Infectious Disease Researchers Make Key HIV Structural Discovery

A team led by HIV researchers at the University of Miami Miller School of Medicine has made an important discovery involving the structure of the virus that could facilitate use of new antibody-based treatment strategies.

“We have found a naturally occurring modification to the HIV envelope protein that protects the virus from a category of anti-HIV antibodies with potent neutralizing activity,” said Ronald C. Desrosiers, Ph.D., professor of pathology and an internationally renowned infectious disease researcher. “The findings have important implications for the use of those antibodies for preventive or therapeutic purposes.”
Dr. Zachary Silver, front, and Dr. Ronald C. Desrosiers in the lab.

Dr. Desrosiers was the submitting author for the study, “Discovery of O-Linked Carbohydrate on HIV-1 Envelope and Its Role in Shielding against One Category of Broadly Neutralizing Antibodies,” published in the February 11 issue of Cell Reports. The first author was Miller School M.D./Ph.D. student Zachary Silver, who performed the work in Dr. Desrosiers’ laboratory. Gordon M. Dickinson, M.D., a UM infectious disease specialist, was a co-author of the study.

“Thirty-six years after the discovery of HIV as the cause of
AIDS, there is an enormous amount of detailed knowledge regarding the structural elements of the virus, replication strategies, and strategies for viral persistence,” said Dr. Desrosiers. “In fact, discovery of new fundamental features of HIV’s structural elements is now quite uncommon.”

Dr. Silver documented for the first time that a subset of HIV isolates possess sugar residues on particular amino acids in a particular region of the HIV envelope surface protein, so-called O-linked glycosylation. These sugar residues were shown to have a dramatic shielding effect, protecting the virus against recognition by a particular category of host-produced antibodies that can neutralize the infectivity of the virus. “This is yet again another example of HIV’s uncanny ability to evolve, to get where it needs to go, to allow continuous unrelenting viral replication,” said Dr. Desrosiers.

Currently, there is great interest in using monoclonal antibodies with potent neutralizing activity against a broad range of HIV-1 isolates as an alternate treatment approach, added Dr. Desrosiers. “The vast majority of HIV-infected people do not make such antibodies but we now have them available for use,” he said.

Dr. Desrosiers’ laboratory team has been investigating a vector-based approach for the delivery of those antibodies, finding that a single intramuscular administration, when successful, results in life-long delivery of the therapeutic antibody. “As these antibody-based approaches advance through the clinic, it will be important to understand the escape and resistance pathways that HIV can use to escape recognition,” said Dr. Desrosiers. “In addition to being an important
discovery at the fundamental level, the findings from this study will help guide the advancement of these antibody-based approaches in the clinic.”