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

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Biology 404 Immunology

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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.

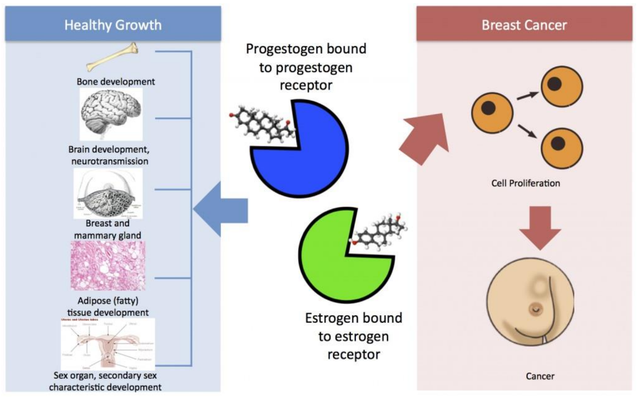


Figure 1: Effect of progesterone and estrogen on the body: Progesterone is show to help bones and tissues grow, whereas increased estrogen can cause cell proliferation

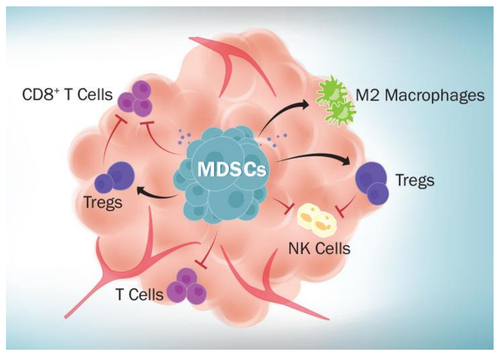


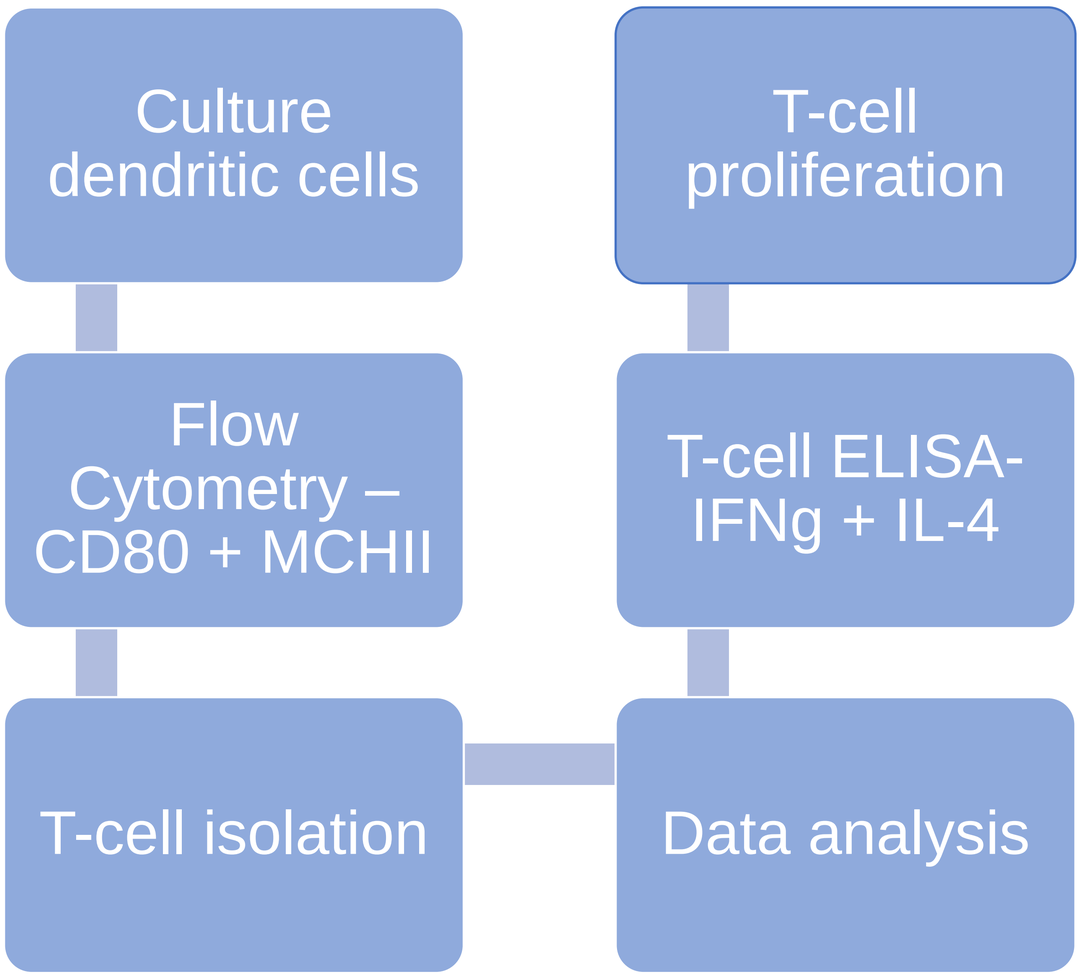
Figure 2: MDSCs in a tumor microenvironment. MDSCs suppress the activation of T cells and NK cells while activating macrophages and Tregs.

