



hhmi

High-fat diet-induced retinal degeneration in *Drosophila melanogaster*

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Retinal Degeneration in Humans & Flies

Objective:

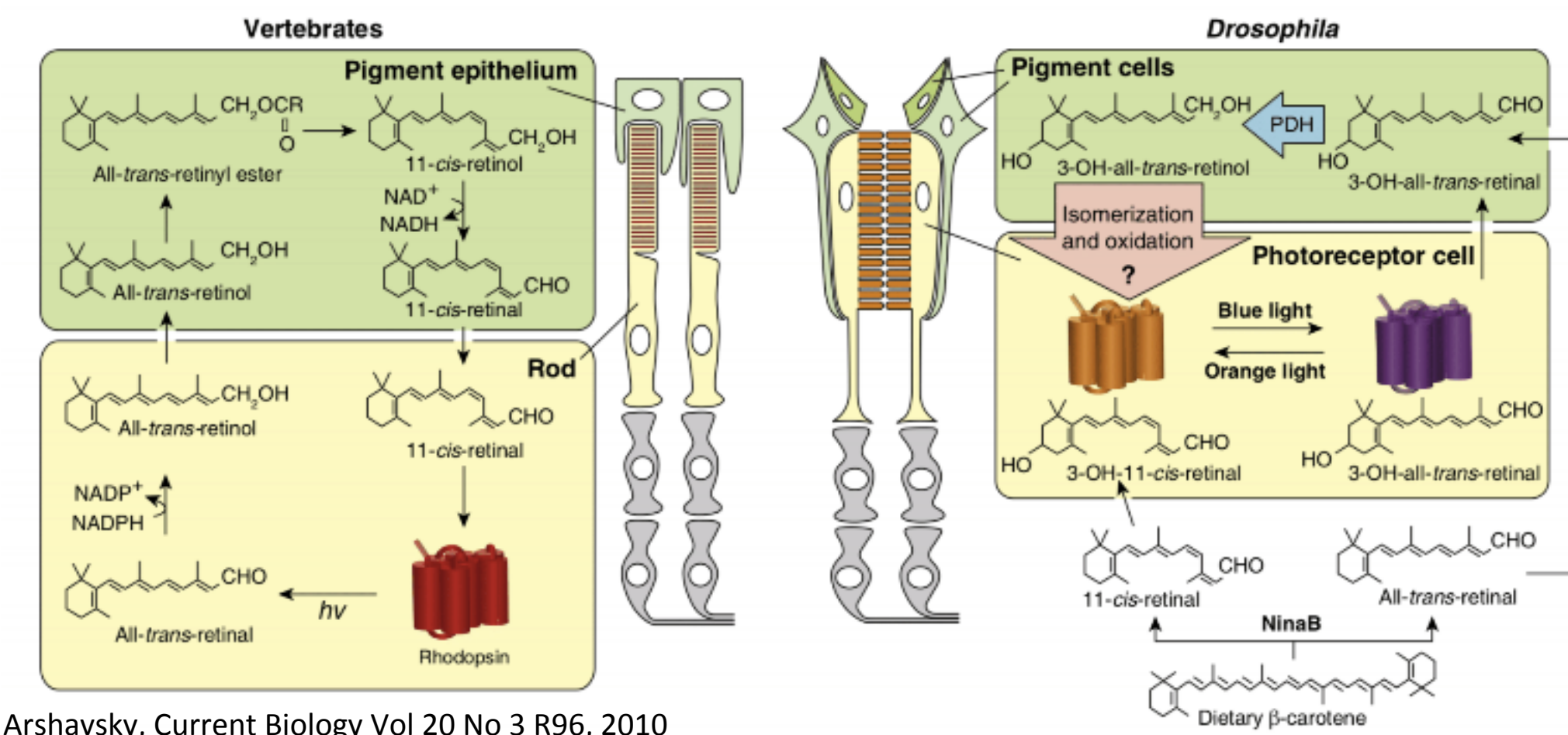
How does a high-fat diet affect retinal degeneration in flies when compared to light-induced retinal degeneration?

