

The Underlying Cause of Multiple Sclerosis

May 7

Tuesday, 12:30 pm

Billings Building—Rosedale Room



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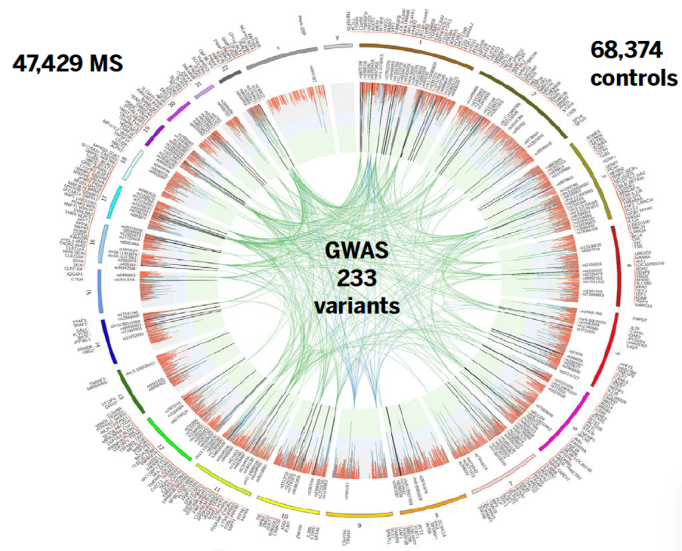
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Abstract

Multiple sclerosis is the most common neurologic disease of young adults. Over the past 30 years, a working model for the disease has emerged based on: 1) the genetic architecture investigated by genome wide associate scans with 233 common genetic variants found predominantly in immune pathways; 2) identification of inflamed myelin reactive T cells in the circulation of patients with MS; 3) loss of immune regulation with dysfunction of FoxP3+ regulatory CD4 cells; (Tregs) 4) epigenetic studies indicating a central role of T cells, Tregs, and B cells in the disease; 5) epidemiologic data strongly indicating that EBV is an environmental factor that may trigger the disease; and 5) finally, the extremely high efficacy of B cell depletion in early relapsing remitting MS with novel mechanisms revealed by this immune intervention. Evidence for this model will be presented and I will explore the question as to whether we know the cause of MS!



Publications:

Sumida TS, Lincoln MR, He L, Park Y, Stillwell HA, Kulminski AM4, Epstein CB, Bernstein BE, Kellis M, **Hafler DA**. Aberrant Short PRDM1 Isoform Drives Dysfunctional Foxp3+ Regulatory T cells in Autoimmune Diseases. *Science Translational Immunology*, in press. bioRxiv 2022.12.02.518871; doi: <https://doi.org/10.1101/2022.12.02.518871>

Wei J, Moon J, Yasumizu Y, Zhang L, Radassi K, Buitrago-Pocasangre N, Deerhake ME, Strauli N, Chan A, Herman A, Pedotte R, Raposo C, Tackenberg B, Yim I, Pappalardo J, Longbrake EE, Sumida TS, Axisa PP, **Hafler DA**. Systems Analysis of Immune Changes after B-cell Depletion in Autoimmune Multiple Sclerosis. bioRxiv [Preprint]. 2024 Feb 9:2024.02.07.576204. doi: 10.1101/2024.02.07.576204. PMID: 38370778 Free PMC article. Preprint.

International Multiple Sclerosis Genetics Consortium; MultipleMS Consortium Locus for severity implicates CNS resilience in progression of multiple sclerosis *Nature*. 2023 Jun 28.

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