Docket #: S18-510

Method to Diagnose Narcolepsy

Researchers at Stanford have developed methods to improve the diagnosis of narcolepsy. Narcolepsy is a disorder in which people experience excessive sleepiness and uncontrollable episodes of falling asleep. Narcolepsy is caused by the loss of specialized neurons that supply hypocretin (HCRT), a critical sleep-wake control hormone. There is no cure for the disease and diagnosis can be complicated as it requires specialized tests that can only be performed in sleep labs or clinics. It would be beneficial to have better methods for diagnosing narcolepsy.

To help meet this need the inventors took advantage of their recent work showing an autoimmune contribution to the development of narcolepsy. They have identified a specific HCRT peptide autoantigen and linked it to narcolepsy-related CD4+ effector responses mediated by the HLA-DQ6 allele and the T cell receptor alpha (TRA) J24 genetic risk allele. In the blood of narcolepsy patients, there are detectable levels of clonally expanded risk-carrying CD4+ T cells that recognize the specific HCRT peptide through antigen presentation restricted to the HLA-DQ allele. Detection of these autoreactive T cells specific for this HCRT peptide autoantigen can be used as a critical complement to the current methods that require sleep studies and a cerebrospinal fluid test for HCRT levels. This technology provides a new method that may be developed to diagnose narcolepsy without sleep studies.

Stage of research
The inventors have identified HCRT-derived peptides that bind HLA-DQ6 and have identified TRAJ24 risk allele-bearing CD4+ T cell clonotypes that bind these peptides.

Applications

- Narcolepsy diagnosis
- Potential for therapeutic development

Advantages

- New, non-sleep related, diagnostic for narcolepsy
- Provides the first evidence demonstrating DQ6-restricted T cell autoreactivity to any self-protein that is associated with HCRT-producing neurons or that has clear narcolepsy relevance

Publications

- Jiang, W., Birtley, J.R., Hung, S. et al. In vivo clonal expansion and phenotypes of hypocretin-specific CD4+ T cells in narcolepsy patients and controls *Nat Commun* 10, 5247 (2019).

Patents

- Published Application: WO2020132063
- Published Application: 20230160890

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