genomics and computational analysis, we have generated a model of that we believe will facilitate our understanding of infectious diseases and expedite the development of new strategies to fight pathogens."

"It is exciting to see that systems biology has the power to unravel how the phagosome works by revealing the intricately woven roles of all the molecules involved in killing infectious

agents," says Joel Bader, Ph.D., Assistant Professor of Biomedical Engineering and a member of the High-Throughput Biology Center at Hopkins. According to Paul L'Archevêque, President and CEO of Génome Québec, this significant new advance is a further illustration of the tremendous talent of Québec scientists and the precision that can be achieved by genomics and proteomics, two approaches that yield concrete results. "I would like to congratulate Dr. Desjardins and his team. Their very important breakthrough further confirms the wisdom of the Québec government's decision to invest in innovation, in this case, genomics, an economic priority for the coming years."

Martin Godbout, President and CEO of Genome Canada expressed his satisfaction to see this proteomics research be widely released. "Peers recognition is very important to scientists and I congratulate Dr. Desjardins and his team for this research and its publication in Nature, a prestigious achievement that will benefit all of Canada. It is our mandate to bring Canada to the forefront of genomics and proteomics research."

"The work of Professor Desjardins, his team, and their American colleagues demonstrates the importance of using a combination of innovative techniques," said Dr. Bhagirath Singh, Scientific Director of the CIHR Institute of Infection and Immunity. "Their research findings, applied to the body's ability to get rid of infections, will help develop new treatments and approaches for the prevention of diseases such as tuberculosis."

Professor Desjardins's research was funded by Génome Québec, Génome Canada, and the Canada Institutes of Health Research (CIHR). Professor Desjardins holds the Canada Research Chair in Cellular Microbiology, and in this project secured the collaboration of the Montreal Proteomics Network based at McGill University. The Massachusetts General Hospital researchers were supported by grants from the Wellcome Trust and the U.S. National Institutes of Health.

About Université de Montréal: www.umontreal.ca

About Massachusetts General Hospital : www.massgeneral.org

About the High Throughput Biology Center at Johns Hopkins:
http://www.hopkinsmedicine.org/ibbs/research/HitCenter/index.html

About Genome Quebec: www.genomequebec.com

About CIHR: www.irsc-cihr.ca

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Information: Sophie Langlois Director, Media Relations Université de Montréal (514) 343-7704 sophie.langlois@umontreal.ca Sue McGreevey Manager, Science and Research Communications Massachusetts General Hospital 617 724-2764 smcgreevey@partners.org Marie-Kym Brisson Génome Québec (514) 603-3100 mkbrisson@genomequebec.com Marie-France Poirier CIHR Media relations (613) 941-4563 mediarelations@cihr-irsc.gc.ca