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Researchers link herpes to Alzheimer's disease

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Laboratories at the University of New Mexico (UNM), Brown University, and House Ear Institute (HEI) have developed a new technique to observe herpes simplex virus type 1 (HSV1) infections growing inside cells. HSV1, the cause of the common cold sore, persists in a latent form inside nerve cells. Re-activation and growth of HSV1 infections contribute to cognitive decline associated with Alzheimer's disease. Details are published in the March 31 issue of *PLoS ONE* magazine from the Public Library of Science.

"Herpes infects mucous membranes, such as the lip or eye, and generates viral particles," submits study Principal Investigator Elaine Bearer, M.D., Ph.D., Harvey Family Professor and Vice Chair for Research, Department of Pathology, UNM School of Medicine. "These viral particles burst out of the cells of the mucous membrane and enter sensory nerve cells where they travel inside the nerve toward the brain. We now can see this cellular transportation system and watch how the newly formed virus engages cellular APP on its journey out of the cell."

Tagging herpes virus inside cells with green fluorescent protein, scientists used live confocal imaging to watch HSV1 particles emerge from infected cells. Newly produced viral particles exit the cell nucleus and then bud into cellular membranes containing amyloid precursor protein (APP). Electron microscopy at HEI detailed the ultrastructural relationship between HSV1 particles and APP.

This dance between viral particles and cellular APP results in changes in

cellular architecture and the distribution of APP, the major component of senile plaques found in the brains of Alzheimer's disease patients. Results from this study indicate that most intracellular HSV1 particles undergo frequent, dynamic interplay with APP, which facilitates viral transport while interfering with normal APP transport and distribution. This dynamic interaction reveals a mechanism by which HSV1 infection leads to Alzheimer's disease.

In developed countries such as the U.S., approximately 20 percent of children are infected with HSV1 prior to the age of five. By the second and third decades of life, as much as 60 percent of the population is infected, and late-in-life infection rate reaches 85 percent.

Symptoms of primary HSV1 infection include painful blisters of the mouth, lips or eyes. After infection, HSV1 persists in nerve cells by becoming latent. Upon re-awakening, new viral particles are made in the neuron and then travel back out its pathways to re-infect the mucous membrane. Many infected people experience sporadic episodes of viral outbreaks as the well-known recurrent cold sore.

"Clinicians have seen a link between HSV1 infection and Alzheimer's disease in patients, so we wanted to investigate what might be going on in the body that would account for this," adds Dr. Shi-Bin Cheng, post-doctoral associate, Department of Pathology and Laboratory Medicine, Alpert Medical School, Brown University. "What we were able to see in the lab strongly suggests a causal link between HSV1 and Alzheimer's Disease."

"It's no longer a matter of determining whether HSV1 is involved in cognitive decline, but rather how significant this involvement is," Bearer asserts. "We'll need to investigate anti-viral drugs used for acute herpes treatment to determine their ability to slow or prevent cognitive decline."

Researchers recommend people treat a cold sore as quickly as possible to minimize the amount of time the virus is actively traveling through a person's nervous system. The faster a cold sore is treated, the faster the HSV1 returns to a dormant stage.

Provided by Brown University