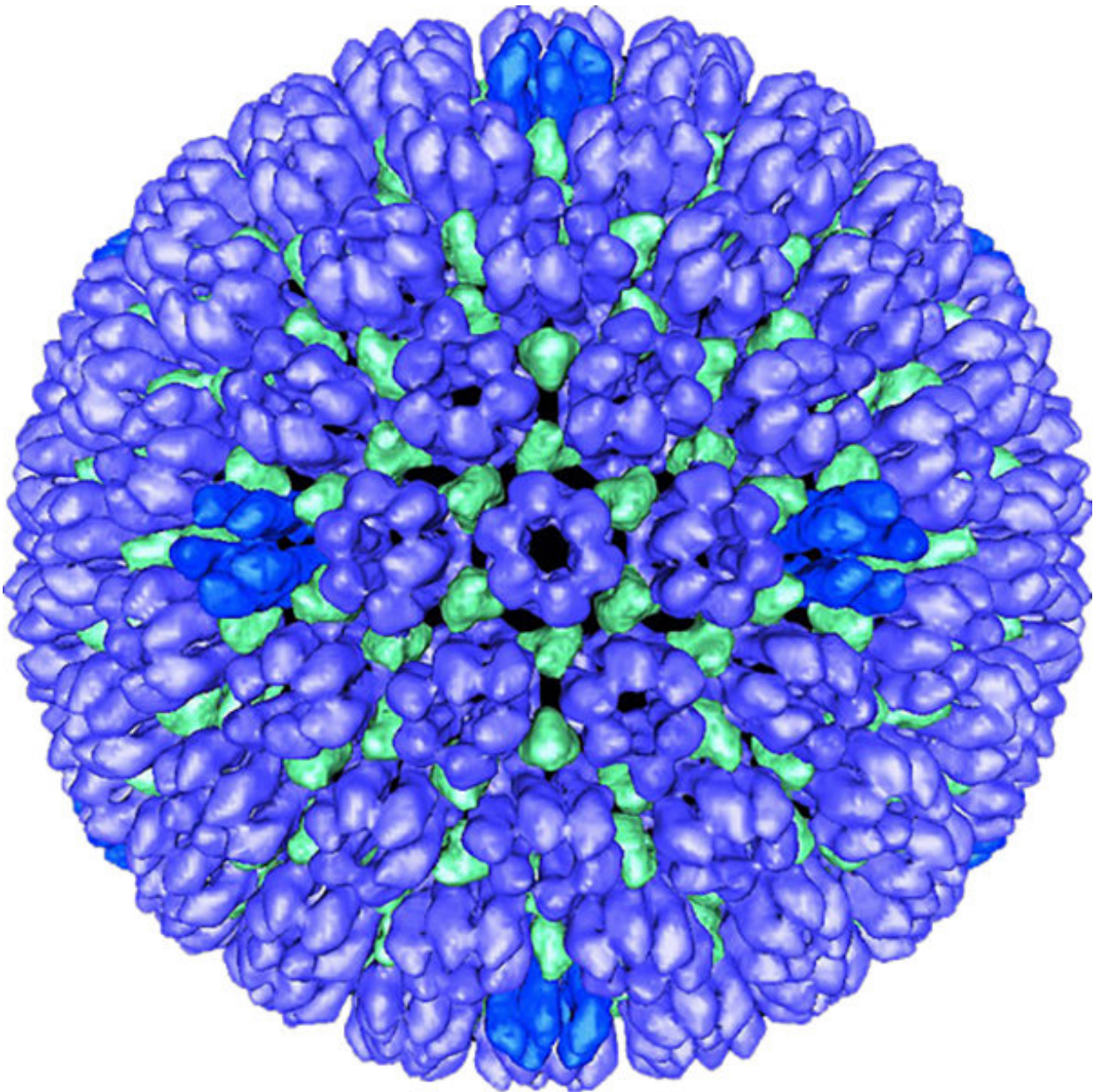


Exploring how herpes simplex virus changes when passed between family members

October 22 2017



The outer protein shell (procapsid) of the herpes simplex virus type 1 (HSV1). A new study explores how HSV1 might change when passed from one individual to another. This information may provide important insight for future development of therapeutics and vaccines. Credit: Bernard Heymann, Ph.D., NIAMS Laboratory of Structural Biology Research, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health

A new study explores how herpes simplex virus might change when passed from one individual to another, information that may prove useful in future development of therapeutics and vaccines. This rare glimpse into a transmission event reveals nearly perfect genetic transmission of the virus from a father to his son and lays the foundation for future studies exploring the genetic diversity of this virus. A paper describing the study appears online October 20, 2017, in the journal *Scientific Reports*.

