Towards Gene Therapy for Uterine Fibroids: Adeno-Associated Virus can Infect Human and Rat Leiomyoma cells

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Objectives: Uterine fibroids are the most common pelvic tumor, affecting 20% to 25% of premenopausal women. Currently there is no effective and sustained non-surgical treatment for uterine fibroids. The development of therapeutic agents capable of reversing the tumor growth in Leiomyomas without serious side effects is urgently needed. We have recently (Am J Obstetrics and Gynecology, 2004,191:00-00) demonstrated the ability of a mutated dominant-negative estrogen receptor gene delivered via an adenoviral vector to induce apoptosis in leiomyoma cells as well as ablate pre-existing fibroids in vivo. One of the potential limitations of adenoviral-based vectors is short term expression. Adeno-associated virus (AAV) has been shown to mediate higher transfection ability and longer gene expression. In this study we aim to explore the potential application of AAV to support gene therapy of uterine leiomyoma.

Methods: Four different cell lines were used; ELT3 rat leiomyoma cell line, HM9 telomerase-immortalized human myometrial cell line, LM176 primary human leiomyoma cells, and HM176 primary human myometrial cells. Cells were grown to 50% confluence and then transfected with different virus to cell ratio ($1x10^5$, $2x10^4$ or $1x10^3$) of DNAase Resistant Particle (DRP) per cell of RSV-green fluorescence protein recombinant AAV2, AAV4, AAV5, AAV6 or BAAV. Four to six days post incubation, the efficiency of viral transduction was assessed with fluorescence microscope.

Results: AAV2 and BAAV were highly efficient in transducing all leiomyoma cell lines tested, with 100% transduction rate achieved at 10^5 DRP/cell. These two vectors were less efficient in transducing normal myometrial cells. AAV4, AAV5, and AAV6 were unsuccessful in transducing neither myometrial nor leiomyoma cells.

Conclusion: AAV2 and BAAV are promising vectors in future development of gene therapy protocols for uterine leiomyoma.