Similarities

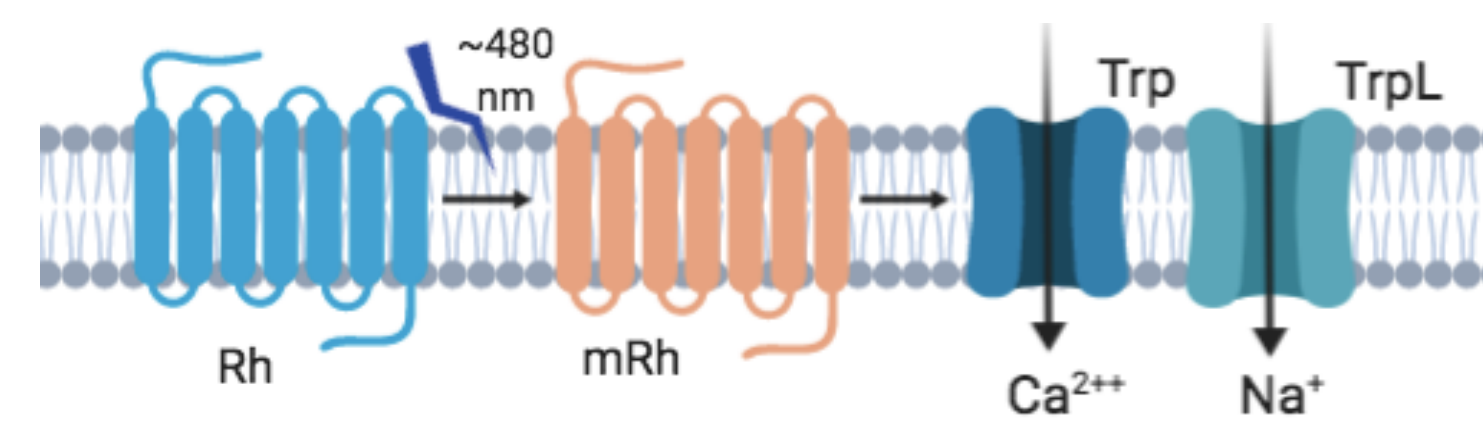
- Photoreceptor cells
- Phototransduction machinery
 - Rhodopsin, Retinal, Ca^{2+} proteins
- Signal transduction

Differences

- Human eye vs Compound eye
- The visual cycle
- Retinal pigment epithelium
- Membrane Discs vs Rhabdomeres



