

Sodium Iodate-Induced Retinal Degeneration Model in Rats and Rabbits

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Introduction

Retinal pigment epithelium (RPE) and photoreceptor dysfunction are characteristic of retinal degeneration diseases. An excessive amount of reactive oxygen species (ROS) is implicated in retinal disorders. Sodium Iodate (NaI), a selective toxic oxidizing agent against RPE, is widely used in rodents to mimic some features of geographic atrophy. Studies in rabbits are fewer despite the rabbit eye having an appropriate size to test therapeutics such as intravitreal compounds or ocular implants. The purpose of this study was to compare the NaI-induced retinal degeneration in rabbits and rats.

Material and Method

Induction of retinal degeneration

Retinal degeneration was induced in ten Brown Norway rats by intraperitoneal injection of 50 mg/kg NaI, and in ten Dutch belted rabbits by intravitreal injection of 400 µg NaI in the right eye.

Animals were handled and cared for according to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research.

Clinical Evaluations

Retinal pigmented epithelium (RPE) and photoreceptor degenerative changes were assessed by optical coherence tomography (OCT), fundus autofluorescence one week and two weeks after NaI injection, using Spectralis™ (Heidelberg Engineering). One vertical section was taken in the superior part and one in the inferior part from the optic nerve head for the rat and in the visual streak below the optic nerve head in the rabbit eye. Photoreceptor layer (PRL) thickness on OCT scan was measured at 4 positions for the rat. A qualitative evaluation was done on OCT scan for the rabbit. Autofluorescence fundus pictures were centered on the optic nerve head for the rat and in the inferior part of the optic nerve head for the rabbit.

Retinal functionality was assessed by ERG on both eyes using a flash intensity of 3 cd.s/m² on dilated eye (system RETI-animal® from Roland Consult for rat and Metrovision® for rabbit). The amplitude of a- and b-wave were measured.

Immunohistochemistry of flatmounted RPE-Choroid-sclera

Eyeballs (EB) were fixed in 4% paraformaldehyde for 1 hour at room temperature. After washing with PBS, the eye cup was dissected, and the retina carefully peeled from retina-choroid-sclera tissue. The flatmounted RPE-choroid-sclera were labelled with Alexa Fluor 488 conjugated Phalloidin (AbCam).

Oil-RedO staining of retinal section

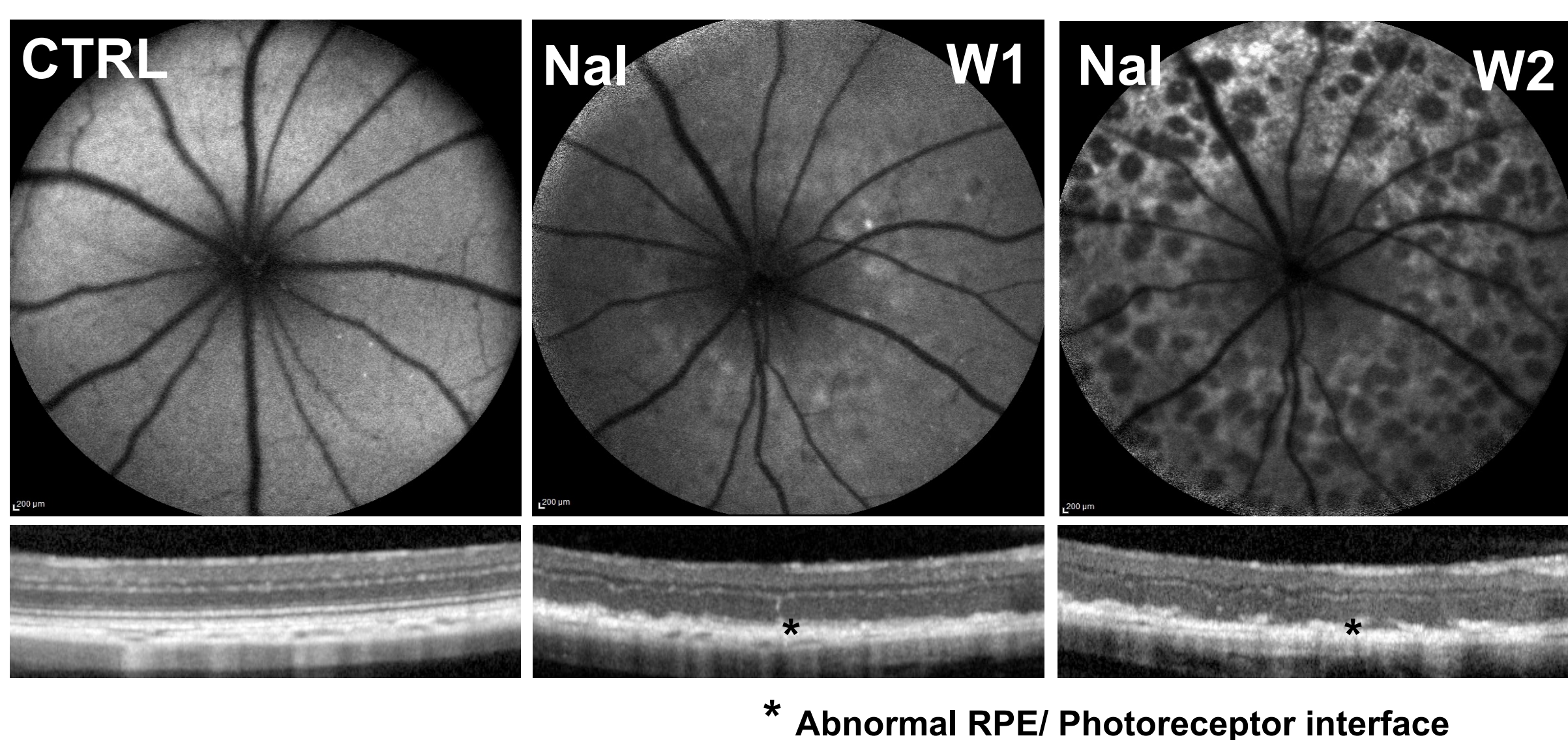
EB were embedded in OCT (optimal cutting temperature) compound, 4 µm cryosection were stained with Oil red O solution for detection of lipid.

