Reduced neonatal regulatory T cell response to microbial stimuli associates with subsequent eczema in high risk infants

ABSTRACT

Background: Regulatory T cells (Treg) play an essential role in early immune programming and shaping the immune response towards a pro-allergic or tolerant state. We evaluated cord blood Treg and cytokine responses to microbial and non-microbial stimuli in infants at high risk of allergic disease and their associations with development of allergic disease in the first year.

Methods: Cord blood mononuclear cells from 72 neonates were cultured with toll-like receptors (TLR2) ligands: lipoteichoic acid (LTA) and heat-killed Lactobacillus rhamnosus GG (HKL); TLR4 ligand: lipopolysaccharide (LPS); ovalbumin (OVA); anti-CD3; or media for 48 h. Treg numbers and Treg cytokines were assessed in relation to allergic disease outcomes during the first year of life (eczema and atopic sensitization).

Results: Infants with eczema (n = 24) had reduced percentages of FoxP3hiCD25hi Treg in LTA ($p = 0.01$, adj $p = 0.005$) and HKL ($p = 0.04$, adj $p = 0.02$) stimulated cultures as well as reduced IL-10 ($p = 0.01$) production following HKL stimulation compared to those without eczema (n = 48). No differences in Treg or cytokine responses to LPS, OVA or anti-CD3 were seen. Infants who developed sensitization had lower percentages of Treg following TLR2 stimulation (but not other stimuli) compared to non-sensitized infants.

Conclusions: High-risk children who develop allergic disease in the first year of life have deficient Treg responses to microbial stimuli but not allergen from the time of birth, which may contribute to failure of immune tolerance development in infancy.

Keywords: Atopic sensitization; Cord blood; Cytokines; Eczema; Infants; Microbial stimuli; Neonates; Regulatory T cell; Toll-like receptor