Arshavsky, Current Biology Vol 20 No 3 R96, 2010



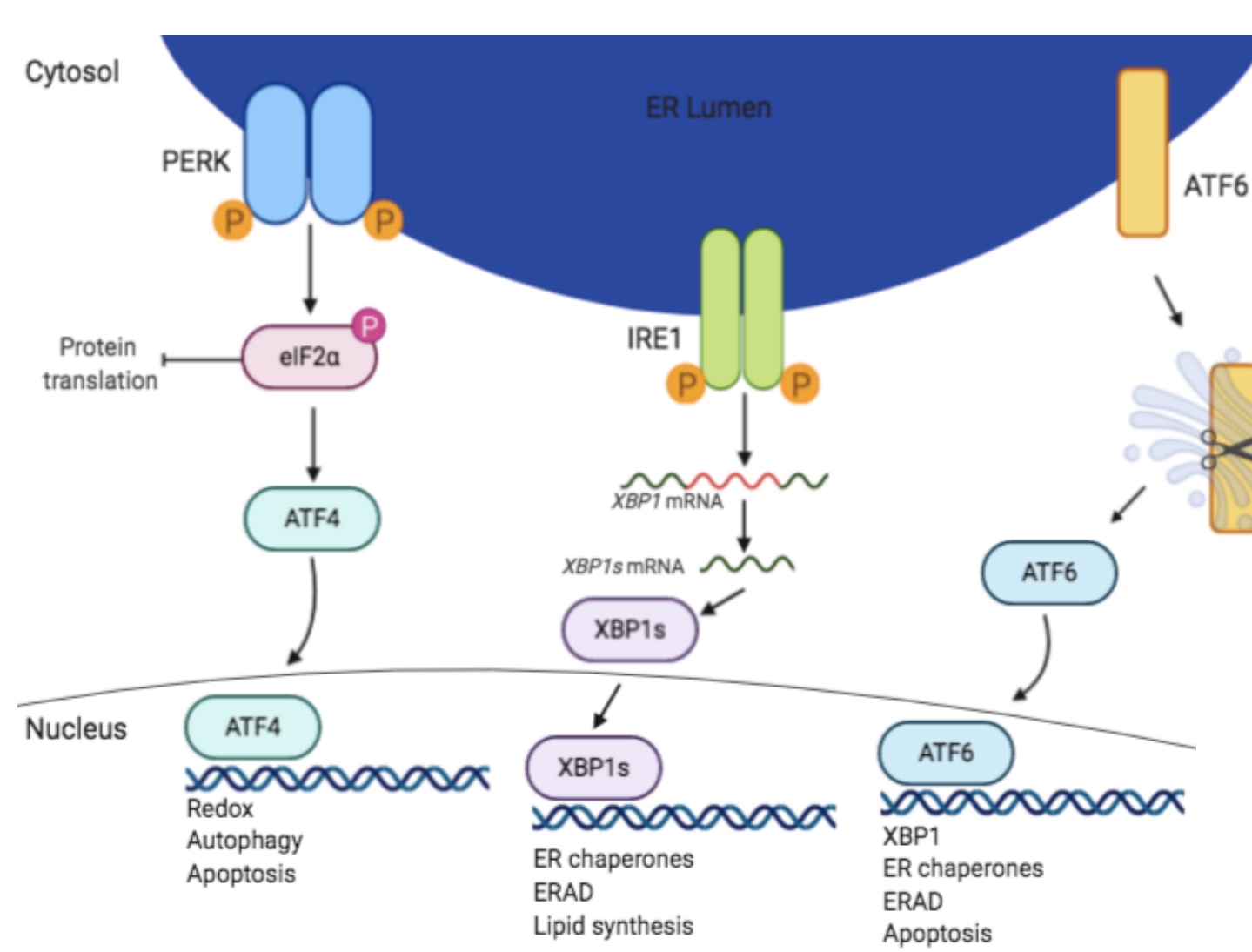
Mechanisms of retinal degeneration:

1. Differentiation of Rhabdomeres
2. Rh1 related pathways
 - Endoplasmic Reticulum Stress
3. Ca^{2+} homeostasis

Light-induced Retinal Degeneration

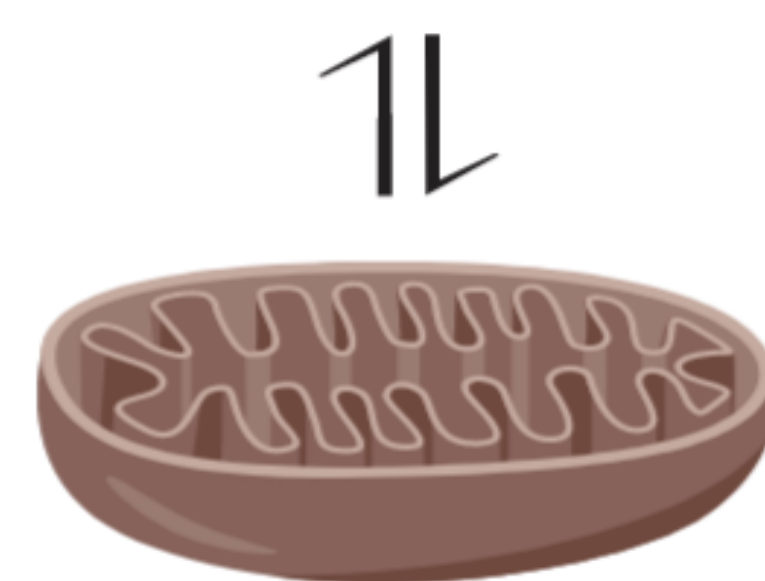
Unfolded protein response (UPR):