Relative mRNA expression

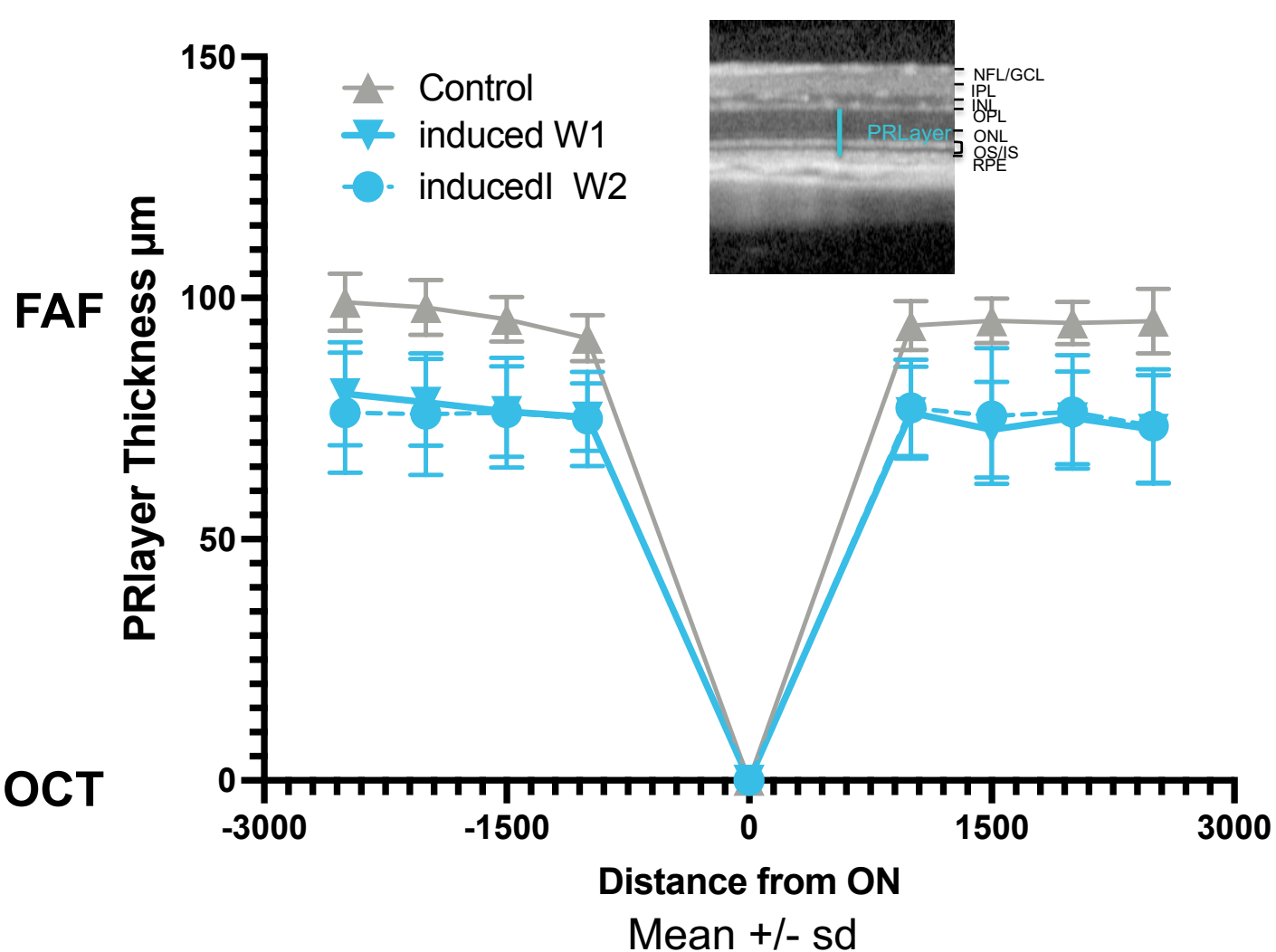
The mRNA levels of selected genes were analyzed by RT-qPCR. Relative gene expression was calculated using the 2-ΔΔCt method by normalizing with the GAPDH reference gene.

