



IMMUNITY AND INFECTION RESEARCH CENTRE

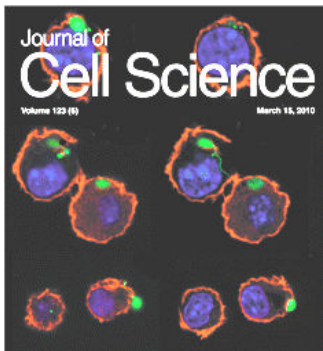
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Vancouver
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Research Institute
Healthier lives through discovery



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Discovering How Parasites Cause Infection



Leishmania (green) releases exosomes inside mouse macrophages.

Leishmania is an intracellular microbe that infects 12 million people worldwide. It causes the disease leishmaniasis, which is characterized by skin ulcers, fever, anaemia, liver and spleen damage, and frequently death.

There is no vaccine for leishmaniasis and the drugs used to treat the disease have limited effectiveness and significant side effects. Recent research from the Reiner Laboratory has discovered how Leishmania secretes the chemicals that allow the parasite to infect the host, which opens up new avenues of research to find better drugs to

treat the disease, and potentially develop a vaccine.

“We are the first to discover a general mechanism of secretion used by Leishmania”, says Dr. Judith Silverman, the lead author of the study. The research examined the proteins secreted by Leishmania and found that over 50% of the proteins matched a mechanism of cellular export found in mammalian cells. The process uses exosomes, which are small spherical containers made from the membrane of the cell. “We were able to observe the formation and movement of exosomes

from Leishmanian into host cells”, says Silverman.

The researchers used Leishmania that were genetically altered to produce a fluorescent green protein. They then added the Leishmania to cultured mammalian cells and examined the cells under a high powered microscope. The resulting images showed the parasite releasing green exosomes into the infected host cells. The research was published in the March 15th edition of the *Journal of Cell Science* and a composite of the cellular images was also chosen for the cover.

Reference:
Silverman JM et al. *Journal of Cell Science*. 2010 Mar 15;123(Pt 6):842-52 .

Congratulations CIHR Grant Winners!



Four IIRC member have received major Operating Grants from CIHR in June:

Dr. Yossef Av-Gay received a five year operating grant focusing on how bacteria that cause tuberculosis sense their surroundings in order to hide from the body's immune system. The Av-Gay lab has already found a *Mycobacterium tuberculosis*

phosphatase, PtpA, which is required for successful infection. By examining the signalling pathways of similar kinases and phosphatases, new therapies can be developed that will improve the health of millions of people that suffer from tuberculosis.

Dr. Vincent Duronio received a five year operating grant study the role of Mcl-1 in cellular responses to DNA damaging agents, including chemotherapy drugs. Abnormal functioning of Mcl-1 allows cells to divide when they should not which leads to a build-up of abnormal cancerous cells. A

better understanding of Mcl-1 will help with understanding many aspects of cell division and the research can lead to drugs designed to interrupt the abnormal processes of Mcl-1.

Dr. Alice Mui received a three year operating grant researching SHIP inhibition of the PI3K pathway to treat multiple myeloma disease processes. The PI3K pathway is implicated in the development of cancer and SHIP is the natural brake for this system which limits cell growth. The known role of SHIP in regulating blood cell function suggests that SHIP activators could

treat cancer effecting cells of the immune system.

Dr. Garth Warnock received a three year operating grant to develop a novel compound to treat type 1 diabetes. In previous research, the Warnock Lab determined that a naturally occurring protein, called B7-H4, can selectively suppress the immune cells that are responsible for killing insulin-secreting beta cells. The Warnock Lab aims to determine if the B7-H4 protein can help prevent and reverse the development of type 1 diabetes.

Provincial Cuts to Medical Research



The growth and continued success of the IIRC over the past seven years has been supported in large part through funding from the Michael Smith Foundation for Health Research. However, the Michael Smith Foundation relies heavily on funding from the BC Provincial Government. In 2009, the government promised the Michael Smith Foundation only enough support to partially cover the Foundation's commitments. The Michael Smith Foundation was also told to not expect any more provincial funding for the next two years. The resulting funding deficits

have dealt a severe blow to health research in BC.

The IIRC has been hit particularly hard by the cuts. With the loss of funding from the Michael Smith Foundation, the IIRC will have to adjust to a 65% decrease in our annual operating budget.

The IIRC is improving health outcomes and health services for the residents of British Columbia and the discoveries made have the potential to benefit people all over the world. This important work merits sustained funding. To learn more about our research, please visit <http://www.iirc.ca>.

You can support the work of the IIRC by:

Becoming a blood donor for IIRC research - http://www.iirc.ca/Opportunities/IIRC_Blood_Drive.htm.

Contacting the Honourable Kevin Falcon, Minister of Health Services for British Columbia, and letting him know that you support funding for health research in BC - kevin.falcon.mla@leg.bc.ca, 250-953-3547.

Making a donation to the VGH & UBC Hospital Foundation - yourgifthelps@supportvgh.ca, 604-875-4676.

Welcome New Members!



Dr. Richard Lester is a new faculty member in the Division of Infectious Diseases with a cross appointment at the BC Centre for Disease Control as the lead physician in sexually transmitted infections. Dr. Lester's research interests include mechanisms of innate immunity, and the use of cell phones to improve patient support and health services. His cell phone work in Africa was featured on CBC's, *The National*.



Dr. Chris Miller is a faculty member in the Department of Respiratory Medicine. He also collaborates closely with the Av-Gay Lab and is a pioneer in nitric oxide technology and therapeutic research. Nitric oxide is a potent antimicrobial and Dr. Miller's most recent work focuses on conducting clinical trials evaluating the safety and efficacy of nitric oxide as a treatment for pulmonary and surface wound infections.

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The Immunity and Infection Research Centre (IIRC) is a highly productive team of basic scientists, clinicians, and health professionals whose expertise spans genomics, molecular microbiology, immunology, infectious diseases, transplantation immunology, medical genetics, epidemiology, health care delivery, and policy development.

We study disease transmission and the basic mechanisms of human immune responses involved in transplantation and infectious diseases in order to improve public health outcomes and health services.