Discovery of a mechanism responsible for chronic inflammation in multiple sclerosis

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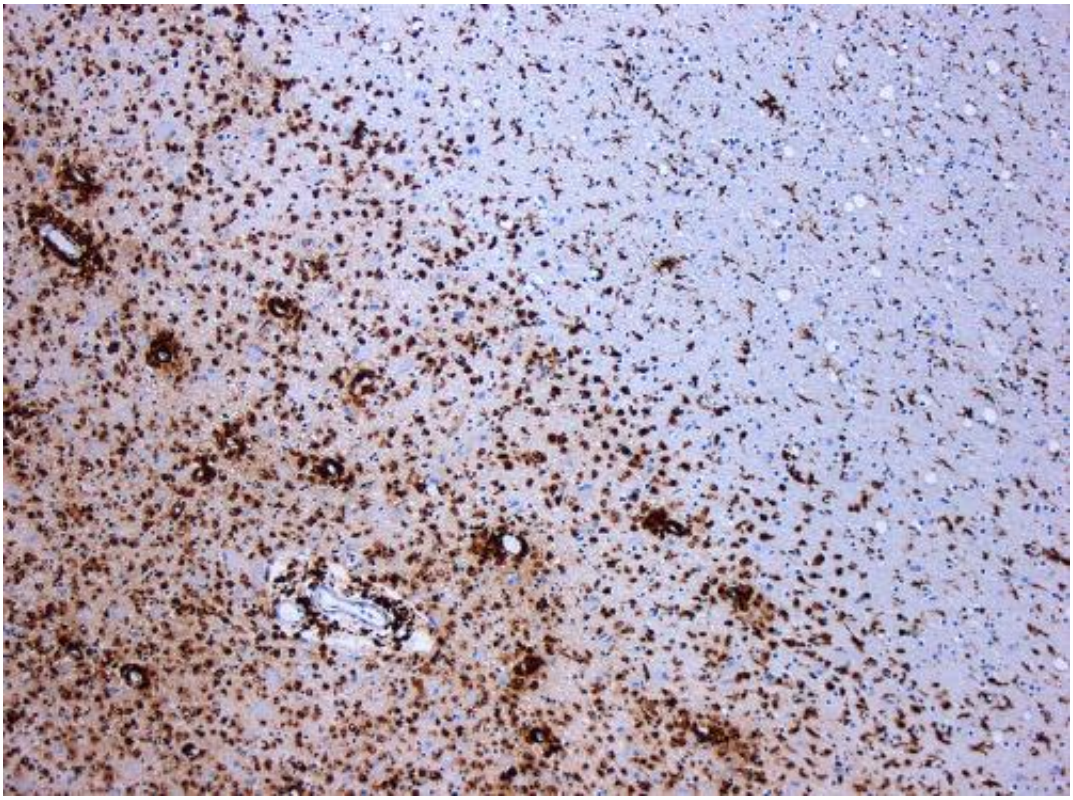

Demyelination by MS. The CD68 colored tissue shows several macrophages in the area of the lesion. Original scale 1:100. Credit: CC BY-SA 3.0 Marvin 101/Wikipedia

Multiple sclerosis (MS) is an autoimmune disease in which the immune system turns on its own cells and attacks them for reasons that are not yet known. Scientists from the Institut Pasteur have shown that ancient

viruses are involved in the acute inflammatory defense response that may contribute to the disease.

Multiple sclerosis (MS) is an incurable inflammatory autoimmune disease that leads to irreversible damage to the brain and spinal cord. It is also associated with the reactivation of ancient viruses that were inserted into human DNA during the evolution of humankind. It was therefore long thought that multiple sclerosis was due to a viral infection.

"Our study shows that reactivation of ancient viruses does not correspond to an infectious phenomenon, but to a defense response of the body when faced with an acute inflammatory phenomenon," explains Christian Muchardt, head of the Epigenetic Regulation Unit at the Institut Pasteur.

Viral sequences were neutralized during evolution and no longer represent a source of infection. But these sequences are a source of external DNA containing information about virus behavior. Cells have therefore been able to control these sequences to detect infections as quickly as possible and turn on their defense genes during an attack.

These viral sequences are used to control defense genes in stem cells. They lie dormant in adult cells, and it is the more traditional sequences that become active. By examining samples from patients with MS, the scientists observed that regulatory sequences of viral origin emerged from their dormant state and were responsible for abnormal expression of several pro-inflammatory genes.

To conclude, in multiple sclerosis, activation of viral sequences does not correspond to an infectious phenomenon but to the unexpected use of regulatory sequences, leading to chronic excessive inflammation. "The discovery of this mechanism, linked to epigenetic phenomena, may one day pave the way for management of MS using small molecules that

inhibit chromatin modification enzymes," says Christian Muchardt.

More information: Saliha Azébi et al, Expression of endogenous retroviruses reflects increased usage of atypical enhancers in T cells, *The EMBO Journal* (2019). DOI: 10.15252/embj.2018101107

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