

## Short-term efficiency and safety of gene delivery into canine kidneys

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**Background.** Gene delivery of biologically active molecules to the kidney may have potential therapeutic applications in renal and cardiovascular diseases. Recombinant adenovirus is one of the most efficient vectors for *in vivo* gene delivery. However, *in vivo* toxicity at the site of administration has to be evaluated for the successful use of adenovirus-mediated gene transfer. The aim of this study was to document precisely the short-term safety of different routes of intra-renal adenoviral administration and to compare their transduction efficiency.

**Methods.** Dog puppies were injected with an adenoviral vector expressing the  $\beta$ -galactosidase reporter gene in both kidneys *via* three different routes, i.e. intra-renal–ureteral route (IU) and intra-renal–arterial route with (IAC) or without (IA) clamping of the renal vein. Toxicity of viral administration was assayed on day 4 at both physiological and histological levels. Renal samples were monitored for the presence of nuclear  $\beta$ -galactosidase-expressing cells.

**Results.** All renal physiological parameters (glomerular filtration rate, effective renal plasma flow, and electrolyte excretion fractions) remained stable whatever the route of viral administration. No histological lesion was detected in any of the haematoxylin–eosin-stained kidney sections, and there was no evidence of ischaemia–reperfusion injury in the kidneys subjected to venous clamping. Efficient transgene expression was obtained in dog kidneys following IAC and IU injection of adenoviral vectors. Gene transfer *via* the IAC route induced gene expression predominantly in the cortical interstitial cells. Retrograde IU adenoviral injection resulted in reduced transduction efficiency compared with the IAC route, with transgene expression occurring mainly in the distal tubular and pyelic epithelial cells.

**Conclusions.** The two major findings of this study were (i) the absence of acute histological and functional renal alteration following intra-arterial and intra-ureteral injections of adenoviral vectors in both kidneys of healthy dogs, and (ii) the efficiency of transgene expression with specific cellular targeting according to the route of administration.

**Keywords:** adenovirus; dog; gene transfer; glomerular filtration rate; kidney; safety

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