STRONG CHILDREN'S RESEARCH CENTER

Summer 2017 Research Scholar

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ABSTRACT

Title: *Role of IL-21 on Neonatal T-Cell Homeostasis*

Background: Interleukin 21 (IL-21) is a member of the common gamma-chain cytokine family with broad pleiotropic actions. It is primarily expressed in activated CD4+ T-cells and assists in immune and inflammatory responses. IL-21 plays a role in T-cell homeostasis through multiple mechanisms including proliferation, differentiation and apoptosis. IL-7, another common gamma-chain cytokine, has cooperative activity with IL-21 in inducing homeostatic proliferation, and neonatal T-cells are highly sensitive to homeostatic proliferation signals. The effects of IL-21 on neonatal T cells have not been studied. Our research shows that plasma IL-21 correlates with CD31+ T-cells in neonates, and CD31+ T cell frequency is highly dependent on gestational age. This correlation suggests that levels of IL-21 may affect T-cell homeostasis during fetal development. Furthering these findings may improve our knowledge of T-cell function in the neonate, leading to novel immune-targeted therapies. We hypothesize that IL-21, through cooperative common gamma-chain signaling, promotes homeostatic proliferation of neonatal CD31+ T-cells.

Objective: The first objective of this study was to determine the role IL-21 plays in T-cell proliferation, differentiation and cell death. The second objective was to determine if IL-21 was differentially expressed between CD31+/- T-cells. The third objective was to identify phenotype and function of IL-21 producing T-cells in neonates.

Results: This experiment was completed using full term umbilical cord blood (n=10) and healthy adult donor blood (n=1) as a control. Cells were stimulated in vitro with cytokine IL-7+/- IL-21 inhibitor, superantigen+/- IL21 inhibitor, media, and IL-21 inhibitor alone. The cells were then characterized using flow cytometry. Neonatal T-cells were higher in IL-21 producing T-cells compared to the adult. IL-21 was produced mainly by CD31+ T-cells and more highly in CD8 T-cells compared to CD4 T-cells. CD31+ IL-21+ CD8+ T-cells were more highly proliferative compared to CD31+ IL-21+ CD4+ T-cells. Homeostatic receptor expression pattern varied by CD31 expression and with IL-7 stimulation, but was not affected by IL-21. IL-21 also inhibited Il-8 production in both CD4 and CD8 T-cells.

Conclusion: The association between CD31+ T-cells and IL-21 may be due to neonatal CD31+ T-cells producing the IL-21, particularly in the CD8+ subset. There is insufficient data from our experiments to comment on the differential effects of IL-21 on CD31+ and CD31- T-cells. IL-21 may play a role in regulating the major cytokine produced by neonatal T-cells, IL-8. If confirmed, our research will be the first to identify Il-21 as a major cytokine produced by neonatal T cells, potentially regulating neonatal T-cell effector function.