

Researchers moving towards ending threat of West Nile virus

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Mosquitoes are buzzing once again, and with that comes the threat of West Nile virus. Tom Hobman, a researcher with the Li Ka Shing Institute of Virology in the Faculty of Medicine & Dentistry, is making every effort to put an end to this potentially serious infection.

West Nile virus infections often result in flu-like symptoms that aren't life-threatening, and some in cases, infected people show no symptoms at all. But a significant percentage of patients develop serious neurological disease that includes inflammation in the brain, paralysis and seizures. In his latest research, published in the journal *PLoS One*, Hobman has discovered how the virus breaks through the normally rocksolid blood-brain barrier to the central nervous system. The virus breaks down two vital proteins that make up what is called the tight junction, a part of the blood-brain barrier.

"What we found in infected cells is there's less of two proteins called claudin and JAM (junctional adhesion molecule)," said Hobman. "The virus replication is causing degradation of two very important molecules that form these intra-cellular barriers. We can quantitate this and we've looked in at least three different cell types and we see the same thing happening."

Now Hobman and his graduate student Zaikun Xu would like to know how this is happening. Cells have built in pathways that regulate tight junctions, in part by controlling the levels of both JAM and claudin. Hobman hypothesizes that West Nile virus infection causes these



pathways to go awry – resulting in accelerated breakdown of claudin and JAM.

"Once we understand how West Nile virus affects the pathways that control the tight junctions of the blood-brain barrier, it may be possible to design drugs that prevent infection of the brain. I expect this will also be the case for related viruses that infect the central nervous system."

This builds on work his lab published last year showing that when they inhibited the expression of a specific cellular protein, infectivity of the West Nile virus went down by more than 100 times.

Provided by University of Alberta Faculty of Medicine & Dentistry

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