

Scientific breakthrough at the IRCM to combat the HIV-1

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The discovery by Dr. Éric A. Cohen's team at the Institut de recherches cliniques de Montréal, could potentially lead to the development of new strategies to combat the human immunodeficiency virus (HIV-1), the causal agent of acquired immunodeficiency syndrome (AIDS). In their article published in the open-access journal *PLoS Pathogens*, Dr. Cohen's team explains how the Vpu viral protein prevents the expression of Tetherin, a host factor inhibiting HIV-1 release, on the surface of infected cells.

Thus, if researchers manage to develop small molecules that prevent Vpu binding to Tetherin, this would restore one of the natural defence mechanisms that prevent the production, transmission and spread of HIV-1.

The study by Dr. Cohen's team allows a better understanding of the strategy used by HIV-1 to facilitate its transmission and its spread in humans. "Tetherin is a cellular protein that captures viruses forming at the surface of infected cells, thereby preventing viral transmission and spread. This antiviral protein, whose production is triggered by interferon, is an effector of the innate immune response against viral infections. However, viruses, and especially HIV-1, have evolved and developed mechanisms that antagonize this restriction factor. In fact, we have discovered how the Vpu protein neutralizes Tetherin, and as such stimulates HIV-1 production," stated Dr. Éric A. Cohen.

By directly binding Tetherin, Vpu adversely affects the transport of the



restriction factor to the cell surface, which is the site of its antiviral activity. Tetherin is therefore stored within the cell, thus preventing it from playing its role as a "barrier" against virus transmission. "Simian immunodeficiency viruses, considered to be precursors of HIV-1, are unable to antagonize human Tetherin. It would appear that the emergence of HIV-1 strains encoding Vpu proteins with the ability to perturb the intracellular transport of human Tetherin, could have contributed to the pandemic spread of certain groups of HIV-1", specified Mathieu Dubé, doctorate candidate at the IRCM's Human Retrovirology Research Unit, and the first author of the article.

"We need to better understand how <u>HIV</u> is transmitted in order to develop new HIV prevention and treatment strategies," said Dr. Marc Ouellette, Scientific Director of the Canadian Institutes of Health Research's Institute of Infection and Immunity. "This is a very important finding by Dr. Cohen's research team and another example of the superb research being done in Canada in this area."

More information: dx.plos.org/10.1371/journal.ppat.1000856

Provided by Institut de recherches cliniques de Montreal

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