Unraveling the spatial dynamics of neurovascular coupling in retinopathy of a mutant MITF mouse model

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MOLECULAR BIOTECHNOLOGY AND DIAGNOSTICS

Background

Ocular health relies on the intricate communication between neurons, glial cells, murine cells and ECs, a phenomenon termed neurovascular coupling. Factors, such as metabolic and genetic factors can drastically offset the balance in communication and cause visual impairment or blindness.
Microphthalmia-associated transcription factor (MITF) gene is specifically expressed in the retinal pigmented epithelium (RPE) and neural crest-derived melanocytes in the eye, where it acts as a master regulator of cell development. Point mutations in the MITF gene are associated with several pathological conditions, such as Waardenburg syndrome and Tietz syndrome. Enu22 mice have a point mutation that truncates three exons from the MITF gene product without abolishing its complete function. However, the Enu22 retina has not been previously characterized to the extent presented here.

Aims

- To characterize homozygote Mitf$^{mi\text{-}enu22(398)}$ mouse model with a point mutation, kindly provided to us by our collaborators from University of Iceland, Prof. Thor Eysteinsson. (García-Llorca *et al.).*
- Gain an idea of what mechanisms are involved in the pathophysiological phenomenon.
- Check therapeutically relevant biomarkers, such as purinergic markers CD39, CD73 and Connexin 43, which partake in neurovascular coupling.

Methodology

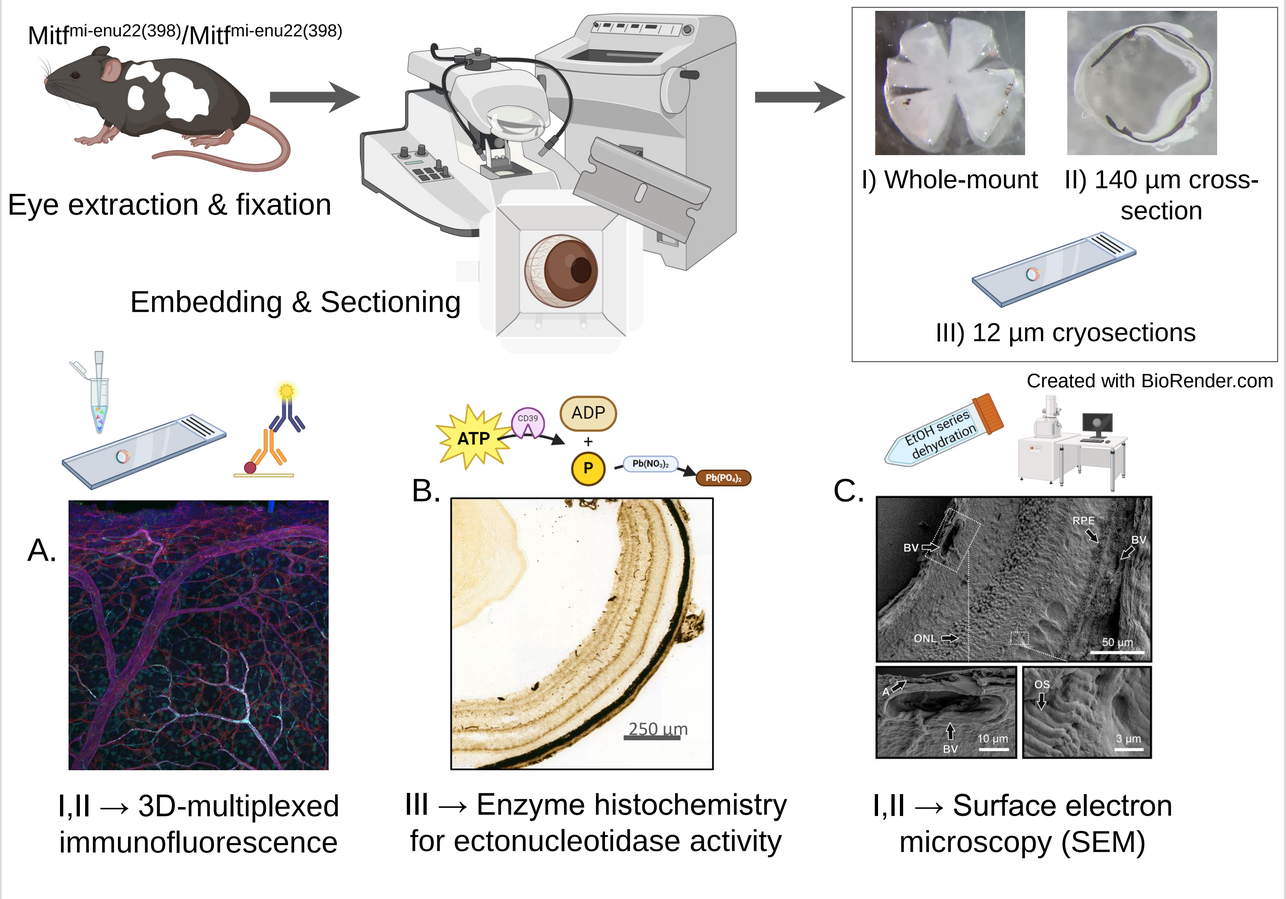
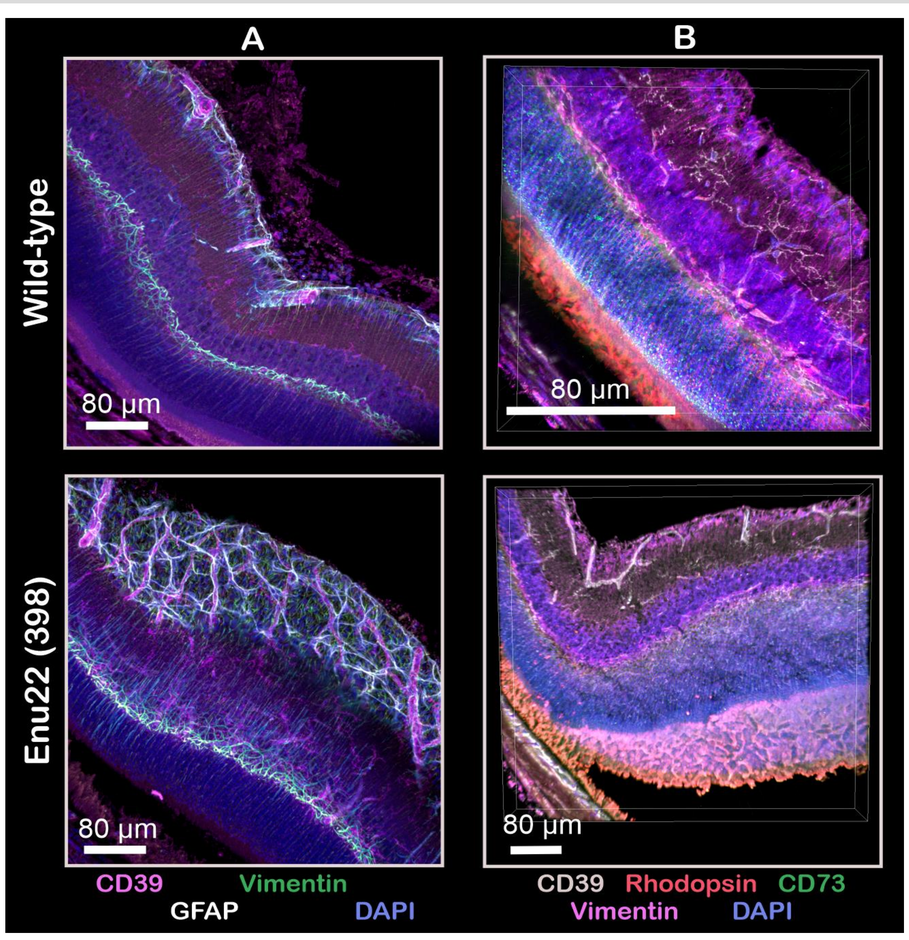


