

# Investigating Mitochondrial Fission, Fusion, and Biogenesis in Pathology of Age-Related Macular Degeneration

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Driven to Discover<sup>SM</sup>



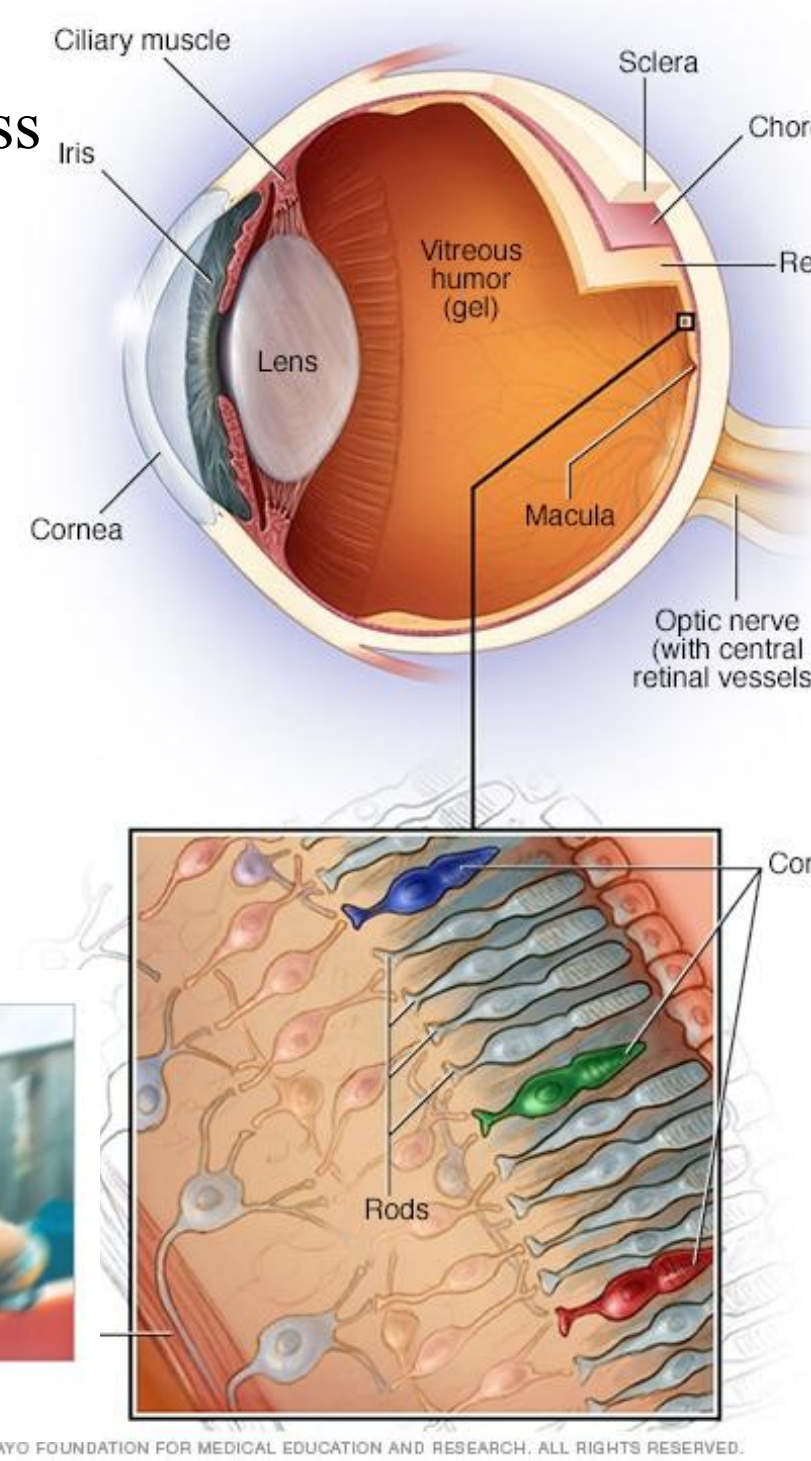
## INTRODUCTION

Age-related macular degeneration (AMD) is characterized by the death of retinal pigment epithelium (RPE), likely a result of increased oxidative stress and mitochondrial dysfunction. The purpose of this study is to determine how RPE's inability to maintain a healthy population of mitochondria contribute to AMD pathology.

