The Effects of Dioxin-like Polychlorinated Biphenyls (PCBs) on the Development of Myeloid Suppressor Cells

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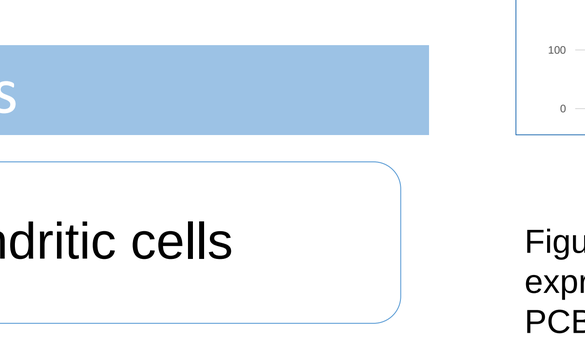
Background

- Polychlorinated biphenyls (PCBs) are man-made organic compounds that are banned in the U.S. due to their estrogen-mimicry.[1]
- PCBs are endocrine-disrupting and have been shown to increase breast cancer risk.[2]
- Increased Estrogen signaling can produce both tumor growth and protective anti-tumor responses.[3]
- Estrogen has two high affinity receptors, Estrogen Receptor α (Erα) and Erβ, which promote cancer through increasing cancer growth factors and inhibiting tumor-suppressing genes.[3]
- Myeloid-derived suppressor cells are immature myeloid cells characterized by its suppression of T cell immune responses and expansion during cancer.
- Estrogens drive Myeloid-derived suppressor cell accumulation.[3,4,5]
- PCB-138 and PCB-153 are the most common forms of PCB.
- PCBs could have cancer-causing properties due to increased development of myeloid-derived suppressor cells through estrogen mimicry.



Chemical composition of PCB-138.[6]

Specific Aims

- Scientific Question: What are the effects of PCB-138 and PCB-153 in Myeloid-derived suppressor cell growth?
- Hypothesis: PCB-138 and 153 will positively influence the production of Myeloid-derived suppressor cells through their ability to mimic estrogen and produce estrogenic effects in the body.

