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Abstracts

Articles appearing in the January 2019 issue

Clinical utility of a molecular signature in inflammatory demyelinating disease

Objective We sought to develop molecular biomarkers of intrathecal inflammation to assist neurologists in identifying patients most likely to benefit from a range of immune therapies.

Methods We used Luminex technology and index determination to search for an inflammatory activity molecular signature (IAMS) in patients with inflammatory demyelinating disease (IDD), other neuroinflammatory diagnoses, and noninflammatory controls. We then followed the clinical characteristics of these patients to find how the presence of the signature might assist in diagnosis and prognosis.

Results A CSF molecular signature consisting of elevated CXCL13, elevated immunoglobulins, normal albumin CSF/serum ratio ($Q_{albumin}$), and minimal elevation of cytokines other than CXCL13 provided diagnostic and prognostic value; absence of the signature in IDD predicted lack of subsequent inflammatory events. The signature outperformed oligoclonal bands, which were frequently false positive for active neuroinflammation.

Conclusions A CSF IAMS may prove useful in the diagnosis and management of patients with IDD and other neuroinflammatory syndromes.

Classification of evidence This study provides Class IV evidence that a CSF IAMS identifies patients with IDD.

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Circulating inflammatory biomarkers are related to cerebrovascular disease in older adults

Objective This investigation aimed at examining whether circulating inflammatory biomarkers C-reactive protein (CRP), interleukin-6 (IL6), and alpha 1-antichymotrypsin (ACT) were related to cerebrovascular disease (CVD) assessed by MRI.

Methods The study included nondemented elderly participants of a community-based, multiethnic cohort, who received baseline MRI scans and had CRP (n = 508), ACT (435), and IL6 (N = 357) measured by ELISA. Silent brain infarcts and white matter hyperintensities (WMH) were derived from all available MRI scans at baseline, approximately 4.4 years after blood sample collection for inflammatory biomarkers. Repeated assessments of infarcts and WMH, as well as microbleeds assessment, were performed at follow-up MRI visits around 4.5 years later. Cross-sectional and longitudinal relationship between inflammatory biomarkers and CVD were analyzed using appropriate logistic regression models, generalized linear models, or COX models.

Results After adjusting for age, sex, ethnicity, education, *APOE* genotype, and intracranial volume, 1 SD increase in $\log_{10}$IL6 was associated with infarcts on MRI {odds ratio [OR] (95% confidence interval [CI]) = 1.28 [1.02–1.60], p = 0.033}, and 1 SD increase in $\log_{10}$CRP and $\log_{10}$ACT was associated with microbleeds (OR [95% CI] = 1.46 [1.02–2.09], p = 0.041; and 1.65 [1.11–2.46], p = 0.013; respectively). One SD increase in $\log_{10}$ACT was also associated with larger WMH at the follow-up MRI (b = 0.103, p= 0.012) and increased accumulation of WMH volume (b = 0.062, p = 0.041) during follow-up. The associations remained significant after additional adjustment of vascular risk factors and excluding participants with clinical stroke.

Interpretation Among older adults, increased circulating inflammatory biomarkers were associated with the presence of infarcts and microbleeds, WMH burden, and progression of WMH.

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V. Lennon, A. Zekeridou. 2015;2: e110. doi.org/10.1212/NXI.0000000000000110

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C. Finke, J. Heine, F. Pache, et al. 2016;3:e229. doi.org/10.1212/NXI.0000000000000229

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C.M. Spencer, E.C. Crabtree-Hartman, K. Lehmann-Horn, B.A.C. Cree, S.S. Zamvil. 2015;2: e76. doi.org/10.1212/NXI.0000000000000076

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. doi.org/10.1212/NXI.0000000000000272

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E. Rissanen, J. Tuisku, T. Vahlberg, et al. 2019;3:e443. doi.org/10.1212/NXI.0000000000000443