

# Dual nature of phytoestrogens as both procancer and anticancer agents

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## Background

- Phytoestrogens are plant-derived, xenoestrogenic dietary compounds that are structurally similar 17- $\beta$ -estradiol, a primary female sex hormone. Thus, phytoestrogens have the ability to disrupt the natural human endocrine system.<sup>5</sup>

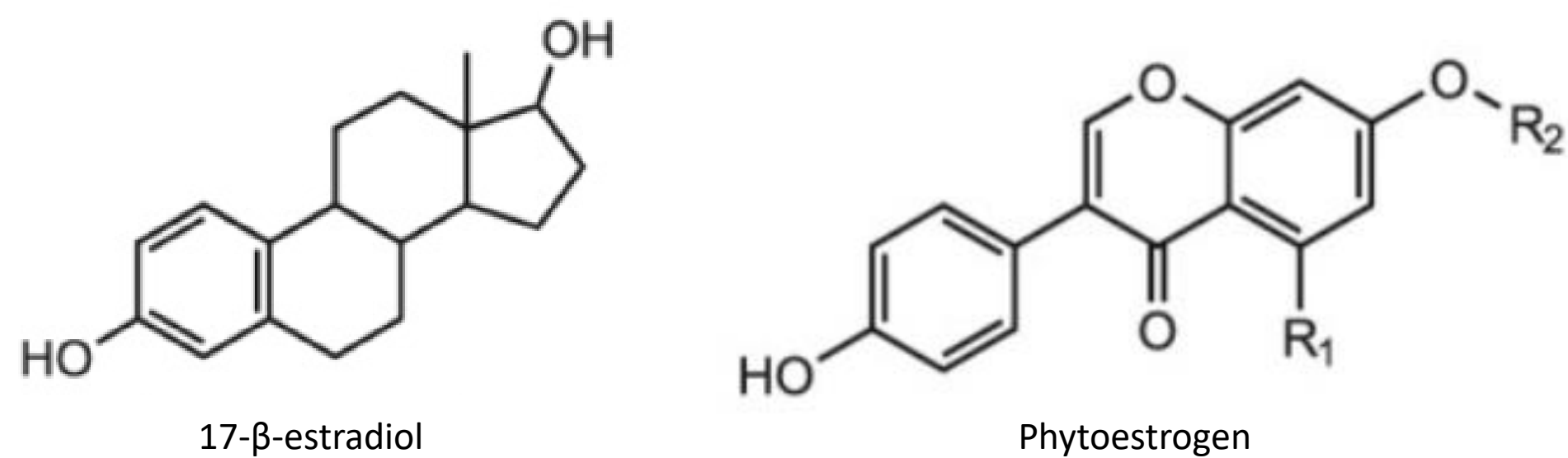


Figure 1: The chemical structures of both human estrogen and phytoestrogens (isoflavones). Adapted from Rietjens et al. 2017.

- Phytoestrogens have been established as having both estrogenic and antiestrogenic effects in breast cancer cells.<sup>1</sup>