**Hypothesis:** Defects in mitochondrial fission, fusion, or biogenesis lead to an accumulation of damaged mitochondria in AMD RPE.

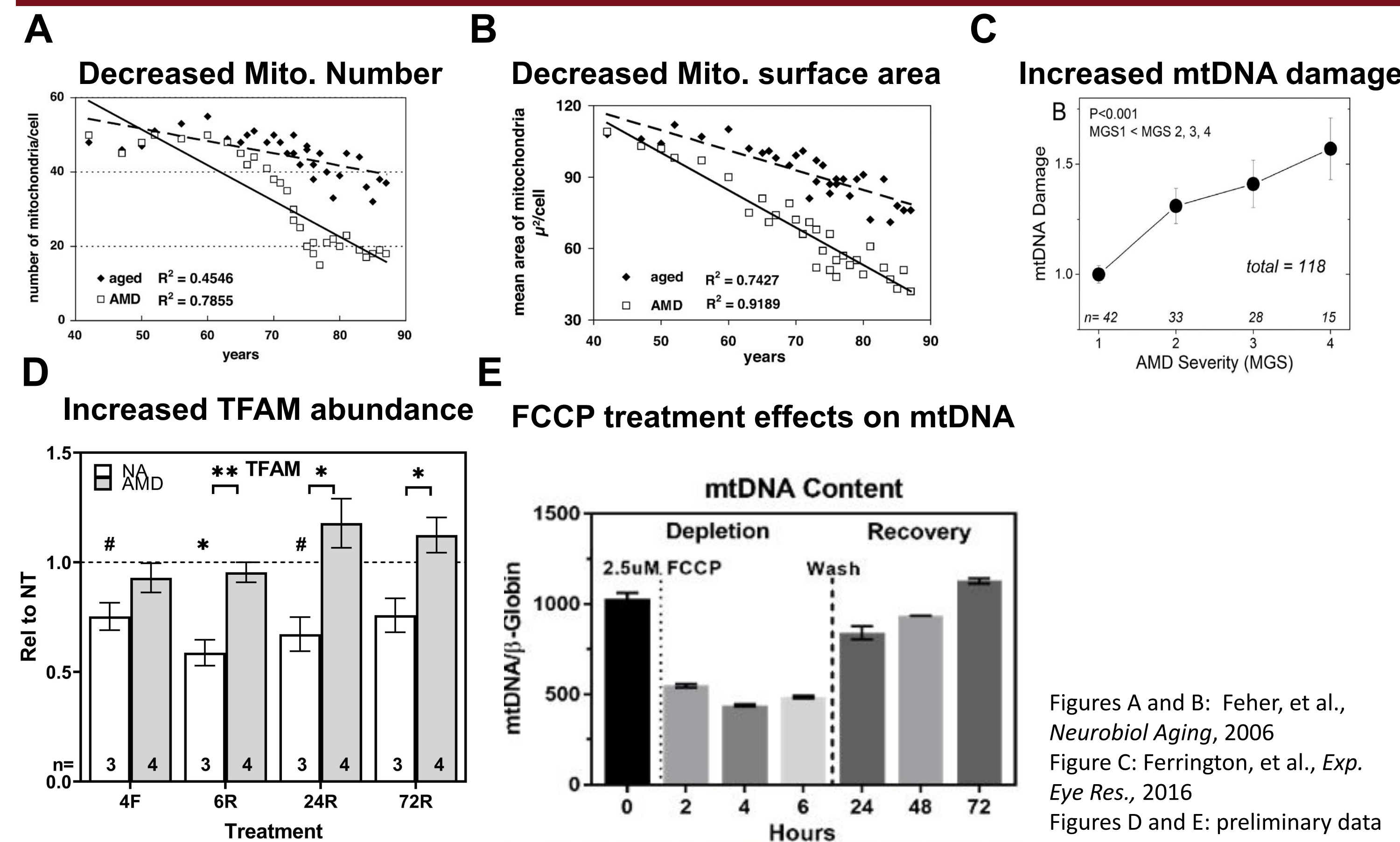
**Significance:**

- AMD is the leading cause of irreversible blindness in developed countries<sup>1</sup>
- 30% of individuals age 75-85 have AMD<sup>1</sup>
- Estimate of individuals with AMD
  - 2020: 196 Million
  - 2040: 288 Million
- No FDA approved treatment for dry-AMD<sup>2</sup>