- 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.

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

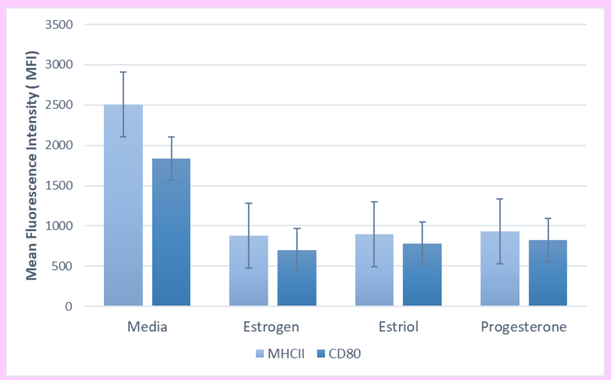
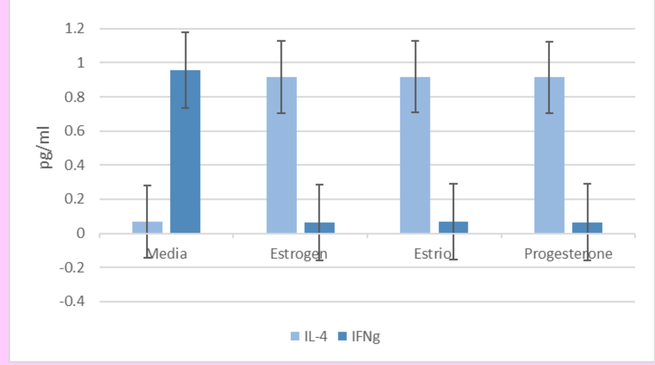


Figure 3: Mean Fluorescence Intensity (MFI): Flow cytometry was used to measure the mean fluorescence intensity. MCHII and CD28 expression was increased in the presence of progesterone. By using a 2 sample T test significant differences were found between MCHII and CD80 in the media (p=3.0301E-7) and 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)



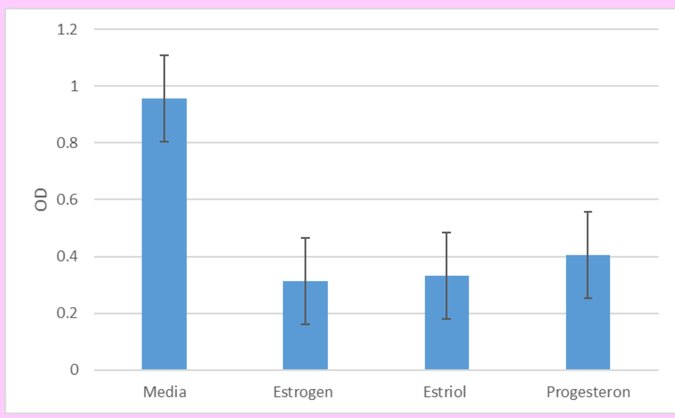


Figure 5: MTT optical density (OD) of T cell proliferation: Average T cell proliferation. There was a significant difference in media to estrogen (p=3.953E-8), and estrogen to progesterone (p=0.000109). There was not a significant difference between estrogen and estriol (p=0.04)

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

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