Washington University in St. Louis
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DRUG TARGET AND BIOMARKER FOR MULTIPLE SCLEROSIS

Klein, Robyn, Williams, Jessica

Han, Nathan

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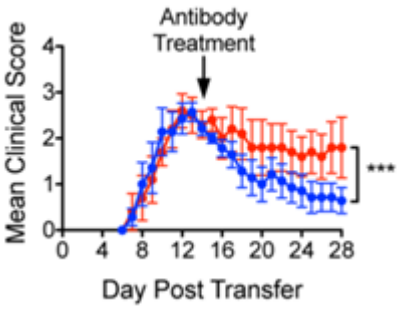
Technology Description

Researchers in Prof. Robyn Klein's laboratory have discovered that interferon lambda (IFN-λ) is a potential target for treating multiple sclerosis (MS), particularly secondary progressive MS (SPMS).

Most patients with MS present with relapsing remitting MS (RRMS) which later progresses to SPMS with increasing clinical deterioration. Currently there are no effective treatments for SPMS. This technology offers a potential SPMS therapy through inhibiting IFN-λ. IFN-λ3 (also known as interleukin 28B, "IL28B") is a cytokine that increases the activity of immune cells which appear to maintain the neuroinflammation underlying multiple sclerosis. Furthermore, IFN-λ3 expression is increased in the brain lesions of patients with SPMS but not those with RRMS. Preliminary studies in a mouse model of MS have demonstrated that a single dose of an antibody that neutralizes IFN-λ3 promotes recovery and significantly improves the clinical MS score of the mice. This therapeutic strategy could be expanded to other drug formats (e.g., small molecule, fusion protein) or to protect against other types of autoimmune inflammation.



In experimental autoimmune encephalomyelitis (EAE) mice, a single dose of Anti-mIL-28b (an antibody that inhibits IFN-λ3) improved clinical scores (blue) compared with control antibody (red).

Stage of Research

- **Human validation** – found increased IFN-λ and IFN-λ receptor expression in brain lesions of patients with SPMS compared with RRMS
- **In vivo mouse studies** – EAE mice (a model of MS) treated with Anti-mIL-28b (an IFN-λ-neutralizing antibody) recovered from EAE symptoms.
- **Future work** - The inventors are planning to develop: a fusion protein that can inhibit IFN-λ; and a hybridoma to produce monoclonal antibodies that neutralize IFN-λ.

Publications

- Manivasagam S, Williams JL, Vollmer LL, Bollman B, … Klein RS. (2022). Targeting IFN-l signaling promotes recovery from central nervous system autoimmunity. *J Immunol* 208(6):1341-1351.

Applications

- **Therapeutic**:
  - targeted treatment for multiple sclerosis or other autoimmune inflammatory disease of the central nervous system
  - demonstrated results with antibody, potential for other drug formats (fusion protein, small molecule)
- **Diagnostic** – IFN-λ as a biomarker for MS

Key Advantages

- **Unmet medical need –** current therapies treat relapsing-remitting multiple sclerosis (RRMS) but there are no therapies for secondary progressive multiple sclerosis (SPMS)
- **Localized effects** – the effects IFN-λ are localized to certain tissues, indicating a lower risk of off-target side-effects if IFN-λ is inhibited

Patents: Pending

Related Web Links: Klein Profile & Lab