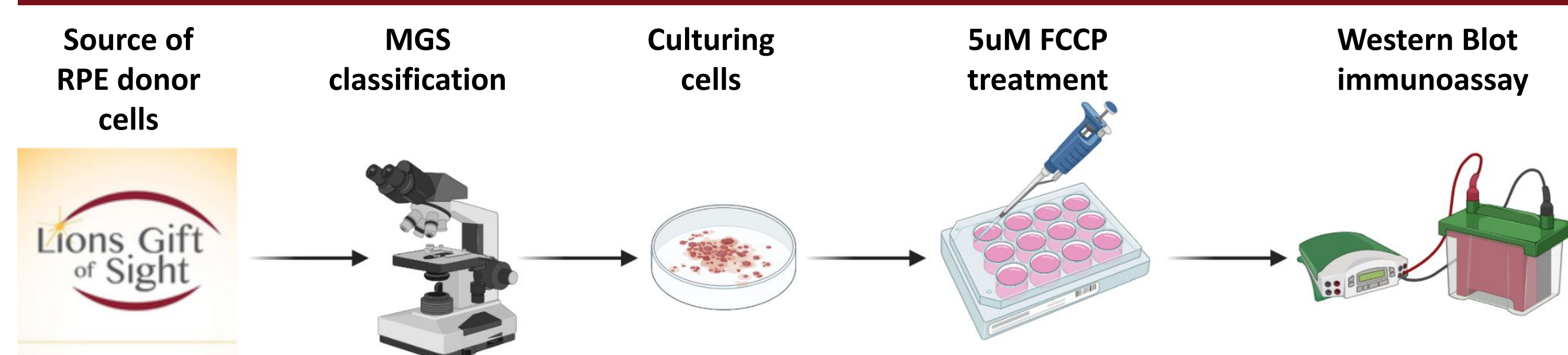
1. Bonilha, et al., *Exp Eye Res*, 2013;  
2. Ferrington, et al., *Redox Biol*, 2017

