Multimodal, High-Resolution, Non-invasive in vivo Tracking of Subretinal Injection of ARPE19 Cells Labeled with Chain-like Gold Nanoparticle Clusters for Regenerative Medicine

Yannis M Paulus, MD
Ann Arbor, MI
Van Phuc Nguyen, PhD, Tianye Zhu, Wen Fan, MD, Wei Qian, PhD, Bing Liu, PhD, Xueding Wang, PhD

Purpose:
Stem cell therapy offers a promising method for the treatment of currently incurable diseases. However, a major challenge of stem cell therapy is to evaluate the treatment outcome and to track the distribution of cells after transplanted in biological tissue. In this study, an advanced non-invasive photoacoustic microscopy (PAM) and optical coherence tomography (OCT) imaging system is developed to monitor progenitor cells in vivo.

Methods:
A high resolution multimodal PAM and OCT imaging system is developed for tracking transplanted cells in living rabbit retina. Ultrapure functionalized chain-like gold nanoparticle (CGNP) clusters were synthesized and used to label human retinal pigment epithelial (ARPE-19) cells prior to injecting them in the subretinal space in rabbits having localized RPE damage via photocoagulation lesions. The biodistribution and migration of the transplanted cells were monitored using multimodal imaging, including color fundus photography, ICGA, PAM, and OCT for up to 90 days.

Results:
PAM images were obtained at two different optical wavelengths of 578 nm to visualize vasculature and 650 nm to visualize ARPE-19 cells and were overlaid on the same image plane and on the OCT image. Transplanted ARPE-19 cells injected into the subretinal space can be selectively identified by PAM at 650nm with high contrast. The laser energy used to perform PAM is 80 nJ, or half of the ANSI safety limit. Co-registration of B-scan OCT with PAM provides information on the anatomic layers in which the ARPE-19 cells are found, which is in the RPE and adjacent layers. ARPE-19 cells localize focally to the grid pattern photocoagulation lesion locations and persist for up to 90 days after injection. Bare CGNP clusters injected into the control eyes do not selectively localize and are rapidly cleared after 14 days. Histology and immunohistochemistry confirm the ARPE-19 cells localize to the regions demonstrated on OCT and PAM at 650nm.

Conclusions:
Multimodal PAM and OCT imaging using CGNP clusters can allow for an imaging and nanoparticle system could be used for labeling and tracking of cell-based regenerative therapies in the retina.