Figure 1. General overview of the workflow for studying retinal samples of Mitf$^{mi\text{-}enu22(398)}$ mice.

Results



◄ Figure 2. Immunofluorescence staining of retinal cross-sections. Wild-type and Enu22 eyes were stained with antibodies against CD39 (co-expressed on blood vessels and microglia), CD73 (expressed on photoreceptor layer), together with molecular markers of Müller glia (vimentin), astrocytes (GFAP), and rods (rhodopsin), as indicated.

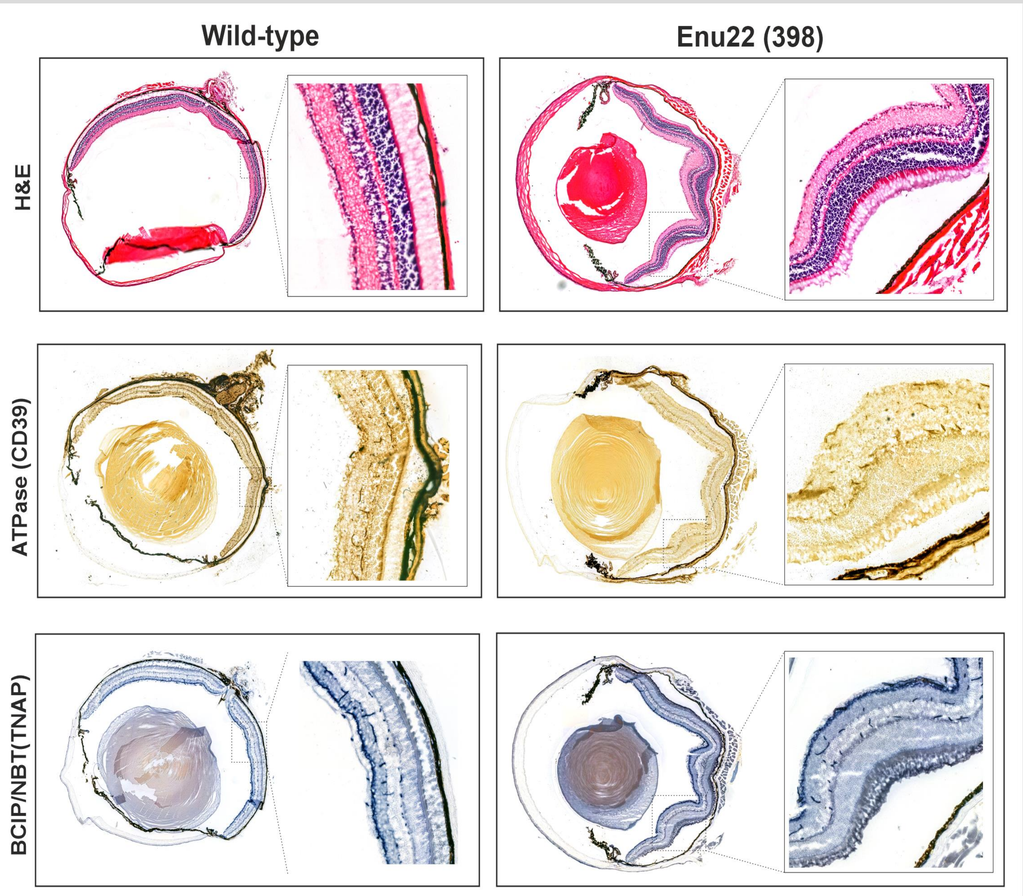
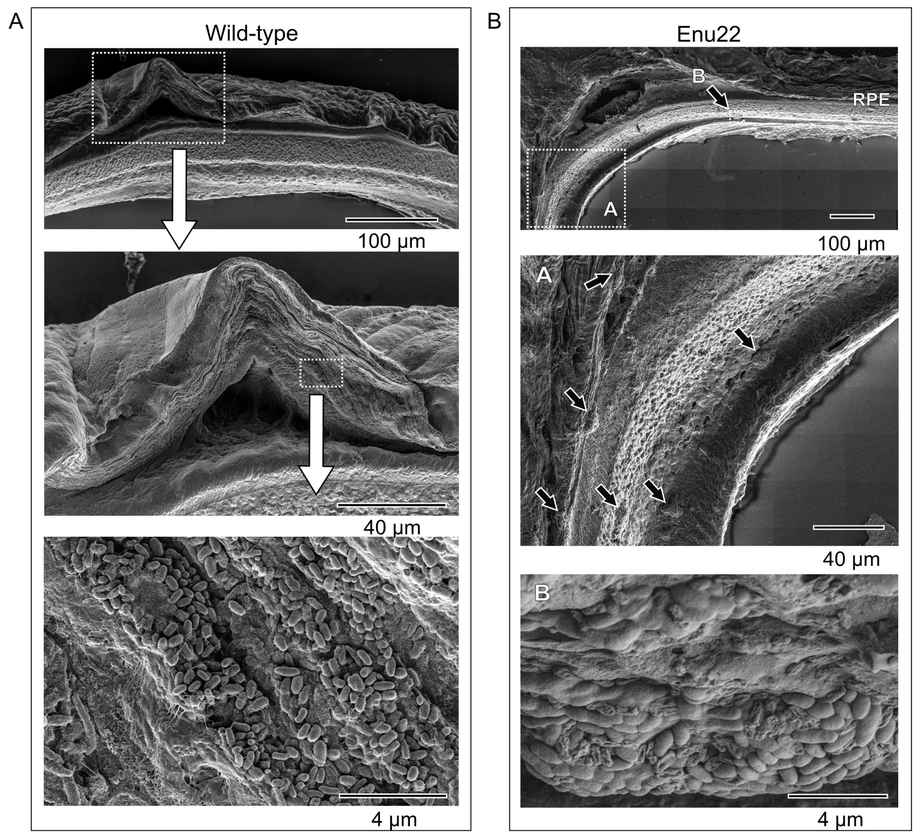


Figure 3. Histochemical stains of WT & Enu22 eyes. Lesions are prominent even in 12 µm sections. However, enzymatic staining is not drastically different.



◄ Figure 4. Surface electron microscopy images acquired for retinal cross-sections of wild-type and Enu22 eyes. Black arrows point to ambiguous melanosome clusters frequently detected in Enu22 eyes.

Conclusions

Homozygote Mitf$^{mi\text{-}enu22(398)}$ do not develop melanosomes normally, which is reflected by the hypopigmentation of the eyes and the unusual distribution of melanosomes. Most importantly, Enu22 mice develop large lesions with hyperproliferating glial cells (astrogliosis), which in turn take a toll on retinal integrity.

References

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