MedicalXpress

Jefferson researchers' discovery may change thinking on how viruses invade the brain

April 19 2007

A molecule thought crucial to ferrying the deadly rabies virus into the brain, where it eventually kills, apparently isn't. The surprising finding, say researchers at Jefferson Medical College in Philadelphia, may change the way scientists think about how central nervous system-attacking viruses such as herpes viruses invade the brain and cause disease.

According to Matthias Schnell, Ph.D., professor of microbiology and immunology at Jefferson Medical College of Thomas Jefferson University, viruses such as rabies must be actively transported to the brain and central nervous system. The LC8 protein was thought to tether viruses to the cellular transport machinery in order to get there.

But Dr. Schnell and his co-workers found that this protein complex is instead a "transcription factor" that plays a role in virus reproduction. "We think that this finding has implications not only for rabies but many viruses that previously were thought to use this complex for transport, such as herpes viruses," he says. They report their results online this week in the journal *Proceedings of the National Academy of Sciences*.

To understand the role of LC8 in rabies disease in the brain, the team compared a rabies virus strain with the LC8 "binding domain" (where the rabies virus and LC8 protein interact) to a virus lacking it. They showed that in mice that were infected with rabies without the LC8 binding domain, the virus was still able to infect the brain, but did not cause disease. The virus' ability to reproduce was greatly diminished.

"What we found has nothing to do with transport," Dr. Schnell says. "We saw that the virus was weakened if we removed the LC8 binding site and viral replication and transcription were affected. But we didn't find a difference in the initial viral entry in the central nervous system. We actually saw that the virus replicated better with the binding site than without it. LC8 is a transcription factor that helps the virus efficiently replicate in cells."

The researchers were surprised by the finding. "The field in general has been focusing on this general dynein-LC8 protein interaction as key to viral transport," says co-author John Williams, Ph.D., assistant professor of biochemistry and molecular biology at Jefferson Medical College. "We found that while transport must happen – it's essential to viral infection and spread and disease progression – it's not through this mechanism. There's more to the story."

"We think we have to have a closer look at how viral transport in general works," Dr. Schnell says. "Viral transport has to be revisited."

Next, the scientists plan to pay closer attention to other parts of the dynein-LC8 interaction, and attempt to find other proteins that could be involved in viral transport.

Source: Thomas Jefferson University

Citation: Jefferson researchers' discovery may change thinking on how viruses invade the brain (2007, April 19) retrieved 11 July 2023 from https://medicalxpress.com/news/2007-04-jefferson-discovery-viruses-invade-brain.html