- Common mechanism
- Three major pathways
- Light-dependent
 - misfolded Rh1
- Can be activated by HFD

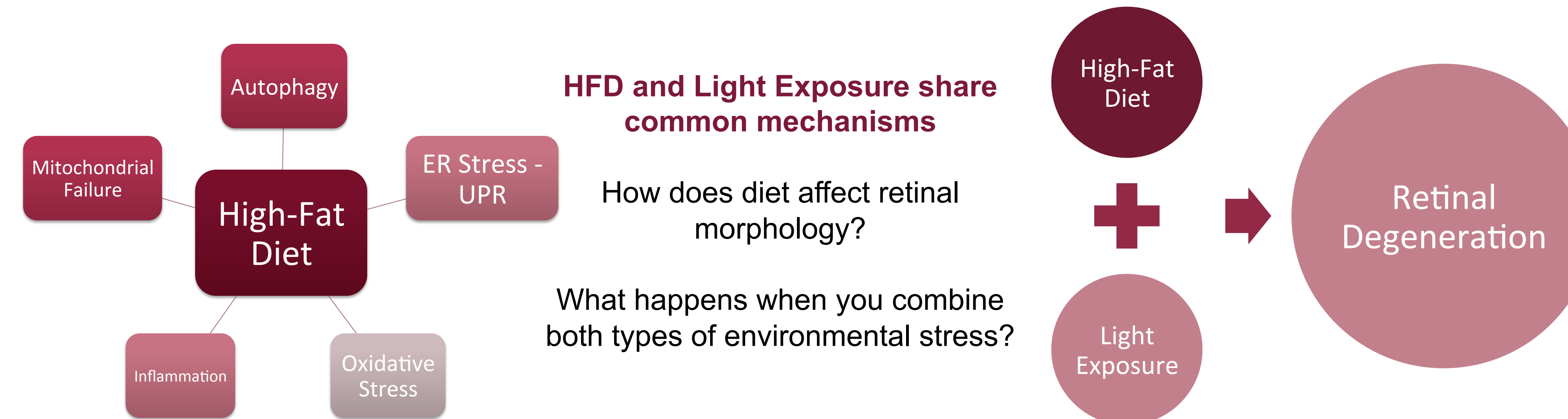


Mitochondria and ER in retinal degeneration:

