Bringing Research to LIFE

Upcoming Events

Café Scientifique

Schizophrenia: Beyond the Social Stigma

Monday, Feb. 28, 2011
at 7 p.m

McNally Robinson Booksellers
1120 Grant Avenue

To assist us in planning seating, RSVP to: (204) 474-9020

For more info: umanitoba.ca/research/cafe_scientifique.html

Café Politique Series Understanding the Manitoba Election

U2011: Understanding Women in Manitoba Politics

With: Dr. Louise Carbert, Dr. Joan Grace, and others

Tuesday, Mar. 8, 2011
at 7 p.m

McNally Robinson Booksellers
1120 Grant Avenue

All are welcome!

Bringing Research to LIFE Speaker Series

A Bird's Eye View of Spatial Cognition

with Canada Research Chair Dr. Debbie Kelly

Wednesday, Mar. 16, 2011
at 7 p.m

McNally Robinson Booksellers
1120 Grant Avenue

To assist us in planning seating, RSVP to: (204) 474-9020

For more info: umanitoba.ca/research/brtl.html

Unraveling The Secrets of a Deadly Virus

Discovering how a virus shuts down our immune system leads to better treatment options

BY MAUREEN PAISLEY

Microbiologist Brian Mark and his team of researchers at the University of Manitoba and colleagues at the Mount Sinai School of Medicine, New York, are studying the tick-borne virus Crimean-Congo hemorrhagic fever (CCHF). CCHF has a mortality rate of about 30%, and current treatment options are scarce. Most commonly transmitted by ticks, the virus can infect domesticated animals such as cattle and goats. The animals don't get sick, but humans do: very sick, in fact, and humans, it appears, are the only species (outside of newborn mice) that get sick from the virus.

Although some of the early reported cases of CCHF date back to 1944/45 in Crimea, the virus, and how it affects the human immune system, was not well understood until the advent of modern analytical techniques such as three-dimensional (3D) protein x-ray crystallography. These techniques, and the high-tech equipment available to Faculty of Science researchers, now enable Mark's team to visualize the 3D structure of a viral protein from CCHF as it interacts with proteins that are part of our innate immune system—ubiquitin and ISG15 (interferon-stimulated gene 15)—part of the body's initial defense against the virus.

One of Mark's collaborators, Adolfo García-Sastre from the Mount Sinai School of Medicine, New York, discovered the ability of CCHF to remove ubiquitin and ISG15 from cellular proteins to shut down the cell's immune response: a major breakthrough. Mark's team uncovered the molecular basis for how CCHF actually carries out this extraordinary viral defense tactic.

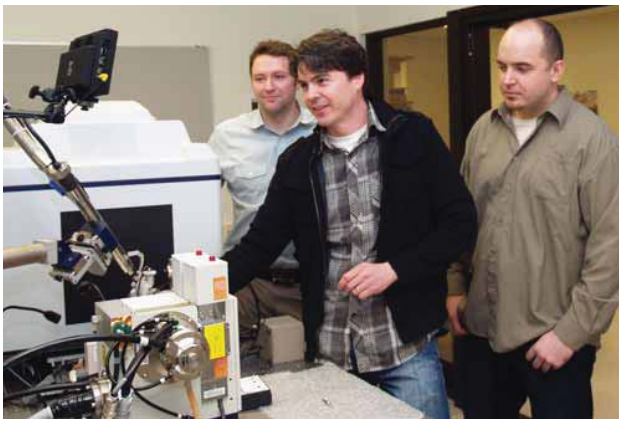

Photo by Maureen Paisley

Brian Mark (centre), with Terrence James (left), a recent M.Sc. graduate from Mark's lab, and John-Paul Bacik (right), who is a post-doctoral fellow in the lab.

How does the virus work?

There is something called an ovarian tumor domain-containing protease: a protease is an enzyme that clips apart other proteins. Ovarian tumor domain proteases have been found in a wide range of species ranging from humans to yeast to fruit flies, and viruses. The CCHF virus may have scavenged an ovarian tumor domain protease from a host at some point in evolutionary history, and evolved the protease into what it is today: a factor that removes (clips apart) ubiquitin and ISG15 from host proteins, thereby inhibiting our innate immune response to the virus. Scary stuff.

How widespread is CCHF?

There are reports of the disease from more than 30 countries in Africa, Asia, southeast Europe and the Middle East. Individuals considered at risk are those susceptible to tick bites from Hyalomma spp. No need to worry here: these ticks aren't endemic to Canada.

Mark explains that, "CCHF is considered an emerging disease, and it uses a previously unknown tactic to avoid our immune system. It is possible that this viral defense mechanism is used by other viruses and is more widespread than we know."

The team's findings have recently been published in the prestigious Proceedings of the National Academy of Sciences, but the work continues. With an understanding of how the virus functions at the molecular level with the host cell, Mark and his colleagues are in a position to target the viruses' weaknesses and to explore effective pharmaceutical interventions.

The Manitoba Health Research Council and the Natural Sciences and Engineering Research Council of Canada funded Mark's research.

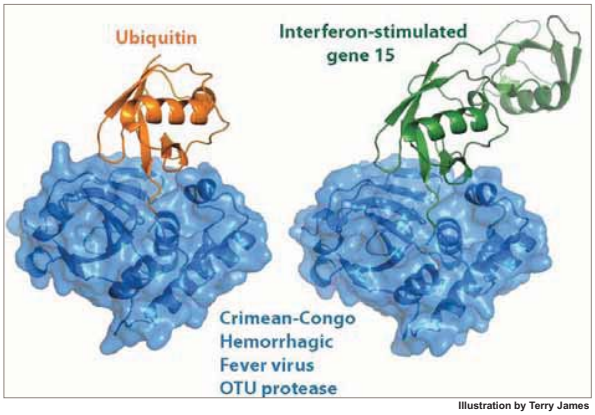

Illustration by Terry James

The Crimean-Congo Hemorrhagic Fever (CCHF) virus OTU protease domain (blue) is shown bound to its two known substrates, Ubiquitin (orange) and Interferon stimulated gene 15 (ISG15)(green). The surface representation of the OTU protease highlights the pocket where Ubiquitin and ISG15 are found during the enzymatic reaction. The structures have revealed how a viral protease is capable of recognizing these two similar substrates, while other OTU proteases only recognize Ubiquitin.

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