

Some genetic causes of ALS may need an epigenetic trigger to activate the disease

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A new research report appearing online in *The FASEB Journal* shows why, for some people, having a genetic predisposition to amyotrophic lateral sclerosis (ALS) may not be enough to actually guarantee having the disease. In short, researchers examined identical twins—one afflicted with familial ALS and one not—and found that environmental factors were likely necessary to alter the expression of some immune genes (epigenetic changes) before the disease could take hold. This discovery may pave the way toward developing preventive strategies for those who are at risk for ALS.

"Inflammation is a cause of damage in the central nervous system in other neurodegenerative diseases, including [mild cognitive impairment](#)," said Milan Fiala, M.D., a senior researcher involved in the work from the David Geffen School of Medicine at the University of California, Los Angeles. "Further studies will show how inflammation can be regulated in different diseases."

To make their discovery, Fiala and colleagues studied a set of identical twins, one with an inherited form of ALS and the other healthy. Both twins had mutations in their genomes related to ALS, but the ALS twin had certain epigenetic changes in the genome suspected to be related to the disease. In particular, the team looked at the production of IL-6 because in previous observations they saw that tocilizumab (an IL-6 receptor antibody) seemed to benefit another ALS patient. In the study they also demonstrated the presence of neurotoxic cytokines in the afflicted twin. Further research is necessary to understand how these

[epigenetic changes](#) relate to actual immune function, and ultimately disease progression.

"We are now beginning to see a number of new clues on both the familial and sporadic ALS pathogenesis landscapes, some quite unanticipated as in this important study," said Thoru Pederson, Ph.D., Editor-in-Chief of *The FASEB Journal*. "Considering the dearth of effective treatments for this devastating disease, all new findings such as these are welcome indeed."

More information: L. Lam et al. Epigenetic changes in T-cell and monocyte signatures and production of neurotoxic cytokines in ALS patients, *The FASEB Journal* (2016). [DOI: 10.1096/fj.201600259RR](https://doi.org/10.1096/fj.201600259RR)

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