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Long-term stability of processed beta-cell autoantibodies is related to their immunoglobulin G subclasses. Type 1 diabetes mellitus (T1DM) is characterized by loss of beta-cell function and insulin production, which leads to dependence on exogenous insulin. The role of autoantibodies is important in the immune-mediated destruction of the beta-cells. We studied the long-term stability of two autoantibodies (IA2, GAD65) and their distribution among the immunoglobulin G (IgG) subclasses in a large T1DM population. Two hundred and forty-three T1DM individuals from a register were followed for up to 4 years. At baseline and at yearly follow-up the IgG subclasses of the autoantibodies were measured in plasma using a commercial multiplex immunoassay and the median and interquartile ranges (IQR) of the IgG subclass distributions were determined. The median duration of follow-up was 2.8 years. The proportion of individuals with each autoantibody decreased from 25% (95% CI 19-32) to 16% (95% CI 12-22) for GAD65 and from 32% (95% CI 25-39) to 22% (95% CI 17-28) for IA2. Both autoantibodies decreased in IgG1, IgG2 and IgG3 subclasses but neither of them decreased in IgG4. Individuals without persistent GAD65 autoantibodies had a median GAD65 concentration of 0.8 $\mu\text{g/l}$ (IQR 0.6-1.1) after 2 years, whereas those with persistent autoantibodies had a median concentration of 1.2 $\mu\text{g/l}$ (IQR 0.8-2.2). Individuals without persistent IA2 autoantibodies had a median IA2 concentration of 5.5 $\mu\text{g/l}$ (IQR 3.8-6.9) after 2 years, whereas those with persistent autoantibodies had a median concentration of 5.2 $\mu\text{g/l}$ (IQR 4.1-5.9). The long-term stability of the autoantibodies was characterized by a decrease in the frequency of GAD65- and IA2-positive individuals and their median concentrations



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