Results

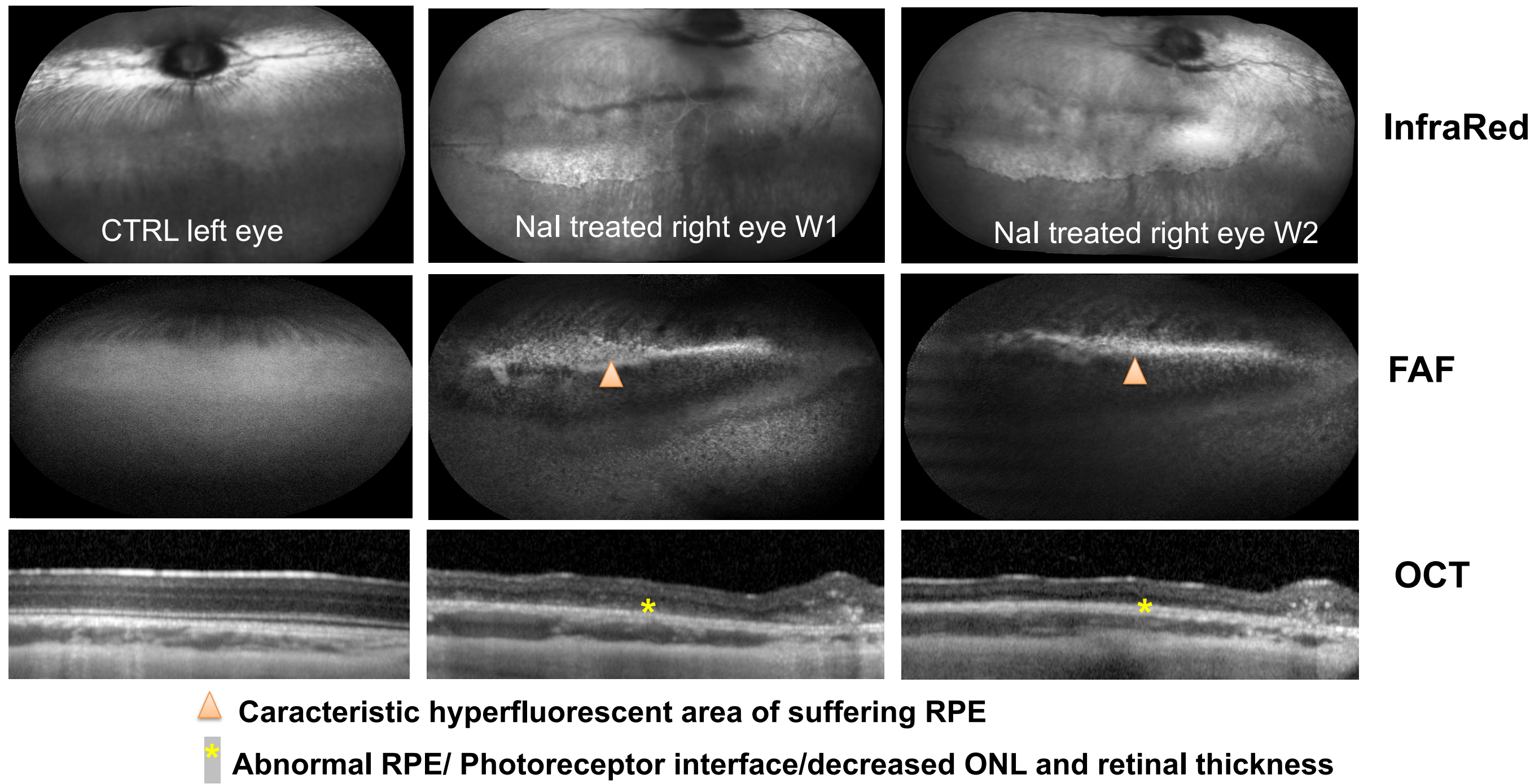
In vivo retinal imaging in rat



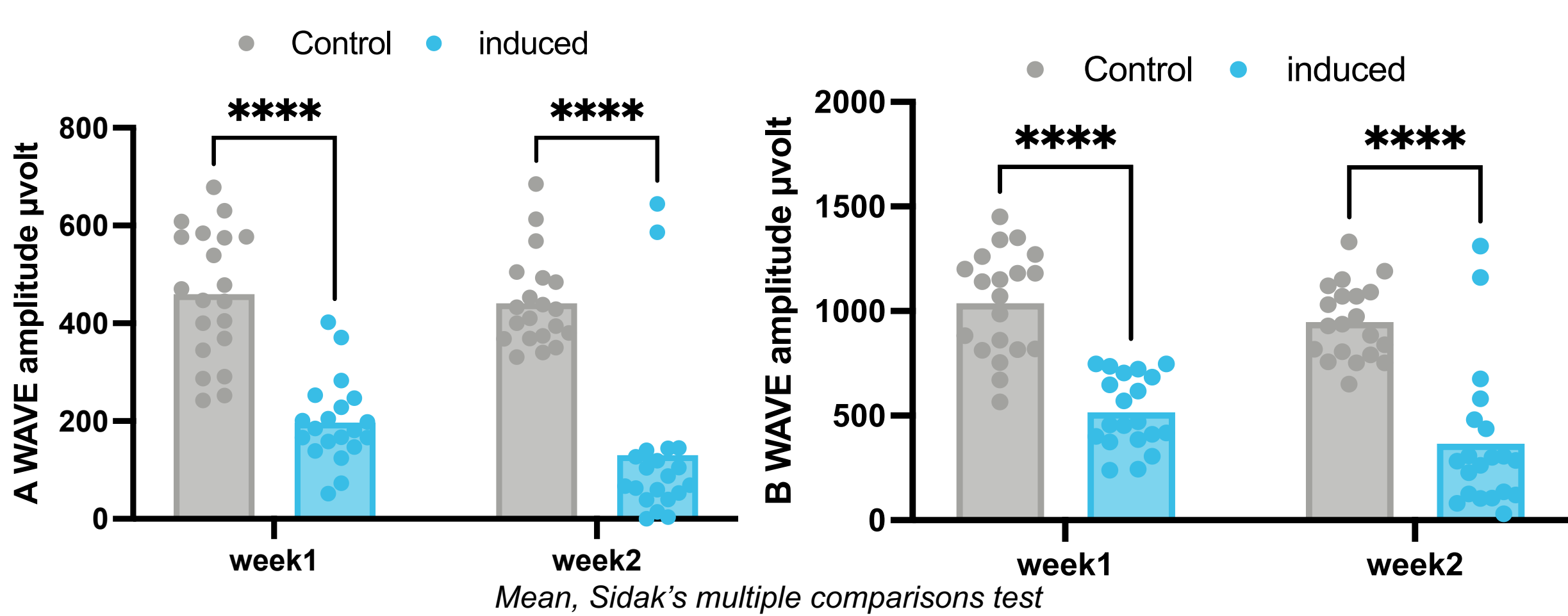
