

Lebercilin Mutations Associated With Photoreceptor Protein Loss

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Introduction

- Photoreceptors are light-detecting retinal cells that are essential for vision
- Photoreceptor damage leads to irreversible vision loss
- Leber Congenital Amaurosis (LCA) is a retinal disease that leads to degeneration and dysfunction of photoreceptors
- LCA5* is a gene that encodes for lebercilin, a ciliary protein involved in IFT
- Prom1 is a protein found in photoreceptor OSs, plays a role in OS structural integrity and disc morphogenesis
- CtBP2 is a protein found in photoreceptor synapses, plays a role in the transmission of sensory information

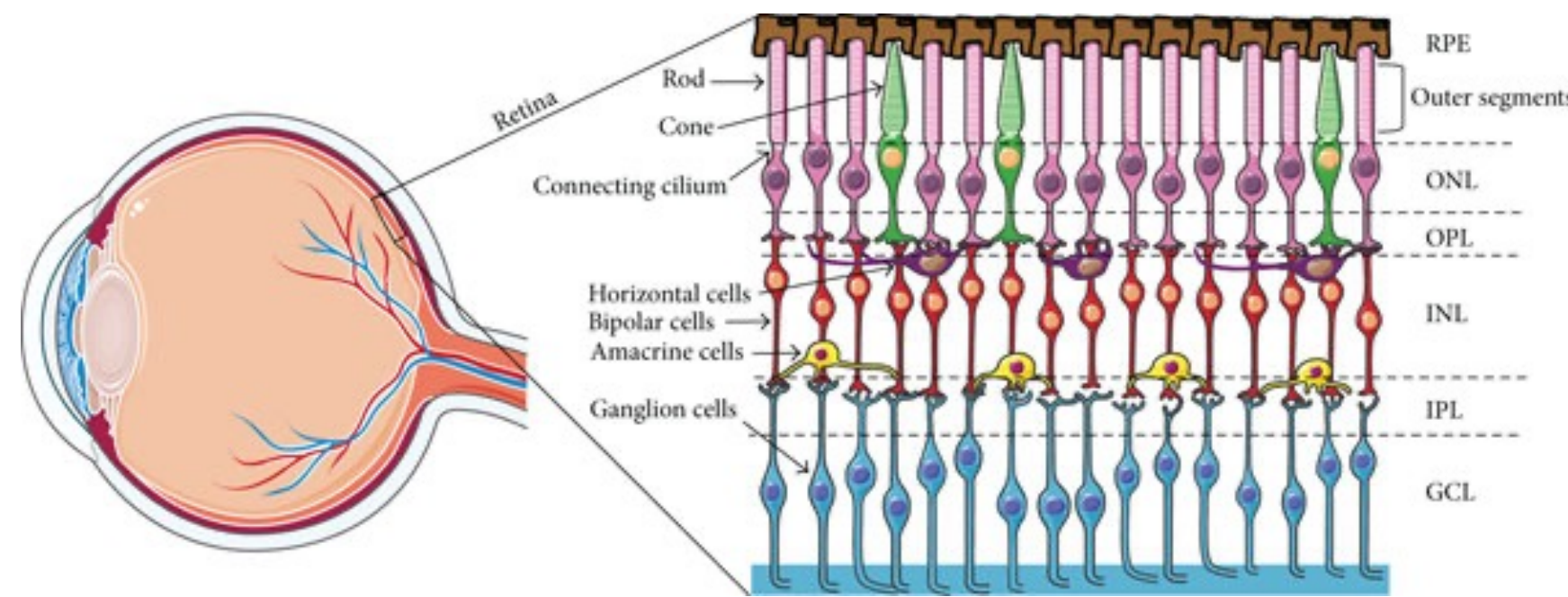


Figure 1. Schematic Representation of the Retina and Retinal Cell Layers. (RPE) Retinal Pigment Epithelium. (OS) Outer Segment. (IS) Inner Segment. (ONL) Outer Nuclear Layer. (OPL) Outer Plexiform Layer. (INL) Inner Nuclear Layer. (IPL) Inner Plexiform Layer. (GCL) Ganglion Cell Layer.

