Activation of islet autoreactive naïve T cells in infants is influenced by homeostatic mechanisms and antigen-presenting capacity.

Islet autoimmunity precedes type 1 diabetes onset. We previously found that islet autoimmunity rarely starts before 6 months of age but reaches its highest incidence already at ~1 year of age. We now examine whether homeostatic expansion and immune competence changes seen in a maturating immune system may account for this marked variation in islet autoimmunity risk in the first year of life. We found naïve proinsulin- and GAD65-responsive T cells in cord blood (CB) of healthy newborns, with highest responses observed in children with type 1 diabetes-susceptible HLA-DRB1/DQB1 genotypes. Homeostatic expansion characteristics with increased IL-7 concentrations and enhanced T-cell responsiveness to IL-7 were observed throughout the first year of life. However, the ability of antigen-presenting cells to activate naïve T cells was compromised at birth, and CB monocytes had low surface expression of CD40 and HLA class II. In contrast, antigen presentation and expression of these molecules had reached competent adult levels by the high incidence age of 8 months. We propose that temporal changes in islet autoimmunity seroconversion in infants are a consequence of the changing balance between homeostatic drive and antigen presentation competence. These
findings are relevant for early prevention of type 1 diabetes.