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**Pronase E improves gene transduction of retinal ganglion cells**

Abstracts of the Royal Australian and New Zealand College of Ophthalmologists 51st Annual Scientific Congress, as published in Clinical and Experimental Ophthalmology, 2019 / vol.47, iss.Suppl. 1, pp.119

***which has been published in final form at <http://dx.doi.org/10.1111/ceo.13632>.***

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**1 July 2021**

<http://hdl.handle.net/2440/130881>

## Pronase E improves gene transduction of retinal ganglion cells

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**Purpose:** Intravitreal injection is used for gene delivery to retinal ganglion cells, but has low efficiencies of transduction. The aim of the present study was to optimise recombinant adenovirus-associated vector (rAAV)-mediated gene transduction of retinal ganglion cells by co-administration with proteolytic enzymes.

**Method:** Female Sprague-Dawley rats (n = 4) received a 5 µL intravitreal injection containing 5e+9 genome copies (gc) rAAV. The rAAV contained a bistrionic cassette expressing green fluorescent protein (rAAV2/2.CAG.NGB.HA.IRES.GFP.pA). Further groups received co-administration of Pronase E (n = 6) or Heparinase III + Hyaluronidase (n = 8). The fellow eye received a vehicle injection. Retinal function was analysed at 2 weeks by scotopic electroretinography (ERG). At 3 weeks, GFP expression was assessed in vivo using a confocal scanning laser ophthalmoscope (cSLO). Animals were then euthanized for whole mount retinas.

**Results:** The mean in vivo GFP expression on cSLO fundal images in rAAV + Pronase E eyes (360 of fundus ± 0) was significantly greater than rAAV + Hep/Hyal (70 ± 35; P < 0.001) or rAAV alone (200 ± 47; P < 0.001) eyes. Analysis of retinal whole mounts supported this pattern of increased transduction with Pronase E. The ERG b-wave of PBS-injected eyes (1195 ± 59 µV) was not different from rAAV-only injected eyes (1246 ± 101 µV; P = 0.46), rAAV + Pronase E eyes (1004 ± 105 µV; P = 0.18) or rAAV + Hep/Hyal eyes (1150 ± 64 µV; P = 0.33).

**Conclusion:** Retinal ganglion cell transduction by rAAV was enhanced by co-administration of Pronase E. Importantly, this effect was not associated with increased retinal toxicity, as assessed by electroretinography. The use of pronase E should be considered for delivery of candidate neuroprotective genes to retinal ganglion cells.