Dokumenttyp: journal article

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Abstract: Islet autoimmunity precedes type 1 diabetes and often initiates in childhood. Phenotypic variation in islet autoimmunity relative to the age of its development suggests heterogeneous mechanisms of autoimmune activation. To support this notion, we examined whether serum metabolite profiles differ between children with respect to islet autoantibody status and the age of islet autoantibody development. The study analyzed 29 metabolites of amino acid metabolism and 511 lipids assigned to 12 lipid clusters in children, with a type 1 diabetic parent, who first developed autoantibodies at age 2 years or younger (n = 13), at age 8 years or older (n = 22), or remained autoantibody-negative, and were matched for age, date of birth, and HLA genotypes (n = 35). Ultraperformance liquid chromatography and mass spectroscopy were used to measure metabolites and lipids quantitatively in the first autoantibody-positive and matched autoantibody-negative serum samples and in a second sample after 1 year of follow-up. Differences in the metabolite profiles were observed relative to age and islet autoantibody status. Independent of age-related differences, autoantibody-positive children had higher levels of odd-chain triglycerides and polyunsaturated fatty acid-containing phospholipids than autoantibody-negative children and independent of age at first
autoantibody appearance (P< 0.0001). Consistent with our hypothesis, children who developed autoantibodies by age 2 years had twofold lower concentration of methionine compared with those who developed autoantibodies in late childhood or remained autoantibody-negative (P< 0.0001).

CONCLUSIONS: Distinct metabolic profiles are associated with age and islet autoimmunity. Pathways that use methionine are potentially relevant for developing islet autoantibodies in early infancy.

Zeitschriftentitel / Abkürzung: Diabetes
Jahr: 2011
Band: 60
Heft / Issue: 11
Seiten: 2740-7
Sprache: eng
Print-ISSN: 0012-1797
TUM Einrichtung: Kinderklinik und Poliklinik
Occurences: · Einrichtungen > Fakultäten > Fakultät für Medizin > Kliniken und Institute > Klinik und Poliklinik für Kinderheilkunde und Jugendmedizin > 2011

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