Research breakthrough opens door to new strategy for battling HIV

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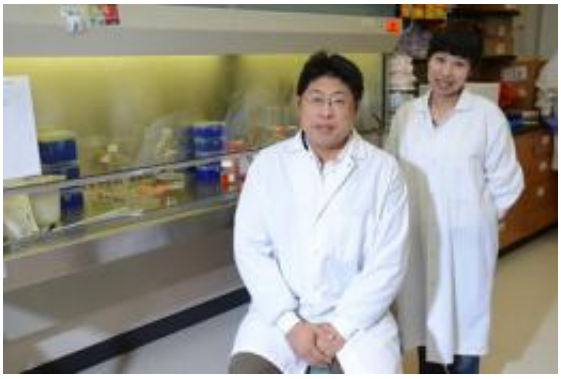

Researchers Yuntao Wu and Jia Guo in Mason's National Center for Biodefense and Infectious Diseases. Photo by Evan Cantwell

(Medical Xpress)—New research showing how the HIV virus targets "veterans" or memory T-cells could change how drugs are used to stop the virus, according to new research by George Mason University.

The research will appear in the Journal of Biological Chemistry's October edition and currently is available online.

"It's a big breakthrough for us," says Yuntao Wu, an author of the study and professor at the Mason-based National Center for Biodefense and Infectious Diseases. "I think this will impact the field."

Helper T-cells support the body's immune system by organizing forces to

fight off infection. The HIV virus hijacks helper T-cells. When helper T-cell numbers plummet, the body is vulnerable to disease.

Not all helper T-cells are the same; some are experienced ones called memory helper T-cells, and others, naive cells or "virgin" cells, haven't encountered an infection. Mason researchers studied why HIV preferentially goes after memory helper T-cells, while shunning their close colleagues. Memory and naive T-cells appear similar.

"In the body, HIV is able to kill most memory helper cells," says Weifeng Wang, the study's main author. "We wanted to pursue what makes the difference between memory and naive T-cells on a molecular level."

Unlike naive helper T-cells, memory T-cells are on the go, and much more mobile. And it's that momentum that attracts the HIV virus and makes the memory cell vulnerable, says Wang, who's currently a research fellow in the Dana-Farber Cancer Institute at Harvard Medical School.

When a memory cell moves, inside the cell, it looks like a waterfall on the moving edge. "It's called 'treadmilling'," Wu says. "The cytoskeleton or the cell's supporting bone is acting like a muscle. The treadmilling of cytoskeleton pushes the cell to migrate. That's how it pushes itself. In the past year we've been studying how HIV infects those memory cells. It has to go to the center, into the nucleus. It has to go past the cytoskeleton barriers to go into the center. For many years we didn't understand how the virus could cross such a structure. It's like a wall. It has to cross that wall."

HIV jumps over the wall by exploiting the cell's treadmilling process, Wu says. "The HIV virus uses a receptor to attach to the cell for entry," he says. "When the virus touches that receptor it's like someone ringing

the doorbell. That triggers a signal—someone comes out and opens the door. Now the HIV virus can start the treadmill to 'walk' along the cytoskeleton towards the center. If the virus goes to naive cells, it cannot do it. Naive cells aren't sensitive enough. The cytoskeleton of these 'virgin' cells is different from the memory cells, and it is not easy for the virus to start the treadmilling process."

HIV's knack for mutating makes it a tough target for drugs, Wang says. By shifting the focus to the cell, away from the virus itself, researchers may find a new way to tackle the virus, he says.

"Basically, our new strategy will be finding a cellular target, something HIV needs to depend on," Wu says. "It's as if the virus says 'give me a house.' The cell is the house. The house has to have electricity and everything so it can live there. Our approach is to look for something the virus needs to live in that house and then to reduce it or shut it down. The challenge will be if you shut that down, that it doesn't impact normal cell functions. It's a very tricky balance. You want to kill the virus but not healthy cells along with it."

Wu is looking at existing drugs, including those used for cancer. "There is something shared between cancer cells and HIV-infected cells because cancer cells also like to migrate. So some drugs that are used to slow down cancer migration could also be used to treat HIV."

More information: www.jbc.org/content/early/2012 … M112.362400.abstract

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