Photoreceptor layer thickness



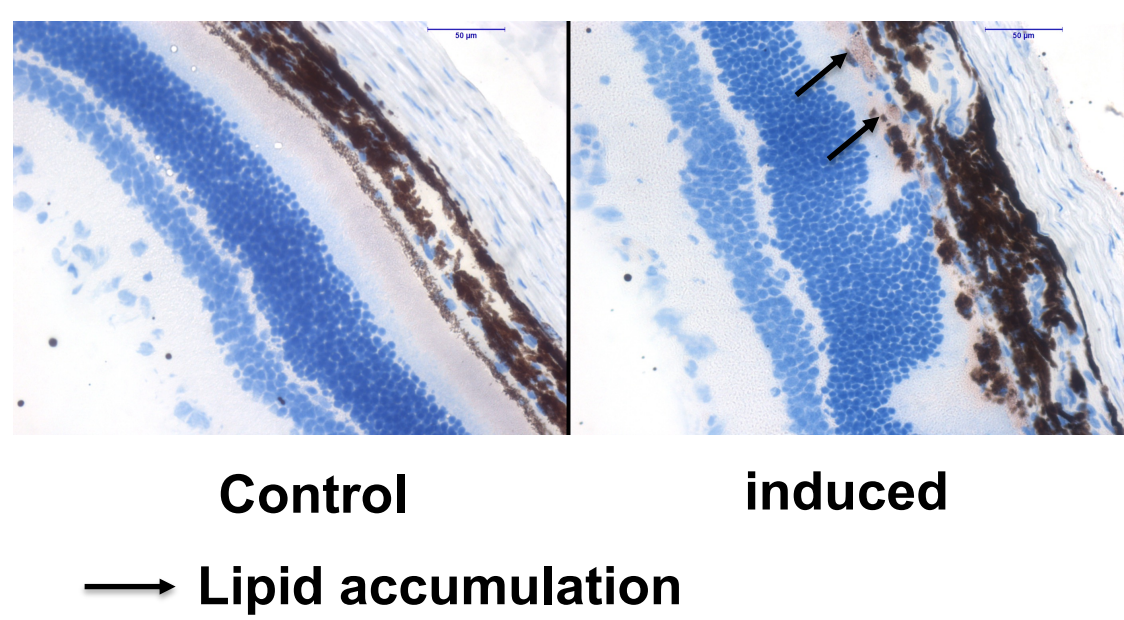
In vivo retinal imaging in rabbit



