



# Effects of estrogen-mimicking compounds, progesterone and estriol, on myeloid-derived suppressor cell development

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## Background

- Myeloid-derived suppressor cells are immature myeloid cells that suppress immunity. MDSCs are known to inhibit T cell responses.
- Estrogen is the primary female hormone that oversees regulation of puberty and menstruation.
- Estrogen is known to play a role in breast cancer development and the amount of MDSCs present.

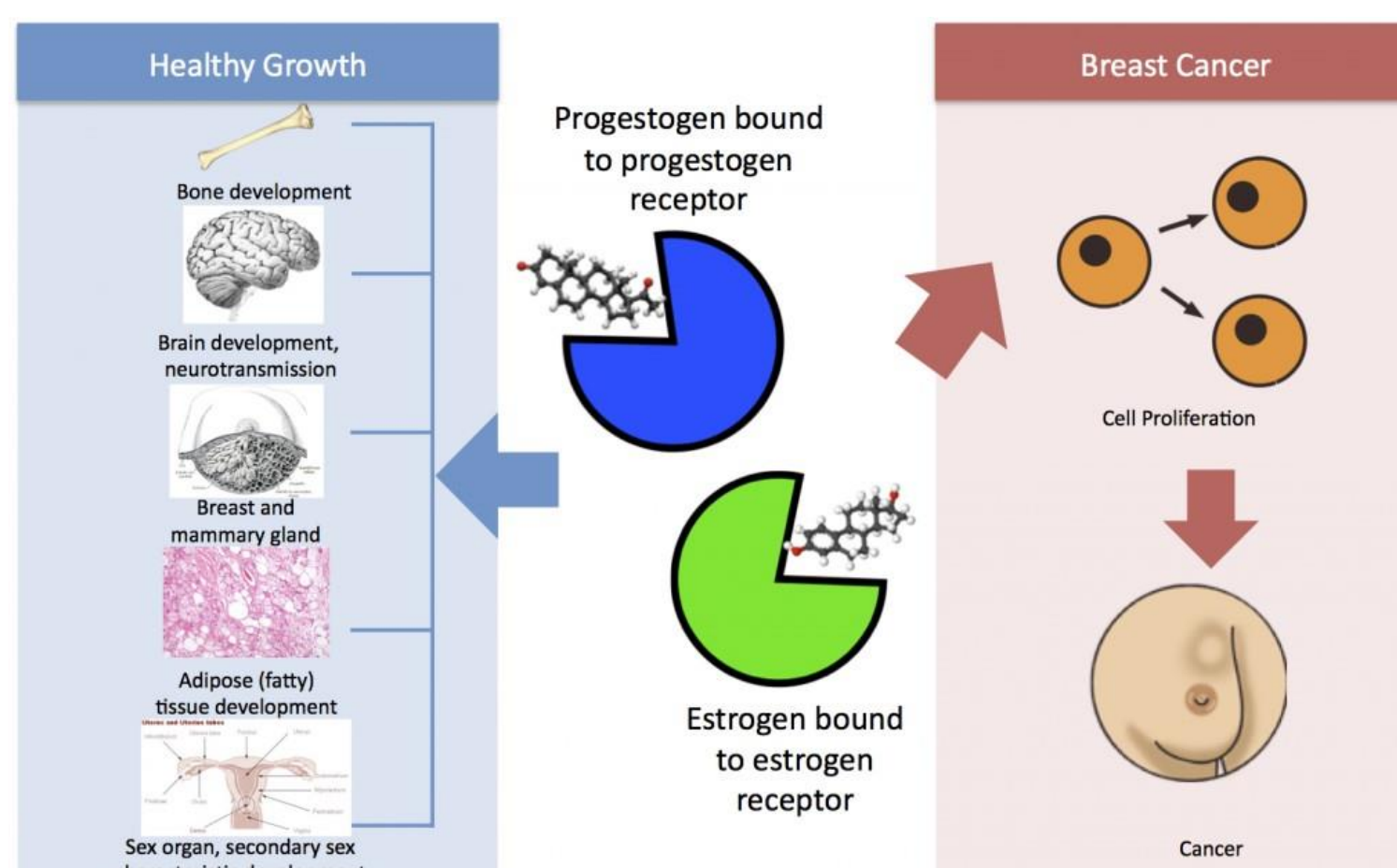


Figure 1: Effect of progesterone and estrogen on the body: Progesterone is shown to help bones and tissues grow, whereas progesterone and estrogen can cause cell proliferation

- Progesterone is a steroid sex hormone found in the body that is associated with menstruation and is commonly found in oral contraceptive pills.
- When your body is being exposed to progesterone in this form it can cause uncomfortable side effects like, emotional changes, abdominal pain, headache.

