Adenoviral therapy

Refers to the use of genetically modified adenoviruses—a type of DNA virus—as tools for treating diseases, particularly cancer. Here's a quick overview adapted to both general understanding and clinical research relevance:

 Definition Adenoviral therapy is a form of gene therapy or oncolytic virotherapy where adenoviruses are engineered to either:

Deliver therapeutic genes into target cells (e.g., p53 tumor suppressor),

Selectively replicate in and kill cancer cells (oncolytic adenoviruses),

Or stimulate an anti-tumor immune response.

⚙ Mechanism of Action Infects host cell via specific receptors (e.g., CAR receptor).

Delivers DNA payload into the nucleus (non-integrating).

Gene expression or viral replication occurs based on design.

Cell lysis (in oncolytic versions) releases tumor antigens → promotes immune response.

 Applications Cancer (Oncolytic virotherapy): Glioblastoma, pancreatic cancer, prostate cancer, etc.

Gene delivery: Cystic fibrosis, cardiovascular disease, vaccines (e.g. COVID-19 vaccines like AstraZeneca use chimpanzee adenovirus).

Immunotherapy adjunct: Boosts immune system via danger signals and antigen presentation.

 Challenges Systemic delivery: Rapid clearance by the immune system and liver uptake.

Pre-existing immunity: Many people have neutralizing antibodies against common human adenoviruses.

Toxicity and inflammation: Especially in high-dose systemic therapy.

Targeting specificity: Tumor-selective replication or gene expression is hard to control.

Repeat dosing: Often limited due to immune memory.

 Next-Generation Approaches Use of non-human adenovirus serotypes (e.g., chimpanzee Ad vectors).

Retargeted capsid modifications for tumor-specific tropism.

Armed oncolytic viruses with immunostimulatory transgenes (e.g., GM-CSF).

Shielding strategies like PEGylation or use of extracellular vesicles.

Combos with checkpoint inhibitors or chemotherapy.

Engineered retargeting to overcome systemic delivery challenges in oncolytic adenoviral therapy

Type of study: Original research (experimental study, engineering approach) **First author:** Leparc et al. **Affiliations:**

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Journal: Molecular Therapy – Oncolytics **Purpose:** To engineer adenoviruses with modified tropism for systemic delivery—aiming to reduce off-target accumulation and enhance tumor retention via retargeting strategies.

Conclusions: Engineered vectors exhibited improved immune evasion, diminished sequestration by non-tumor tissues, and improved intratumoral delivery, indicating the feasibility of retargeting modifications for systemic adenoviral therapy.

Critical Review

Methodology: The study lacks transparency in the engineering protocol. Crucial elements such as ligand selection, targeting affinity, and vector modifications are insufficiently described. No rigorous dose-responsiveness or replication kinetics are provided.

Experimental Limitations: Only limited xenograft models were used. The absence of immunocompetent or metastatic models weakens any extrapolation to clinical practice.

Immunological Oversight: There is no data on host immune responses or neutralizing antibody development over time. This omission is critical for systemically delivered viral therapies.

Safety and Toxicology: Claims of reduced off-target effects are unsupported by comprehensive toxicity or biodistribution data. Lack of liver, lung, or spleen histopathology undermines safety assertions.

Comparative Context: The study fails to benchmark against existing retargeting approaches like bispecific adaptors or nanoparticle-based carriers, weakening claims of novelty or superiority.

Data Accessibility: Raw data including viral load, distribution curves, and replication efficiency are omitted. Figures are descriptive but lack statistical rigor.

Final Verdict

While conceptually relevant, this study lacks empirical robustness and critical comparative analysis.

Its translational impact is unsubstantiated due to poor methodological and immunological validation.

Takeaway for Neurosurgeons

Systemic delivery of engineered oncolytic adenoviruses is promising, but this study’s incomplete immunological and toxicological evaluation renders it clinically unconvincing for neuro-oncology application.

Bottom Line

High-concept, low-rigor: currently inadequate for informing clinical or translational strategies.

Rating

2 / 10

Citation

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