

New study explains how a common virus can cause multiple sclerosis

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Researchers at Karolinska Institutet in Sweden have found further evidence for how the Epstein-Barr virus can trigger multiple sclerosis or drive disease progression. A new study published in *Science Advances*

shows that some individuals have antibodies against the virus that mistakenly attack a protein in the brain and spinal cord.

The Epstein-Barr virus (EBV) is a herpesvirus that infects most people early in life and then remains in the body, usually without causing symptoms. It is one of the most widespread viruses in humans. Over 90% of the world's population are infected with EBV and carry the virus for life as a latent, usually asymptomatic, infection. Most people are infected as children with few or no symptoms but in young adults, the virus often causes [infectious mononucleosis](#), also known as glandular fever or "kissing disease."

The link between EBV and the neurological disease multiple sclerosis (MS) was discovered many years ago and has puzzled researchers ever since. Increasing evidence, including two papers published in [Science](#) and [Nature](#) last year, suggests that EBV infection precedes MS and that antibodies against the virus may be involved. However, the [molecular mechanisms](#) seem to vary between patients and remain largely unknown.

"MS is an incredibly complex disease, but our study provides an important piece in the puzzle and could explain why some people develop the disease," says Olivia Thomas, postdoctoral researcher at the Department of Clinical Neuroscience, Karolinska Institutet and shared first author of the paper. "We have discovered that certain antibodies against the Epstein-Barr virus, which would normally fight the infection, can mistakenly target the brain and spinal cord and cause damage."

Misdirected antibodies

The researchers analyzed [blood samples](#) from more than 700 patients with MS and 700 healthy individuals. They found that antibodies that bind to a certain protein in the Epstein-Barr virus, EBNA1, can also bind to a similar protein in the brain and [spinal cord](#) called CRYAB, whose

role is to prevent protein aggregation during conditions of cellular stress such as inflammation. These misdirected, cross-reactive antibodies may damage the nervous system and cause severe symptoms in MS patients, including problems with balance, mobility and fatigue. The antibodies were present in about 23% of MS patients and 7% of control individuals.

"This shows that, whilst these antibody responses are not required for disease development, they may be involved in disease in up to a quarter of MS patients," says Olivia Thomas. "This also demonstrates the high variation between patients, highlighting the need for personalized therapies. Current therapies are effective at reducing relapses in MS but unfortunately, none can prevent [disease progression](#)."

T cells may also be involved

The researchers also found that there is likely a similar cross-reactivity among T cells of the immune system.

"We are now expanding our research to investigate how T cells fight EBV infection and how these immune cells may damage the [nervous system](#) in multiple sclerosis and contribute to disease progression," says Mattias Bronge, affiliated researcher at the Department of Clinical Neuroscience, Karolinska Institutet and shared first author of the paper.

More information: Olivia Thomas, Cross-reactive EBNA1 immunity targets alpha-crystallin B and is associated with multiple sclerosis, *Science Advances* (2023). [DOI: 10.1126/sciadv.adg3032](https://doi.org/10.1126/sciadv.adg3032).
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