1. **The immunotherapeutic potential of soy extract in the treatment of urothelial carcinoma of the bladder**

**Global Integrative Oncology: Use in Cancer Treatment & Patient Management**

Urothelial carcinoma of the bladder is the second-most prevalent cancer of the genitourinary system, with approximately 80,470 new cases estimated to have occured in the United States in 2019. Phytochemicals are biologically active compounds produced by plants that have been shown to play important roles in tumor proliferation, apoptosis, and radiosensitization. Our lab has previously demonstrated the synergistic anti-tumor effect of resveratrol, a phytochemical found in grapes and berries, as an adjunct to radiation therapy for treatment of prostate cancer. The current study was designed to investigate the role of soy extract on the growth bladder urothelial carcinoma.

**Methods**: Clonogenic survival assay, cell proliferation, and caspase-3 activity kits were used to evaluate the effects of soy extract, alone and with radiation therapy (RT), on cell survival, proliferation, and apoptosis in the widely studied bladder urothelial carcinoma cell line J82. We further investigated possible molecular mechanisms using RT-PCR and immunocytochemistry.

**Results**: While the percentage of colonies of J82 urothelial carcinoma cells did not significantly decrease with either soy extract or RT alone, we did observe a significant decrease in the percentage of colonies treated with a combination of soy extract and RT. This was paralleled with a decrease in OD value of J82 cells in the presence of soy extract and RT. Furthermore, relative caspase-3 activity in J82 cells increased significantly in the presence of soy extract and RT. The anti-tumor effect of soy extract on J82 cells correlated with increased expression of the anti-proliferative molecule p21. The pro-apoptotic effect correlated with increased expression of the anti-apoptotic molecule TRAILR1.

**Conclusions**: Soy extract may radiosensitize bladder urothelial carcinoma through inhibition of proliferation and promotion of apoptosis via modulation of p21 and TRAILR1. Such a study might pave the way towards development of a new immunotherapy for urothelial carcinoma of the bladder.

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