

## **S010** Technologies for gene delivery to cancer

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Gene therapy often uses nanoparticles, either synthetic or viral, and adenovirus is a monodisperse particle that provides a useful paradigm for the challenges of gene delivery. Adenovirus is particularly useful for cancer gene therapy, however its usefulness is often limited by inefficient tumour cell transduction. The coxsackie-adenovirus receptor (CAR) is expressed at low levels in many carcinomas, however the epidermal growth factor receptor (EGFR) is often upregulated and would be an attractive candidate for retargeting infection.

The normal tropism of adenovirus can be ablated using a multivalent reactive copolymer based on poly[N-(2-hydroxypropyl)methacrylamide] (pHPMA). Polymer-coated virus (pc-virus) conjugated with EGF could infect cells expressing the EGF receptor, providing a therapeutic virus with selectivity for target cells.

Polymer coating with pHPMA also ablates unwanted CAR-mediated infection in vivo and results in an increased level of adenovirus in the plasma. Intravenous administration of clodronate liposomes to mice destroys tissue macrophages in the liver and 100% of the administered dose of pc-virus was present in the bloodstream of clodronate-treated mice, compared with only 1% of the non-coated virus.

Ablation of the natural tropism of adenovirus can be coupled with temporary suppression of host scavenging mechanisms to permit efficient systemic delivery of therapeutic adenovirus, possibly useful for systemic gene therapy of metastatic cancer.