

Study identifies DNA region linked to severity of herpes simplex infections

March 21 2014, by Keith Herrell



Researchers Richard Thompson, PhD, and Nancy Sawtell, PhD, have collaborated for almost 25 years in an effort to gain insight into the herpes simplex virus.

(Medical Xpress)—In a study that has important implications for how the herpes simplex virus causes blindness and fatal brain disease, researchers at the University of Cincinnati (UC) and Cincinnati

Children's Hospital Medical Center have identified a host DNA region associated with severity and mortality of herpes simplex infections.

The researchers—Richard Thompson, PhD, and Nancy Sawtell, PhD—co-authored the study that appeared Thursday, March 20, in *PLOS ONE*, a peer-reviewed, open-access journal published by the Public Library of Science (PLOS). Thompson is a professor in the UC Department of Molecular Genetics, Biochemistry and Microbiology; Sawtell is a professor in the UC Department of Pediatrics and a researcher in the division of infectious diseases at Cincinnati Children's.

The [herpes simplex virus](#) type 1 (HSV-1) is the leading infectious cause of herpetic stromal keratitis, a cloudiness of the cornea that leads to blindness, and acute sporadic encephalitis, an inflammation of the brain that is fatal in more than half of untreated cases, according to the National Institute of Neurological Disorders and Stroke (NINDS). Primary infection is usually acquired during childhood, most likely from a family member.

As many as 80 percent or more of people are infected with HSV. Most of the time, people carrying the [virus](#) do not have symptoms, although they can still transmit the virus.

To gain insight into host gene variants important for HSV-1 disease severity, Thompson and Sawtell conducted a forward genetic analysis of the offspring of two different strains of mice, with one parent highly resistant to HSV-1 and the other highly susceptible to it.

"We infected them with the virus and we asked, 'What do these phenotypes look like in each mouse line?'" says Thompson, who noted that he and Sawtell started out with no hypothesis.

To their surprise, the two properties (severity of herpetic stromal

keratitis and invasion of the brain) mapped to the same location on the mouse genome. Specifically, a quantitative trait locus on chromosome 16 was found to associate with both percent mortality and HSK severity.

"And what's really exciting is that they mapped very close to a place that is homologous (having the same properties) on the human genome that is associated with the frequency of cold sores, which are also caused by HSV-1," says Sawtell.

The finding suggests that a single host locus may influence these seemingly diverse HSV-1 pathogenic phenotypes by as yet unknown mechanisms. The genes residing in the region have no obvious connection to the immune system or known virus resistance genes. One likely possibility, Thompson and Sawtell are hypothesizing, is that a host gene in this region regulates the ability of the virus to travel back and forth through the nervous system instead of acting directly on infection of the eye.

"There's much more work to be done, but our findings indicate that the interaction of the virus with the nervous system is actually very important for what is happening in the eye," Thompson says.

Sawtell, noting that only about 10 percent of people infected with HSV-1 in the eye actually develop cloudiness in their corneas, notes that the findings could eventually lead to better methods of predicting who might be more susceptible to herpetic stromal keratitis or acute sporadic encephalitis.

"From a medical point of view, finding markers that allow us to assess risk would allow us to identify people who might be more susceptible to disease and encourage them to seek appropriate intervention," says Thompson.

More information: Thompson RL, Williams RW, Kotb M, Sawtell NM (2014) "A Forward Phenotypically Driven Unbiased Genetic Analysis of Host Genes That Moderate Herpes Simplex Virus Virulence and Stromal Keratitis in Mice." *PLoS ONE* 9(3): e92342. [DOI: 10.1371/journal.pone.0092342](https://doi.org/10.1371/journal.pone.0092342)

Provided by University of Cincinnati

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