

Cell type-specific delivery of short interfering RNAs by dye-functionalised theranostic nanoparticles.

Press AT, Traeger A, Pietsch C, Mosig A, Wagner M, Clemens MG, Jbeily N, Koch N, Gottschaldt M, Bézière N, Ermolayev V, Ntziachristos V, Popp J, Kessels MM, Qualmann B, Schubert US, Bauer M (2014) Cell type-specific delivery of short interfering RNAs by dye-functionalised theranostic nanoparticles. *Nat Commun* 5, 5565. [PubMed](#)

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Abstract

Efficient delivery of short interfering RNAs reflects a prerequisite for the development of RNA interference therapeutics. Here, we describe highly specific nanoparticles, based on near infrared fluorescent polymethine dye-derived targeting moieties coupled to biodegradable polymers. The fluorescent dye, even when coupled to a nanoparticle, mimics a ligand for hepatic parenchymal uptake transporters resulting in hepatobiliary clearance of approximately 95% of the dye within 45 min. Body distribution, hepatocyte uptake and excretion into bile of the dye itself, or dye-coupled nanoparticles can be tracked by intravital microscopy or even non-invasively by multispectral optoacoustic tomography. Efficacy of delivery is demonstrated in vivo using 3-hydroxy-3-methyl-glutaryl-CoA reductase siRNA as an active payload resulting in a reduction of plasma cholesterol levels if siRNA was formulated into dye-functionalised nanoparticles. This suggests that organ-selective uptake of a near infrared dye can be efficiently transferred to theranostic nanoparticles allowing novel possibilities for personalised silencing of disease-associated genes.

Identifier

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