

Examine the effect of 3,3'-Diindolylmethane(DIM) treatment on cellular metabolism

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Abstract

Diindolylmethane or DIM is made in the body from a chemical called indole-3-carbinol or I3C . I3C can be found in vegetables including cabbage, Brussels sprouts, cauliflower, and broccoli. Both I3C and DIM have shown to help prevent cell death, cancer in cells, and promote cell growth. The aim of our study was to determine if DIM and I3C affect cellular metabolism. We did this by first collecting T-cells from the spleens of mice, and treating cells with 25mM of DIM or I3C to see if reduced or increase genes associated with cellular metabolism. The result that we came up with was that DIM and I3C does increase genes associated with cellular metabolism.

Introduction

3,3'Diindolylmethane(DIM)- a phytonutrient and plant indole found in cruciferous vegetables that is potential beneficial for cells

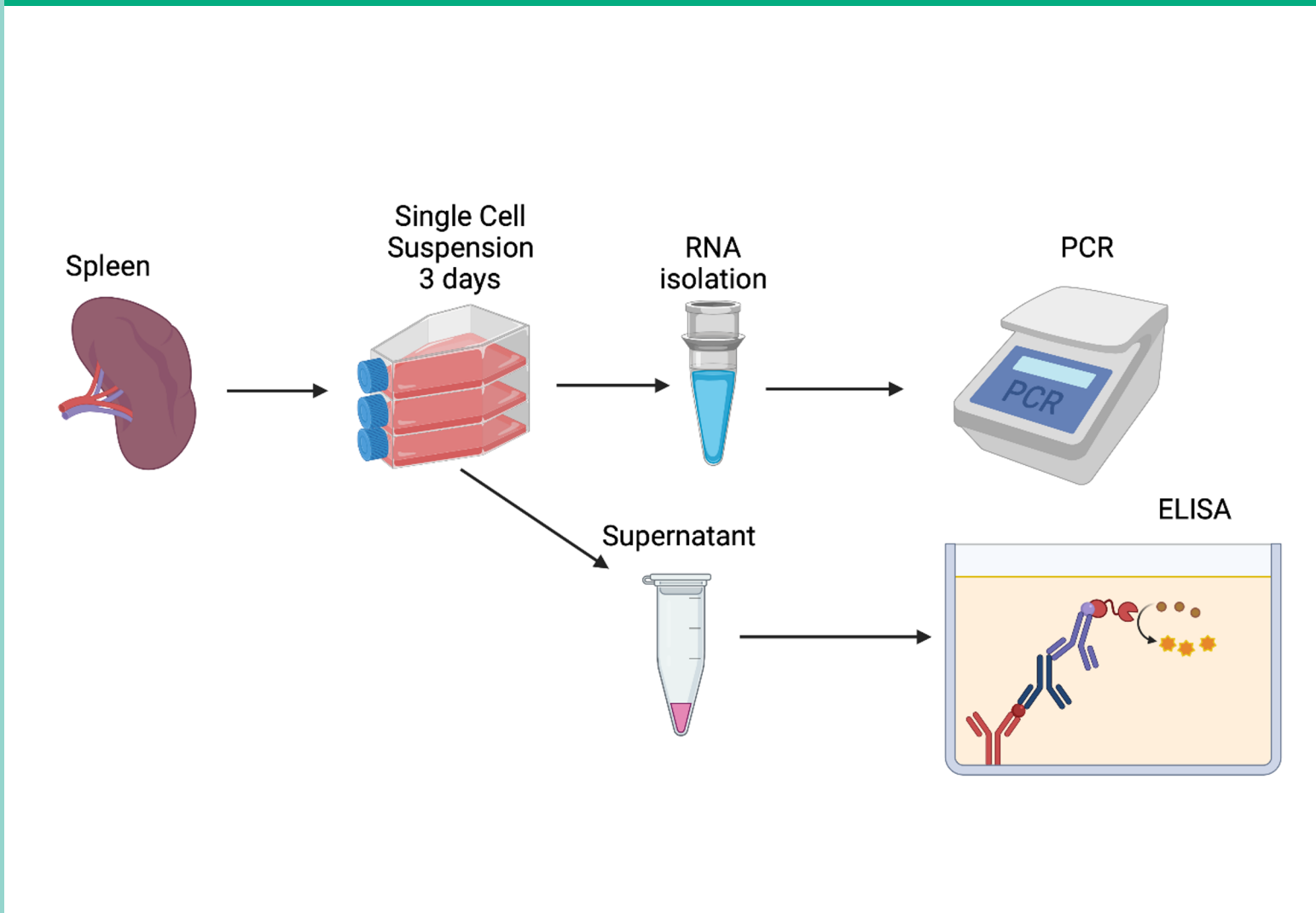
Indole-3-carbinol(I3C)- is produced by the breakdown of glucobrassicin which can be found in cruciferous vegetables

AHR - is a protein that in humans is encoded by the AHR gene. The aryl hydrocarbon receptor is a transcription factor that regulates gene expression.