## BACKGROUND



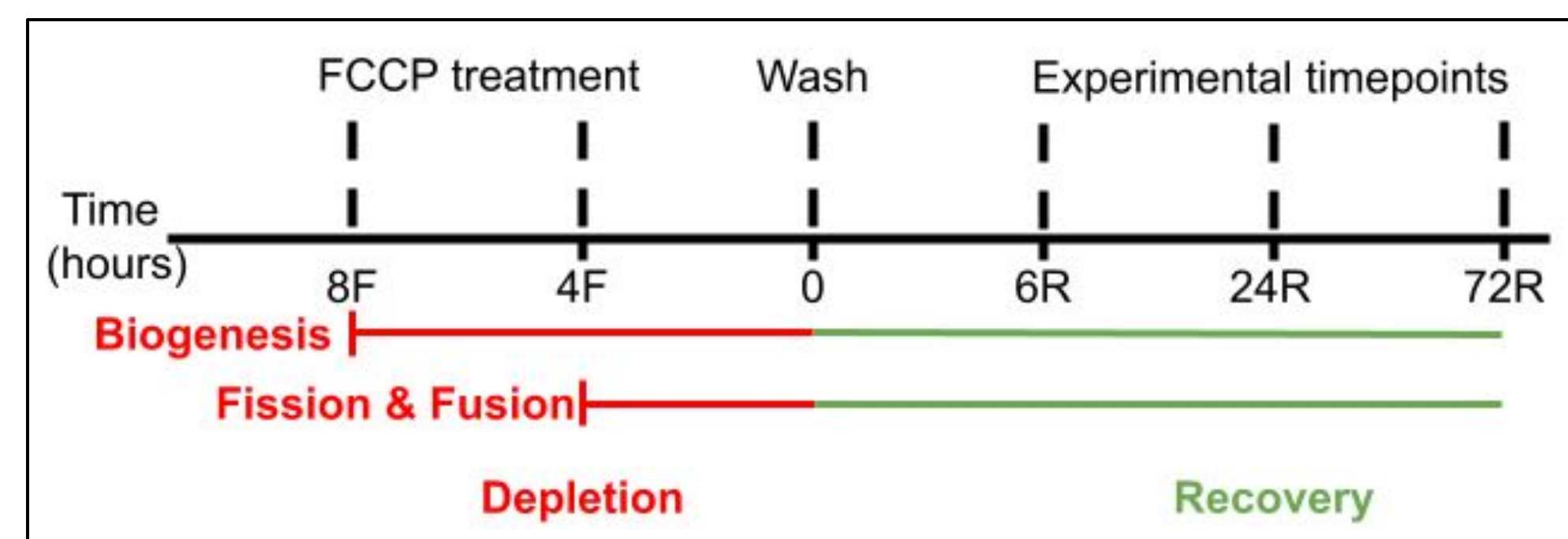
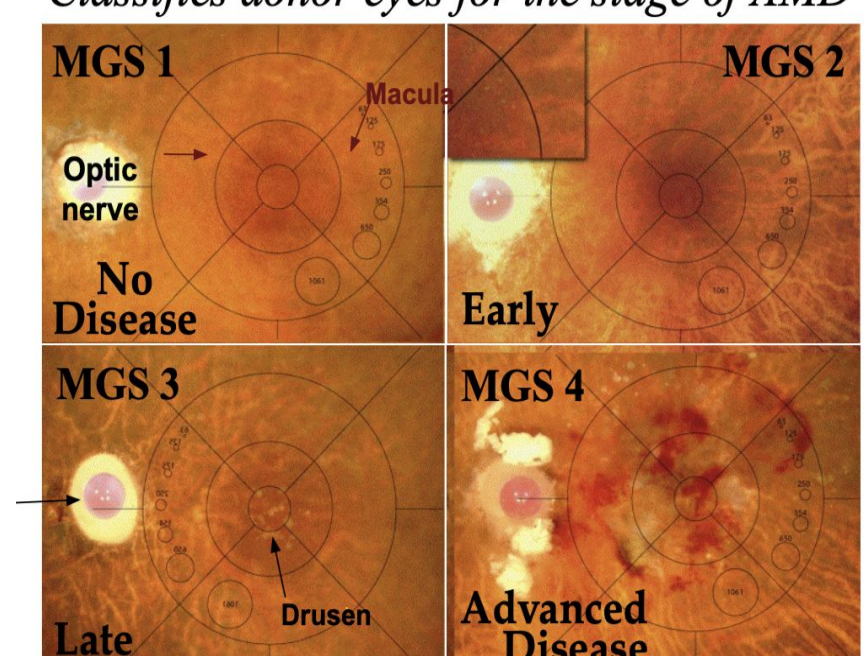
Figures A and B: Feher, et al., *Neurobiol Aging*, 2006  
 Figure C: Ferrington, et al., *Exp. Eye Res.*, 2016  
 Figures D and E: preliminary data

