Establishing a new model of light-induced retinal degeneration in zebrafish larvae

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1. Abstract

Until now, eye research relied on the mouse model, which is suboptimal for anatomical and ethical reasons. Zebrafish, however, represent a suitable alternative due to their anatomical similarity to the human eye, as well as their economic and practical advantages. As the project was still in its initial stage, the first objective was to establish a model of light-induced retinal degeneration (LIRD) in zebrafish larvae by investigating changes in visual acuity at different timepoints following light induction. For this purpose, four models were evaluated in terms of either acute or chronic retinal damage. Acute damage was induced using 100’000 lux for 30 minutes or 2 hours, whereas chronic damage was induced using 20’000 lux for 16 or 24 hours. Behavioural analyses were then performed at specific timepoints after induction, alongside histological examinations to assess structural alterations, retinal degeneration and regeneration. Based on the results, one model each was defined for acute and chronic LIRD.

2. Introduction

Zebrafish larvae as a model organism in eye research

Zebrafish are becoming increasingly popular as a model organism in research. This is not only due to their genetic similarity, as they share 70 % of their genome with humans, but also because they offer multiple economic and practical advantages. [1]
One major advantage is their fast embryonic and larval development. As each mating can result in up to 200 offspring, high-throughput experiments or drug screenings can be conducted. External fertilisation and the transparency of the chorion and embryo allow real-time observation of zebrafish early development and organogenesis. [2]
As no food needs to be supplied until they reach six days post fertilisation (dpf) and due to their small size, resources, time and costs associated with research projects can be reduced. [3]

Anatomy of the zebrafish eye

Zebrafish possess an eye structure that is very similar to the human eye. The retina detects light, which is why it plays a key role in visual acuity. It consists of three main cell layers: the ganglion cell layer (GCL), the inner nuclear layer (INL) and the outer nuclear layer (ONL). The ONL is made up of photoreceptor cells that detect incoming light and transform it into electrical signals for further processing. [2]
Extensive exposure to intense light, can result in retinal damage through degeneration of the photoreceptor cells. This exposure can be either chronic or acute, depending on the light intensity (measured in lux) and the exposure duration. Unlike us humans, zebrafish can regenerate their retina after damage. [4]

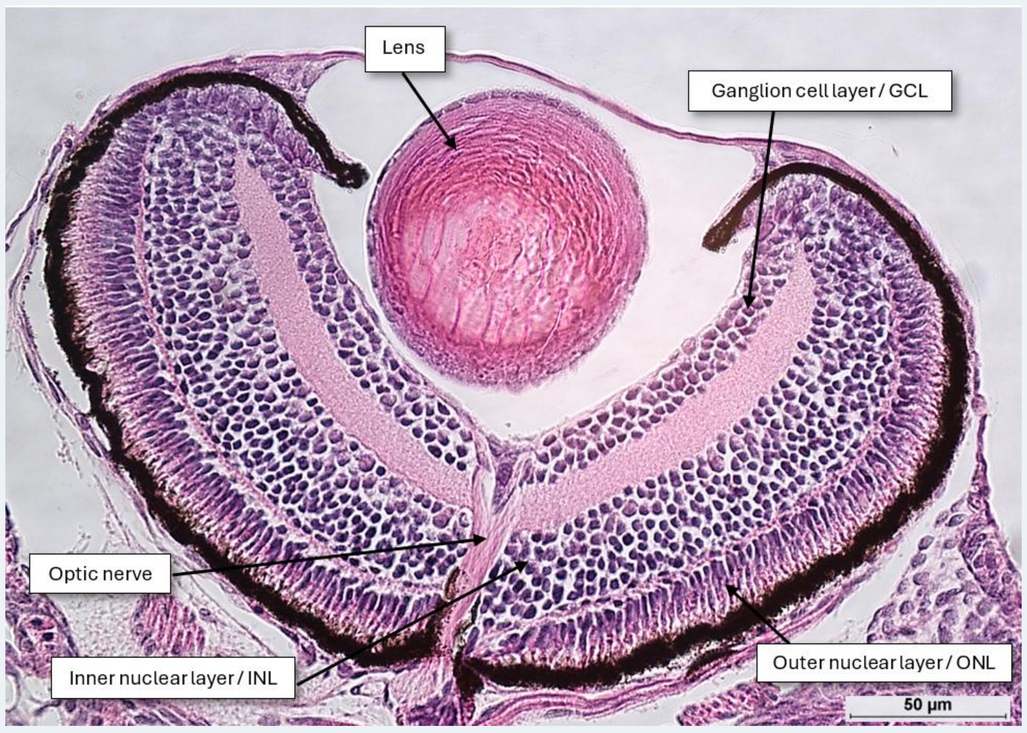

Figure 1: Histological image of a zebrafish eye (5 dpf) showing the different layers of the retina (Linder N., 2026)

3. Aims and leading questions

Investigate changes in visual acuity at different timepoints following light induction and subsequently establish one model each for acute and chronic LIRD for future studies.

