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Site-targeting nanotherapeutics for micro vascular normalization

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Abstract

Blood capillaries (microvessels) play a critical role in tissue formation and function as they ensure proper nutrient and oxygen delivery to tissues. Indeed, microvascular dysfunctions in the form of regression and chronic inflammation lead to severe pathologies such as cardiovascular diseases and chronic wounds. Conventional microvascular normalization strategies involve systemic administration of high doses of pharmacological or biological agents that often cause drug tolerance and/or undesirable side effects. To address these limitations, our lab is developing injectable site-targeting nanoparticles that can selectively home to microvascular defect sites and locally deliver low doses of a drug to achieve effective microvascular normalization. The simultaneous increase in drug half-life, control of the rate of drug release and reduction in toxic sideeffects achieved by this targeted nanotherapeutic approach makes it superior to conventional strategies. Specifically, these therapeutic nanoparticles achieve microvascular normalization by increasing the local production of nitric oxide (NO). NO is a gaseous molecule that promotes capillary formation and function and depletion in NO levels leads to various microvascular complications. To enhance NO production, the nanoparticles are loaded with a conventional clinically-used NO-enhancing vasodilatory drug that, we have recently shown, also exhibit novel anti-inflammatory and vasculogenic properties. Finally, the site-targeting capability is achieved by modifying the surface of drug-loaded nanoparticles with an antibody for E-selectin, a cell-surface marker that is overexpressed at sites of microvascular defects. Identification of the unique microvascular normalization properties of a clinically-approved drug and development of a nanotherapeutic approach for its targeted delivery to vascular defect sites may lead to superior clinical management of microvascular dysfunctions and the related pathological conditions.

Biography

Kaustabh Ghosh., Ph.D. is an Assistant Professor of Bioengineering at the University of California, Riverside. Prior to joining UCR, he was a postdoctoral fellow at the Wyss Institute for Biologically Inspired Engineering at Harvard University and the Vascular Biology Program at Children's Hospital & Harvard Medical School. He obtained his Ph.D. in Biomedical Engineering from SUNY at Stony Brook in 2006. Dr Ghosh has received several awards during his research career, including an NIH Postdoctoral Training Grant, has published 19 peer-reviewed papers in reputed journals such as Nano Letters and PNAS, and serves as an editorial board member of the Journal of Regenerative Medicine and Tissue Engineering.