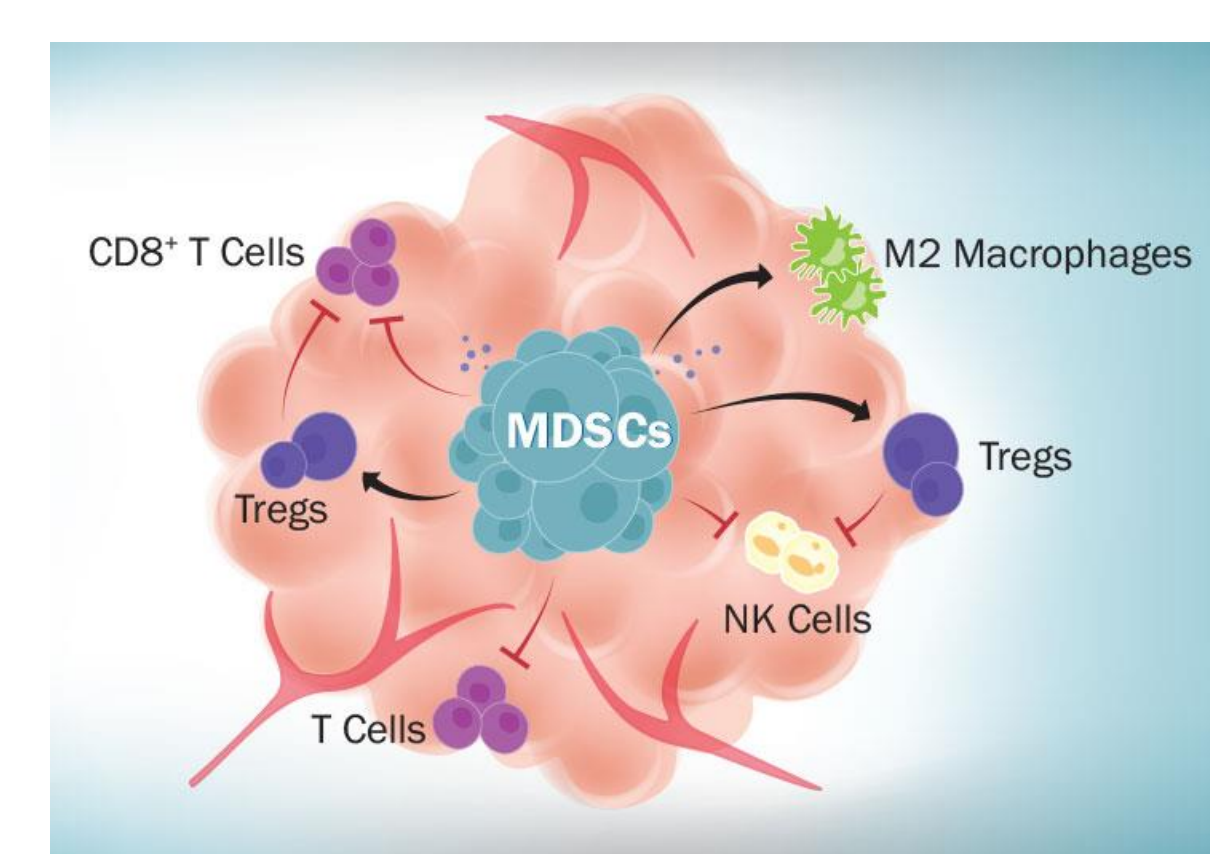
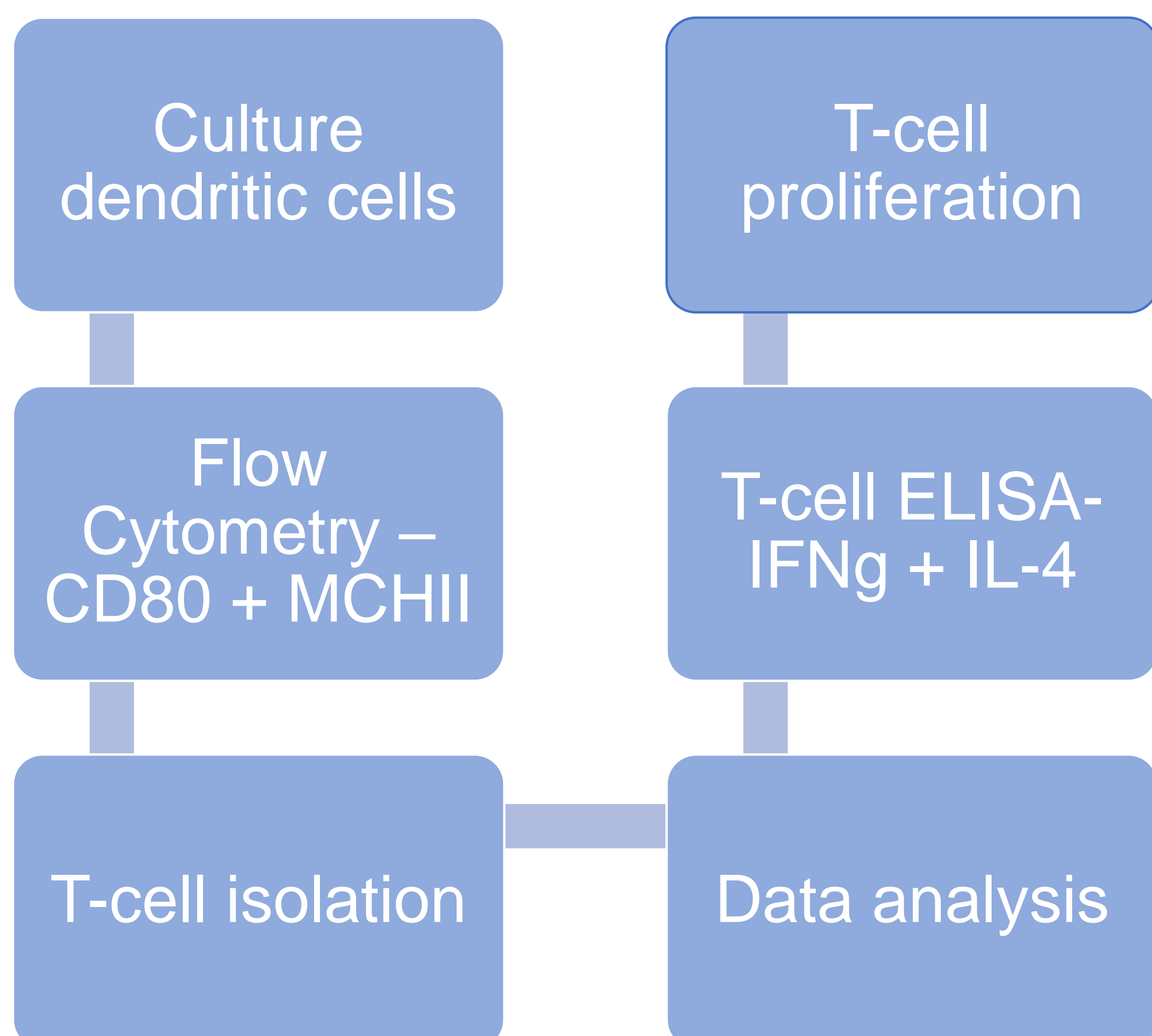


