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Researchers pave the way for a better understanding of HIV infection and AIDS

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Dr. Eric A. Cohen, Director of the Human Retrovirology research unit at the Institut de recherches cliniques de Montreal (IRCM), and his team published yesterday, in the online open-access journal *PLos Pathogens*, the results of their most recent research on the role of the Vpr protein in HIV (human immunodeficiency virus) infection and AIDS (acquired immune deficiency syndrome).

"We previously identified that HIV, when infecting target cells, blocks cell division and induces cell death," says Dr. Cohen. "We then discovered that the Vpr protein was involved in this process."

HIV-1 encodes several proteins, including the viral protein R (Vpr), which plays an important role in the development of acquired immunodeficiency syndrome (AIDS). Vpr blocks normal cell division, a process believed to increase viral replication and to trigger immune cell death. The researchers recently showed that Vpr performs this activity by interacting with a cellular protein complex (E3 ligase) involved in ubiquitination. Ubiquitination is characterized by the conjugation of a small protein called ubiquitin to various other proteins to regulate their degradation or activities. They also demonstrated that Vpr engages this protein complex to ubiquitinate a yet to be discovered host factor, whose degradation triggers the arrest of cell division.

"We understand the process, but we still don't know which cellular factor is targeted by Vpr to block cell division and where these events are occurring within the infected cell," explains Dr. Jean-Phillippe Belzile, a

postdoctoral fellow in Dr. Cohen's research unit and first author of the article. "If we can identify this unknown host factor and determine its role in the cell cycle, it will undoubtedly have an impact on our understanding of HIV infection and the processes of immune cell death that characterize AIDS. We believe that the identification of this host factor could, in the long run, lead us to new potential therapeutic targets."

In this study, the researchers demonstrated that Vpr forms mobile structures called foci on the DNA of host cells. They also found that formation of these nuclear foci by Vpr is required to block cell division. They further showed that Vpr engages the E3 ligase within these mobile structures, and uses them to find a DNA-bound cellular protein and target it for degradation. This mechanism, in turn, results in the activation of a host cell response leading to a cell division block.

"Getting such insight into this process is very important, as it gives us and the scientific community a direction to focus our efforts to identify this unknown host factor, thereby contributing to a better understanding of the role of Vpr during HIV infection and AIDS pathogenesis," adds Dr. Cohen.

Provided by Institut de recherches cliniques de Montreal