Abstract

Due to high incidence, medical and socioeconomic burden and impact on individual quality of life and productivity, allergic disorders are a crucial issue for 21st century immunology. Much still remains to be elucidated, particularly regarding the very early processes in allergy development. In order to introduce timely, effective preventive measures, novel, more reliable predictive factors of allergy risk also need to be established.

Dysregulation of proper balance between the branches of immune response, particularly unwarranted dominance of Th2, is the underlying cause of allergy. After birth, new immune balance needs to be established to prepare the neonate for adequate reactivity towards newly encountered environmental stimuli. Regulatory T cells (Treg) play a central role in finely setting this balance and inducing tolerance towards harmless environmental antigens, including allergens. Interactions with external factors, most importantly microbiota, modulate this process during the early postnatal "window of opportunity."

Analysis of cord blood Treg of children of allergic mothers uncovered decreased presence of function-associated surface markers and lower production of IL-10. Furthermore, decreased proportion of Helios^{-} induced Treg was observed in children with higher risk of allergy. Together, these findings hint at delayed functional maturation of Treg in the high-risk group, consistent with observation of increased dendritic cell (DC) reactivity of these children.

Supplementation with probiotic bacteria is considered a potentially promising approach for allergy prevention. In our studies, we show that early postnatal colonisation with probiotic *E. coli* strain O83:K24:H31 (EcO83) is able to reduce allergy incidence in colonised children of allergic mothers, likely owing to normalisation of IL-10 and IFN-γ production in the colonised children. This effect may be due to promotion of regulatory responses by EcO83 administration to the neonate. Upon *in vitro* stimulation with EcO83, we observed increase in production of IL-10 and IFN-γ by cord blood mononuclear cells, higher ability of DC to produce IL-10 and higher induction of IL-10^{+} CD4^{+} T cells in coculture with the stimulated DC.

Keywords: Treg, allergy, cord blood, immune regulation, cytokines, probiotics, *E. coli* O83:K24:H31