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Abstracts

Articles appearing in the January 2018 issue

Anti-LINGO-1 has no detectable immunomodulatory effects in preclinical and phase 1 studies

Objective To evaluate if anti-LINGO-1 antibody has immunomodulatory effects.

Methods Human peripheral blood mononuclear cells (hPBMCs), rat splenocytes, and rat CD4+ T cells were assessed to determine if LINGO-1 was expressed and inducible. Anti-LINGO-1 Li81 (0.1–30 μg/mL) effect on proliferation/cytokine production was assessed in purified rat CD4+ T cells and hPBMCs stimulated with antibodies to CD3 ± CD28. In humans, the effect of 2 opicinumab (anti-LINGO-1/BIIB033; 30, 60, 100 mg/kg) or placebo IV administrations was evaluated in RNA from blood and CSF samples taken before and after administration in phase 1 clinical trials; paired samples were assessed for differentially expressed genes by microarray. RNA from human CSF cell pellets was analyzed by quantitative real-time PCR for changes in transcripts representative of cell types, activation markers, and soluble proteins of the adaptive/innate immune systems. ELISA quantitated levels of CXCL13 protein in human CSF supernatants.

Results LINGO-1 is not expressed in hPBMCs, rat splenocytes, or rat CD4+ T cells; LINGO-1 blockade with Li81 did not affect T-cell proliferation or cytokine production from purified rat CD4+ T cells or hPBMCs. LINGO-1 blockade with opicinumab resulted in neither significant changes in immune system gene expression in blood and CSF nor changes in CXCL13 CSF protein levels (clinical studies).

Conclusion These data support the hypothesis that LINGO-1 blockade does not affect immune function.

Classification of evidence This study provides Class II evidence that in patients with multiple sclerosis, opicinumab does not have immunomodulatory effects detected by changes in immune gene transcript expression.

NPub.org/N2/9009a

A multiplex family with GAD65-Abs neurologic syndromes

Objective Neurologic autoimmune syndromes associated with anti–glutamate acid decarboxylase 65 antibodies (GAD65-Abs) are rare and mostly sporadic.

Method We describe a niece and her aunt with GAD65-Abs neurologic syndromes. High-resolution human leukocyte antigen (HLA) typing of Class I and Class II alleles was performed using next-generation sequencing.

Results The proband had cerebellar ataxia and probable limbic encephalitis features while her niece had stiff-person syndrome. Both had high titer of GAD65-Abs in the serum and CSF and showed signs of inflammation in the CSF. Both affected members carried the same rare recombinant DRB1*15:01:01~DQA1*01:02:01~DQB1*05:02:01 haplotype, which may or may not be involved in disease susceptibility. Interestingly, other unaffected members of the family had either the same HLA haplotype but normal serum GAD65-Abs or had different HLA types but high titer of serum GAD65-Abs without neurologic symptoms, suggesting cumulative effects.

Conclusion This unique association strengthens the concept that hereditary factors, possibly including specific HLA haplotypes, play a role in neurologic syndromes associated with GAD65-Abs.

NPub.org/N2/9010b

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