Identification of biomarkers of progression to type 1 diabetes

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The incidence of type 1 diabetes (T1D) is increasing at a rate of 3% per year with the most dramatic increases in children diagnosed under the age of five years. The condition results from a breakdown in immune regulation leading to expansion of autoreactive T cells. The presence of specific genetic markers and islet autoantibodies increases risk but the mechanisms dictating why some individuals with ongoing islet autoimmunity do not develop diabetes, or do so only after many years, represents a critical gap in our understanding of the pathogenesis of T1D. The presence of two or more islet autoantibodies in unaffected first degree relatives of individuals with T1D is associated with >25% risk of developing diabetes within 5 years in adults and >50% within 7 years in children. It is however increasingly clear that in some multiple islet autoantibody positive individuals, progression to diabetes is delayed for decades. Through international collaboration, we have identified a unique population of individuals, called "Slow Progressors", who have been positive for two or more islet autoantibodies for more than 10 years but remain diabetes free. Longitudinal serum samples as well as DNA samples are available on most participants. Understanding the nature of relative protection in Slow Progressors and identifying improved biomarkers to predict the rate of progression to type 1 diabetes are the aims of this project. This will involve refining current biomarker assays and comparing proteomic profiles in serum from our well characterised population of slow progressors, with those of islet antibody negative relatives and individuals who progress rapidly to T1D. In this way we hope to identify strategies for delaying or preventing the onset of clinical T1D.