Uterine Fibroids Gene Therapy: Adenovirus-Mediated Herpes Simplex Virus Thymidine Kinase/Ganciclovir Treatment Inhibits Growth of Human and Rat Leiomyoma Cells

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Introduction: Adenovirus-mediated herpes simplex virus thymidine kinase gene transfer in combination with ganciclovir (Ad-TK/GCV) is one of the major gene therapy strategies to eradicate tumor cells. Leiomyoma is a benign uterine tumor that affects high percentage of women in their reproductive age. Unfortunately, there is no effective and safe medical treatment available. Leiomyom is developed as discrete well-defined tumor, easily accessible with imaging techniques which makes it a good candidate for localized gene therapy approaches.

Objective: To determine the in vitro efficacy of Ad-TK/GCV as a potential gene therapy for leiomyomas using rat ELT3 leiomyoma cell line and human leiomyoma cells (LM) as surrogate system.

Methods: ELT3 cells and five LMs were infected with different MOI (10-100 PFU/cells) of Ad-TK and treated with different concentrations of GCV (5, 10, or 20 μg/ml) for 5 days followed by cell count (DNA content). To test the bystander effect, Ad-TK-transfected ELT3 cells (100 PFU/cell) or LM cells (10 PFU/cell) were co-cultured with corresponding non-transfected cells at different percentage and treated with GCV (10 μg/ml) for 5 days followed by cell count.

Results: In ELT3 cells transfected with different MOIs of Ad-TK/GCV (10, 20, 50, or 100 PFU/cell), the cell number were reduced by 24%, 42%, 77%, or 87 %, respectively compared to the control cells (transfected with Ad-LacZ/GCV). Similarly, in LM cells transfected with Ad-TK/GCV (10, 50, or 100 PFU/cell), cell count was reduced by 31%, 62%, or 82%, respectively, compared to the control. A strong bystander effect was noted in both ELT3 and LM cells with significant killing (P=0.001) at a ratio of infected: uninfected cells of only 1:90 and maximal killing at 1:4.

Conclusion: This study demonstrates the potential efficacy of Ad-TK/GCV approach in Leiomyoma gene therapy.