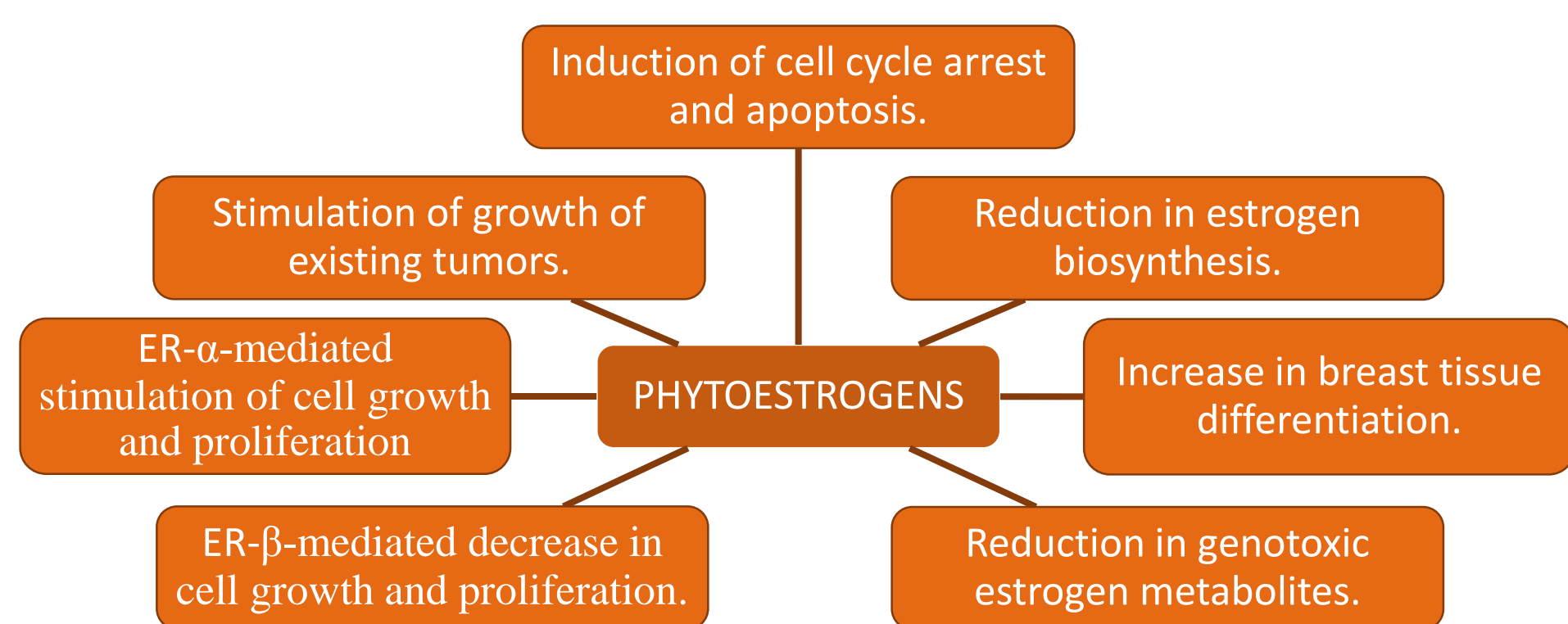


Figure 2: Phytoestrogens have both pro-cancer and anti-cancer properties. Adapted from Mense et al. 2008.

- Recent research suggests phytoestrogens do more good than harm in the fight against breast cancer cell proliferation and that regions with higher spice and herb consumption correlate to a lower incidence of various cancers.<sup>2,3</sup>

## Specific Aim

- To investigate the potential duality of phytoestrogens - 6-gingerol, curcumin, and capsaicin - as both estrogen receptor antagonists in cancer cells and potential activators of myeloid-derived suppressor cells.

## Methods

Culture dendritic cells in the presence of media, 50  $\mu$ g/mL of estrogen, 6-gingerol, curcumin, and capsaicin for 24 hours.

Flow cytometry for MHC II and CD80.

Isolate CD4 T cells and culture with dendritic cells and stimuli for 7 days.

Measure T cell proliferation using MTT assay.

IFN $\gamma$  and IL-4 ELISA assay on T cell supernatants.

Data analysis.

