Notch Signaling During Vertebrate Eye Regrowth

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Abstract

Exposure to low gravity can have long term detrimental effects on the eye and vision. If space travel is to become commonplace, we must develop tools to heal the eye following damage. In the Tseng lab, we are interested in identifying and studying the mechanisms that induce regeneration of the eye. The Notch1 gene is involved in normal eye development but also plays a key role in maintaining neural stem cells. Using the clawed frog *Xenopus laevis* as a model, we seek to assess the role of the Notch signaling pathway in eye regrowth. By inhibiting Notch signaling during eye regrowth, we have determined that this pathway's activity is required for regrowth of the eye. Further experiments show that this is likely due to the requirement of Notch signaling for cell proliferation following injury. This project will help to define how a developmental mechanism can be used to induce successful regrowth.

Xenopus laevis as a model for eye regrowth

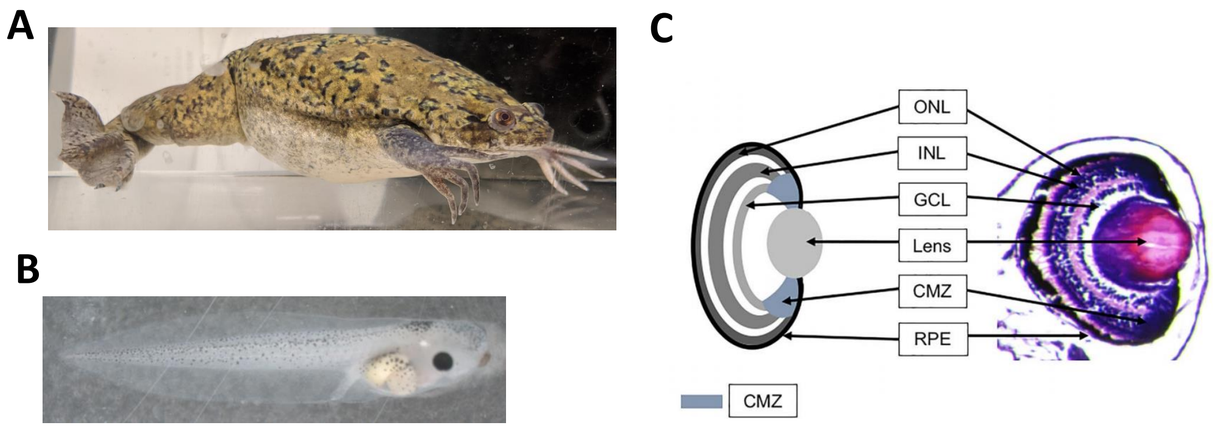
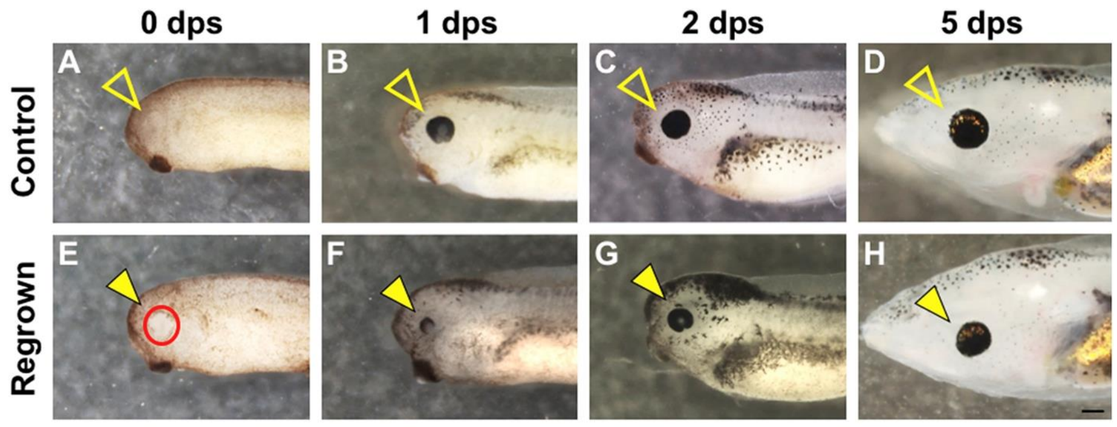


Figure 1. (A) Adult *Xenopus* frog. (B) *Xenopus* tadpole. (C) *Xenopus* and human eyes are physiologically homologous.