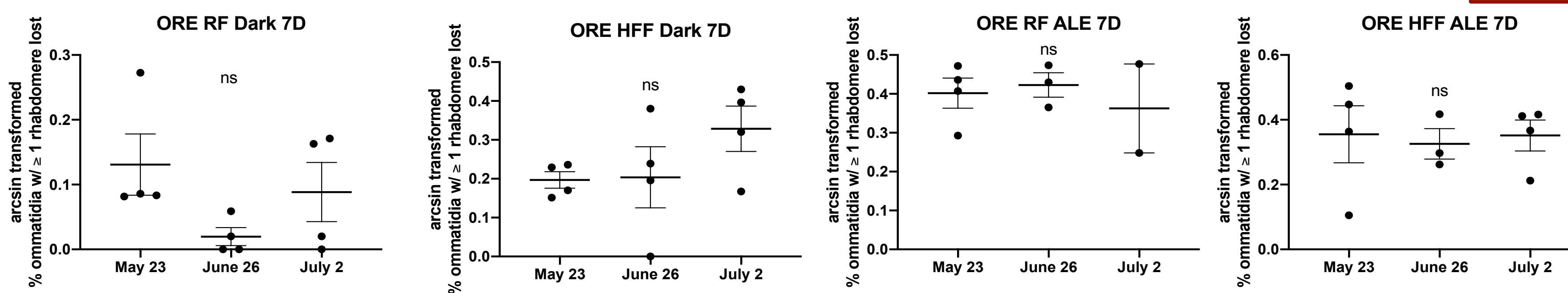
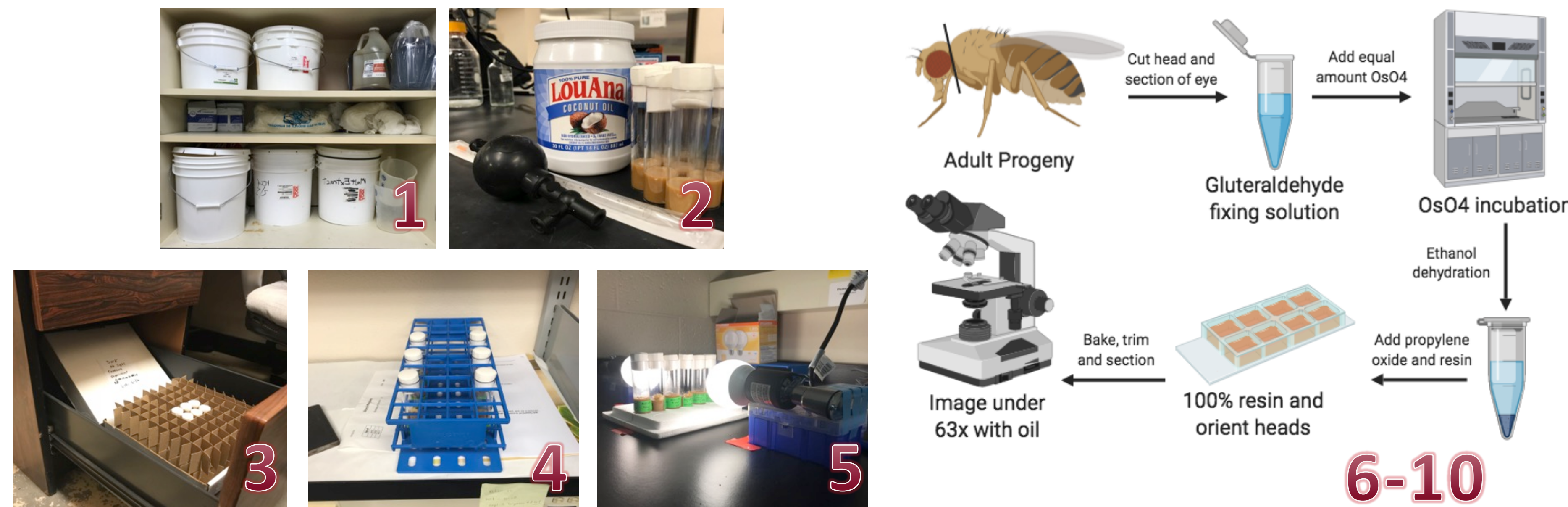
- Rh1-mutant flies → mitochondrial failure
- ER stress → ER-mitochondria coupling



