Researchers discover enzyme suppressing immune response to viral infections

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Viruses such as HIV, hepatitis B and hepatitis C evade or disrupt the immune system to create persistent infections. These viruses remain a serious health threat, but researchers from the University of Missouri

School of Medicine have discovered how an enzyme that regulates several cellular processes might be a key target to preventing viruses from disarming the human immune response.

"There is very little research on how the sphingosine kinase 2 (SphK2) enzyme affects the immune responses to viral infections," said senior author Bumsuk Hahm, Ph.D., associate professor of surgery and molecular microbiology and immunology. "We hypothesized that this enzyme suppresses the T cells that fight infections and allows viruses to persist."

Hahm and his team tested their hypothesis by infecting mice with the lymphocytic choriomeningitis virus, a common rodent-borne virus. Mice in the study that received an oral therapy that briefly inhibited the SphK2 enzyme experienced a robust immune response and an accelerated destruction of the virus.

"SphK2 is shown to regulate immune cell responses during a viral infection, and inhibition of this enzyme is effective in clearing a persistent viral infection," Hahm said. "We believe targeting SphK2 may provide a promising route for developing a drug to elicit protective immunity against viral infections that have a devastating impact on human health."

Another key finding from the study demonstrated that SphK2 plays a role in preventing the immune system from attacking the kidneys during an infection. Hahm's team found SphK2 deficient mice died within two weeks of infection from kidney failure. All showed evidence of immune cell infiltration in the kidneys.

Hahm's team also discovered SphK2 inhibition may also treat some types of cancer by promoting activation of the immune system. Other clinical trials are already exploring the idea that SphK2 inhibition can slow

cancer cell growth by directly blocking cancer cell proliferation.

"Our study suggests that SphK2 can be targeted for restoring T cell immunity to circumvent an immune suppressive environment," Hahm said. "This finding may be applicable to cancer studies as well as other diseases caused by immune disruption."

Their study, "Sphingosine kinase 2 restricts T cell immunopathology but permits viral persistence," was recently published in the *Journal of Clinical Investigation*.

More information: Caleb J. Studstill et al, Sphingosine kinase 2 restricts T cell immunopathology but permits viral persistence, *Journal of Clinical Investigation* (2020). DOI: 10.1172/JCI125297

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