

The Effect of Resveratrol on Proliferation and Apoptosis in Uterine Leiomyoma Cells

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Background: Epidemiological evidence has revealed wide geographical variations in the incidence of leiomyomas and a clear impact of diet in the progression of this disorder. Estrogen receptor (ER) alpha is over expressed in leiomyomas, compared to normal adjacent myometrium. Resveratrol, a polyphenolic plant phytoalexin present in many dietary sources has high affinity for, and acts as a selective and potent antagonist of ER alpha. Resveratrol has anti-proliferative activity against a variety of neoplastic tissues including breast, ovarian, colon, and prostate cancer.

Objectives: To determine if proliferation or apoptosis of the estrogen responsive ELT-3 rat uterine leiomyoma cell line is altered *in vitro* by resveratrol at physiologically relevant concentrations.

Methods: ELT-3 cells (ELT-3 cells courtesy of Dr. Cheryl Walker, MD Anderson Cancer Center, Smithville, TX) were cultured in estrogen-free DF8 media containing 10% FBS. Cells were plated and treated with various concentrations of resveratrol or vehicle (DMSO). A non-treated control group was also assessed. Cell growth was determined at 24-72 hours by sulforhodamine B assay and apoptosis was assessed by flow cytometry.

Results: The results of sulforhodamine B assay indicated that resveratrol inhibited cell growth. Resveratrol exhibited an IC_{50} between 50-100 μ M. Apoptosis was demonstrated in response to resveratrol in both a time and dose dependent manner.

Conclusion: The growth of ELT-3 uterine leiomyoma cells *in vitro* was inhibited by resveratrol in part by the induction of apoptosis. Mechanistic studies are underway to define the molecular mechanisms leading to cell growth inhibition and apoptosis and determine whether ER modulation is involved. The study of resveratrol may be an important lead to develop novel compounds to prevent or treat early phases of uterine leiomyoma pathogenesis. R01 HD46249 (GMC).