Figure 2: MDSCs in a tumor microenvironment. MDSCs suppress the activation of T cells and NK cells while activating macrophages and Tregs.

## Specific Aim

- Does Progesterone and Estradiol increase MDSC activity similar to Estrogen?
- Conducting Flow cytometry, T-cell isolation, T-cell proliferation, and ELISA help to determine the production of MHC II and B7.
- Progesterone and Estriol will both have a decreased production of MHC II and B7

## Methods



## Results

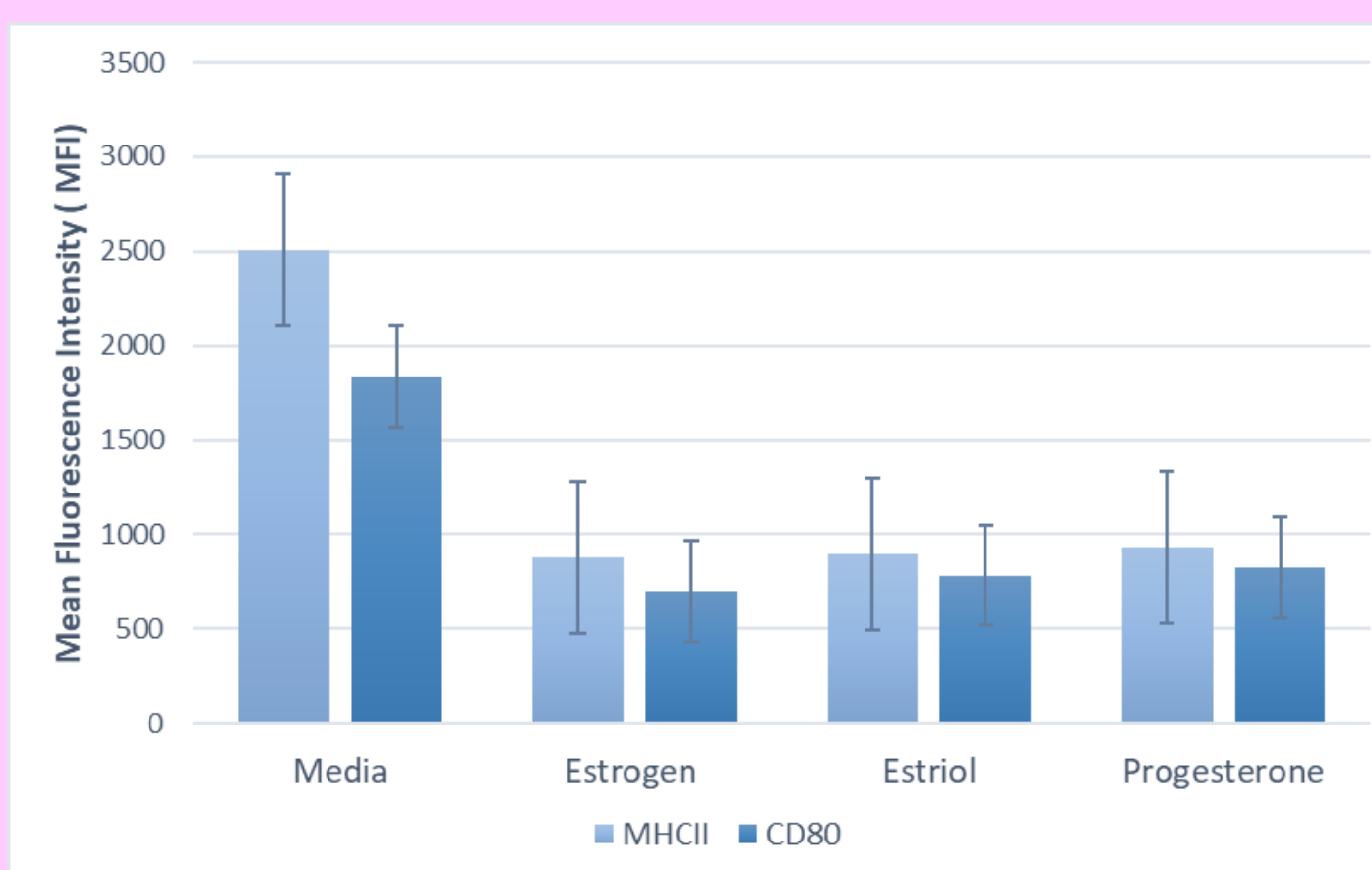


Figure 3: Mean Fluorescence Intensity (MFI): Flow cytometry was used to measure the mean fluorescence intensity. MCHII and CD80 expression was increased in the presence of progesterone. By using a 2 sample T test significant differences were found between MCHII and CD80 in the media ( $p=3.0301E-7$ ) and estrogen ( $p=7.291E-10$ ).

Figure 4: Cytokine expression in the presence of different hormones. IL-4 secretion was measured by an ELISA test and there was no significant difference in IL-4 expression between the different hormones. IFNg expression was measured by an ELISA test. By using a 2 sample T test significant differences were found between each compound – Media ( $p=2.973E-10$ ), Estrogen ( $p=2.004E-10$ ), Estriol ( $p=7.14E-10$ ), Progesterone ( $p=1.749E-10$ )

