Phase I clinical trial of systemically administered TUSC2(FUS1)-nanoparticles mediating functional gene transfer in humans.


The clinical data generated in the report by Lu et al. involving 31 advanced lung cancer patients convincingly support clinical validation of non-viral delivery mechanisms for safe systemic-targeted delivery of DNA plasmids to cancer patients with pulmonary disease.

A critical limitation of DNA-based therapeutics is delivery to the target cell population. Lu et al. in their paper in PLoS ONE demonstrated convincing proof of principle that tumor-specific delivery of DNA can be achieved via systemic infusion of non-viral delivery vehicle. They specifically studied a therapy utilizing a non-viral DOTAP:cholesterol cationic nanoparticle delivery vehicle (1) to deliver an expressive TUSC2 (FUS1) plasmid to patients with advanced lung cancer (2). They demonstrated in 31 patients safe delivery and expression of the intended transgene within primary and metastatic disease sites following systemic delivery in a subset of patients. Functional effect related to delivered transgene expression, as evidenced by induction of intracellular pro-apoptotic signals, was also observed. These results are consistent with a prior publication utilizing the same DOTAP:cholesterol cationic nanoparticle for systemic delivery of another DNA plasmid (GNE gene) in a patient with a rare muscle disorder called hereditary inclusion body myopathy (see [3]), on which I am an author. Moreover, as pointed out by Lu et al. and others, multiple examples in preclinical testing have further supported successful systemic delivery, and functional capacity involving several different experimental DNA therapeutics (see [2], [4, 5], on which I am an author and [6, 7]), Trial registration: NCT00505605.

References
2. Myelosuppression of the T cells required for tumor suppression in human lung cancer cells. Ueno F, Sasaoka J, Nishizaki M, Carboni G, ... Kondo M, Minna JD, Roth JA, Ji L. Cancer research 2004 May 1; 64(9): 2669-76. PMID: 15123327

Competing interests
None declared