Delivery Method	Safety	Efficacy	Tissue Tropism	Considerations	References
Non-Viral Delivery					
Lipid nanoparticles	*Toxicity:* low *Off-target effects:* minimal *Immunogenicity:* high *Other:* biocompatible and biodegradable	*Transfection efficiency:* lower compared to viral delivery systems *Currently approved and administered beyond clinical trials?: Y*es	Broad, but mostly in the liver and spleen.	*Genetic Payload:* limited to size of nanoparticle *Production feasibility:* large-scale production achievable and fairly inexpensive *Other:* unstable in long-term storage, low encapsulation efficiency	(Ghasemiyeh & Mohammadi-Samani, 2018) (Qiu et al., 2022) (Sharma et al., 2012)
Engineered lipid nanoparticles	*Toxicity:* low *Off-target effects:* minimal *Immunogenicity:* None *Other:* low risk of integration into host genome	*Transfection efficiency:* lower compared to viral delivery systems *Currently approved and administered beyond clinical trials?:* No (only proven in mouse models)	Limited to lungs, spleen, and liver.	*Genetic Payload:* multiple mRNA in one dose *Other:* Has yet to be used in human trials	(Melamed et al., 2023)
Viral Vector Systems					

Lentivirus	*Toxicity:* *Off-target effects:* potential alteration to host genome upon integration *Immunogenicity:* low *Other:* potential of mutagenesis in proliferating cells	*Transduction efficiency:* high *Currently approved and administered beyond clinical trials?:* Yes	Broad	*Genetic Payload:* up to 9 kB *Production feasibility:* best for small-scale use due to expensive production costs *Other:* commonly used and well characterized, stable expression	(Sadelain & Rivière, 2002) (Han, 2012) (Martínez-Molina et al., 2020)
Adeno-associated virus (AAVs)	*Toxicity:* high *Off-target effects:* moderate *Immunogenicity:* high *Other:* low mutagenesis and carcinogenesis risk	*Transduction efficiency:* high but small transgene capacity *Currently approved and administered beyond clinical trials?:* Yes	Broad (mostly liver, striated muscles, CNS)	*Genetic Payload:* up to 50 kB *Production feasibility:* high manufacturing costs *Other:* stable expression	(Wang et al., 2019) (Zacchinga et al., 2014) (Smith, 2008)

Adenovirus	*Toxicity:* high *Off-target effects:* high *Immunogenicity:* high *Other:* minimal risk of insertional mutagenesis	*Transduction efficiency:* high and transient gene expression *Currently approved and administered beyond clinical trials?:* Yes	Broad	*Genetic Payload:* up to 4.6 kB *Production feasibility:* large-scale manufacturing at a low cost *Other:* easy to manipulate, requires other vector modifications to overcome immunological and structural barriers of the tumour microenvironment	(Ferreira et al., 2021) (Wold & Toth, 2013). (Sayedahmed et al., 2019)
Gutless adenovirus (GLAd)	*Toxicity:* low *Off-target effects:* low *Immunogenicity:* low	*Transduction efficiency:* high and transient gene expression *Currently approved and administered beyond clinical trials?:* No (currently in clinical trials)	Broad	*Genetic Payload:* up to 40 kB *Production feasibility:* difficult to produce at large-scale	(Kaspar et al., 2009) (Lee at al., 2019)

Oncolytic virus	*Toxicity:* moderate *Off-target effects:* moderate *Immunogenicity:* high *Other:* high selectivity for cancerous cells	*Transduction efficiency:* dependent on target tissue, but most efficient on endothelial tissues *Currently approved and administered beyond clinical trials?:* Yes	Cancerous tissues	*Genetic Payload:* up to 140 kB *Production feasibility:* readily scalable at a moderate cost *Other:* limited efficacy against solid tumours	(Zheng et al., 2019) (Gao et al., 2021) (Ungerechts et al., 2016)
Herpes Simplex Virus (HSV)	*Toxicity:* moderate *Off-target effects:* moderate *Immunogenicity:* moderate *Other:* can become latent	*Transduction efficiency:* high *Currently approved and administered beyond clinical trials?:* No	Broad, but mainly epithelial cells	*Genetic Payload:* up to 150 kB *Production feasibility:* expensive at large-scale	(Mody et al., 2020 (Miyagawa et al., 2015)
Human Papillomavirus (HPV)	*Toxicity:* moderate *Off-target effects:* unknown *Immunogenicity:* High	*Transduction efficiency:* moderate *Currently approved and administered beyond clinical trials?:* No	Epitheliotropic, but a strong tropism for cancer cells	*Genetic Payload:* up to 8 kB *Production feasibility:* difficult at large-scale *Other:* rapid degradation can become an issue	(Cerqueira et al., 2017) (Gilson et al., 2020)

Red Blood Cell Extracellular Vesicles (RBCEVs)	*Toxicity:* low *Off-target effects:* low *Immunogenicity:* low *Other:* biocompatible	*Transduction efficiency:* high *Currently approved and administered beyond clinical trials?:* No (currently in stage III clinical trials)	Broad	*Genetic Payload:* up to 30 kB *Production feasibility:* cost-effective *Other:* highly stable	(Biagiotti et al., 2023) (Chiangjong et al., 2021).

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