## Results

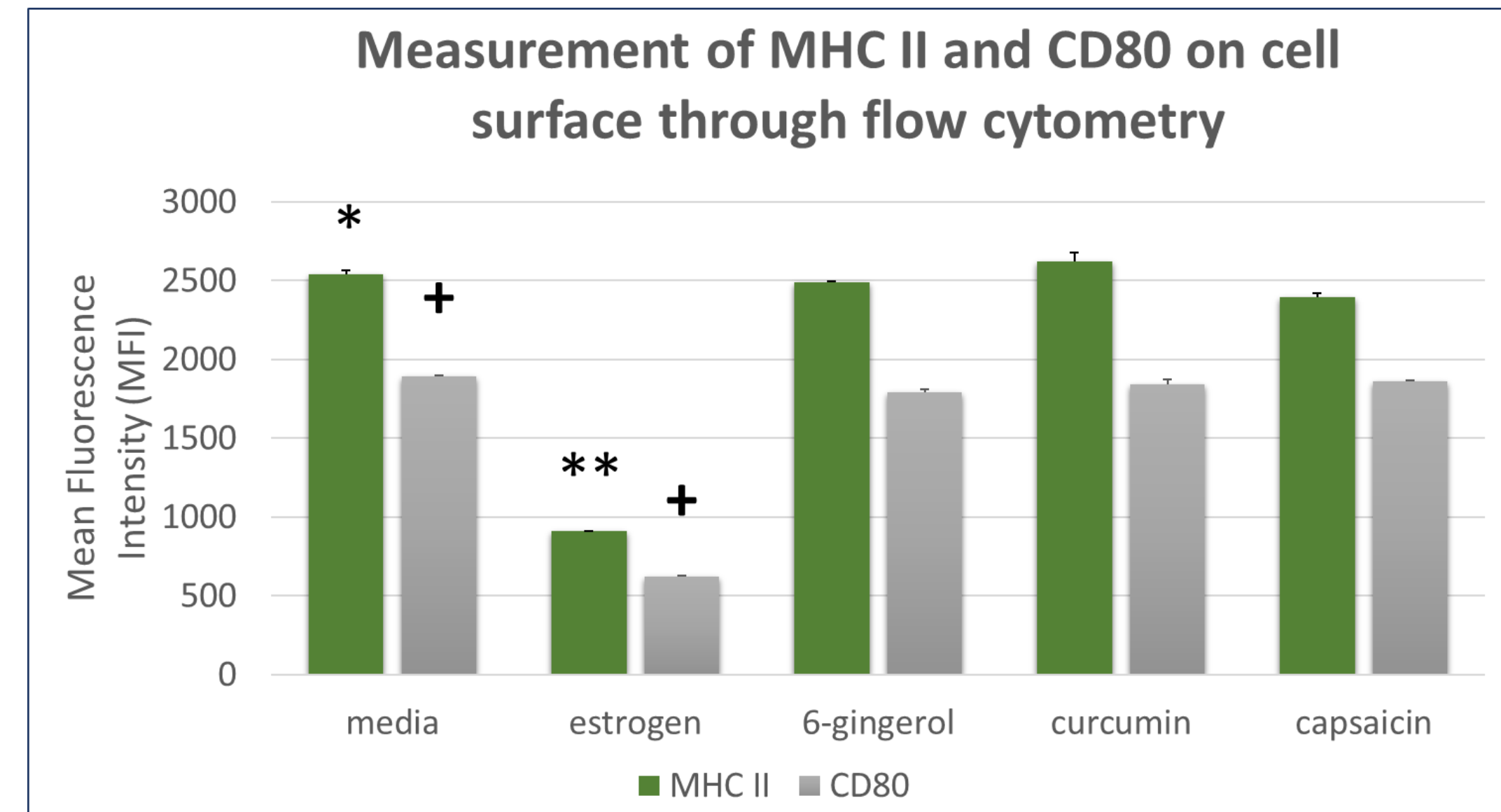


Figure 3: Estrogen decreases expression of MHC II and CD80 on dendritic cells compared to phytoestrogens. Phytoestrogens showed significantly different values from estrogen for MHC II and CD80 flow cytometry.

