Unique Interaction in Immunity to Infection, Study Shows

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The immune system's recognition and the ongoing struggle for survival of the fittest.

In an unprecedented study, researchers at Sunnybrook provide evidence of a unique molecular interaction in immunity to infection that suggests longer-term clinical implications for treatment of cytomegaloviruses (CMVs), a family of herpesviruses causing chronic and sometimes fatal infections.

Published online today in the journal Immunity, the study provides definitive molecular evidence of ongoing evolution and counter-evolution in host-pathogen interactions. Researchers characterized innate immunity to CMV during the initial stages of infection, and identified an interaction between a rat CMV protein and the inhibitory immuno-receptor, NKR-P1B. A similar inhibitory receptor is conserved in humans, known as NKR-P1A or CD161.

Key findings of the study include the evolution of a decoy mechanism by which CMV has co-opted a lectin-like host gene in order to gain protection from killing by the host's natural killer (NK) cells. As a result, infected cells are mistakenly recognized as normal "self" cells, because the viral decoy mimics the natural host ligand by interacting with the inhibitory NKR-P1B receptor. Key findings also demonstrate that individual variations in host NKR-P1 receptors have evolved to avert the CMV viral decoy strategy while maintaining "self" recognition to avoid autoimmunity. Similar lectin-like genes have been found in poxviruses, suggesting this may be a common theme for viral evasion of innate immunity.

"For the first time, an MHC-independent 'missing-self' recognition system has been shown to be involved in innate immunity to infection," says Dr. James Carlyle, lead investigator, scientist at Sunnybrook Research Institute and assistant professor, Department of Immunology, University of Toronto. "We are always looking at the evolution of pathogens to give us insight into the normal operation of the immune system, but we are equally interested in the counter-evolution of host mechanisms to avert infectious disease. In the long term, this helps us to develop targeted strategies for the treatment and prevention of chronic infections like CMV."

CMV causes life-long infections that are normally well-controlled in individuals with healthy immune systems, and evidence of CMV infection is found in up to two-thirds of any given population. When the immune system is weakened, such as in infants, patients undergoing chemotherapy, transplant recipients, or those afflicted with AIDS or other immune deficiencies, CMV infections often escalate, leading to complications that can sometimes be fatal.

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