

NEWS RELEASE

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Montreal researchers identify defects of immune cells that give rise to a fungal infection commonly found in HIV patients

Montréal, June 21st, 2006 — Researchers at Université de Montréal and the Institut de recherches cliniques de Montréal (IRCM) have successfully identified a defective immune cell population that determines susceptibility to candidiasis, a common and often debilitating infection in individuals infected with the human immunodeficiency virus (HIV). These findings, revealed using a model of candidiasis in transgenic mice expressing HIV developed by the same research group, represents a milestone in developing a treatment for the infection and, eventually, preventing it. They are described in an article of the July 1st issue of *The Journal of Immunology*.

Oral and esophageal *Candida albicans* infections, which often affect individuals infected with HIV, may limit food consumption and lead to weight loss, threatening patients' general health and well-being. Of added concern, treatment of candidiasis in these patients is often complicated by strains of *Candida albicans* resistant to conventional antifungal therapies. The research project was carried out jointly by **Dr. Louis de Repentigny**, Director of the Medical Mycology Laboratory and Professor in the Department of Microbiology and Immunology at the Faculty of Medicine of Université de Montréal, and at CHU Sainte-Justine, and **Dr. Paul Jolicœur**, Director of the Molecular Biology Research Unit at the Institut de recherches cliniques de Montréal (IRCM), researcher in the Department of Microbiology and Immunology at the Faculty of Medicine of Université de Montréal, associate member of the McGill University Faculty of Medicine and holder of the Canada Research Chair on Infectious and Parasitic Diseases and **Dr Zaher Hanna**, Associate Director in the same Unit, researcher in the Department of Medicine at the Faculty of Medicine of Université de Montréal, associate member of the McGill University Division of Experimental Medicine.

Drs de Repentigny, Jolicœur and Hanna have for the first time succeeded in demonstrating that defective CD4+ T lymphocytes primarily determine the susceptibility to oral candidiasis in transgenic mice expressing HIV-1 and developing an AIDS-like disease. Findings from this research further indicated that a diminution and functional defects of both dendritic cells and CD4+ cells cause susceptibility to candidiasis in these transgenic mice by preventing T lymphocyte mediated acquired immunity to *Candida albicans*. The results also showed extensive perturbations in the production of cytokines required for protection against oral candidiasis in the transgenic mice.

"These findings regarding the specific immune defects which trigger candidiasis are very promising," explains Dr. de Repentigny. "This new knowledge will be instrumental in designing more powerful and effective treatments, which will directly improve the health status of HIV-infected patients who suffer from candidiasis. Defective CD4+ T lymphocytes have long been suspected to be the leading cause of candidiasis, however, it never had been directly demonstrated. Now, they become designated targets for the development of novel treatments not only for candidiasis but other mucosal infections."

"Secondary infections are the major cause of morbidity and mortality in people infected by HIV/AIDS. Fungal infection due to candidiasis is one of these debilitating conditions," said Dr. Bhagirath Singh, Scientific Director of the Canadian Institutes of Health Research (CIHR) Institute of Infection and Immunity. "This work provides a new understanding of why candidiasis is not controlled by the body's immune cells, particularly the CD4+ T lymphocytes. It will also help us to develop better treatments to prevent these opportunistic infections in HIV patients."

The research was funded by the Canadian Institutes of Health Research (CIHR). The research work by Dr. Jolicœur's team at the IRCM is also funded by Canadian Network for Vaccines and Immunotherapeutics and the National Institutes of Health (NIH).

About the IRCM

The IRCM is a non-profit research centre devoted to the study of the causes of disease, development of new diagnostic techniques and discovering new therapies that help improve general health. The *Institut* is affiliated with Université de Montréal, associated with the Centre hospitalier universitaire de Montréal (CHUM) and also maintains close collaborative ties with McGill University. The IRCM has 37 research units specializing in fields as varied as medicinal chemistry, molecular biology, functional genomics, clinical research, biomedical engineering and bioethics. Its researchers are key players in the broader network of medical and scientific research and are actively involved in national and international collaborations that are essential to the advancement of science.

About Université de Montréal

Founded in 1878, the Université de Montréal today has 13 faculties and together with its two affiliated schools, HEC Montréal and École Polytechnique, constitutes the largest centre of higher education and research in Québec, the second largest in Canada, and one of the major centres in North America. It brings together 2,400 professors and researchers, accommodates nearly 55,000 students, offers some 650 programs at all academic levels, and awards about 3,000 masters and doctorate diplomas each year.

About the Canadian Institutes of Health Research (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 health care system. Composed of 13 Institutes, CIHR provides leadership and support to over 10,000 health researchers and trainees across Canada. <http://www.cihr-irsc.gc.ca>

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