Hypothesis

Prom1 and CtBP2 levels decrease in the *Lca5* mouse model.

Methods

- Obtained retinal samples from WT and *Lca5* ^{-/-} mice at P15, P30, and P90 for immunofluorescent analysis (**figure 2**)
- Imaged samples through confocal microscopy
- Obtained cDNA from WT and *Lca5* ^{-/-} mice at P15, P30, and P90 for qPCR analysis (**figure 2**)

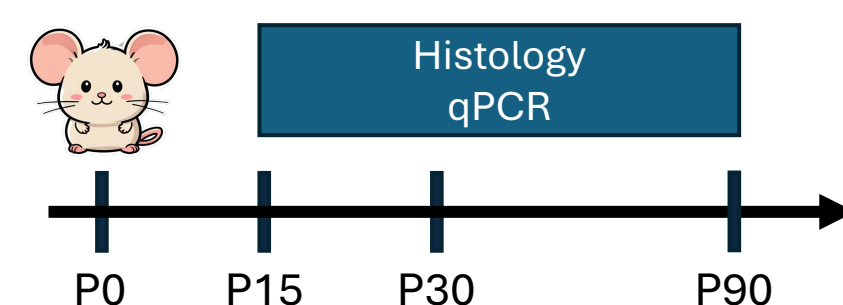


Figure 2. WT and *Lca5* ^{-/-} mice retinas harvested at P15, P30, and P90.

