

New study suggests amyotrophic lateral sclerosis could be caused by a retrovirus

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A retrovirus that inserted itself into the human genome thousands of years ago may be responsible for some cases of the neurodegenerative disease amyotrophic lateral sclerosis (ALS), also known as Lou Gherig's disease. The finding, made by Johns Hopkins scientists, may eventually give researchers a new way to attack this universally fatal condition.

While roughly 20 percent of ALS cases appear to have a genetic cause, the vast majority of cases appear to arise sporadically, with no known trigger. Research groups searching for a cause of this so-called sporadic form had previously spotted a protein known as reverse transcriptase, a product of retroviruses such as HIV, in ALS patients' serum samples, suggesting that a retrovirus might play a role in the disease. However, these groups weren't able to trace this reverse transcriptase to a specific retrovirus, leaving some scientists in doubt whether retroviruses are involved in ALS.

Seeking to verify whether a culprit retrovirus indeed exists, Avindra Nath, M.D., a professor of neurology at the Johns Hopkins University School of Medicine, and colleagues examined brain samples from 62 people: 28 who died from ALS, 12 who died from chronic, systemic diseases such as cancer, 10 who died from accidental causes and 12 who had another neurodegenerative disease, Parkinson's disease, at the time of their deaths. Using a technique known as polymerase chain reaction, the researchers searched for [messenger RNA](#) (mRNA) transcripts from retroviruses, a chemical signature that retroviruses were active in these patients.

In samples from the ALS and chronic disease patients, the search turned up mRNA transcripts that came from human endogenous retrovirus K (HERV-K). This retrovirus is one of thousands that became a part of the human genome after infecting our ancestors long ago. Nowadays, these retroviruses are no longer contagious, but are

instead passed along through inheritance in part of the genome that scientists consider "junk" DNA.

When Nath and his colleagues took a closer look at the mRNA, they saw that the transcripts seemed to originate from different parts of the genome in the samples from ALS and systemic disease patients. The transcripts also came from different tissues in the brain. While patients with ALS tended to have HERV-K transcripts present in areas surrounding the motor cortex of the brain - the area affected by the disease - the other patients' transcripts were spread more diffusely through the brain.

Although the researchers express caution, the findings, reported in the January *Annals of Neurology*, suggest that HERV-K might be the ALS retrovirus that researchers have been looking for.

"This paper doesn't establish causation beyond the level of doubt, but it does provide some promising links between HERV-K and ALS," Nath says. "We've never found a putative retrovirus for this disease before, so this opens up a whole new area."

He and his colleagues plan to study whether HERV-K might cause neuronal damage, a step closer to linking this [retrovirus](#) to ALS. They also plan to study what factors may cause HERV-K to reactivate in some people and lead to ALS symptoms. Researchers might eventually be able to fight ALS, Nath adds, using antiretroviral drugs specific to HERV-K.

Provided by Johns Hopkins Medical Institutions

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