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Researchers discover how the kissing disease virus hijacks human cells

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University of Montreal researchers have discovered how a component of the Epstein Barr (EBV) virus takes over our cells gene regulating machinery, allowing the virus to replicate itself. The EBV virus causes a variety of diseases such as Hodgkin's lymphoma and Burkitt's lymphoma, with the most prevalent disease being infectious mononucleosis commonly known as "kissing disease" because of its mode of transmission between humans. It turns out that the diseases begin with kiss of a molecular sort; a viral protein contacting the molecules that control our genes.

Viruses such as EBV use sophisticated strategies to subvert human cells during an infection. The viruses cannot survive outside of human cells and for this reason they have developed strategies to mimic key components of human cell function such as the RNA polymerase. "Unraveling the atomic level details of these interactions using structural biology allows us to understand how the virus tricks the human defense systems. Having this knowledge is the first step towards developing new therapeutic treatments for viral infections", explained Dr. James Omichinski, senior author of this work conducted in collaboration with his colleague Dr. Jacques Archambault at the Institut de recherches cliniques de Montréal (IRCM).

Using cutting-edge nuclear magnetic resonance techniques at the University of Montreal facility for structural biology in the Department of Biochemistry and Molecular Medicine, the scientists studied how the EBNA2 protein of the EBV virus binds to one of the proteins of the

TFIIH complex that helps regulate another protein called RNA polymerase II, a molecule that is responsible for the control of most of our genes. "We were able to unravel the molecular details of the interaction between these proteins", explains Dr. Omichinski.

To unravel the molecular details of this interaction, the lead author Philippe Chabot labeled the EBNA2 protein and TFIIH with stable isotopes and determined the molecular structure of their interaction using NMR spectroscopy. "This type of instrumentation costs several millions dollars, but thanks to generous investments made by the Canada Foundation for Innovation (CFI) we are able to conduct such studies with the most modern equipment", explained Dr. Omichinski. A direct benefit of this work is that the "kissing" interaction between EBNA2 proteins and TFIIH could be a target for drug development to better treat kissing disease and cancers caused by EBV viruses in future.

The study was published in *PLOS Pathogens*.

Provided by University of Montreal