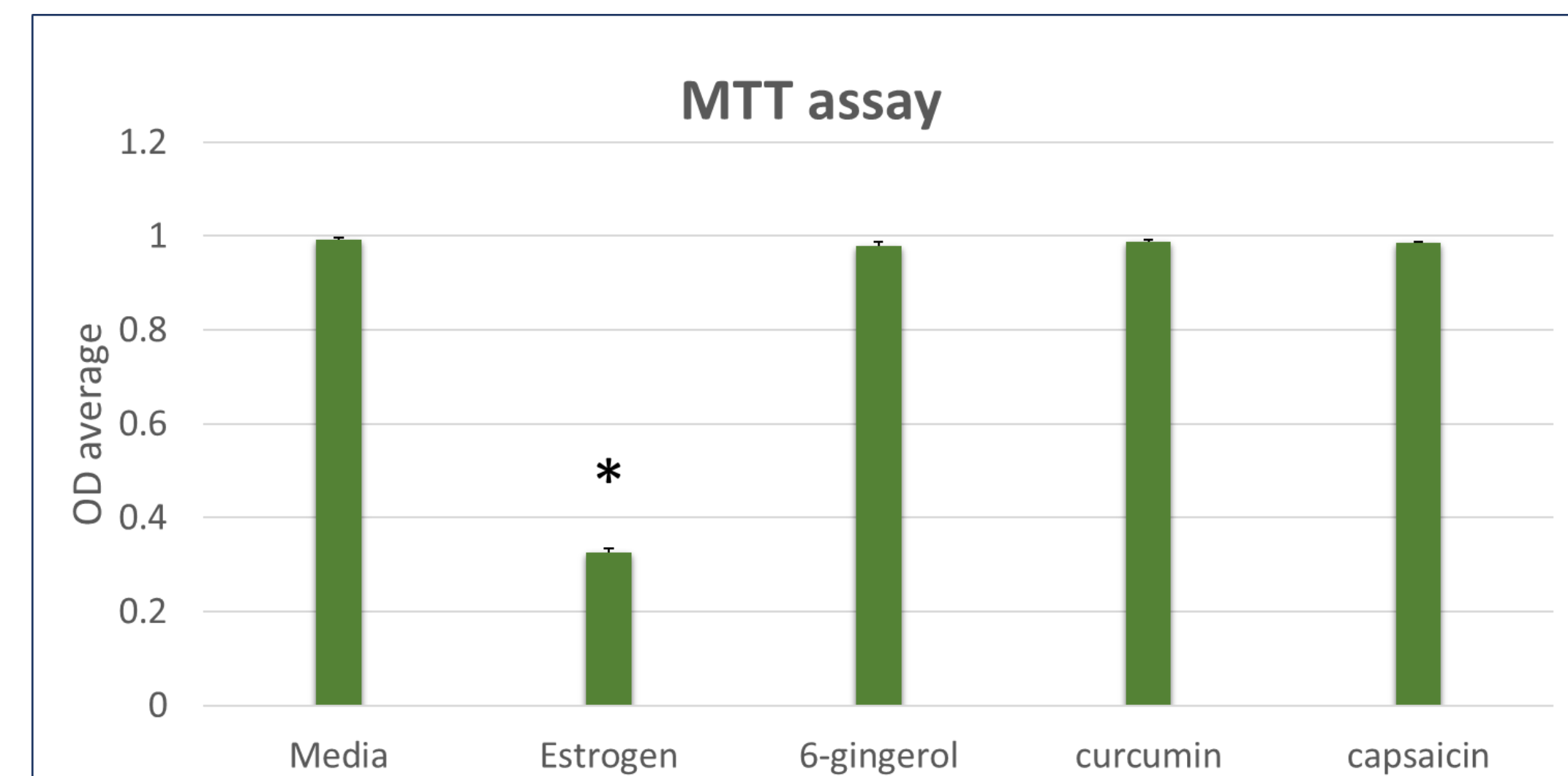


Figure 4: T cell proliferation is significantly decreased in the presence of estrogen, but not phytoestrogens. All three phytoestrogens showed significantly different values from estrogen for MTT.