Xenopus embryos can regrow their eyes



Kha et al., 2018

Figure 2. *Xenopus* embryos regrow their eyes in five days following removal of the optic vesicle. Top panels are control developing eye. Bottom panels show regrowth of the eye following removal of the area within the red circle. Arrowheads indicate the eye.

Inhibition of Notch signaling impairs eye regrowth

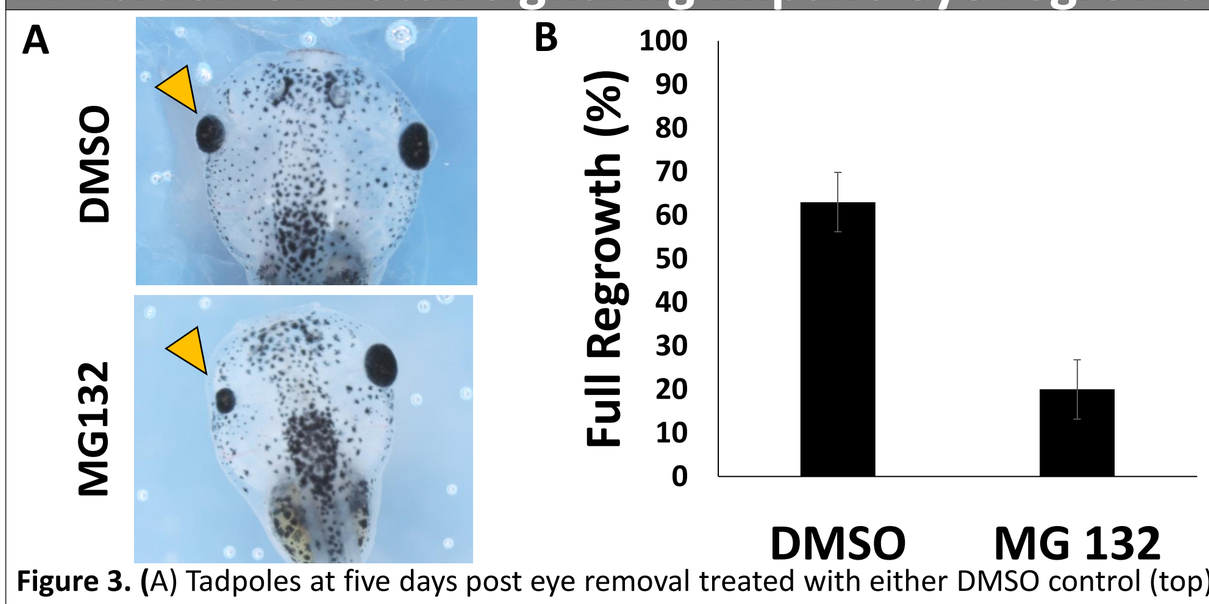


Figure 3. (A) Tadpoles at five days post eye removal treated with either DMSO control (top) or the Notch inhibitor MG 132 (bottom). Arrows indicate the regrown eye. (C) Percent of tadpoles that fully regrew their eye when treated with vehicle control (DMSO) or Notch inhibitor (MG 132).

