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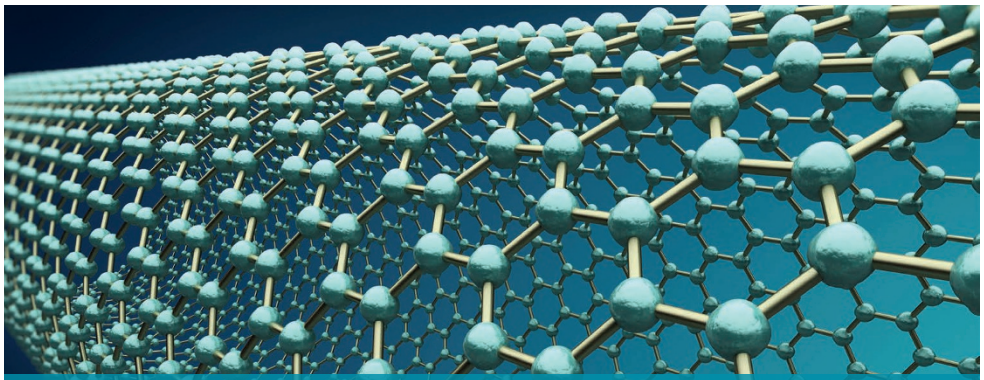

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NANOMEDICINE

Nanocarbon-mediated siRNA delivery to the kidney

> The fCNT safely mediated delivery of the siRNA cargo to the proximal tubule

The development of effective therapeutics based on RNA interference (RNAi) to prevent or treat acute kidney injury (AKI) has been hindered due to confounds such as poor tissue-specific delivery and off-target effects. Now, Michael McDevitt and colleagues report the development of a fibrillar carbon nanomaterial that exhibits tissue-specific and cell-specific pharmacology, which they successfully used as a delivery vehicle for small interfering RNA (siRNA) to target cells of the proximal tubule in mice and silence two genes that are involved in the pathology of AKI.

The researchers previously reported that fibrillar nanocarbon is cleared by glomerular filtration, and that a marked fraction of the dose accumulates in cells of the proximal tubule. They found that small, duplex RNA could be non-covalently bound to this nanocarbon platform and reported a mechanism for deployment of the RNA cargo *in vivo*. These findings led McDevitt and his team to investigate the effects of intravenous administration of an ammonium functionalized carbon nanotube (fCNT) loaded with siRNA in mice, prior to inducing nephrotoxin-associated AKI.

The fCNT safely mediated the delivery of the siRNA cargo to the proximal tubule and permitted successful, concomitant knock down of two target genes, *p53* and *Mep1b*, that have known roles in apoptosis and loss of tubule cell polarity during AKI, respectively. Improved progression-free survival following fCNT–siRNA-mediated knockdown of *p53* and *Mep1b* was realized in both the acute and chronic stages of renal injury, supporting a role for *Mep1b* in AKI and demonstrating that this approach can be used to rapidly target tubule cells.

Finally, the researchers evaluated the effects of delivering the fCNT to non-human primates and found that the pharmacokinetic profile and lack of toxicity of the nanocarbon platform was very similar to that observed in rodent models. "The tissue-specific and cell-specific delivery of bioactive siRNA solves a long-standing problem in the field of therapeutic RNAi", says McDevitt. "We are now exploring the utility of this approach in other models of renal injury, and have commenced toxicological experiments to support the application to clinically evaluate fCNT-mediated RNAi in humans".

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ORIGINAL ARTICLE Alidori, S. *et al.* Targeted fibrillar nanocarbon RNAi treatment of acute kidney injury. *Sci. Transl. Med.* http://dx.doi.org/10.1126/scitranslmed.aac9647

FURTHER READING Ruggiero, A. *et al.* Paradoxical glomerular filtration of carbon nanotubes. *Proc. Natl Acad. Sci. USA* **107**, 12369–12374 (2010)