MS drug Tysabri shows promise in efforts to combat HIV's 'viral reservoirs'

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Biologists from Boston College, Cornell University, University of Florida College of Medicine and Harvard Medical School have unlocked new clues about the formation of debilitating viral reservoirs in HIV patients and how they can be blocked. Credit: Lee Pellegrini/Boston College

A drug used to treat patients with Crohn's disease and multiple sclerosis has helped scientists confirm how "viral reservoirs" form in patients living with HIV and also proven effective in animal trials at blocking the pathways to those reservoirs in the brain and gut, a team of researchers reported recently in the journal *PLOS Pathogens*.

The drug, a humanized antibody called natalizumab, is produced by Biogen Idec Inc. under the brand name Tysabri and prescribed to patients suffering from Crohn's disease and relapse of multiple sclerosis. In their experiments, university researchers found the antibody effectively blocks a molecule that two types of white blood cells use to travel to the brain and the gut, where they collect in viral reserves linked to debilitating illnesses that strike people living with HIV, said Boston College Professor of Biology Ken Williams, a senior author of the report.

The researchers found a three-week course of natalizumab, applied four weeks after infection, reversed lesions on the central nervous system. Furthermore, the experiments showed for the first time that the traffic of the virus to the brain - transported in disease-fighting cells known as monocytes and macrophages - could be physically blocked, Williams said.

In a parallel trial, a three-week course of treatment with natalizumab at the time of experimental infection completely blocked the traffic of the virus to the brain and the gut in animal subjects, according to the report. These tests confirmed the roles of monocytes in seeding the central nervous system with the virus and leukocytes leading to the infection of the gut - both precursors to a range of illnesses.

"We actually stopped all traffic and showed that if you physically block monocytes and macrophages, the virus does not enter the brain," said Williams, whose research focuses on the long-term impact of the

immune system's response to HIV/AIDS infection. "And even if full and major lesions of the central nervous system are present, application of the antibody can heal that damage and eliminate the virus, underscoring the necessity for continued traffic of cells to the central nervous system and the gut to maintain infection and lesions."

The team - which included additional researchers from Boston College, as well as colleagues at Harvard Medical School, Cornell University, and the University of Florida College of Medicine - studied the antibody based on earlier research that showed natalizumab blocked monocyte traffic in laboratory mice in trials focused on the treatment of multiple sclerosis, Williams said.

"So our question was if we can do that with HIV, does it stop virus replication in the brain, stop seeding and does it reverse injury?" said Williams. "The answer to each of those questions, we now know, is 'yes'."

The findings suggest that potential treatment regimens for humans at the time of HIV infection could include the use of the antibody in combination with antiretroviral drugs, a pairing that could serve to halt the seeding of HIV reservoirs in the brain and gut, while traditional antiretroviral therapies can target lymphoid organs to contain infection, Williams said. Human clinical trials would have to be conducted to pave the way for that potential use of the drug by patients, he said.

The latest report is viewed as a critical step in the effort to combat illnesses linked to HIV infection, including nerve damage, cardiac disease, gut disorders and dementia, which strike patients living with HIV and AIDS even though they are largely symptom free thanks to treatment from antiretroviral drugs.

Despite drug therapies that help hold HIV/AIDS symptoms in check,

researchers have centered on the presence of viral reservoirs that persist in the brain and the gut. Earlier research from the Williams lab has shown that cells and molecules from these stockpiles are present in illnesses such as neuropathy in the hands and feet, AIDS-related dementia, "leaky gut" syndrome and heart inflammation in people living with HIV and AIDS.

The Williams lab is also involved in a $39-million human clinical trial led by researchers at Massachusetts General Hospital and funded by the National Institute of Allergy and Infectious Diseases to determine whether treatment with a statin drug can reduce the elevated risk of cardiovascular disease in individuals infected with HIV. The REPRIEVE trials are slated to begin this spring.

As calls grow louder for a push to a "cure" for HIV/AIDS, researchers have focused on monocytes and macrophages - as well as T-cells - as another route to the development of new drug therapies that can fully arrest the damaging impact of the virus.

"When people talk about a 'cure' for aids, it's really about eradicating these viral reservoirs," said Williams.

Provided by Boston College

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