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Magnetically targeted drug delivery to stented blood vessels

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Abstract

The potential of magnetic nanoparticles (MNP) for targeted therapy, as well as for diagnostic purposes, has been extensively explored both experimentally and clinically. MNP typically used for therapeutic applications are synthetic biodegradable particles in the size range of 50-500 nm with magnetic responsiveness imparted by nanocrystalline iron oxide and the capacity to carry a therapeutic payload either in the bulk of the particle or attached to the MNP surface. MNP formulated in this size range and targeted to steel stents magnetized by a uniform field provide a novel approach for in-stent restenosis treatment that can be readily adapted for clinical use. MNP targeting can address a number of therapeutic challenges facing vascular disease therapy, such as achieving a clinically relevant local effect in the absence of systemic toxicity, extending the drug presence at therapeutically adequate levels at the site of arterial injury with minimal redistribution to non-target tissues, and adjusting the drug dose to the disease status of a treated blood vessel. We recently showed the feasibility of a novel two-source magnetic targeting scheme for guiding therapeutic agents to injured arteries implanted with a magnetizable stent. In this approach a stent is used as the physical platform for targeted delivery due to its ability to focus the magnetic force in its vicinity and attract therapeutic agents configured in magnetically responsive particles to the site of stent implantation. Notably, this targeted delivery scheme is potentially applicable to deep blood vessels and is not restricted to superficial regions, does not require the use of permanently magnetic materials (thus obviating safety concerns), and can be realized using magnetic field intensities and sources that are currently widely used in the clinic (e.g. MRI scanners and magnetic navigation systems). The effectiveness of this strategy was shown in a rat model of carotid stenting, where biodegradable polymer-based magnetic nanoparticles loaded with paclitaxel effectively inhibited neointima formation compared with non-magnetically treated control animals. Targeted delivery of therapeutic agents configured in magnetically responsive nanocarriers using the two-source guidance strategy is a promising experimental direction that has a great potential in vascular disease therapy.

Biography

Michael Chorny finished his PhD in School of Pharmacy of the Hebrew University of Jerusalem. Since 2009 he is a Research Assistant Professor at the University of Pennsylvania and the Children's Hospital of Philadelphia. His research is focused on biodegradable nanoparticles for targeted delivery of drugs, gene vectors and cells for cardiovascular disease applications and cancer therapy. He has published a number of papers describing novel magnetic carrier formulations for site-specific therapy of injured blood vessels.