

Kayla Cooksey
Adrianna Doggett
Debbie Pitt
Maya Young
January 28th, 2020

Lycopene and Trans-Resveratrol Phytoestrogens and Their role in the production of myeloid-derived suppressor cells (MDSC)

According to the CDC (2016), breast cancer is the most common cancer amongst women in the United States with 245,210 cases in 2016. The large number observed cases can be due to the steroid hormone estrogen within the female body. Estrogen is a pleiotropic steroid that can affect biological functions and increases the likelihood of developing cancer (Svoronos et al., 2017). As cancer proliferates, the body is unable to suppress the tumor cells due to MDSC, a specific type of suppressor cell that blocks T-cells and natural killer cells which reduces the efficacy of the innate immune response (Umansky et al., 2016; Joseph et al., 2019; Svoronos et al., 2017). Currently, one method to reduce tumor cells is tamoxifen however it is specific for breast cancer and does not inhibit MDSC (Patisaul et al., 2010). Other methods, such as phytoestrogens, have recently been studied for its health benefits against hypertension and cancers involving estrogen (Alice et al., 1998). Phytoestrogens are plant compounds that mimic estrogenic activity. Based on the structure of phytoestrogen, they can be classified as flavonoids, isoflavonoids, stilbenes, lignans, and carotenoids (Cos et al., 2003). This paper will study the effects of two phytoestrogens, Trans-Resveratrol and Lycopene, on MDSCs. We believe that these phytoestrogens will bind to estrogen receptors and block estrogenic activity, effectively decreasing the production of MDSCs in murine cells.

Resveratrol, a stilbenoid found in red grapes, has been seen to precipitate cancer proliferation and cell growth by fueling ER α -positive and HER2-positive breast cancer cells. They increase tumor multiplicity by inducing the down-regulation of ER α + and an overexpression of HER2+ carcinomas in the mammary glands (Andreani et al., 2017). The analog structure of Resveratrol — Trans-Resveratrol — has been seen to inhibit the growth of estrogen-dependent breast cancer cells and exhibits anti-proliferative activity on the MCF-7 receptor by a separate mechanism than what is observed in Resveratrol (Yenugonda et al., 2012).

Lycopene, a carotenoid found in tomatoes, mimics estrogen by binding to the ER α and ER β receptors. When Lycopene binds to the receptor, estrogen cannot bind to the receptor and the production of estrogen is blocked (Raj et al., 2013). This makes lycopene a good anticancer compound because many cancers proliferate in the presence of estrogen.

In conclusion, the introduction of Trans-Resveratrol and Lycopene on estrogen receptors may decrease the production of MDSCs which will decrease the likelihood of acquiring cancer.

Bibliography

- Alice L. Murkies, Gisela Wilcox, Susan R. Davis, Phytoestrogens, *The Journal of Clinical Endocrinology & Metabolism*, Volume 83, Issue 2, 1 February 1998, Pages 297–303, <https://doi.org/10.1210/jcem.83.2.4577>
- Andreani C., Bartolacci C., Wijnant K., Crinelli R., Bianchi M., ... Marchini C. 2017. Resveratrol fuels HER2 and ER α -positive breast cancer behaving as proteasome inhibitor. *AGING*. Volume 9. 508-520.
- Bao-xing X., Jing-jing Z., Shi-wei S., Wei S., Guang-wen S., Yan-wei H., and Hou-cheng L. 2019. Supplemental blue and red light promote lycopene synthesis in tomato fruits. *Journal of Integrative Agriculture*. Volume 18:3, 590–598.
- Centers for Disease Control and Prevention. 2016. United States Cancer Statistics: Data Visualizations. <https://gis.cdc.gov/Cancer/USCS/DataViz.html>
- Cos P., Bruyne D T., Apers P., Berghe V D., Pieters L., and Vlietinck J A. 2003. Phytoestrogens: recent developments. *Planta med.* Volume 69, 588-599.
- Joseph, A. M., Parker, D., Hawkins, T., Ciavattone, N., & Davila, E. 2017. TLR-stimulated T cells acquire resistance to MDSC mediated suppression.
- Raj M., Selvakumar K., Kirshnamoorthy G., Revathy S., Elumalai P., and Arunakaran J. 2013. Impact of Lycopene and Epididymal Androgen and Estrogen Receptors' Expression in Polychlorinated Biphenyls-Exposed Rats. *Reproductive Sciences*. Volume 21:1, 89-101.
- Patisaul, H. B., & Jefferson, W. 2010. The pros and cons of phytoestrogens. *Frontiers in neuroendocrinology*, 31(4), 400–419. doi:10.1016/j.yfrne.2010.03.003.

- Svoronos, N., Perales-Puchalt, A., Allegrezza, M. J., Rutkowski, M. R., Payne, K. K., Tesone, A. J., ... & Eruslanov, E. B. 2017. Tumor cell-independent estrogen signaling drives disease progression through mobilization of myeloid-derived suppressor cells. *Cancer discovery*. Volume 7:1, 72-85.
- Umansky, V., Blattner, C., Gebhardt, C., & Utikal, J. 2016. The Role of Myeloid-Derived Suppressor Cells (MDSC) in Cancer Progression. *Vaccines*, Volume 4:4, 36.
- Yenugonda M V., Brown L M., Deb B T., Kong Y., Riggins B R., and Yang Y. 2012. Trans-Resveratrol boronic acid exhibits enhanced anti-proliferate activity on estrogen-dependent MCF-7 breast cancer cells. *Cancer Biology and Therapy*. Volume 13:10, 925-934.