Novel Risk Prediction and Diagnosis of Type 1 Diabetes using Deamidated Proinsulin

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Technology description

SHORT DESCRIPTION

A diagnostic method to detect autoantibody reactivity for deamidated insulin in diabetes

BACKGROUND

Type 1 diabetes (T1D) is classified as an autoimmune disease. In this disease, the immune system mounts misguided destruction of "self" insulin-producing islet cells while trying to defend against infectious microbes and potentially harmful foreign substances. The exact nature of T1D autoimmunity has yet to be fully understood. A large variety of diagnostic and population screening tests have been developed for various islet autoantibodies, all of which are native forms of protein antigens as testing substrates. However, there are no existing tests that detect anti-islet immune responses to pathogenically modified antigens. Such substrates might enable improved risk stratification and diagnosis of diabetes.

ABSTRACT

Northwestern researchers made a recent discovery-- that insulin undergoes a novel chemical modification called deamidation, making it liable to be recognized as "non-self." Diabetic mouse models confirmed this finding, as these animals produce antibodies that specifically cross-react with deamidated insulin. The abnormal auto-antibodies could be utilized as diagnostic markers and therapeutic targets for T1D. This is the first discovery of its kind in identifying the pathogenic processing of pro-insulin deamidation and the production of auto-antibodies which are arguably causative to T1D onset and progression. In addition to identifying a strong correlation between positive antibody reactivity against deamidated proinsulin and onset of diabetes, the Northwestern researchers also narrowed down the specific portion of antibody reactivity on the deamidated insulin molecule. They have developed a detection method to better diagnose and stratify risk of diabetes patients, using a pair set of normal and deamidated human proinsulin mimotopes. The sequences of these mimotopes can additionally be used to design chimeric antigen receptors in adoptive T cell therapy.

Application area

Risk stratification in pre-onset Type 1 diabetes

Type 1 diabetes diagnostic test
Type 2 diabetes islet health assessment

Advantages

Novel form of insulin, not previously identified
Measurement of neoautoantigenic reactivity against post-translational modification of deamidation, not native autoantigens
Strong correlation between deamidation and disease pathogenesis

Institution

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