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Abstracts

Articles appearing in the January 2018 issue

Immune response to vaccines is maintained in patients treated with dimethyl fumarate

Objective To investigate immune response to vaccinations in patients with relapsing forms of multiple sclerosis treated with delayed-release dimethyl fumarate (DMF) vs nonpegylated interferon (IFN).

Methods In this open-label, multicenter study (clinicaltrials.gov NCT02097849), patients received 3 vaccinations: (1) tetanus diphtheria toxoid to test T cell–dependent recall response; (2) pneumococcal vaccine polyvalent to test T cell–independent humoral response; and (3) meningococcal (groups A, C, W-135, and Y) oligosaccharide CRM_{197} conjugate to test T cell–dependent neoantigen response. Eligible patients were 18–55 years of age, diagnosed with relapsing-remitting multiple sclerosis (RRMS), and treated for ≥6 months with DMF or for ≥3 months with nonpegylated IFN. Primary endpoint was the proportion of patients with ≥2-fold rise in antitetanus serum immunoglobulin G levels from prevaccination to 4 weeks after vaccination.

Results Seventy-one patients (DMF-treated, 38; IFN-treated, 33) were enrolled. Mean age was 45.3 years (range 27–55); 86% were female. Responder rates (≥2-fold rise) to Td vaccination were comparable between DMF- and IFN-treated groups (68% vs 73%). Responder rates (≥2-fold rise) also were similar between DMF- and IFN-treated groups for diphtheria toxoid (58% vs 61%), pneumococcal serotype 3 (66% vs 79%), serotype 8 (95% vs 88%), and meningococcal serogroup C (53% vs 53%), all $p > 0.05$. In a post hoc analysis, no meaningful differences were observed between groups in the proportion of responders when stratified by age category or lymphocyte count.

Conclusions DMF-treated patients mount an immune response to recall, neoantigens, and T cell–independent antigens, which was comparable to that of IFN-treated patients and provided adequate seroprotection.

Classification of evidence This study provides Class II evidence that patients with RRMS treated with DMF respond to vaccinations comparable to IFN-treated patients.

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Multiple sclerosis *AHI1* genetic risk promotes IFN-γ+ 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 was examined in T cells from genotyped healthy participants who were recruited the PhenoGenetic Project, and the function of *AHI1* was explored using T cells from *Ahi1* knockout mice.

Results Chromatin state analysis reveals that the LD block containing rs4896153, 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 the subsequent decreased *AHI1* expression was associated with reduced CD4+ T-cell proliferation and a specific differentiation into IFN-γ-positive T cells when compared to 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 IFN-γ+ T cells that have previously been implicated in MS and its mouse models.

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Most Cited Articles

As of December 15, 2017

Treatment of spontaneous EAE by laquinimod reduces Tfh, B cell aggregates, and disease progression

M. Varrin-Doyer, K.L. Pekarek, C.M. Spencer, et al. 2016;3:e272.

CSF isoprostane levels are a biomarker of oxidative stress in multiple sclerosis

F. Mir, D. Lee, Hl. Ray, S.A. Sadiq 2014;1:e21.

Aquaporin-4 autoimmunity

A. Zekeridou, V.A. Lennon 2015; 2:e110.

Normal volumes and microstructural integrity of deep gray matter structures in AQP4+ NMOSD

C. Finke, J. Heine, F. Pach 2016; 3:e229.

NMDA receptor antibodies associated with distinct white matter syndromes

Y. Hacohen, M. Absoud, C. Hemingway 2014;1:e2.