## METHODS



### Minnesota Grading System (MGS)

Classifies donor eyes for the stage of AMD



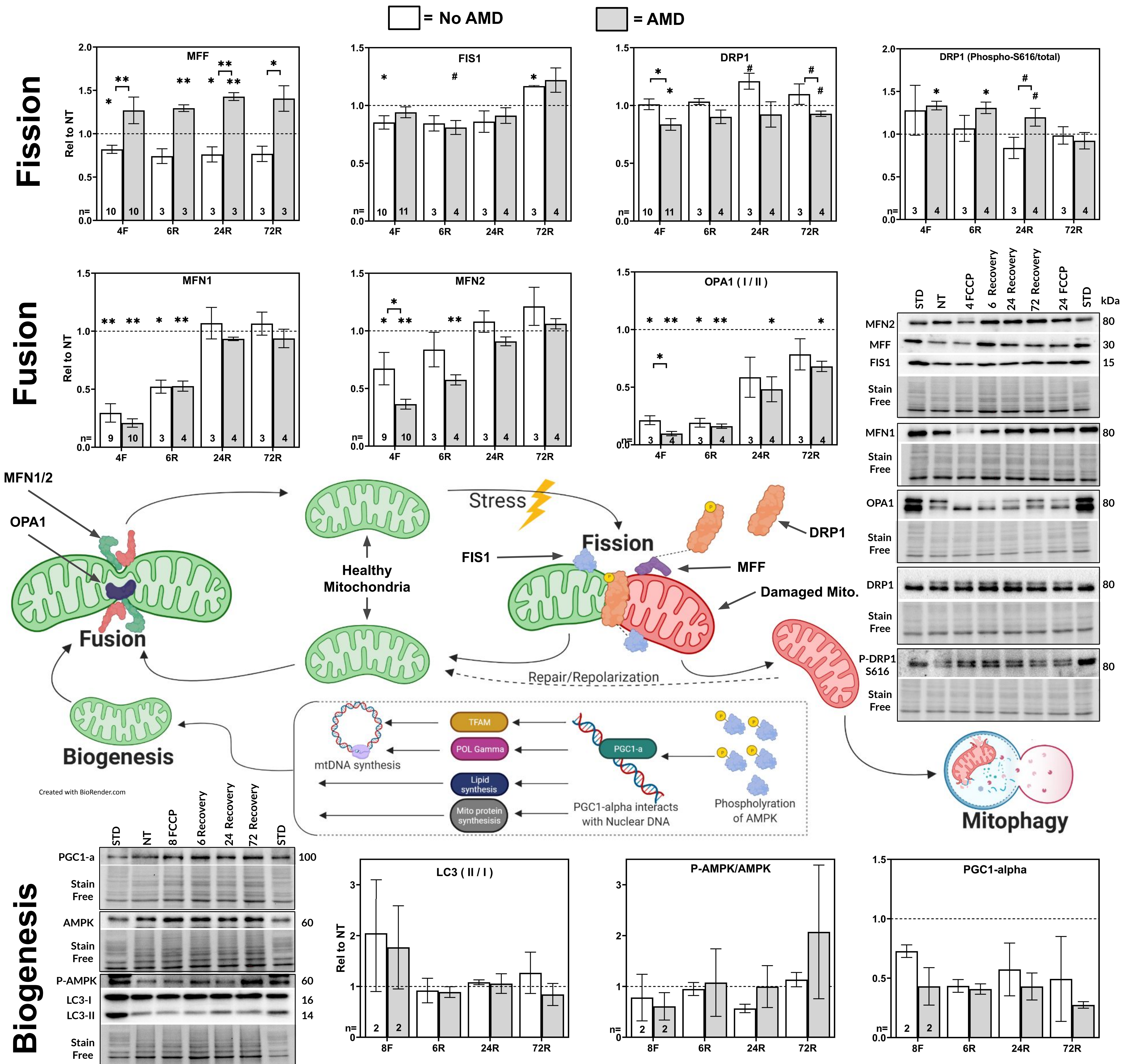
Decanini A, et al., *Am J of Ophthalmol*, 2007; Olsen and Feng, *IOVS*, 2004

Methods figure: BioRender.com

## ACKNOWLEDGMENTS

- Dr. Sandra Montezuma for grading our donors using MGS
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- Lindsay Family Foundation
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## RESULTS



## SUMMARY and FUTURE DIRECTIONS

- **Fission and Fusion**
  - AMD donors have significantly **increased fission** machinery (MFF, pS616-Drp1)
  - AMD donors have significantly **decreased fusion** machinery (OPA1 and MFN2) during stress (4F), though no differences during recovery.
- **Biogenesis**
  - TFAM showed significant difference between AMD and No AMD during Recovery, indicating potential differences in biogenesis (fig. D, background).
  - P-AMPK/AMPK and PGC1-a did not show significant difference with this sample size.
- **Future Directions**
  - Increase sample size for Biogenesis Western blots
  - CoCl<sub>2</sub> treatment to stimulate Hypoxia, a physiologically relevant mitochondrial stressor
  - Imaging experiments as an alternative method to quantify fission, fusion, and biogenesis

