Autoantibodies to zinc transporter 8 (ZnT8A) are associated with risk of type 1 diabetes. Apart from the SLC30A8 gene itself, little is known about the genetic basis of ZnT8A. We hypothesise that other loci in addition to SLC30A8 are associated with ZnT8A. The levels of ZnT8A were measured in 2,239 British type 1 diabetic individuals diagnosed before age 17 years, with a median duration of diabetes of 4 years. Cases were tested at over 775,000 loci genome wide (including 53 type 1 diabetes associated regions) for association with positivity for ZnT8A. ZnT8A were also measured in an independent dataset of 855 family members with type 1 diabetes. Only FCRL3 on chromosome 1q23.1 and the HLA class I region were associated with positivity for ZnT8A. rs7522061T>C was the most associated single nucleotide polymorphism (SNP) in the FCRL3 region ($p = 1.13 \times 10^{-16}$). The association was confirmed in the family dataset (pG was the most associated variant in the HLA region ($p = 2.06 \times 10^{-9}$) and $p = 0.0014$ in family cases). The presence of ZnT8A was not associated with HLA-DRB1, HLA-DQB1, HLA-A, HLA-B or HLA-C ($p > 0.05$). Unexpectedly, the two loci associated with the presence of ZnT8A did not alter risk of having type 1 diabetes, and the 53 type 1 diabetes risk loci did not influence positivity for ZnT8A, despite them being disease specific. ZnT8A are not primary...
pathogenic factors in type 1 diabetes. Nevertheless, ZnT8A testing in combination with other autoantibodies facilitates disease prediction, despite the biomarker not being under the same genetic control as the disease.