SIGNIFICANCE STATEMENT

Almost 50 years after it was first proposed, gene therapy is now entering into regular clinical use. The most common method of delivery of genetic material for gene therapy approaches is the adeno-associated virus (AAV). A major gap in the field has been the lack of an AAV capable of transducing the kidney. This paper reports the first systematic examination of AAV subtypes for delivery of genetic material to the kidney. The study identifies a synthetic AAV (Anc80) with efficient transduction of kidney pericytes and perivascular fibroblasts and reports on dosing, timing, and cell specificity. Anc80 is shown to be able to delete floxed genes in mouse mesenchymal cells and transduce kidney mesenchymal cells in human kidney organoids, providing a proof of principle for use in humans.