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Controlled-release siRNA nanoparticles for sustained gene silencing

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RNA interference (RNAi) has shown tremendous potential in the treatment of diverse diseases including cancer. Numerous nanoparticle (NP) platforms have been developed to facilitate the safe and effective delivery of RNAi therapeutics (e.g., siRNA), which represents a major hurdle for the clinical applications of RNAi. Nevertheless, majority of these NP systems including those in the clinical trials lack the sustained siRNA release property, and thus can only induce transient gene silencing due to the short lifetime of siRNA. Herein, we present an innovative controlled-release NP platform for sustained siRNA delivery, which can be developed through self-assembly of biodegradable and biocompatible polymers and lipids. The lipid-polymer hybrid NPs show excellent knockdown efficacy at low doses of siRNA. More importantly, these NPs can control the temporal release of siRNA for long-term, sustained silencing of target gene expression. For example, obtained results demonstrate that the expression of a target protein PHB1 can be effectively inhibited for over two weeks after short-term transfection with the NPs. The NP-mediated sustained silencing of PHB1 in turn generates more effective tumor cell growth inhibition in vitro and in vivo than the lipofectamine-siRNA complexes. Furthermore, we have applied this NP platform to simultaneously deliver siRNAs against drug resistance and chemotherapeutic drugs for synergistic cancer treatment. It is expected that the lipid-polymer hybrid NP platform with the property of sustained siRNA release could be of interest in both fundamental biological research and clinical applications.

Biography

Jinjun Shi is an Assistant Professor at Harvard Medical School, and directs the laboratory for Nanoengineering and Drug Delivery at Brigham and Women's Hospital, Boston. He has published more than 25 papers and is an inventor of over 15 issued/pending patents. Some of his nanomedicine research work has formed the foundation for the launch of two biotechnology companies–Selecta Biosciences and Koan Therapeutics; and resulted in the clinical trial of a first-in-class synthetic nanoparticle vaccine for smoking cessation. He has also received many awards, including the K99/R00 Award from National Cancer Institute and Young Investigator Award from Prostate Cancer Foundation.

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