- In which retinal cell layer of zebrafish larvae are the most severe light-induced structural alterations observed and how do these alterations change across different recovery timepoints?

4. Methods and material

Retinal degeneration was induced as soon as the zebrafish reached three to four dpf using four different modalities: **100’000 lux for 30 minutes or 2 hours** for acute damage and **20’000 lux for 16 hours or 24 hours** for chronic damage. Afterwards, the fish were placed in low light intensity for regeneration.

To analyse the difference between diverse recovery durations, six different timepoints were set:
0 minutes, **1 hour**, **3 hours**, **6 hours**, **12 hours** and **24 hours**.
At these specific timepoints changes in visual acuity were investigated on the 4 to 5 dpf zebrafish using behavioural analysis, alongside histological examinations to assess structural alterations.
For histological processing the zebrafish were cut in into 3 µm sections and subsequently stained with haematoxylin and eosin (H&E).

5. Results

To assess structural alterations to the retina, the histological slides were analysed by counting the cells of the three retinal cell layers and evaluated by the non-normalised ANOVA test for group analysis.

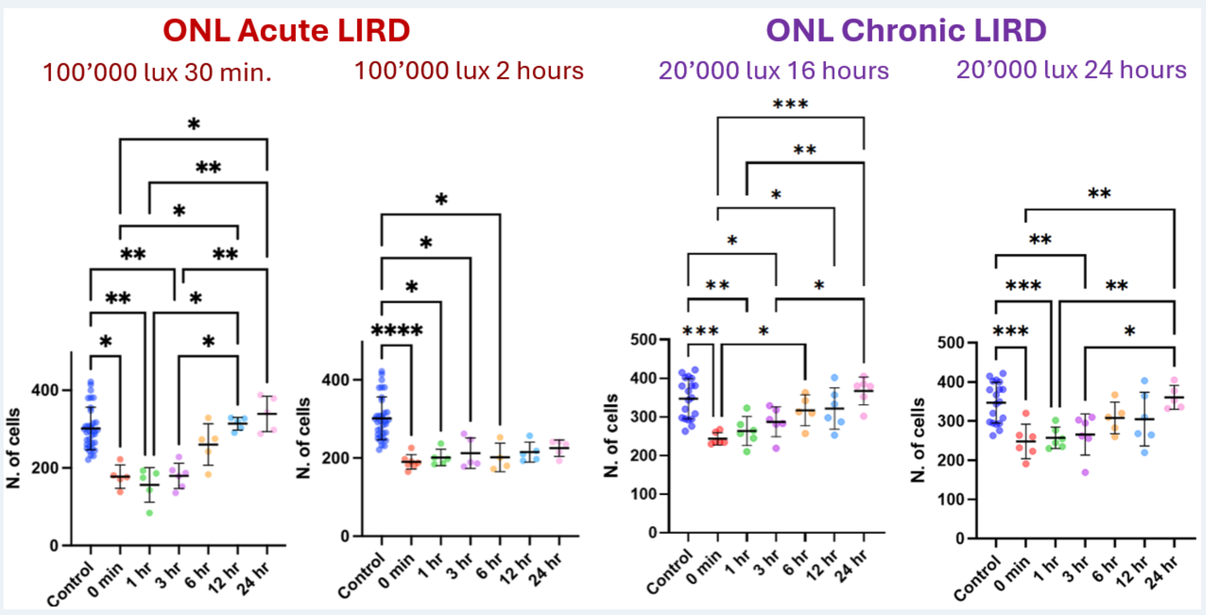

Figure 2: Comparison of the number of cells counted in the ONL after light-induced retinal damage (Linder N., 2026)

6. Discussion

For future experiments, it would be the best to focus on the acute modality involving 30 minutes of light induction at 100’000 lux and the chronic modality involving 16 hours of light induction at 20’000 lux. The 2 hours modality will no longer be pursued, as it caused too severe damage. For the chronic LIRD model, the shorter light exposure duration was established because both exposure durations yielded very similar results. So, to reduce stress and thereby improve the ethical aspect, it is preferable to choose a shorter treatment.

Furthermore, future experiments will focus on the 1-, 6- and 24-hour timepoints. This is because LIRD progressed the most in the first hour after induction, then started to recover after 6 hours, reaching normal levels again after 24 hours.

List of references
[1] Canedo et al., 2022, p. 3-4
[2] Chhetri et al., 2014, p. 1-4
[3] Meyers, 2018, p. 1-5
[4] Fogerty et al., 2022, p. 9, 11

Figures