IA-2 autoantibody affinity in children at risk for type 1 diabetes.

Abstract: Autoantibodies to insulinoma-associated protein 2 (IA-2A) are associated with increased risk for type 1 diabetes. Here we examined IA-2A affinity and epitope specificity to assess heterogeneity in response intensity in relation to pathogenesis and diabetes risk in 50 children who were prospectively followed from birth. At first IA-2A appearance, affinity ranged from 10(7) to 10(11)L/mol and was high (>1.0×10(9)L/mol) in 41 (82%) children. IA-2A affinity was not associated with epitope specificity or HLA class II haplotype. On follow-up, affinity increased or remained high, and IA-2A were commonly against epitopes within the protein tyrosine phosphatase-like IA-2 domain and the homologue protein IA-2?. IA-2A were preceded or accompanied by other islet autoantibodies in 49 (98%) children, of which 34 progressed to diabetes. IA-2A affinity did not stratify diabetes risk. In conclusion, the IA-2A response in children is intense with rapid maturation against immunogenic epitopes and a strong association with diabetes development.