

# Receptor variation influences fingolimod efficacy in mouse multiple sclerosis models

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Multiple sclerosis (MS) is an autoimmune disorder that results in demyelination of neurons. The FDA-approved drug fingolimod (Gilenya, FTY-720) modulates signaling by the bioactive lipid sphingosine-1-phosphate (S1P), which is linked to MS pathogenesis. Fingolimod treatment reduces relapse rates and neurologic disability in many individuals with MS; however, the drug is less effective in some patients.

In this issue of *JCI Insight*, May Han of Stanford University and colleagues tested the hypothesis that genetic variants of the [cell surface receptor](#) that responds to S1P, S1PR1, may influence the efficacy of fingolimod. In mouse MS models, fingolimod protected control mice from central nervous system damage, but was not effective in animals expressing an S1PR1 variant that could not be modified by phosphorylation.

Mutant animals had elevated expression of CCR6, a molecule that promotes migration of inflammatory cells, in the central nervous system. Treatment of these mice with fingolimod and an antibody targeting CCR6 delayed disease progression.

The results of this study indicate that S1P1R variation may underlie differential patient responses to fingolimod treatment.

**More information:** Hsing-Chuan Tsai et al, Effects of sphingosine-1-phosphate receptor 1 phosphorylation in response to

FTY720 during neuroinflammation, *JCI Insight* (2016). DOI: [10.1172/jci.insight.86462](https://doi.org/10.1172/jci.insight.86462)

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