adenovirus serotype 5 (Ad5) may be low due to variable expression of coxsackie-adenovirus receptor (CAR) on advanced PrCa cells. CRAds can be retargeted and genetically modified for tumor enhanced replication. Targeting Ads to the serotype 3 receptor might enhance transduction of tumor cells. A molecule, such as βhCG, secreted in conjunction with viral replication might provide a means to detect viral replication and kinetics non-invasively in vivo. Radiotherapy is a commonly used treatment for PrCa but cannot cure advanced disease. Interaction of radiation with Ad infection is poorly understood. Moreover, Ad E1A might theoretically enhance irradiation induced apoptosis.

Methods and results: Transduction of PrCa cells was tested with capsid modified luciferase expressing Ads. A vector containing the serotype 3 knob was found most effective. In MTS assays improved transduction translated into enhanced oncolysis by a serotype 3 capsid modified replicative agent. A new virus, Ad5/3Δ24hCG, containing a 24 bp deletion in the E1A region and expressing βhCG from a native E3 promoter, was created and studied for oncolysis and replication in PrCa cells. The CR2 deletion in E1A results in replication selectivity for Rb-p16 pathway dysfunctional cells. Ad5/3Δ24hCG was effective in killing of PrCa cells. Moreover, increasing amounts of βhCG were detected as viral replication proceeded. The same effects were observed in a mouse model resulting in tumor growth inhibition and detection of βhCG in blood samples of Ad5/3Δ24hCG treated mice. Ad5/3Δ24hCG induced production of βhCG was tested in tissue samples of PrCa and non-malignant prostate and resulted in high production of βhCG in PrCa tissue when production remained low in normal tissue. To determine if irradiation could potentiate the oncolytic effect of CRAds, PrCa cells were irradiated at different doses of γ-radiation. Since it has been proposed that radiation prior to infection increases the expression of receptors relevant for Ad entry, we assayed if there was a difference in oncolysis when cancer cells were infected before or after irradiation.

Conclusions: Ad5/3Δ24hCG effectively infects and kills PrCa cells and produces βhCG in concordance with virus replication. The virus is effective in suppressing growth of PrCa tumors in mice, and replication *in vivo* was confirmed by detection of βhCG in serum samples. Ad5/3Δ24hCG induced higher βhCG in fresh malignant prostate tissue than in non-malignant, suggesting tumor specific replication. Combining Ad5/3Δ24hCG treatment to irradiation potentiates cancer cell death.

951. A New Vector Based on Baculovirus Was Effective in Inhibiting Glioma Cell Growth in the Rat Brain

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The baculovirus *Autographa californica multiple nucleopolyhedrovirus* (AcMNPV)-based vectors are emerging as a new type of gene delivery vehicles. However, gene therapy application of the virus is still in its infancy and no practically useful application in cancer therapy has yet been produced, even in preclinical animal studies. We have constructed a baculoviral expression cassette containing an engineered GFAP promoter to restrict gene expression to astrocytes. Using this recombinant baculovirus, we observed extended *in vivo* transgene expression in the rat brain at 90 days postinjection, by which time the gene expression from baculovirus vectors with the CMV promoter had already become undetectable. The astrocyte specificity of the GFAP promoter was well preserved, as demonstrated by immunohistological analysis of brain samples and an axonal retrograde transport assay. Also, this recombinant baculovirus provided significantly improved transgene expression in glioma cells, with almost 100% of cells being transduced in certain glioma cell lines. When used to produce the A-chain of diphtheria toxin intracellularly in a rat glioma xenograft model, the baculoviruses effectively suppressed tumor development. The new baculovirus vector circumvents some of the inherent problems associated with mammalian viral vectors and provides an additional option for cancer gene therapy.

952. Human Mesenchymal Stem Cells Migrate to Colon Cancer Xenografts: Potential Carriers of Cancer Therapeutics

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Mesenchymal stem cells (MSC) are found in the bone marrow and give rise to adipocytes, osteocytes, chondrocytes, and potentially other tissues. It has recently been shown that MSCs have affinity for lung and glioma tumors in xenograft models. We investigated MSC migration to colon cancer xenografts in conjunction with MSC transduction by a lentiviral vector as a way to deliver cancer therapeutics to the local tumor microenvironment. Subcutaneous colon or glioma tumor xenografts were generated in nude mice followed by intravenous infusion of DiOC18 fluorescently labeled MSCs. MSC pluripotentcy was confirmed by in vitro differentiation into osteocytes and adipocytes. Tumors and other organs were harvested 1 wk following MSC infusion and cryosections prepared in order to observe the presence of MSCs. We found that colon cancer tumors were selectively populated by labeled MSCs, compared to liver and spleen. MSCs were also observed to some extent in the lung. The distribution of tumor-associated MSCs were predominately at the tumor periphery and within loose clusters. In glioma xenografts, labeled MSCs were detected to a lesser extent and were mainly distributed as single cells. MSCs were then analyzed for their susceptibility to lentiviral transduction for eventual use to target cancer therapeutics to the tumor mass. We analyzed MSC transduction by a lentiviral vector harboring a luciferase-IRES-GFP cassette over a range of MOI. MSCs were easily transduced, with essentially complete transduction at an MOI of 18, and substantial transduction observed at MOIs as low as 2 when analyzed for GFP expression by flow cytometry. Luciferase expression was likewise high. These studies show that MSCs have the capacity for high lentiviral transduction and the ability to migrate to colon cancer xenografts, suggesting potential use to deliver transgene-expressed anti-cancer therapeutics to solid tumors in vivo.

953. Therapeutic Ultrasound Mediated Anti-Angiogenic Gene Delivery Results with Prostate Tumors Inhibition

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Gene therapy using angiogenic inhibitors is a promising approach for the therapy of prostate cancer (PCa), which depends on the angiogenesis process for its growth. Therapeutic ultrasound (TUS), which utilizes low intensities and non-continuous waves, has emerged as a method to safely deliver genes to cells and tissues. In the present study, the efficacy of TUS for gene-delivery, in combination with Optison, is studied on endothelial cells and PCa *in vitro* and on tumors *in vivo* using two genes encoding for anti-angiogenic proteins: PEX and Endostatin (Endo).

In the *in vitro* studies, PCa and primary endothelial cells were successfully transfected with luciferase (Luc) and GFP using TUS and Optison. Similarly, cells were transfected with pPEX or pEndo and protein expression was detected by Western Blot analysis and