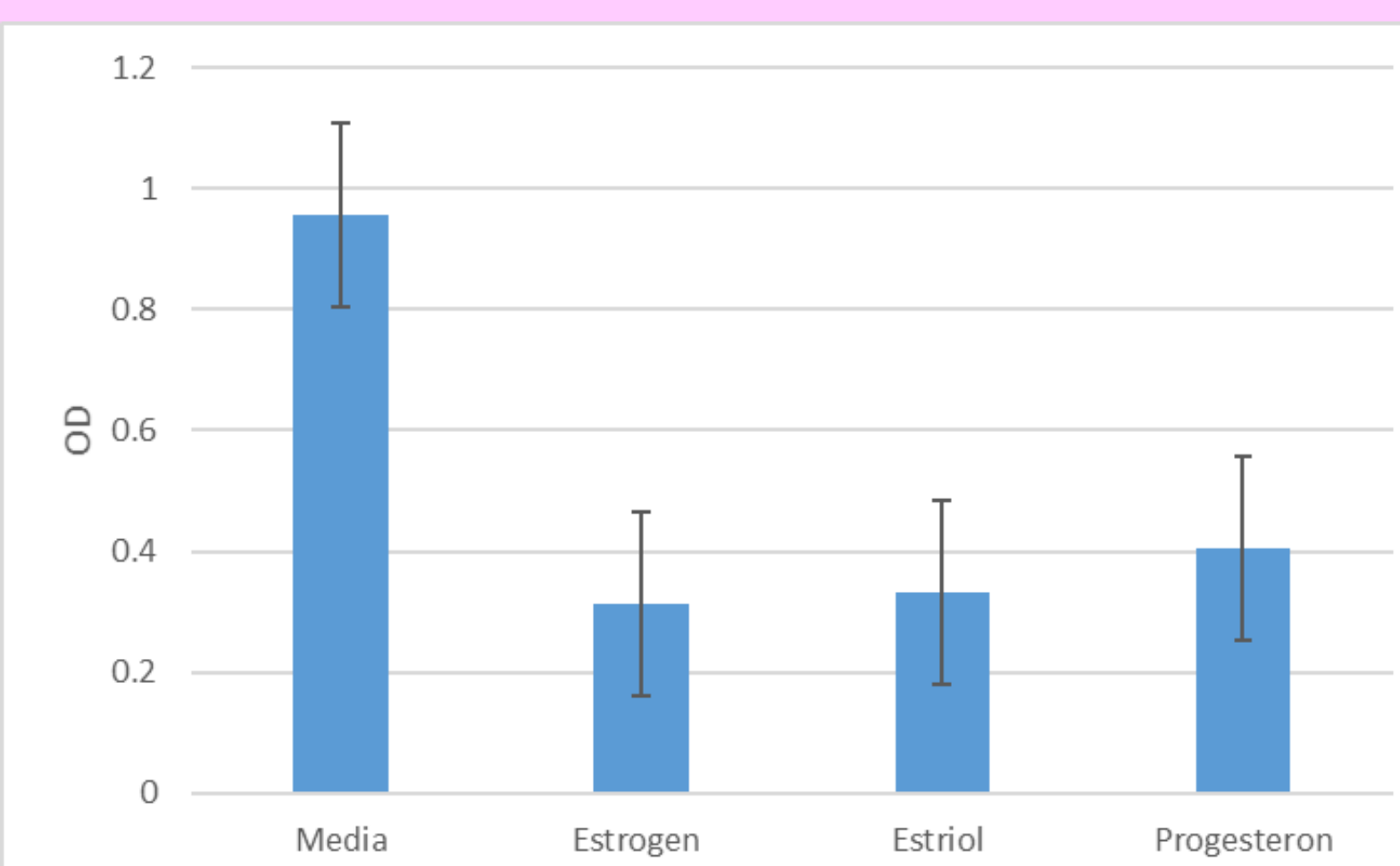
