Divergent Response Profile in Activated Cord Blood T cells from First-born Child Implies Birth-order-associated in Utero Immune Programming

**Background:** First-born children are at higher risk for development of a range of immune-mediated diseases. The underlying mechanism of 'birth-order-effects' on disease risk is largely unknown, but in utero programming of the child's immune system may play a role. **Objective:** We studied the association between birth-order and the functional response of stimulated cord blood T cells. **Method:** Purified cord blood T cells were polyclonally activated with anti-CD3/CD28-coated beads in a subgroup of 28 children enrolled in the COPSAC 2010 birth cohort. Expression levels of seven activation markers on helper and cytotoxic T cells as well as the percentage of CD4$^+$CD25$^+$ T cells were assessed by flow cytometry. Production of IFN-γ, TNF-α, IL-17, IL-4, IL-5, IL-13 and IL-10 was measured in supernatants. **Results:** IL-10 secretion ($P = 0.007$) and CD25 expression on CD4$^+$ helper T cells ($P = 0.0003$) in activated cord blood T cells were selectively reduced in first-born children, while the percentage of CD4$^+$CD25$^+$ cord blood T cells was independent of birth-order. **Conclusion:** First-born infants display a reduced anti-inflammatory profile in T cells at birth. This possible in utero 'birth-order' T cell programming may contribute to later development of immune-mediated diseases by increasing overall immune reactivity in first-born children as compared to younger siblings.