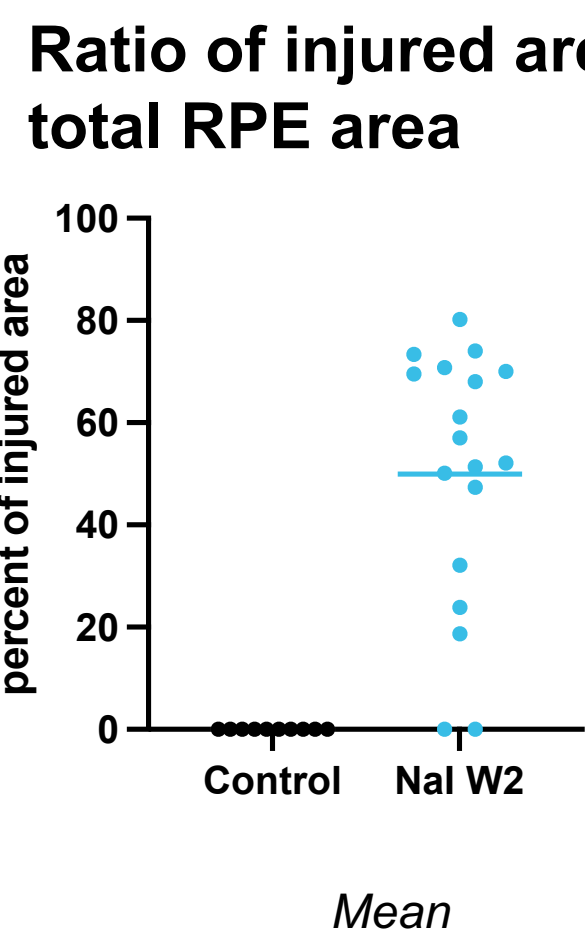
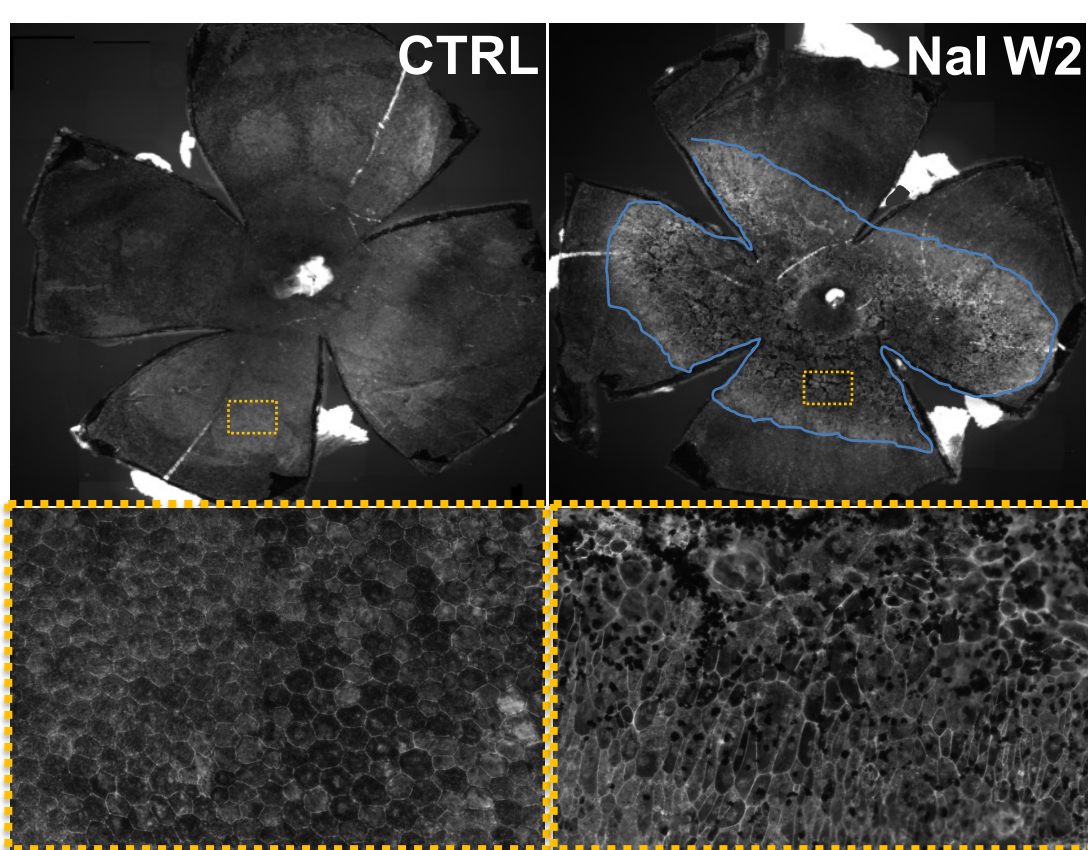
ERG A wave – B wave rat