Results

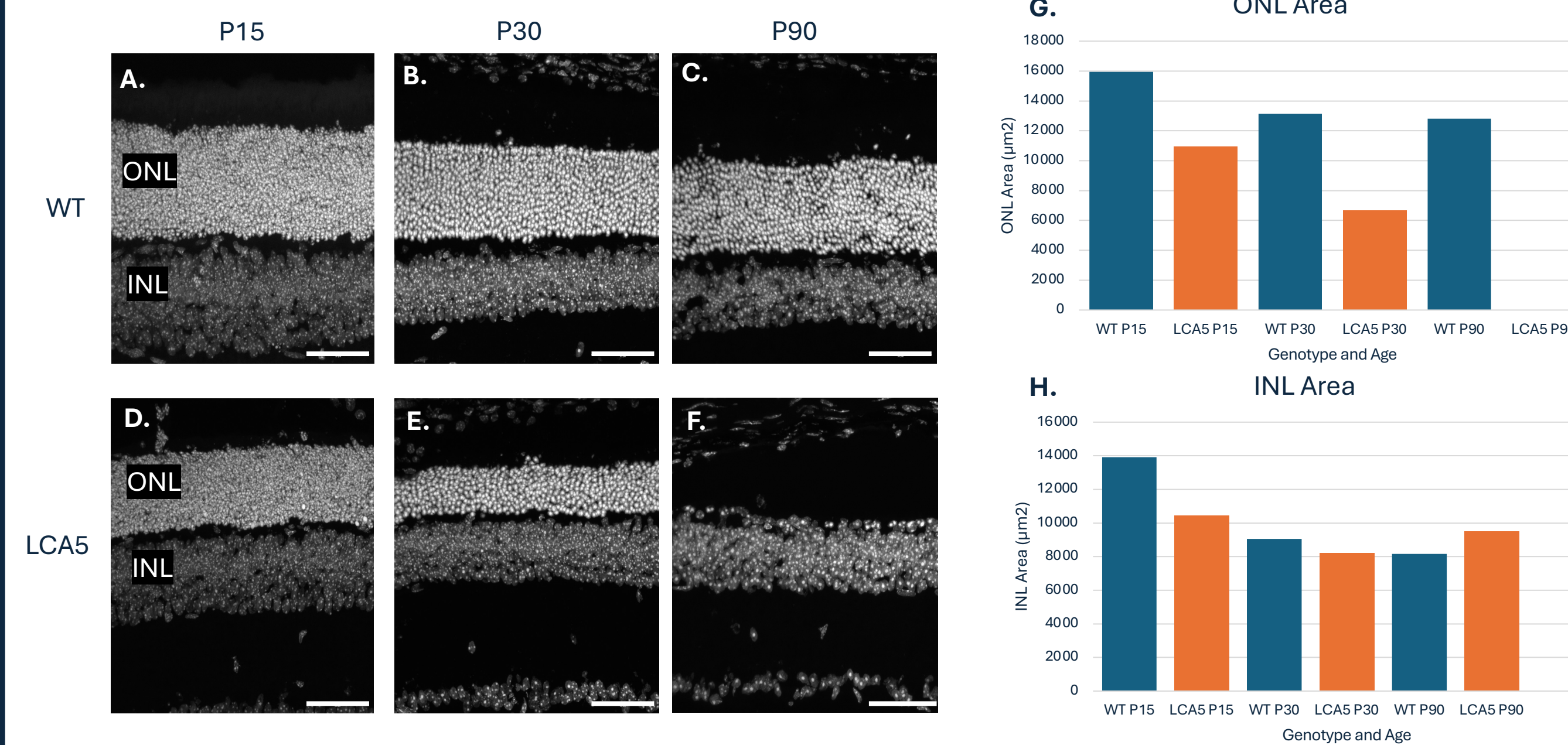


Figure 3. ONL and INL Area Decrease Over Time in *Lca5* ^{-/-} Mice. Samples A-F stained with Hoechst. (A-C) are WT, (D-F) are *Lca5* ^{-/-} mice. (G) ONL Area of WT and *Lca5* ^{-/-} mice over time. (H) INL Area of WT and *Lca5* ^{-/-} mice over time. Scale Bar: 50 µm.