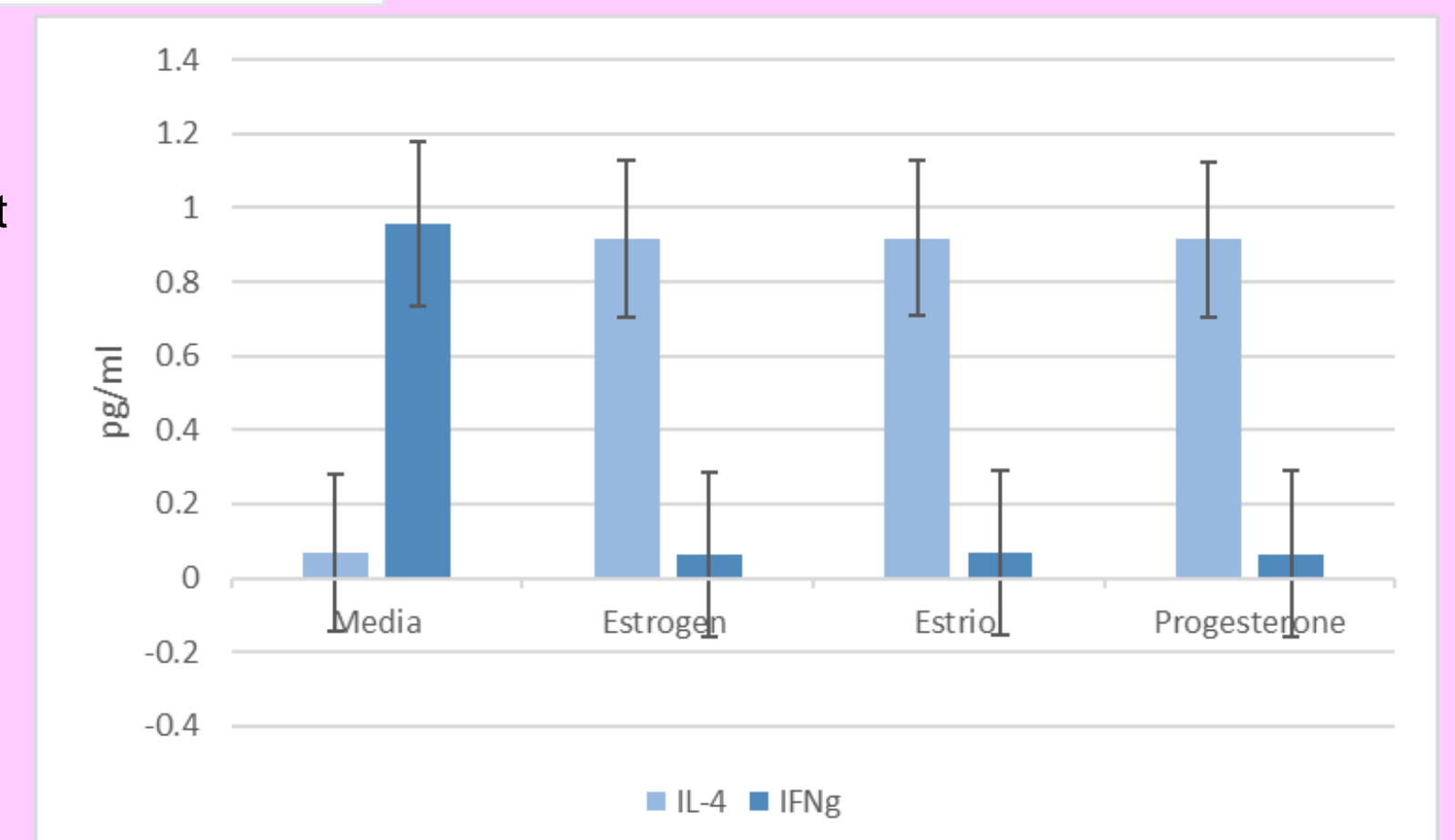