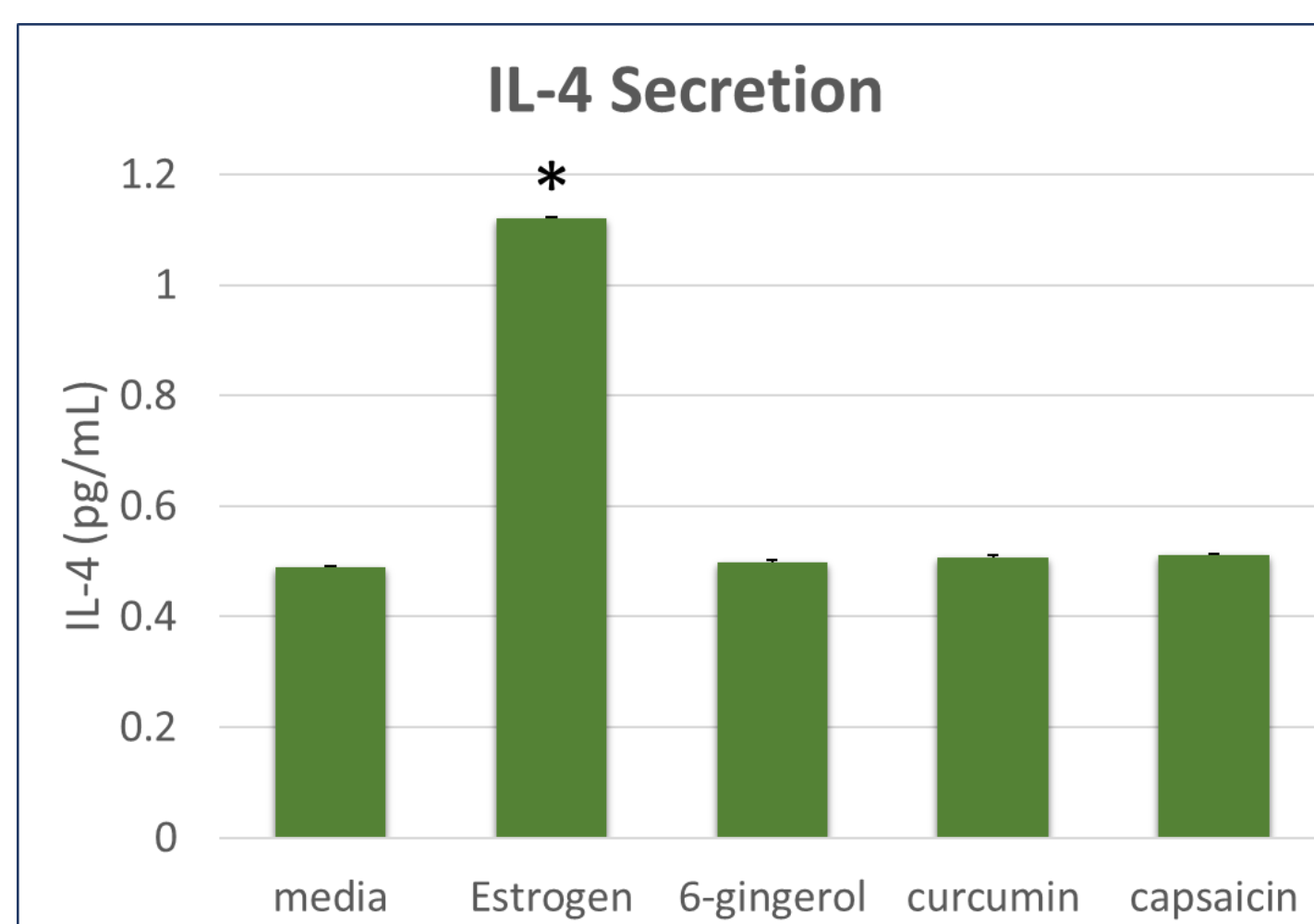


Figure 5: Estrogen causes an increase in IL-4 secretion. All three phytoestrogens showed significantly different values from estrogen for the IL-4 ELISA.