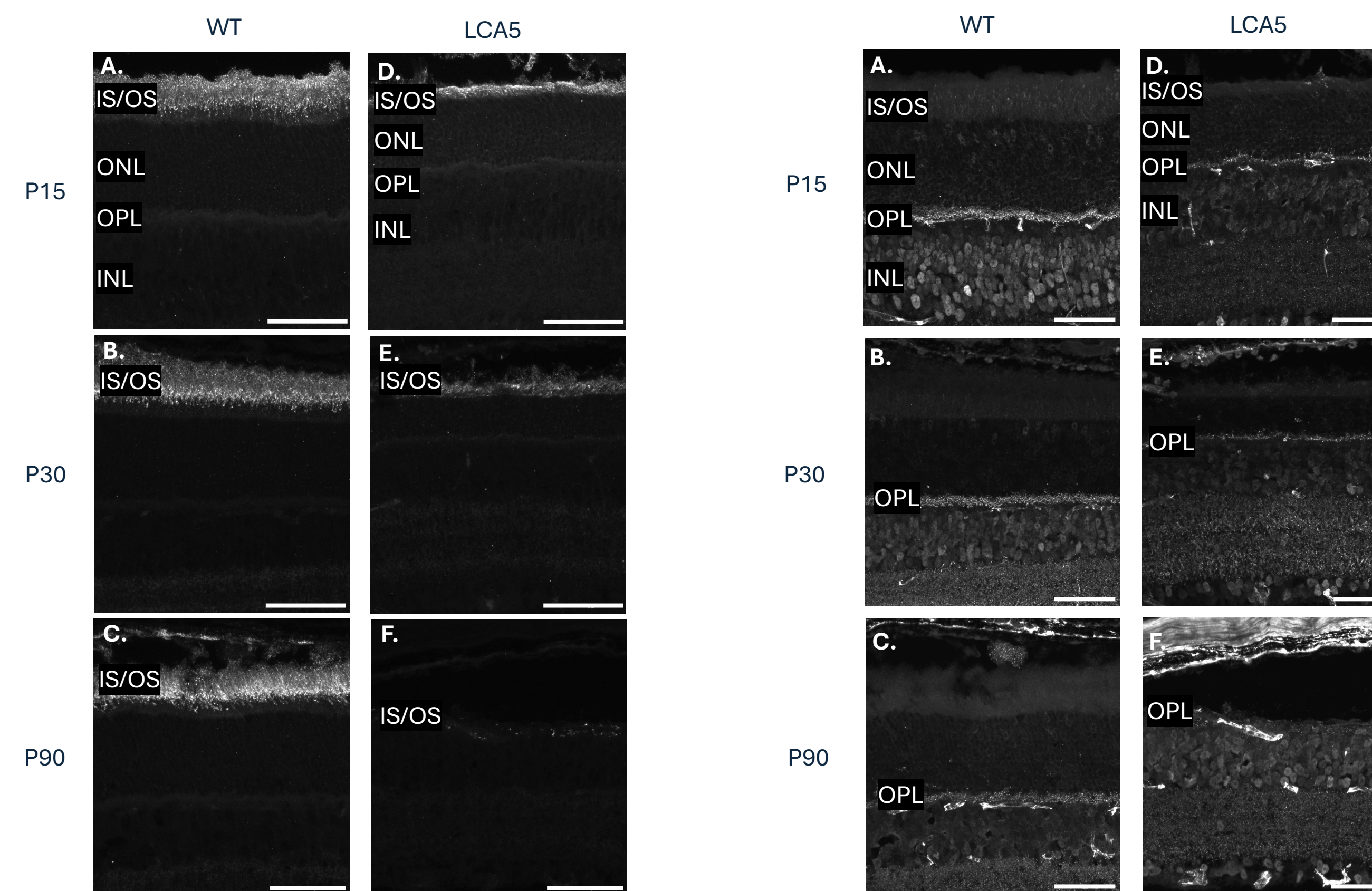


Figure 4. Prom1 Levels Decrease Over Time in *Lca5* ^{-/-} Mice. (A-C) show a constant level of Prom1 in the OS in WT mice. (D-F) show decreased Prom1 levels in the OS in *Lca5* ^{-/-} mice. Scale Bar: 50 µm.

Figure 5. CtBP2 Levels Decrease Over Time in *Lca5* ^{-/-} Mice. (A-C) show a constant level of CtBP2 in the OPL in WT mice. (D-F) show decreased CtBP2 levels in the OPL in *Lca5* ^{-/-} mice. Scale Bar: 50 µm.

