Innovations
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Insulin Mimotope for the Identification, Monitoring & Treatment of Type 1 Diabetes

Category
Therapeutic/Diagnostic – Novel Chemical Entity

Problem
Difficulty in monitoring T cell response to T1D therapeutics and developing effective treatment to delay/prevent disease onset

Solution
Mimotope of insulin B chain activates T cells and can elicit Treg response in T1D patients

Intellectual Property
- Issued patent for diagnostic
- Patent pending for therapeutic
- Available for exclusive and nonexclusive licensing

Value Proposition
- Ability to monitor efficacy of T1D therapeutics during administration
- Can be developed as a diagnostic or therapeutic
- Ability to measure response of T cells in peripheral blood samples

Market Attractions
- Predicted 2.2 million T1D cases in USA, 4.7 million worldwide by 2026
- Global T1D market expected to reach 2.8 B US$ by 2025

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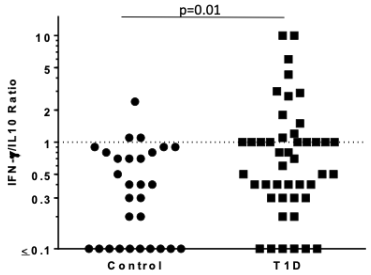
Problem:

Type I diabetes (T1D), the autoimmune form of diabetes, results from T cell-mediated destruction of insulin producing beta cells within pancreatic islets. The disease incidence doubled in the last two decades and, although it is predictable with the measurement of antibodies directed against proteins found in β-cells, T1D onset cannot be prevented. Major efforts at disease prevention have been undertaken with preparations of insulin to induce tolerance and delay the onset of clinical symptoms. Measuring insulin-specific T cell responses from the peripheral blood is a challenging task but doing so would allow the assessment of therapeutic response, which has been a major obstacle in clinical trials of potential drug candidates. Therefore, there exists a need for improved methods of identifying and monitoring T1D-associated T cell responses in individuals, to select and administer individualized therapies to prevent or treat the disease, and to efficiently and effectively monitor T1D disease progression after immune therapies.

Technical Solution and Key Value Propositions:

Dr. Aaron Michels and team at the University of Colorado has developed a mimotope of insulin B chain amino acids 9-23 (B:9-23). These amino acids represent a key epitope for T cells targeting pancreatic beta cells, but the basic arginine residue at B22 is a very poor match for binding to disease relevant HLA molecules. A substitution of glutamic acid for arginine shows a 100-fold better binding to the HLA-DQ8 molecule and allows for binding in a register that activates CD4 T cells in the nonobese mouse model of spontaneous autoimmune diabetes and human peripheral blood. This allows for the ability to measure robust T cell responses in peripheral blood samples from T1D patients with the secretion of the inflammatory cytokine IFN-γ, and can lead to monitoring of therapeutic efficacy in T1D patients (Figure). Interestingly, non-diabetic control subjects also responded to the peptide but with a predominant regulatory phenotype marked the anti-inflammatory cytokine, IL-10. With this data, the team then sought to elicit a regulatory T cell (Treg) response from new onset T1D patients using the same mimotope which showed an expansion of Tregs. When cultured with peripheral blood mononuclear cells, those new-onset T1D patients showed at least a 1.4-fold expansion of CD4+Foxp3+Tregs while there was no change when presented with the wild type insulin B chain peptide. Dr. Michels' data suggests T1D risk is related partly to the nature of insulin-specific T cell response (inflammatory versus regulatory cytokine production), and insulin antigen-specific immunotherapies with the B chain mimotope have the potential to induce regulatory immune responses.



The nature of the T cell response to the insulin B chain mimotope differentiates those with and without T1D. Peripheral blood T cells in controls produce IL-10> IFN-γ, while new-onset T1D secrete IFN-γ > Il-10.

Resources & Documents

Proc Natl Acad Sci U S A. 2015 Apr 7;112(14):4429-34

"Insulin Mimotopes and Methods of Using the Same" US201562103429P