Full-Length Znt8 Self-Antigen for Type 1 Diabetes Diagnosis

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Technology description

Unmet Need

Type I diabetes (T1D) is an autoimmune disorder characterized by destruction of pancreatic beta-cells, leading to insulin deficiency and high blood glucose levels. In 2015, 1.3 million Americans had T1D, with approximately 1.5 million new cases of diabetes diagnosed each year. Despite advances in research, the incidence of T1D in children continues to increase by 3-5% annually, indicating a need for highly sensitive and specific diagnostics. The detection of T1D autoantibodies, including those against insulin, islet antigen 2 (IA2), and glutamic acid decarboxylase (GAD), can predict one’ s risk for the onset of symptomatic disease. In addition to these major biomarkers, autoantibodies to zinc transporter 8 (ZnT8A) have recently been identified as another biomarker detected in 60-80% of newly diagnosed T1D cases. Due to the fact that ZnT8A occurs in the prodromal phase of disease prior to clinical onset, including it in biomarker panel would greatly improve accuracy of T1D prediction. However, due to the inability to maintain proper folding of the ZnT8 protein outside of its native environment, existing assays for detecting ZnT8A are limited to only the protein’ s soluble domains. Consequently, in order to improve ZnT8A detection and sensitivity, there is a need for a more effective method to express full length protein in vitro that maintains all accessible autoreactive ZnT8A binding sites for improved T1D prediction and diagnosis, particularly at very early stages of disease.

Technology Overview

The PLR-ZnT8 achieved a 76% sensitivity and 97% specificity, which far surpassed the sensitivities achieved when using only soluble domains of the protein. The researchers also successfully multiplexed the IA2 and GAD proteins with ZnT8 for a more comprehensive assay for the detection of T1D autoantibodies. Although the current studies were accomplished on a plasmonic gold chip (pGOLD), the assay is tunable to other multiplexed systems.

Application area

Johns Hopkins researchers developed a proteoliposome-based full length ZnT8 self-antigen (PLR-ZnT8) for efficient detection of Znt8A.

Advantages

The lipid matrix of the proteliposome provided a protective environment that improved folding and structural stability of ZnT8, allowing for complete access to all autoreactive sites and high affinity capture of ZnT8A from T1D sera.

Institution

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