Explore the immunological changes associated with Th22 activation

SMART

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Abstract

Th22 cells, a subset of T helper cells, play an essential role in the body's immune response. Th22 secretion of IL-22 helps with rebuilding alveoli during acute lung injury. However, IL-22 is generally produced in combination with IL-17 by Th17/Th22 cells during an inflammatory state. IL-17 is a proinflammatory cytokine that exacerbates inflammation. Interestingly, polarization of Th22 cells, secretion of IL-22, and the downregulation of IL-17 are controlled by transcription factors such as a ligand-activated aryl hydrocarbon receptor (AHR), which is activated by ligands such as indole-3-carbinol (I3C). Our studies aim to determine whether treatment with I3C affects the expression and secretion of IL-17 and IL-22 in T cells. Towards this, naïve T cells (Th0) and Th22 cells were treated with 25mM of I3C in vitro. After 72 hours, we took supernatants from cultures as well as isolated total RNA for cells. I3C increases the gene expression of IL-22 in Th22 cells and decreases IL-17 secretion. In addition, Il-22 production was increased, and IL-17 was decreased in Th0 cells treated with I3C, but not to the same extent as Th22+I3C cells. However, gene expression of IL-22 was not altered in Th0+I3C, Th22+Veh vs. Th22+I3C cells. Lastly, the expression of AhR and EGLN3, genes associated with Th22 polarization, was decreased in Th22 cells and I3C treated Th0 cells. In conclusion, our studies suggest that AhR ligand I3C-induced immunological changes are associated with the polarization of Th22 secreting IL-22 cells and the downregulation of IL-17.

Introduction

-CD4+ T helper cells play an essential role in the immune response and are classified by the cytokines they release.

-**Th22** cells are a type of T helper cell characterized by the production and release of the cytokine of **IL-22**.

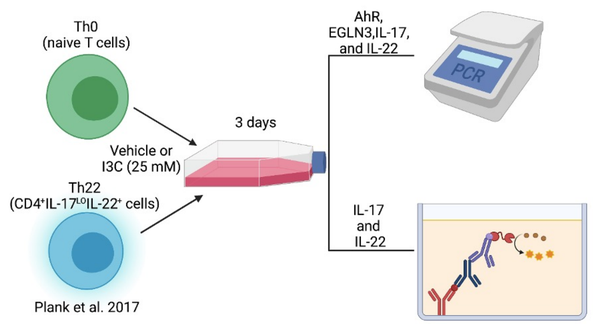
-**IL-22** have been shown to exert anti-inflammatory and tissue rebuild properties.

-However, **IL-22** is generally produced in combination with **IL-17** by **Th17**/**Th22** cells during an inflammatory state.

-**IL-17** is a proinflammatory cytokine that exacerbates inflammation.

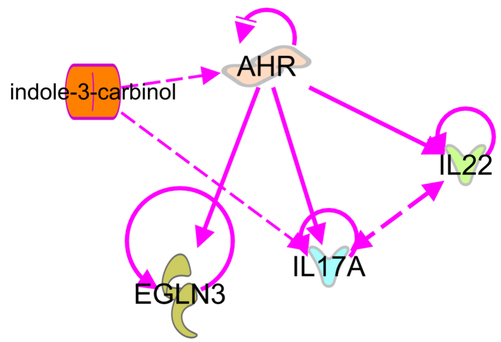
-The polarization of **Th22** cells and the secretion of **IL-22** is controlled by transcription factors such as a ligand-activated aryl hydrocarbon receptor (AHR), which is activated by indole-3-carbinol (I3C), a natural compound found in some vegetables which have shown to decrease **IL-17** production.

Methodology



Research Question

Question: Does the AhR ligand I3C activate AhR, which guides the polarization of Th22 secreting IL-22 cells?



Hypothesis: I3C activates AhR which guides the polarization of Th22 secreting IL-22 cells. A. Ingenuity Pathway Analysis of compounds, genes, and cytokines associated with Th22 polarization.

Results

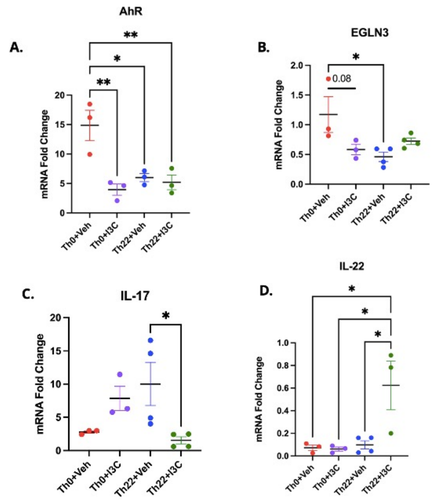


Figure 1. I3C upregulates the gene expression of IL-22 in Th22 cells but downregulates the expression of AhR, IL-17, and EGLN3. A-D. AhR, EGLN3, IL-17, and IL-22 expression detected by RT-PCR.

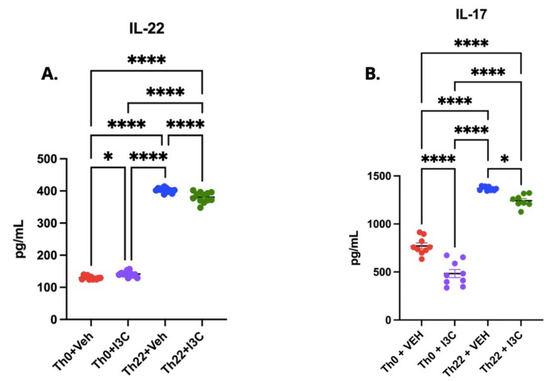
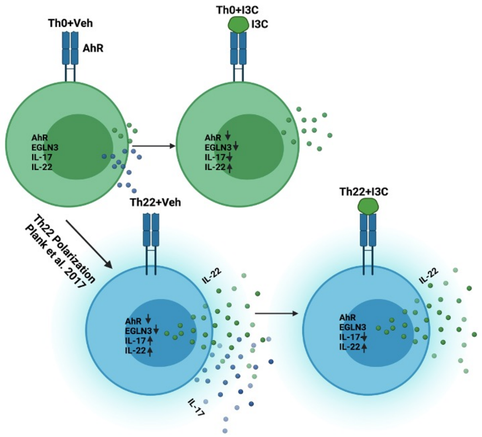


Figure 2. Treatment of Th22 cells with both vehicle and I3C increases the production of IL-22 but I3C decreases the secretion of IL-17 in Th0 and Th22 cells. A. IL-22 protein level detected by ELISA test. B. IL-17 protein level detected by ELISA test

Conclusion



In conclusion, I3C does activate AhR in Th22 cells and guides the polarization of the cells secreting IL-22. The upregulation of IL-22 gene expression and the production of IL-22 without IL-17 in Th22 cells in the presence of I3C points to its role in the differentiation of Th22 cells. Therefore, the immunological changes associated with the polarization of Th22, the secretion of IL-22, and the downregulation of pro-inflammatory cytokine IL-17 are linked to the AhR activated by I3C.

Acknowledgements

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