HelmholtzZentrum münchen
German Research Center for Environmental Health

Scientific Highlight April 2016

☐ co-ordinated with the Director of the Institute / Research Unit

Institute of Diabetes Research (IDF)

PSP-Element:
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Title of the highlight:
Islet autoantibody phenotypes and incidence in children at increased risk for type 1 diabetes

Keywords:
Incidence . Islet autoantibodies . Type 1 diabetes

Central statement of the highlight in one sentence:
Children of different ages have differing susceptibilities to autoimmunisation against specific beta cell autoantigens.

Text of the highlight:
Autoantibodies that precede type 1 diabetes frequently develop in early childhood and target distinct beta cell proteins. The aim of this study was to determine the heterogeneity of islet autoantibody development and fate. The ages of development of insulin autoantibodies (IAA) and GAD autoantibodies (GADA), followed by multiple islet autoantibodies and progression to diabetes were examined in 2,441 children participating in two German birth cohorts. In 218 children who developed islet autoantibodies, the first islet autoantibody-positive sample was characterised by single IAA in 80 (37%), multiple islet autoantibodies in 68 (31%) and single GADA in 63 (29%) children. Of the children who were single antibody positive at seroconversion, 35 (44%) IAA-positive and 15 (24%) GADA-positive children developed multiple islet autoantibodies. Single persistent antibodies had heterogeneous affinities; GADA were also heterogeneous in their binding to N-terminally truncated GAD65 and in an ELISA. Progression to diabetes occurred in >50% of children within 10 years in all groups that developed multiple islet autoantibodies and in 44% of children with persistent single high-affinity IAA or persistent single GADA that were positive in both a radiobinding assay and ELISA. The earliest autoantibody development was seen in children with single IAA that progressed to multiple islet autoantibodies or in those with persistent high-affinity single IAA, with a

sharp peak in incidence observed at age 9 months. The peak incidence occurred at age 2 years for children who underwent seroconversion directly to multiple islet autoantibodies and at 5 years for children who first seroconverted to GADA and subsequently developed other autoantibodies. Seroconversion to low-affinity IAA or persistent single GADA occurred at alow incidence after the age of 9 months.
Therefore, children of different ages have differing susceptibilities to auto-immunisation against specific beta cell autoantigens.

Publication:
Giannopoulou EZ, **Winkler C,** Chmiel R, Matzke C, Scholz M, **Beyerlein A,** Achenbach P, Bonifacio E, **Ziegler AG**. Islet autoantibody phenotypes and incidence in children at increased risk for type 1 diabetes. Diabetologia. 2015 Oct;58(10):2317-23.

Taking account of the HMGU mission:
Our results show important differences in the temporal immunisation profiles for islet autoantigens. These may imply differences in the aetiology of islet autoimmunity in infancy. We suggest that there may be important benefits to categorising the autoantigen and the age period of autoimmunity development when investigating the genetic and environmental aetiology of type 1 diabetes. We also suggest that these findings could have implications for the timing of antigenspecific prevention using autoantigens such as insulin, proinsulin and GAD.

The internal HMGU co-operation partners with whom the highlight was compiled, if appropriate:
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