Induction and characterization of bacterial and fungal-specific T-cell responses

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Summary of the project:
Neonates and infants are very susceptible for infections. The immune system of neonates and infants is clearly distinct from that of adults. Newborns cannot readily mount Th1 cell antibacterial responses. Instead they show a predominance of Th2 immune responses, which, together with the immune regulatory functions, are thought to limit the potential for inflammatory damage, while simultaneously permitting intestinal colonization by commensals.

Yet relatively little research effort has focused on neonatal immune development. To redress this situation we need a more precise understanding of bacterial and fungal-specific T-cell responses. Moreover the characterization of molecular bases of T-cell responses is required.

Introduction:
T cells in human neonates, infants, and adults differ dramatically in the initiation, strength, and stability of their responses. In this study, we investigate cellular mechanisms of $CD4^+$ T cells from neonates, infants and adults to study the antigen specific response to *Staphylococcus aureus*, *Staphylococcus epidermis*, *Bifidobacterium longum biovar infantis*, *Aspergillus fumigatus*, and *Candida albicans.*

Methods:
T cells from surgically excised adenoids, cord blood and peripheral blood from healthy donors were characterized by flow cytometry and functional assays. Intracellular stainings and CFSE-dilution experiments were performed. $CD14^+$ monocytes were incubated with extracts of *Staphylococcus aureus*, *Staphylococcus epidermis*, *Bifidobacterium longum biovar infantis*, *Aspergillus fumigatus*, and *Candida albicans* to stimulate T cells. In addition, cryo tissue sections of the adenoids were analyzed by Imaging Cycler Microscopy (ICM).

Results and discussion:
$CD4^+$ CD45RA and $CD4^+$ CD45R0 T cells proliferate and up regulate the activation-associated molecule CD25 in response to *Staphylococcus aureus*, *Staphylococcus epidermis*, and *Candida albicans*. The antigen-specific T-cell proliferation can be reduced by blockade of HLA-DR.

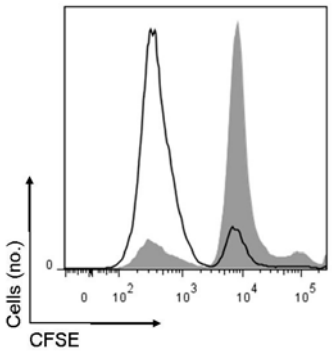

Figure 1: **Staphylococcus aureus-specific T cell response in vitro**. $CD4^+$ CD45RA T cells were isolated from adult donors, labelled with CFSE, and stimulated with monocytes pulsed with Staphylococcus aureus in absence (black line) or presence (gray filled) of an antibody blocking HLA-DR.

High numbers of responsive T cells are identified in human adenoids compared to peripheral blood. An inverse correlation between the percentages of proliferating T cells and age of infants is observed in adenoids.

Functional bacterial and fungal-specific T cells are identified in cord blood, adenoids of infants, and adults with age-dependent characteristics.

Perspectives:
This work highlights the gap between specific T-cell responses of neonates, infants, and adults in terms of quality and quantity.

For therapeutic interventions, an adenoid-specific hierarchical pattern of T cell surface and intracellular makers should be identified in adenoids.

Findings will help to understand the relationship between pathogens and T cells and to optimize intervention strategies.

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