WHAT'S HAPPENING IN

Neurology® Neuroimmunology & Neuroinflammation

Neurology.org/NN

Abstracts

Articles appearing in the January 2018 issue

MS AHI1 genetic risk promotes IFNγ+ CD4+ T cells

Objective To study the influence of the Abelson helper integration site 1 (*AHI1*) locus associated with multiple sclerosis (MS) susceptibility on CD4+ T-cell function.

Methods We characterized the chromatin state of T cells in the MS-associated *AHI1* linkage disequilibrium (LD) block. The expression and the role of the *AHI1* variant were examined in T cells from genotyped healthy participants who were recruited from the PhenoGenetic Project, and the function of *AHI1* was explored using T cells from *Ahi1* knockout mice.

Results Chromatin state analysis revealed that the LD block containing rs4896153, which is robustly associated with MS susceptibility (odds ratio 1.15, $p = 1.65 \times 10^{-13}$), overlaps with strong enhancer regions that are present in human naive and memory CD4+ T cells. Relative to the rs4896153^{A} protective allele, the rs4896153^{T} susceptibility allele is associated with decreased *AHI1* mRNA expression, specifically in naive CD4+ T cells ($p = 1.73 \times 10^{-74}$, n = 213), and we replicate this effect in an independent set of participants ($p = 2.5 \times 10^{-9}$, n = 32). Functional studies then showed that the rs4896153^{T} risk variant and subsequent decreased *AHI1* expression were associated with reduced CD4+ T-cell proliferation and a specific differentiation into interferon-γ (IFNγ)–positive T cells when compared with the protective rs4896153^{A} allele. This T-cell phenotype was also observed in murine CD4+ T cells with genetic deletion of *Ahi1*.

Conclusions Our findings suggest that the effect of the *AHI1* genetic risk for MS is mediated, in part, by enhancing the development of proinflammatory IFNγ^{+} T cells that have previously been implicated in MS and its mouse models.

NPub.org/N2/9008b

Fingolimod-associated PML with mild IRIS in MS: A clinicopathologic study

Objective To clarify the clinical, neuropathologic, and virologic characteristics of progressive multifocal leukoencephalopathy (PML) and its immune reconstitution inflammatory syndrome (IRIS) in a patient with fingolimod-treated multiple sclerosis (MS).

Methods Case study.

Results A 34-year-old patient with MS using fingolimod for 4 years had a gradual progression of right hemiparesis and aphasia with a new subcortical white matter lesion in the precentral gyrus by initial MRI. Blood tests were normal, except for lymphopenia (160 cells/μL). One month after the cessation of fingolimod, brain MRI depicted a diffusely exacerbated hyperintensity on fluid-attenuated inversion recovery and diffusion-weighed imaging in the white matter with punctate gadolinium enhancement, suggesting PML-IRIS. A very low level of JC virus (JCV) DNA (15 copies/mL) was detected in the CSF as judged by quantitative PCR. Brain tissues were biopsied from the left frontal lesion, which showed some small demyelinated foci with predominant loss of myelin-associated glycoprotein with infiltrations of lymphocytes and macrophages, but clear viral inclusion was not observed with hematoxylin & eosin staining. JCV DNA was uniquely detectable in an active inflammatory demyelinating lesion by in situ hybridization, possibly suggesting an early phase of PML. DNA extracted from the brain sample was positive for JCV DNA (151 copies/cell). It took 3 months to normalize the blood lymphocyte count. The patient was treated with 1 g IV methylprednisolone for 3 days and a weekly oral dose (375 mg) of mefloquine, and her symptoms gradually improved.

Conclusion Low CSF JCV DNA and unfound viral inclusions initially made diagnosis difficult. The clinical course of fingolimod-associated PML may be associated with mild immune reconstitution.

NPub.org/N2/9009b

Most-Read Articles

As of February 23, 2018

Pleocytosis is not fully responsible for low CSF glucose in meningitis

M.O. Baud, J.R. Vitt, N.M. Robbins, et al. 2018;5:e425. doi.org/10.1212/NXI.0000000000000425

Characterization of lymphopenia in patients with MS treated with dimethyl fumarate and fingolimod

M. Nakhaei-Nejad, D. Barilla, C.H. Lee, G. Blevins, and F. Giuliani. 2018;5:e432. doi.org/10.1212/NXI.0000000000000432

Proinflammatory B-cell profile in the early phases of MS predicts active disease

T. Guerrier, M. Labalette, D. Launay, et al. 2018;5:e431. doi.org/10.1212/NXI.0000000000000431

Neurofilament light chain predicts disease activity in relapsing-remitting MS

K.N. Varhaug, C. Barro, K. Bjørnevik, et al. 2018;5:e422. doi.org/10.1212/NXI.0000000000000422

Serum neurofilament light chain in relapsing-remitting MS: Unchaining disease activity prediction?

R.A. Marrie. 2018;5:e421. doi.org/10.1212/NXI.0000000000000421

