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Why human body cannot fight HIV infection? Study results could lead to new drug therapies

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University of Washington researchers have made a discovery that sheds light on why the human body is unable to adequately fight off HIV infection.

The work, directed by Dr. Michael Gale, Jr., a professor in the Immunology Department, will be featured in the August print issue of the Journal of Virology.

The researchers discovered that the viral protein vpu, which is created by HIV during infection, directly interferes with the immune response protein IRF3 to dampen the ability of the immune system to protect against virus infection.

"By understanding exactly what HIV does to hamper the innate immune response during early infection, we can develop a clearer picture of how the virus is able to evade immunity to establish a long-term infection," said Dr. Brian Doehle, a postdoctoral fellow and lead author of the article.

The research expanded on an earlier discovery by the Gale lab that HIV directly antagonizes the early innate immune response in infected cells by impairing IRF3 function.

The new studies found that the HIV protein vpu specifically binds to the

immune protein IRF3 and targets it for destruction, thereby, preventing IRF3 from functioning to trigger an immune response within the infected cell.

The scientists also found that HIV strains engineered to lack vpu, which is made during infection, did not impair the immune response.

"We have effectively identified a new Achilles heel in the arsenal that HIV uses to overcome the defenses present in the body's immune system", stated Dr. Gale. "This knowledge can be used to design new HIV antiviral therapeutics that prevent vpu from interacting with IRF3 and targeting it for destruction, thus enhancing immunity.

The development of new HIV antiviral therapeutics is critical to successfully treating HIV-infected people. Even though HIV antiviral therapeutics have already been developed and can effectively treat HIV infections, over time they lose their effectiveness due to the ability of the virus to adapt and spread despite the therapy, said Gale. "Therefore, the identification of new targets for treatment therapy is essential to providing the most effective treatment for HIV-infected patients".

Gale's laboratory has already begun translating the knowledge from these discoveries to tracking the molecular events that occur in patients during infection.

Arjun Rustagi, an MD/PhD student in the UW Medical Scientist Training Program, has developed a procedure to measure IRF3 activity in human blood cells. This new methodology will be used to measure IRF3 function over the course of HIV infection -- from the early stages of acute infection to the later stages of chronic infection that lead to AIDS.

By linking IRF3 function with infection over time, researchers will be

able to understand how antiviral therapeutics that are designed to improve IRF3 function might impact the overall course of the disease in an HIV-infected individual.

More information: Details on the development of the new assay will be published in the August 2012 issue of the journal, *Methods*.

Provided by University of Washington