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Accelerating endothelium recovery in injured arteries with magnetically guided cell delivery

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Increased susceptibility to thrombosis and restenosis due to slow and often incomplete regrowth of the endothelial layer severely damaged as a result of extensive mechanical injury remains a critical limitation of interventional strategies currently used clinically to relieve atherosclerotic obstruction. Rapid endothelium recovery has the potential to both prevent the thrombotic events and limit post-angioplasty restenosis, providing the rationale for developing strategies aimed at accelerating arterial reendothelialization. In the present study, we evaluated feasibility of achieving stable homing of endothelial cells (EC) in stented arteries using a two-source magnetic guidance strategy. EC functionalized with biodegradable magnetic nanoparticles (MNP) exhibited strong magnetic responsiveness, unaltered proliferation rates, and capacity for targeted delivery effectively confining the cells to the region of stent placement in a rat model of stent angioplasty. Using bioluminescent imaging and fluorimetric tissue analysis, we showed that: 1) Magnetically guided cells will home and expand at the site of stent implantation, 2) Targeted cell delivery realized with a brief exposure to a uniform magnetizing field of a clinically applicable strength can markedly improve site specificity as evidenced by the target:non-target ratio strongly increased in comparison to nonmagnetically treated control animals, and 3) Elimination of MNP used for EC functionalization will take place concomitantly with cell expansion after the completion of the targeted delivery step. The present study contributes to establishing effectiveness and safety of magnetically guided cell delivery and shows the potential of this approach for accelerating the healing of injured blood vessels and reducing vulnerability to untoward effects associated with stent angioplasty.

Biography

Michael Chorny earned his PhD in Pharmaceutical Sciences at the Hebrew University of Jerusalem. Since 2009, he is an Assistant Professor of Pediatrics at the University of Pennsylvania and the Children's Hospital of Philadelphia. His research focuses on development and evaluation of biodegradable nanocarriers for targeted delivery of drugs, gene vectors and cells for cardiovascular disease applications and cancer therapy.

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