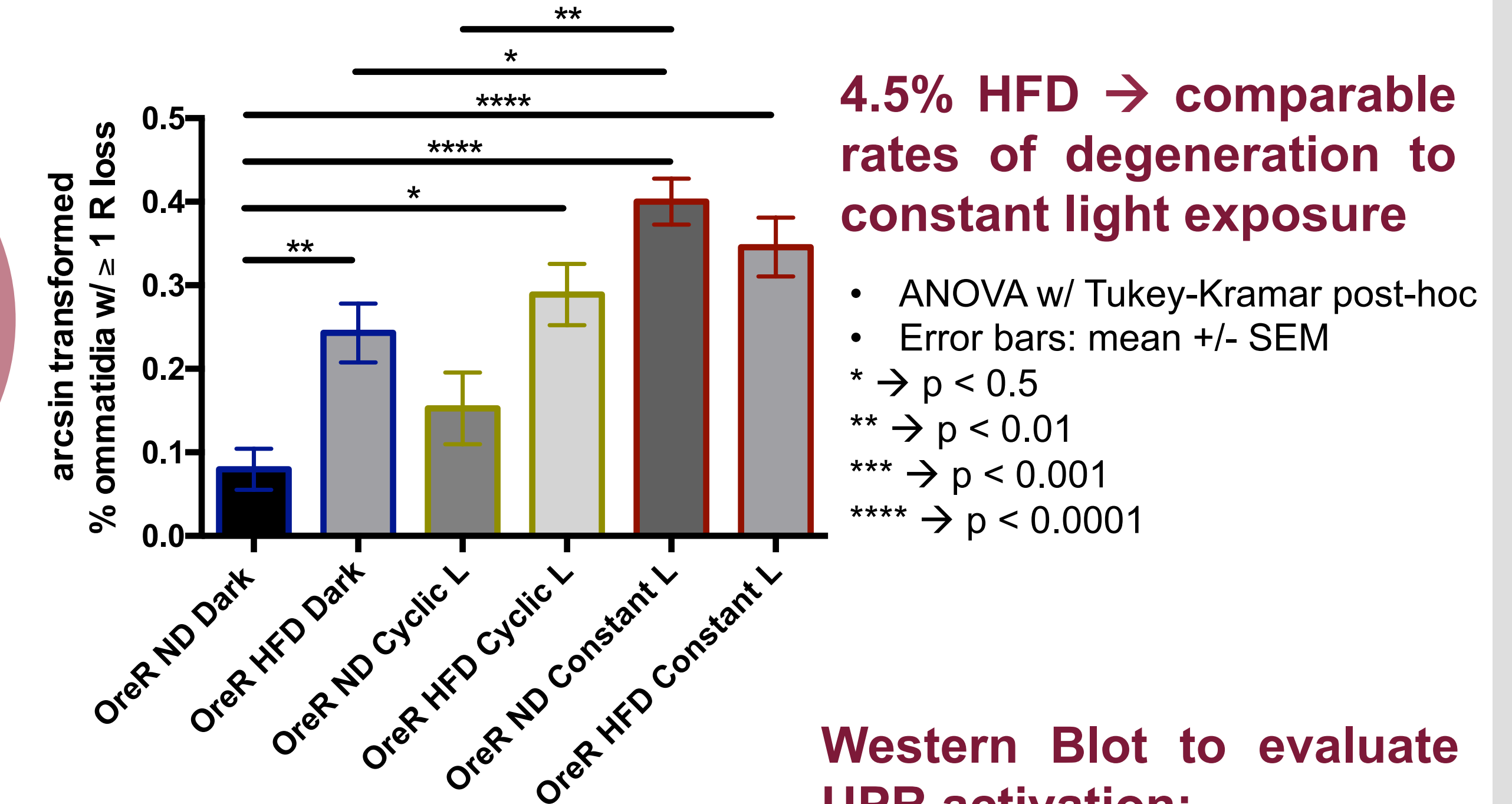
Why High-Fat Diet AND Light Exposure?