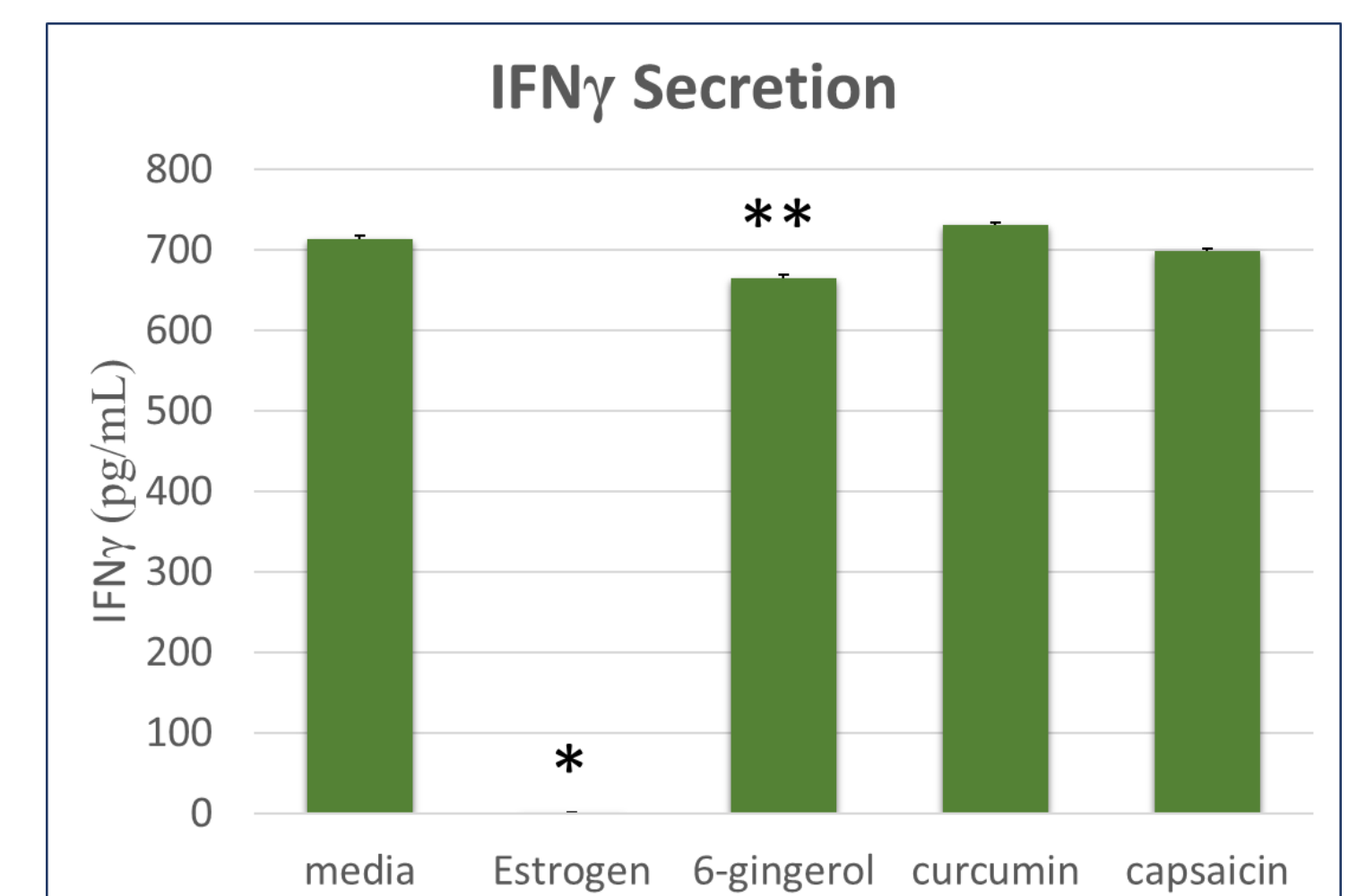


Figure 6: Phytoestrogens cause an increase in IFN $\gamma$  secretion. All three phytoestrogens showed significantly different values from estrogen for the IFN $\gamma$  ELISA.

## Conclusions

- Overall, estrogen limits the immune system's ability to clear cancer by decreasing antigen presentation, decreasing T cell proliferation, and skewing humoral immunity, which is not useful against cancer.
- On the other hand, phytoestrogens had no effect on antigen presentation or T cell proliferation, and they skewed cell-mediated immunity, allowing CD4 T cells to be activated.

## Future Directions

- Further analysis should be done for other phytoestrogens, such as soy, in order to determine if they have similar effects on the immune system.
- Further examination of the reported anti-cancer benefits of phytoestrogens should be done in order to determine their validity.

## References

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