Zinc Transporter 8 (ZnT8) antibodies

General Information

The assessment of autoantibodies to pancreatic β cell antigens is an important serological marker of type 1 diabetes mellitus (Type 1 DM). The antigens recognised by these antibodies include Zinc transporter 8 (ZnT8), insulinoma associated antigen 2 (IA-2), glutamic acid decarboxylase (GAD) GAD65kDa isoform and insulin.

The epitopes principally recognised by ZnT8 antibodies reside in residues 268-369 of the C terminal domain. Single nucleotide polymorphisms at the 325 residue lead to expression of arginine (R), tryptophan (W) or, rarely, glutamine (Q). Autoantibodies have been discovered that are known to be specific to either the R or W alleles or residue 325 non-specific. Autoantibodies specific to the Q allele are extremely rare. In a study of 1170 children with a genetic predisposition to diabetes, 58 went on to develop ZnT8 autoantibodies. Of these antibodies, the majority (67.7%) could recognise all alleles and only 15.5% were reactive to a single allele, none of which were reactive only to the Q allele (Achenbach et al, 2009). The RSR kit will detect the R, W and reside 325 non-specific alleles.

ZnT8 antibodies can be ordered individually, or as part of a panel containing ZnT8 antibodies, IA-2 antibodies and GAD antibodies.

Assay interferences: Haemolysed and lipaemic samples should not be used.

Laboratory Information

Analyte: Zinc transporter 8 (ZnT8) antibodies

Units: U/mL

Specimen type: Serum (Brown top serum gel bottle)

Frequency of analysis: At initial diagnosis and in patients with suspected type 1 diabetes. Highest accuracy seen at initial presentation.

Turnaround times: 10 days

Specimen transport: At room temperature

Additional/special requirements: None

Method: ELISA

Participation in EQA scheme: UK NEQAS for Diabetic Markers

Clinical information

Interpretation: Autoimmune diabetes associated autoantibodies (ADAA) can be seen before clinical symptoms and used to stratify risk of progression to overt diabetes. In patients without a current diabetes diagnosis the likelihood of progression to diabetes within 5 years increases as additional antibody positivity increases. The 5-year risk of progression with only Islet cell antibody positivity is 2.2% but this increases up to 70% when 3 additional antibodies (including ZnT8, IA-2 and GAD65) are also present (Polly, 2010). ADAA positivity can be lost as islet cell destruction progresses leading to misleading negative results. NG17 states the false negative rate can be reduced by carrying out quantitative tests for 2 different diabetes specific autoantibodies (with at least 1 being positive). Serum C-peptide should be used if there is still diagnostic uncertainty after the use of autoantibody testing.

Reference Range: Negative is <10 U/mL

Achenbach, P., Lampasona, V. and Landherr, U. (2009) Autoantibodies to zinc transporter 8 and SLC30A8 genotype stratify type 1 diabetes risk. *Diabetologia*, **52**, 1881-1888
Polly J. Bingley (2010) Clinical Applications of Diabetes Antibody Testing, *The Journal of Clinical Endocrinology & Metabolism*, **95**, 25–33

(Last updated July 2023)