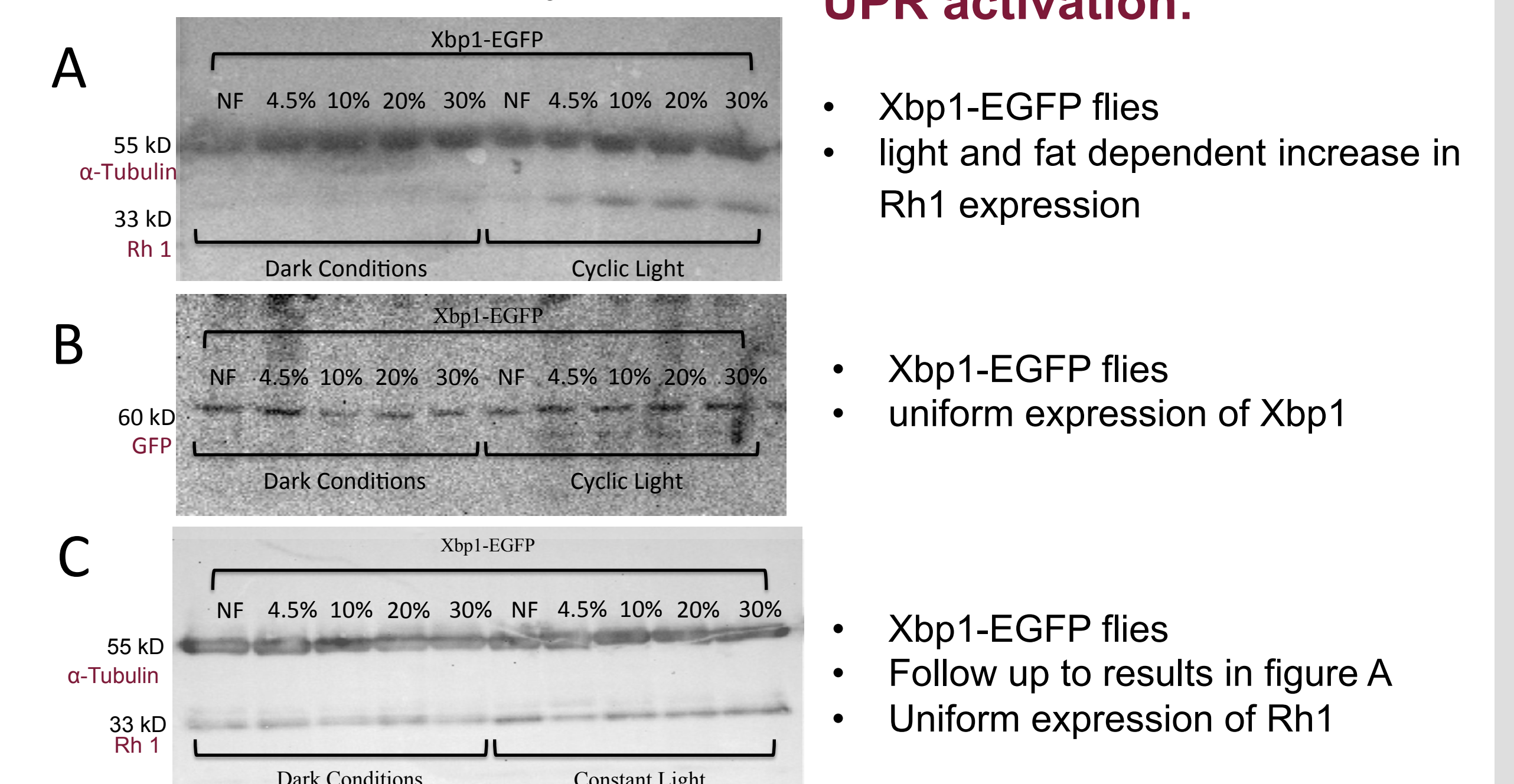
High-Fat Diet vs Regular Food



HFD Flies Show Retinal Degeneration



Western Blot to evaluate UPR activation:



Conclusions/Future Directions

- These results suggest a possible connection between high-fat diet consumption and retinal degeneration.
- This project has made me aware of the gaps in my methodology, and future work will include simpler assays to evaluate the affect of a HFD at varying concentrations on retinal morphology.

Refocus on just HFD... use new techniques like:

1. Transmission Electron Microscopy
2. Whole eye retinal dissections
3. Lipid composition assay
4. Redo Western blots for UPR activation and Rh1 expression

Questions I'm interested in:

1. Is a HFD directly causing retinal degeneration?
2. What are the mechanism?
3. Are energy producing pathways being affected because of the diet?

Acknowledgements

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References

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