AB034. *In vivo* laser-mediated retinal ganglion cell optoporation using Kv1.1 conjugated gold nanoparticles

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Background: There is a current void in efficient, cell-specific, retinal drug delivery systems, thus developing a safe, effective, selective drug delivery system would open novel therapeutic avenues. We previously demonstrated that femtosecond (fs) laser irradiation can transfect DNA plasmids into cultured cells in the presence of gold nanoparticles (AuNPs). These AuNPs locally amplify laser energy at a submicron range creating transient pores allowing exogenous genetic material or cell impermeable dyes to enter the cell. Here, we sought out to selectively optoporate retinal cells *in vivo* with functionalized AuNPs and a 800 nm femtosecond (fs) laser.

Methods: The cell-surface Kv1.1 voltage-gated channel was chosen to selectively target retinal ganglion cells (RGC) in the rat retina. Citrate-capped spherical 100 nm AuNPs functionalized with orthopyridyl-disulfide-poly(ethylene glycol) (5 kDa)-N-hydroxysuccinimide (OPSS-PEG-NHS) conjugated to a Kv1.1 monoclonal antibody were injected intravitreally in Sprague Dawley rats 3 hours prior to irradiation, concomitantly to a FITC-dextran dye to detect optoporation. The eyes of anesthetized rats were placed in the beam path of a laser system consisting of an 800 nm, 100 fs laser and a Heidelberg Spectralis HRA ophthalmoscope for fundus visualization. The rat retina was irradiated at powers ranging from 20–750 mW, the eyes fixed in 4% paraformaldehyde, dissected, rinsed, mounted and imaged by confocal microscopy.

Results: Our novel laser system coupled to a Heidelberg ophthalmoscope allowed for a clear visualisation of the rat ocular fundus. A timecourse of AuNP intravitreal injections revealed that optimal nanoparticle dispersion on the retinal surface occurred at 3 hours post injection. Following Kv1.1-AuNP and FITC-dextran intravitreal injection and incubation, irradiation at 120–750 mW resulted in FITC uptake by retinal cells.

Conclusions: Since living biological tissues absorb energy very weakly at 800 nm, this non-invasive tool may provide a safe, cost effective clinically relevant approach to selectively target retinal cells and limit complications associated with surgical interventions, and potential biological hazards associated with viral-based gene therapy.

Keywords: Nanoparticle; laser; optoporation

doi: 10.21037/aes.2018.AB034

Cite this abstract as: Wilson AM, Mazzaferri J, Bergeron É, Patskovsky S, Costantino S, Meunier M, Sapieha P. *In vivo* laser-mediated retinal ganglion cell optoporation using Kv1.1 conjugated gold nanoparticles. Ann Eye Sci 2018;3:AB034.