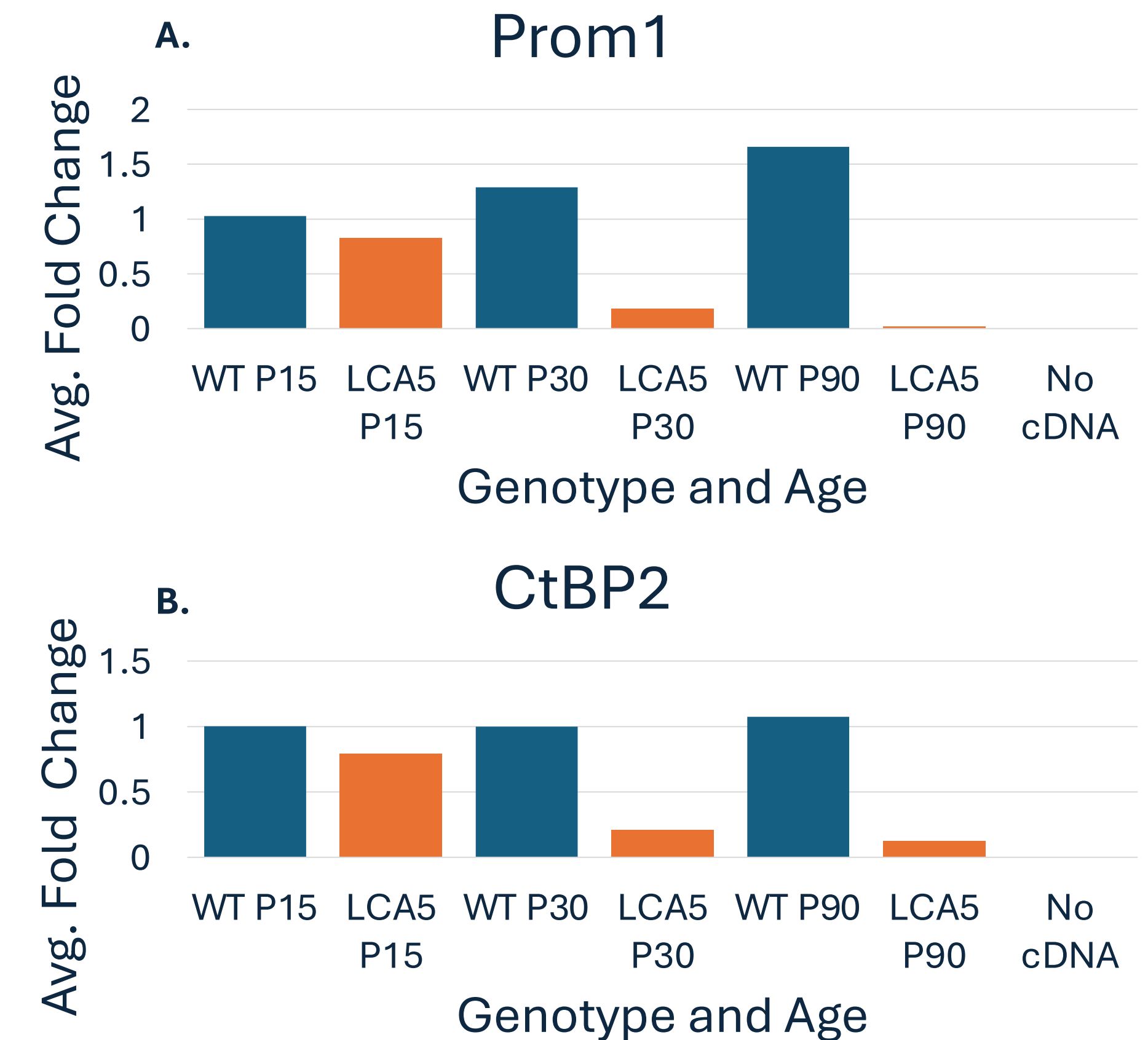


Figure 6. Prom1 and CtBP2 Gene Expression Levels Decrease in *Lca5* ^{-/-} Mice. (A) qPCR analysis of Prom1 in WT and *Lca5* ^{-/-} mice. (B) qPCR analysis of CtBP2 in WT and *Lca5* ^{-/-} mice.

Summary

- Lca5* ^{-/-} mice show degeneration of the ONL and INL over time
- Lca5* ^{-/-} mice show decreased protein levels of Prom1 in the OS and CtBP2 in the OPL over time
- Lca5* ^{-/-} mice show decreased gene expression levels of Prom1 and CtBP2 over time

Future Directions

- Look into the specific mechanisms behind photoreceptor loss and Prom1/CtBP2 loss due to *Lca5* ^{-/-}
- Determine if the loss of Prom1/CtBP2 is due to the loss of retinal cells or causally linked to *Lca5* ^{-/-}
- Examine the levels of Prom1 and CtBP2 in other mouse models of retinal degeneration

Acknowledgements

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References

- Sanjurjo-Soriano, Carla & Kalatzis, Vasiliki. (2018). Guiding Lights in Genome Editing for Inherited Retinal Disorders: Implications for Gene and Cell Therapy. *Neural Plasticity*. 2018. 1-15. 10.1155/2018/5056279.