Methods

Culture dendritic cells

Flow cytometry- MDSC

ELISA - MDSC

Isolate T cells

T cell proliferation - MTT

T cell skewing - ELISA

Results

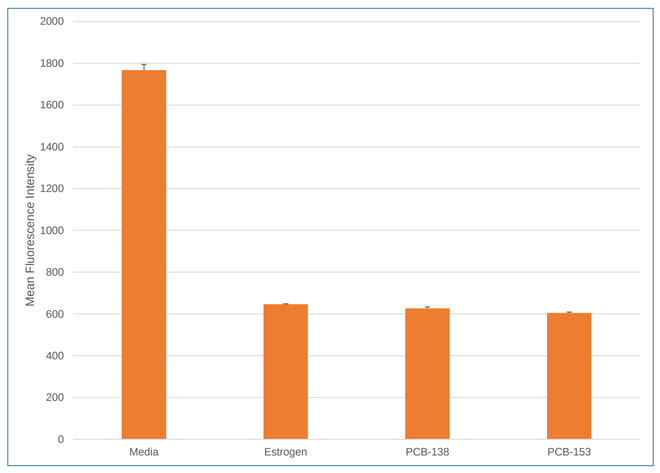


Figure 1A: CD80 Averages

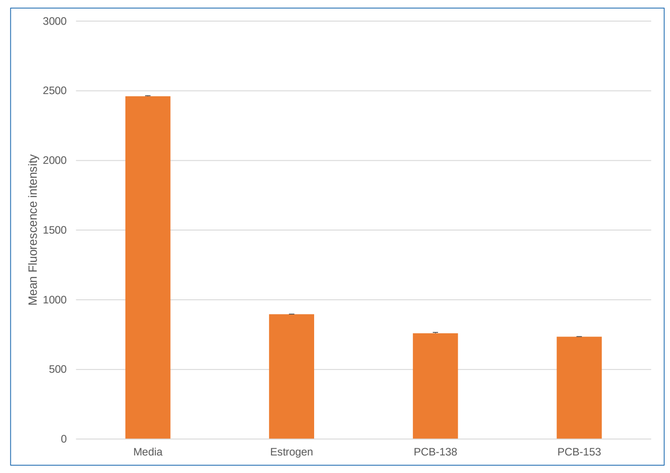


Figure 2B: MHC II Averages

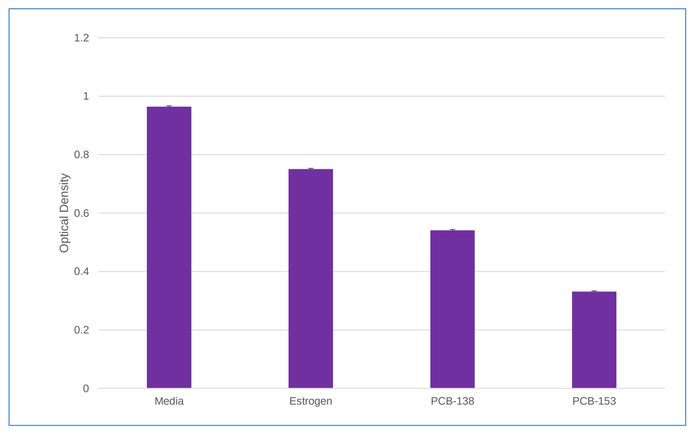


Figure 2: MTT assay

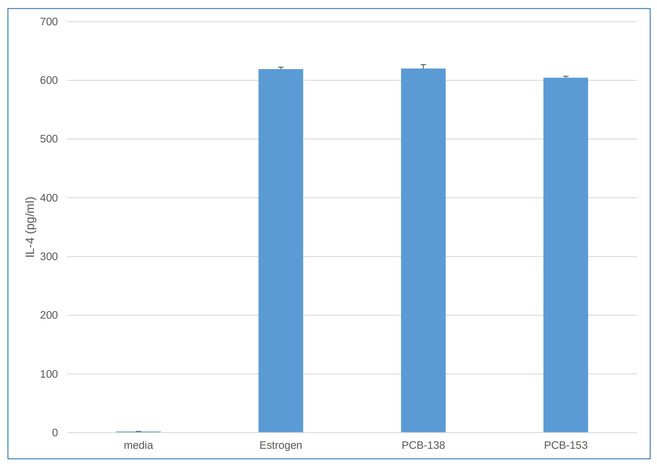


Figure 3A: IL-4 ELISA Data

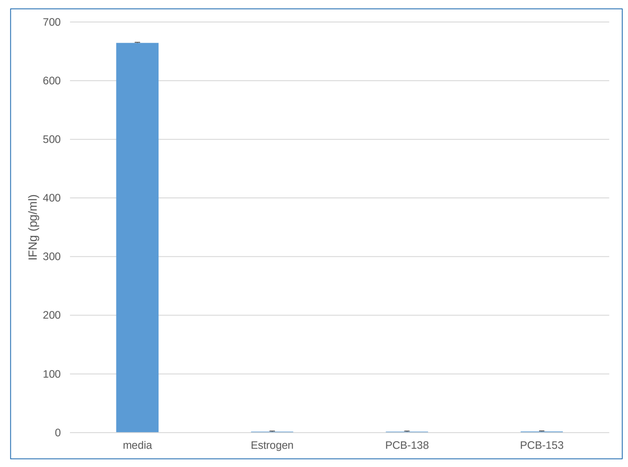


Figure 3B: IFNg ELISA Data

Figure 1: Flow cytometry was conducted to the amount of (A) CD80 and (B) MHCII expression in media, estrogen, PCB-138 and PCB-153. Averages are shown. Estrogen, PCB-138, and PCB-153 inhibited MHCII and CD80 expression compared to controls. Both PCB-138 and PCB-153 showed significantly higher CD80 and MHCII expression than estrogen ($p<0.05$).
Figure 2. MTT averages were taken of media, estrogen, PCB-138 and PCB-153 to measure cell proliferation. Estrogen and PCB-138 averages were significantly higher than PCB-153.
Figure 3. ELISA assay was used to determine IL-4 and IFNg secretion levels in media, estrogen, PCB-138 and PCB-153. Averages are shown for (A) IL-4 and (B) IFNg. PCB-138 IL-4 secretion was significantly higher than Estrogen and PCB-153 ($p<0.05$). IFNg secretion was not statistically significant between estrogen, PCB-138, and PCB-153 ($p>0.05$).

Conclusions

- Results conferred with past research showing similarly estrogenic effects in PCB-138 and PCB-153.
- Decreases in MDSC cytokine markers CD80 and MHCII displayed an even greater effect in PCBs on immune responses than estrogen.
- PCB-138 displayed a significant difference in cell proliferation compared to PCB-153. Similar levels were seen in estrogen.
- Pro-inflammatory markers IL-4 and IFNg for PCB-138 and PCB-153 were at levels similar to estrogen compared to controls. PCB-138 maintained significantly higher IL-4 secretion compared to Estrogen or PCB-153
- Further study is needed to ascertain whether other forms of PCB similarly drive myeloid-derived suppressor cells and to what extent.

Citations

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3. Conejo-Garcia, Jose et al. Estrogens drive myeloid-derived suppressor cell accumulation. *Oncoscience* vol. 4,1-2 5-6. 24 Feb. 2017.
4. Atretkhany K-SN, Drutskaya MS. Myeloid-derived suppressor cells and proinflammatory cytokines as targets for cancer therapy. 2016;81(11):1274–1283.
5. Svoronos N, et al. Tumor Cell–Independent Estrogen Signaling Drives Disease Progression through Mobilization of Myeloid-Derived Suppressor Cells. 2016;7(1):72–85.
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