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## Nanotechnology guided delivery of siRNA in retinal vascular disease

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Cell adhesion molecules (CAMs) are markers of inflammation expressed on retinal endothelial cell surfaces in a broad spectrum of ocular vascular diseases, including retinal neovascularization, and therefore constitute potential targets for promoting homing, binding, and internalization of nanoscale imaging and therapeutic agents. We have developed a series of nanocarriers targeted against CAMs which can bear imaging or therapeutic payloads and deliver them to the cytoplasm of dysfunctional endothelial cells. The goal of this study was to demonstrate the utility of CAM targeted nanocarriers for site-specific delivery of antiangiogenic siRNAs in two animal models of retinal neovascularization. CAM targeted nanocarriers bearing VEGFR2 siRNAs were synthesized and characterized to determine optimal size, surface charge, and encapsulation efficiencies. Cytotoxicity, delivery efficiency, and functional knockdown of several molecular targets were determined in retinal microvascular endothelial cells. Biodistribution and efficacy of nanocarriers in animal models of laser-induced choroidal neovascularization and oxygen-induced retinopathy were analyzed. CAM targeted nanocarriers were capable of specific targeting of ICAM-1, endoglin, and VCAM-1 on inflamed retinal endothelial cells *in vitro* and triggered release of siRNA following internalization was observed. Specific targeting of neovascular endothelial cells was observed in both animal models of vascular disease, using CAMs on neovessel endothelial cells as a portal for delivery of therapy. Knockdown of molecular targets via siRNAs was achieved *in vitro* and *in vivo* without adverse effects on cell and tissue function. CAM targeted nanocarriers are a promising framework for the delivery of diverse imaging and therapeutic payloads to diseased retinal endothelial cells *in vivo*.

### Biography

Ashwath Jayagopal is an Assistant Professor of Ophthalmology and Visual Sciences at the Vanderbilt Eye Institute of Vanderbilt University Medical Center in Nashville, TN. He also holds an appointment in Molecular Physiology and Biophysics at Vanderbilt. A biomedical engineer by training, Jayagopal's research interests are focused on imaging and therapy of diabetic retinopathy and neovascular age related macular degeneration. He is a recipient of the 2013 Dolly Green Special Scholar Award from Research to Prevent Blindness. His research program is currently funded by the National Eye Institute, American Diabetes Association, American Health Assistance Foundation, Research to Prevent Blindness, and the International Retinal Research Foundation.

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