Notch signaling is required during the first day

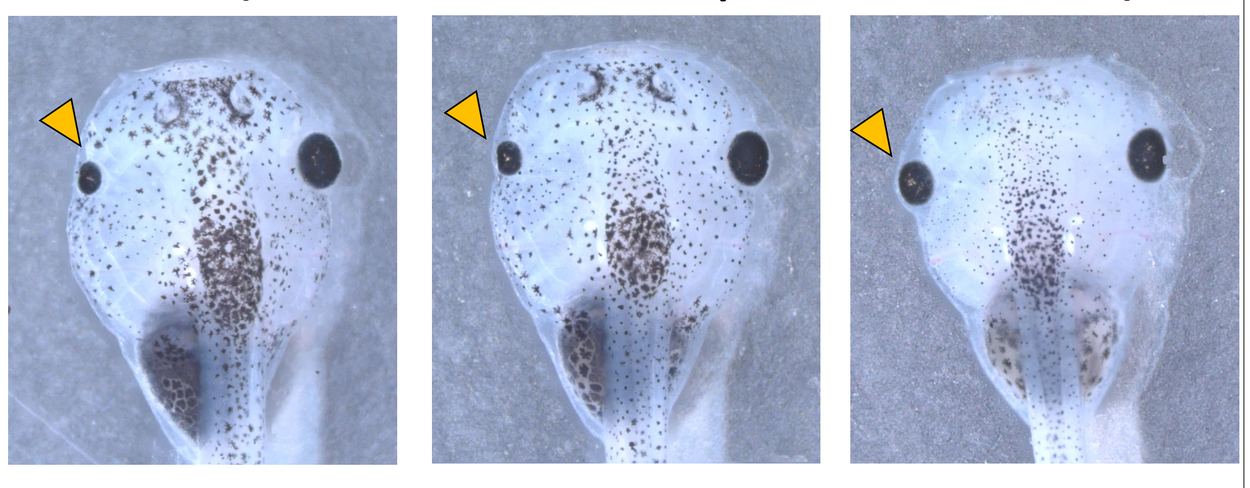


Figure 4. Tadpoles at five days post surgery treated with Notch inhibitor MG132 for different durations. Full duration of regrowth (0-5dps) left. Only first day of regrowth (0-1dps) center. After the first day of regrowth (1-5dps) right. Arrows indicate regrown eye.

Notch inhibition reduces cell proliferation

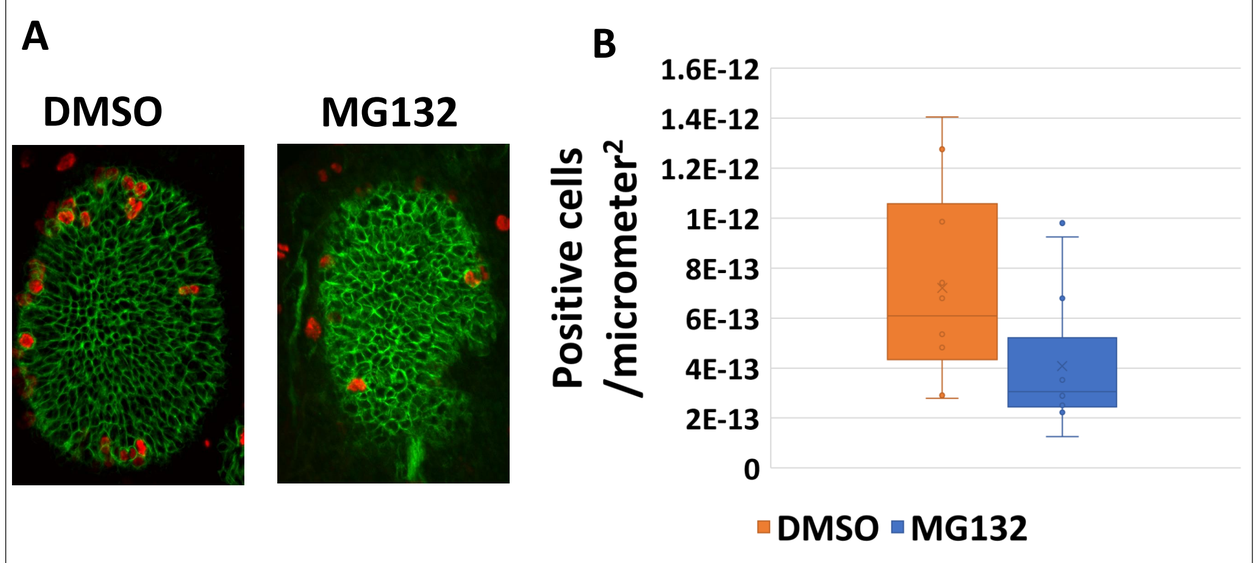


Figure 5. (A) Fluorescence images of regrowing eyes at 1day post surgery with proliferating cells in red (anti- phosphorylated histone 3) and neural tissue in green *(Xenopus* engrailed1). (B) Quantification of proliferating cells per eye area.

Summary

- Inhibition of Notch signaling results in decreased eye regrowth following removal
- Inhibition of Notch signaling during the first day of regrowth is sufficient to reduce regrowth. Inhibition on subsequent days has no affect.
- Inhibition of Notch signaling reduces cell proliferation within the regrowing eye

Acknowledgements

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References

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