HIF1A- is a subunit of a heterodimeric transcription factor hypoxia-inducible factor 1 that is encoded by the *HIF1A* gene

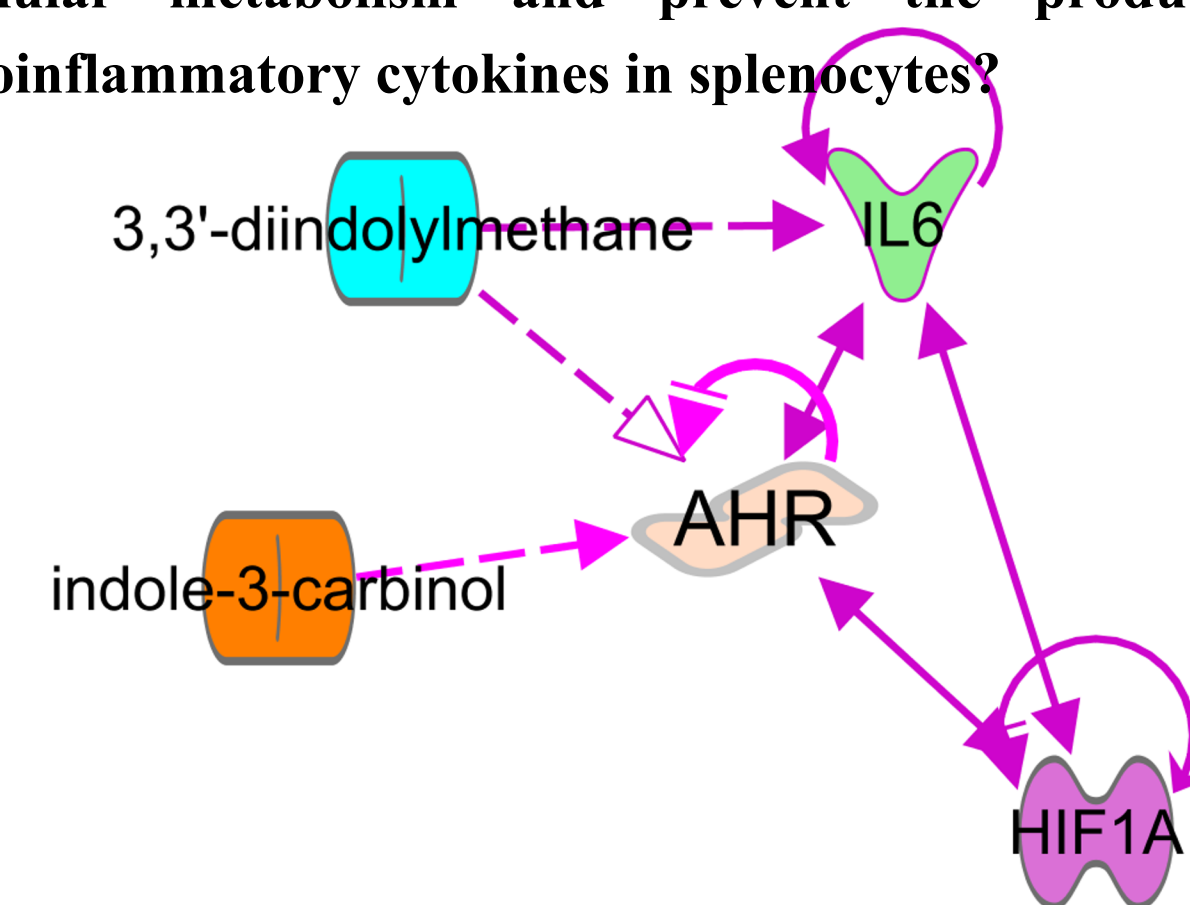
IL6- a proinflammatory cytokine that is produce by many cells that regulate immune cells

Methodology



Research Question

Question: Does DIM and I3C binding to AhR affect cellular metabolism and prevent the production of proinflammatory cytokines in splenocytes?



Symbol	Entrez Gene Name	Location	Family
3,3'-diindolylmethane		Other	chemical drug
AHR	aryl hydrocarbon receptor	Nucleus	ligand-dependent nuclear receptor
HIF1A	hypoxia inducible factor 1 subunit alpha	Nucleus	transcription regulator
IL6	interleukin 6	Extracellular Space	cytokine
indole-3-carbinol		Other	chemical drug

Hypothesis: DIM and I3C activates AhR which downregulates cellular metabolism gene HIF1A and the production of proinflammatory cytokines. A. Ingenuity Pathway Analysis of compounds, genes, and cytokines associated with AhR activation.