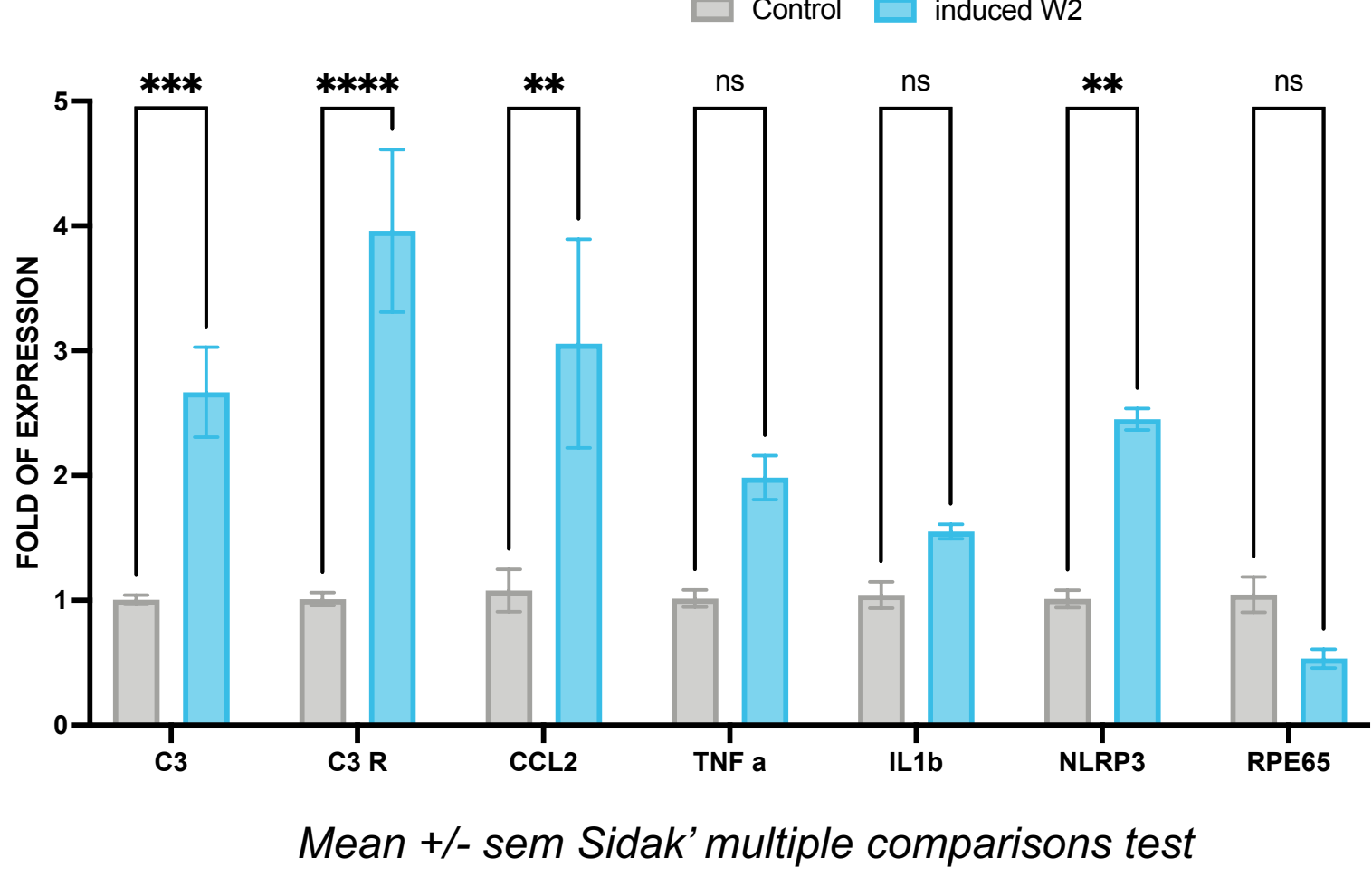
Oil-RedO staining of retinal section



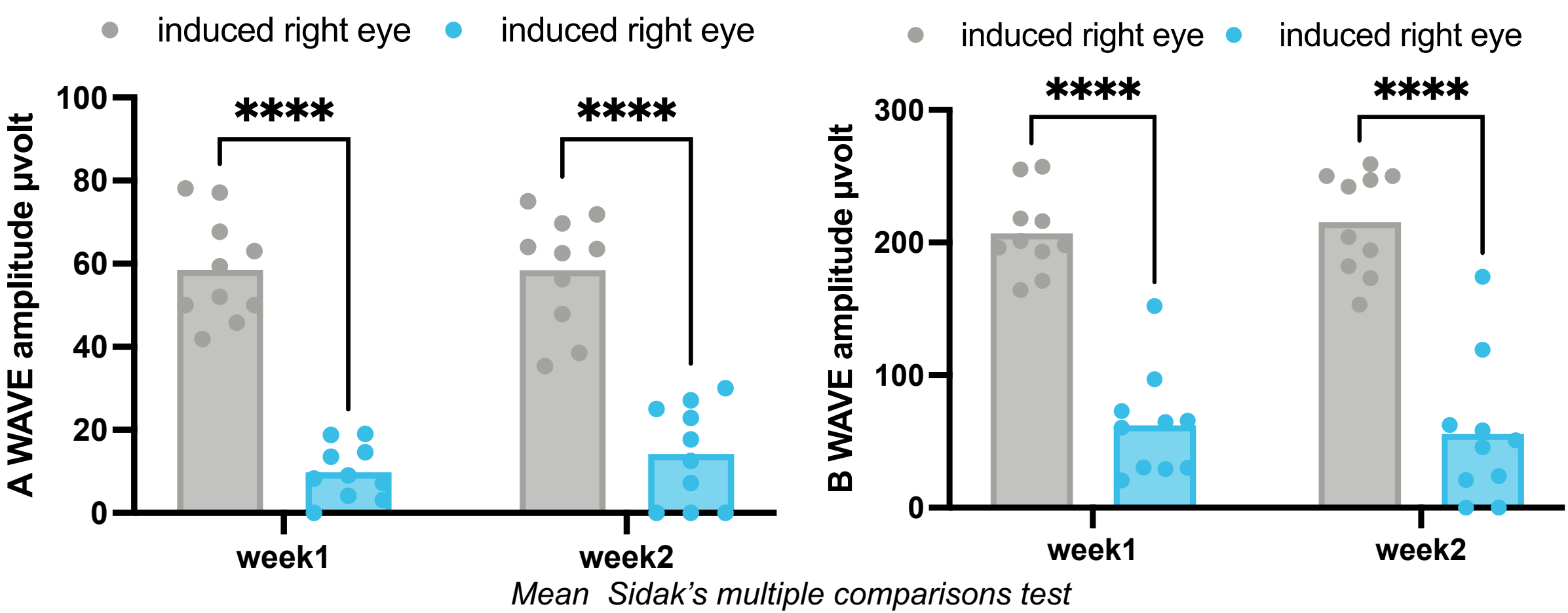
Phalloidin staining of the RPE/choroidal flatmount



