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In vivo molecular imaging of retinal vascular disease

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Molecular imaging strategies for early detection of retinal vascular diseases are needed for improving clinical diagnosis, timeliness of therapeutic intervention, and assessment of therapeutic response. Approaches for molecular imaging of the retina have been limited by a lack of molecularly-targeted imaging agents capable of targeting disease biomarkers *in vivo* with sufficient sensitivity and safety. To address the need for clinically-relevant retinal molecular imaging agents, hairpin DNA functionalized gold nanoparticles (hAuNP) featuring optical contrast agents and RNA-specific nucleic acid targeting sequences were developed to noninvasively imaging any messenger RNA or microRNA biomarker in the retina. The goal of this study was to evaluate the utility of hAuNP for longitudinal imaging of mRNA and microRNA biomarkers in an animal model of laser-induced choroidal neovascularization (LCNV) which models ocular angiogenesis exhibited in human age related macular degeneration, with the long-term goal of developing imaging agents for clinical detection of subclinical and advanced CNV. hAuNP designed to specifically target the CNV-relevant mRNA biomarkers HIF1α and VEGFR2, as well as the microRNA 23-24-27 family members, were evaluated using *in vitro* endothelial cell cultures and mouse models of LCNV. Nonspecific control hAuNP and hAuNP targeting housekeeping mRNA transcripts were utilized in parallel as negative controls and normalization of emission signal, respectively. hAuNP were specific for their targets in cell cultures and tissue as evaluated by confocal imaging, *in situ* FISH analysis, flow cytometry, and spectrophotometry. Specific imaging of RNA biomarkers was achieved in retinal tissue using *in vivo* retinal fluorescence imaging of LCNV animal models. Intravenous or subretinal administration of hAuNP was not associated with adverse effects on retinal tissue as evaluated by cell proliferation, ERG and TUNEL analysis. hAuNP are promising nanoscale imaging agents which can be utilized in conjunction with clinically-available ophthalmic imaging instrumentation for noninvasive, high sensitivity, and high specificity imaging of RNA disease biomarkers in retinal vascular disease. The nanoparticle is readily amenable for imaging virtually any RNA target in living tissues, and may also be valuable for elucidating molecular mediators of retinal disease in preclinical studies.

Biography

Ashwath Jayagopal is an Assistant Professor in the Departments of Ophthalmology and Visual Sciences at the Vanderbilt Eye Institute, and Molecular Physiology and Biophysics of Vanderbilt University Medical Center in Nashville, TN. His laboratory is focused on the development of nanotechnology-based imaging and therapeutic strategies for retinal diseases. He received his doctoral degree in biomedical engineering from Vanderbilt University in 2008, and an MBA from Kelley School of Business, Indiana University, in 2011. His research interests are primarily focused on imaging and therapy of diabetic retinopathy (DR) and neovascular age related macular degeneration (nvAMD), with emphasis on targeting dysfunctional endothelial cells. In addition, his laboratory has developed a number of optical nanoparticle-based imaging contrast agents for imaging specific disease biomarkers, including proteins and RNAs, in neovascular endothelial cells and retinal ganglion cells in animal models of DR, nvAMD, and glaucoma. 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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