Results

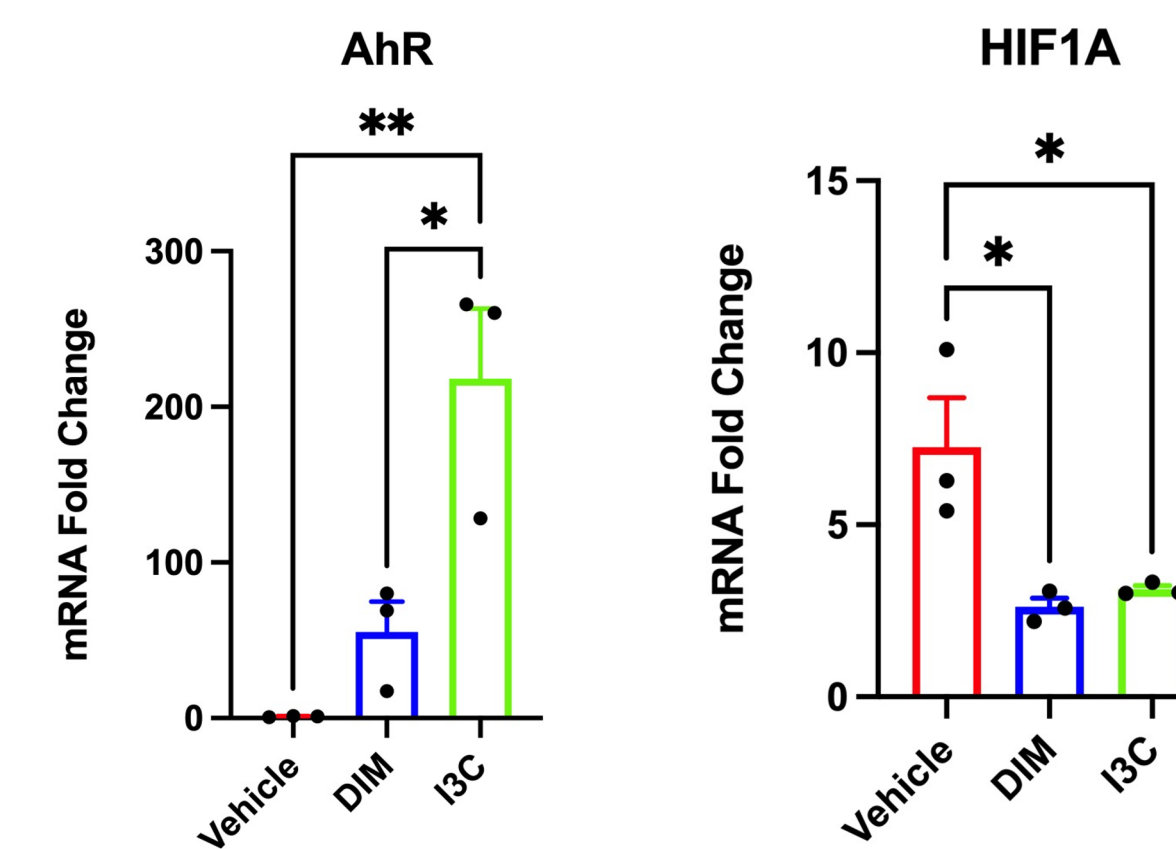


Figure 1. I3C upregulates the gene expression of AhR in splenocytes but downregulates the expression of HIF1A. A-B. AhR and HIF1A expression detected by RT-PCR.

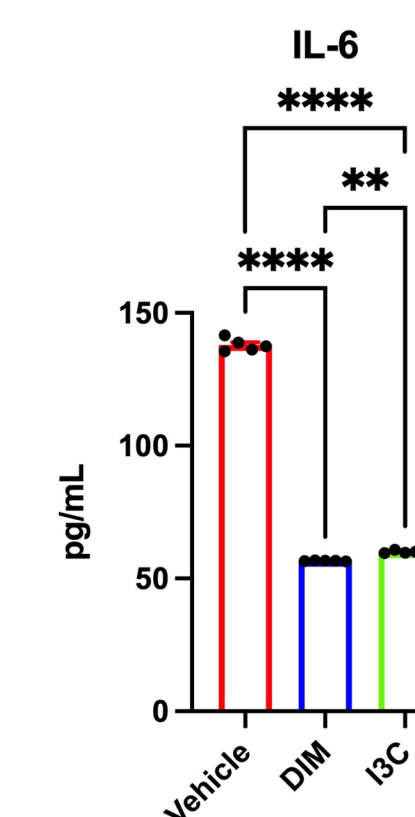


Figure 2. Treatment of splenocytes with both DIM and I3C decreases the production of proinflammatory cytokine IL-6. A. IL-6 protein level detected by ELISA test.

Conclusion

-HIF1A and AhR sense metabolic changes in immune cells and tumor cells.

-HIF1A and AhR drives metabolic reorganization, in which regulates the metabolism of immune cells.

-However, HIF1A and AhR competes for the Aryl hydrocarbon receptor nuclear translocator (ARNT).

-The ARNT translocate HIF1A and AhR bind to different promoter sequences, which leads to varies changes in cellular metabolism.

-In our studies we shown that activation of AhR ligand DIM and I3C upregulates AhR. Conversely, I3C and DIM downregulates HIF1A.

-Lastly, I3C and DIM reduces the production of IL-6 in splenocytes

Acknowledgements

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