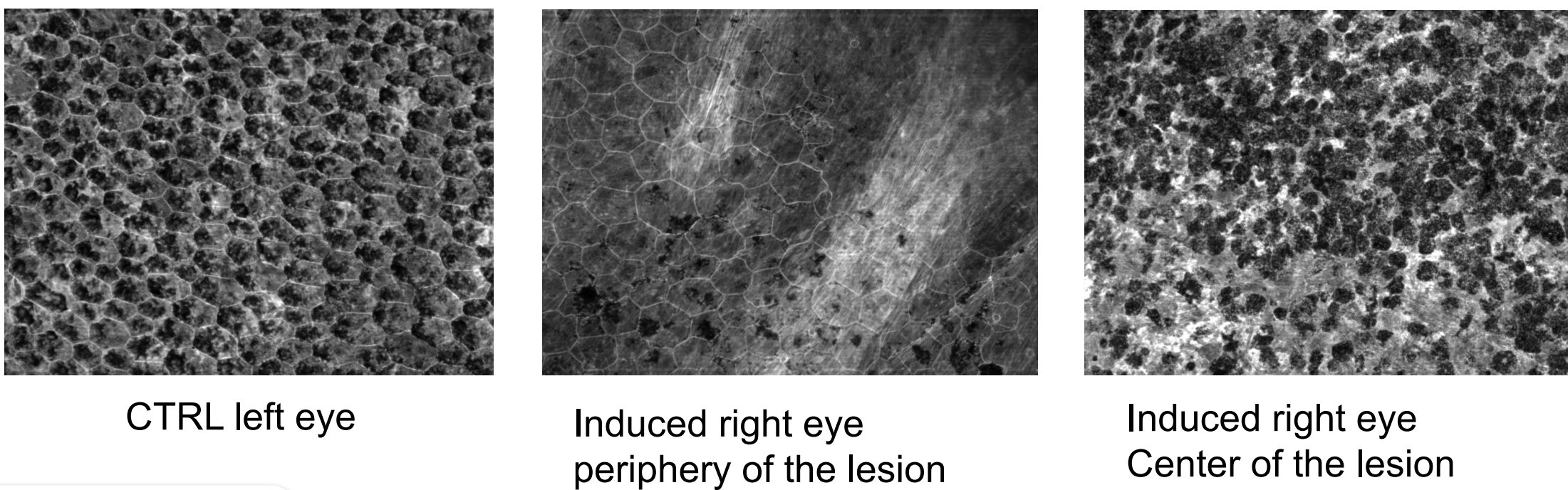
Relative mRNA expression in rat



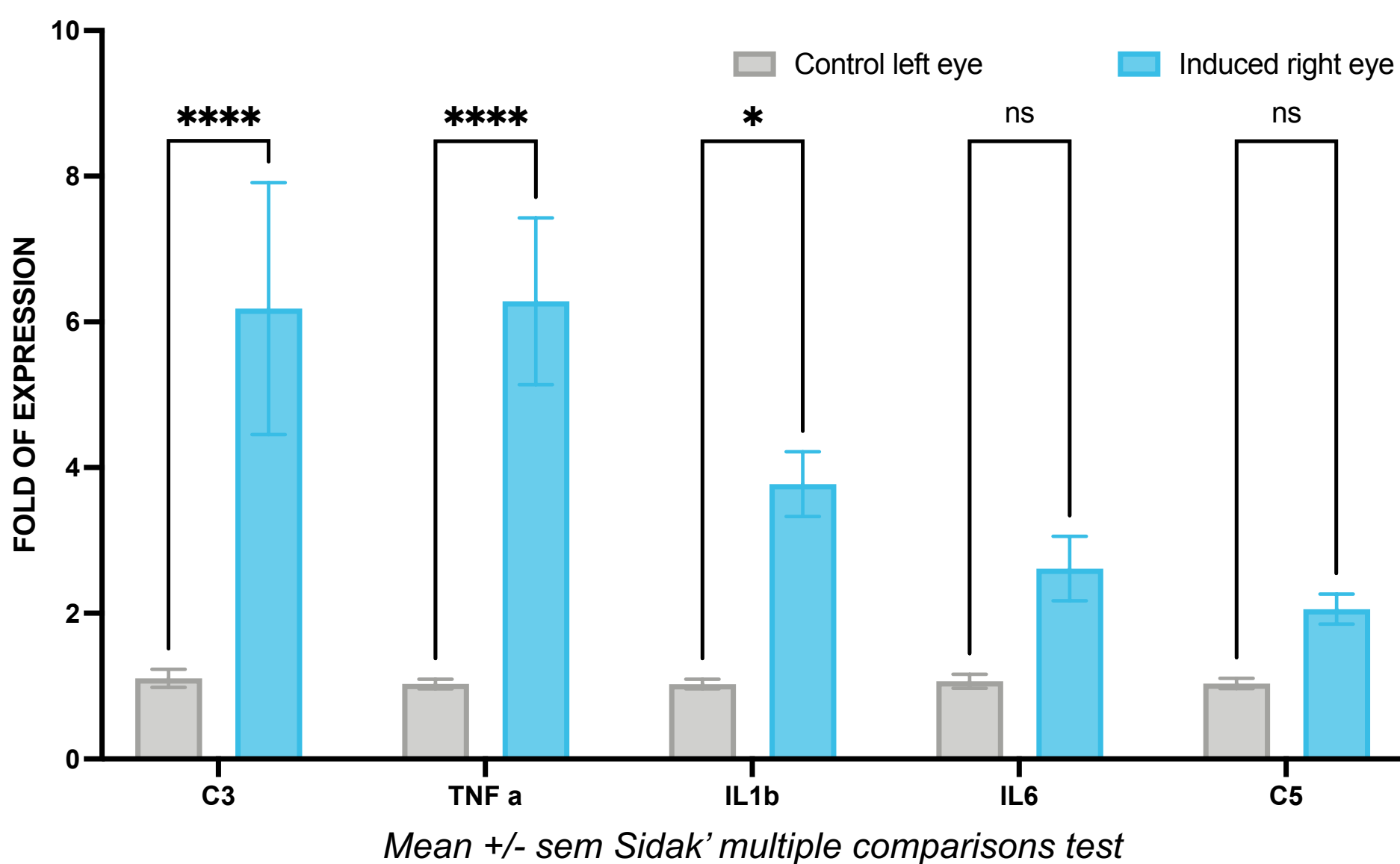
ERG A wave – B wave rabbit



Phalloidin staining of the RPE/choroidal flatmount in rabbit



Relative mRNA expression in rabbit



Conclusions

Sodium iodate treatment induced retinal lesion in the RPE/photoreceptor interface, showing patchy lesions of the RPE after one week, as an alteration of ERG response in both species. An accumulation of lipid deposits in rat histological sections compared to healthy rats was observed. An increased mRNA levels of inflammatory cytokines and complement components, especially C3, were also observed in both species. Sodium iodate induction in rabbits as well as in rats are reliable models for studying retinal degeneration and testing therapeutic interventions, particularly those targeting the complement.

References

Yang Y, Ng TK, Ye C, et al. Assessing sodium iodate-induced outer retinal changes in rats using confocal scanning laser ophthalmoscopy and optical coherence tomography. Invest Ophthalmol Vis Sci. 2014;55:1696–170
So Min Ahn, et al. The effects of intravitreal sodium iodate injection on retinal degeneration following vitrectomy in rabbits. Sci Rep. 2019 Oct 30;9(1):15696.