"Millions of people worldwide have herpes simplex virus," said Moriah Szpara, assistant professor of biochemistry and molecular biology at Penn State and an author of the paper. "We see locally distinct variants of the virus with distinct genetic fingerprints in different regions around the world, and, with the prevalence of international travel, we're starting to see a lot of different variants of the virus appearing in one place. This could have implications for how the virus evolves and how we design therapeutics to combat it. Studies of a related virus - human cytomegalovirus - suggest that the virus diversifies after transmission, and we wanted to see if this was also the case for herpes simplex virus."

Herpes simplex virus type 1 (HSV-1) is a highly contagious infection that commonly causes oral and genital lesions. More severe symptoms can also occur, such as eye disease and, in rare cases,

encephalitis—inflammation of the brain that can cause flu-like symptoms, confusion, seizures, or problems with movement. Although some medications can reduce the severity and frequency of the symptoms, there is no cure for HSV-1 and no guaranteed way to prevent transmission. HSV-1 can be transmitted through contact with sores or saliva around the mouth - as is often the case in familial transmission - or sexually.

"Capturing transmission of herpes simplex virus is incredibly difficult," said Szpara, "in part because the social stigma associated with having the virus makes it unlikely for sexual partners to admit when they transmit it. The virus also lasts a lifetime. Unlike the flu, which comes and goes, HSV remains in an individual's body for the remainder of their life. Periods of latency and reactivation make it hard to know exactly when the virus was first transmitted."

"In this study, we had a known case of familial transmission," said Nancy Sawtell, professor at the Cincinnati Children's Hospital Medical Center and an author of the paper. "Samples from a father and son were cultured in the lab, enabling us to investigate potential differences of the virus after transmission. To gain a comprehensive look at the results of transmission, we used genetic sequencing, and we examined each virus in an animal model to compare the level of virulence, or the ability to cause disease. Animal models have the ability to reflect the interactions of all the body's systems at once—the outer surface, the immune system, and the nervous system all interact during the response to herpes simplex virus infection."



A new study by researchers from Penn State, the Cincinnati Children's Hospital Medical Center, and the University of Cincinnati provides a rare look at the genetics behind transmission of HSV1 from a father to his son. Credit: Moriah Szpara, Penn State

Genetically, the viruses taken from the father and son were a near-perfect match. The viruses also had similar pathology when tested in

mice - they grew at a similar rate and had a similar ability to set up long-term infection in the brain. Although the viruses from the father and son were not completely identical, these results suggest that HSV-1 may not change much when transmitted between closely related individuals. However, the researchers suspect that transmission between unrelated hosts may provide a more dramatic opportunity for change.

"An individual's immune system exerts selection pressure on a virus," said Utsav Pandey, graduate student at Penn State and first author of the study. "The son got at least half of his immune system from his father, so it was probably a similar selective environment. Unrelated individuals likely differ more in their immune system, which could shape the virus."

The research team also compared the performance of the viruses from the father and son to two separate clinical cultures of HSV-1. The variants from the father and son were less virulent—less severe—when tested in mice. Additionally, the genome sequence of the viruses in the father and son, who were from the United States, did not fit in as expected with other HSV-1 genomes that have been genetically sequenced from the United States or Europe.

"This study broadens our knowledge of what [herpes simplex virus](#) variants are circulating in the U.S.," said Szpara. "It's not just the United States/European variants that are used in vaccine development and clinical studies. When we think about designing therapeutics and vaccines, we need to know how the virus can differ or we may design something that only controls the virus from a particular region."

To further understand how [genetic diversity](#) of HSV-1 is generated, the researchers plan to turn their attention to studying [transmission](#) of the virus between unrelated individuals. "If we could understand how much the virus changes when passed between unrelated individuals and how the virus' genetics influences the level of virulence or level of harm the

[virus](#) can do," said Szpara, "then hopefully we can design better treatments for HSV-1."

More information: Utsav Pandey et al, Inferred father-to-son transmission of herpes simplex virus results in near-perfect preservation of viral genome identity and in vivo phenotypes, *Scientific Reports* (2017). [DOI: 10.1038/s41598-017-13936-6](https://doi.org/10.1038/s41598-017-13936-6)

Provided by Pennsylvania State University

Citation: Exploring how herpes simplex virus changes when passed between family members (2017, October 22) retrieved 14 August 2024 from <https://medicalxpress.com/news/2017-10-exploring-herpes-simplex-virus-family.html>

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