Figure 5: MTT optical density (OD) of T cell proliferation: Average T cell proliferation. There was a significant difference in media to estrogen ( $p=3.953E-8$ ), and estrogen to progesterone ( $p=0.000109$ ). There was not a significant difference between estrogen and estriol ( $p=0.04$ )

## Conclusion

- In conclusion we are able to see that progesterone as well as estriol have similar effects on myeloid-derived suppressor cell development as estrogen has. This is most likely because progesterone, estriol, and estrogen are all hormones.
- Estradiol and progesterone caused more expression of MCH II and CD28 cells to be present, compared to estrogen.
- More IL-4 was produced than IFNg in the presences of different hormones. IL-4 is a cytokine that promotes tumor growth and IFNg is suppressed in the presence of tumors.

## Future Directions

- To take this project to the next step animal models could be used to gain more accurate data.
- Analyze more female sex hormones and hormones that are used in different oral contraceptive pills.

## Reference section

- Bork K. Recurrent episodes of skin angioedema and severe attacks of abdominal pain induced by oral contraceptives or hormone replacement therapy. The American Journal of Medicine. 114(4):294–298. doi:10.1016/S0002-9343(02)01526-7
- Graham JD, Clarke CL. (1997) Physiological Action of Progesterone in Target Tissues\*. Endocrine Reviews.18(4):502–519
- Horwitz KB, McGuire WL. Estrogen Control of Progesterone Receptor in Human Breast Cancer. The Journal of Biological Chemistry. 253(7):2223–2228.
- Scheibl P, Zerbe H. Effect of progesterone on the immune system in consideration of bovine placental retention. PubMed. 107(6):221–227.
- Williams WV. Hormonal contraception and the development of autoimmunity: A review of the literature. The Linacre Quarterly. 84(2):275–295. doi:10.1080/00243639.2017.1360065