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# Molecular Pathways of Chemokine Receptor Desensitization by IL-16 Pertinent to Multiple Sclerosis

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## Article:

### Reduction of CD8+ T lymphocytes in multiple sclerosis patients treated with dimethyl fumarate

Spencer CM, Crabtree-Hartman EC, Lehmann-Horn K, Cree BA, Zamvil SS. Reduction of CD8(+) T lymphocytes in multiple sclerosis patients treated with dimethyl fumarate. *Neurol Neuroimmunol Neuroinflamm*. 2015 Feb 12;2(3):e76. doi: 10.1212/NXI.0000000000000076

## Letter in Response to Above Article:

### Molecular pathways of chemokine receptor desensitization by IL-16 pertinent to multiple sclerosis

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Multiple sclerosis (MS) is a progressive, autoimmune CD4+ T cell - mediated, inflammatory, demyelinating disease of central nervous system (CNS). Long-term MS therapy increases risk of opportunistic viral infections due to non-specific immune down-regulation. The important study from Spencer et al. revealed distinct changes within lymphocyte and leukocyte subsets in MS patients treated with dimethyl fumarate (DMF). [1]

An overall reduction in immune cell counts and pronounced down-regulation of CD8+ T cells weaken innate immune responses to viruses in DMF treated MS patients. Viral infection can trigger autoimmune responses primary to development or progression of MS. Migration of chemokine receptor expressing activated autoimmune cells can be potentially controlled by viral chemokines. Crystallography data revealed interaction between viral vMIP-II and CXCR4. [2] CXCR4 and its endogenous ligand chemokine CXCL12 are implicated in MS. A CD4+ T cell specific chemotactic factor, cytokine IL-16, by binding to CD4 co-receptor induces receptor desensitization of CXCR4 independent of p56lck enzymatic activity. [3] Production of IL-16 corresponds to CD4+ T cell inflammation, demyelination, and axonal degeneration in MS lesions. [4] Multifaceted properties of IL-16 include regulation of autoimmune and viral responses. [5] I propose use of IL-16 in combination MS therapy to avert complications of immune suppression.

1. Spencer CM, Crabtree-Hartman EC, Lehmann-Horn K, et al. Reduction of CD8+ T lymphocytes in multiple sclerosis patients treated with dimethyl fumarate. *Neurol Neuroimmunol Neuroinflamm* 2015;2:e76.
2. Qin L, Kufareva I, Holden LG, et al. Crystal structure of the chemokine receptor CXCR4 in complex with a viral chemokine. *Science* 2015;347:1117-1122.
3. Van Drenth C, Jenkins A, Ledwich L, et al. Desensitization of CXC chemokine receptor 4, mediated by IL-16/CD4, is independent of p56lck enzymatic activity. *J Immuno* 2000;165:6356-6363.

4. Skundric DS, Cai J, Cruikshank WW, Gveric D. Production of IL-16 correlates with CD4+ Th1 inflammation and phosphorylation of axonal cytoskeleton in multiple sclerosis lesions. *J Neuroinflammation* 2006;3:13.

5. Cruikshank W, Little F. Interleukin-16: the ins and outs of regulating T-cell activation. *Crit Rev Immunol* 2008;28:467-483.

For disclosures, please contact the editorial office at [nnjournal@neurology.org](mailto:nnjournal@neurology.org).

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