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

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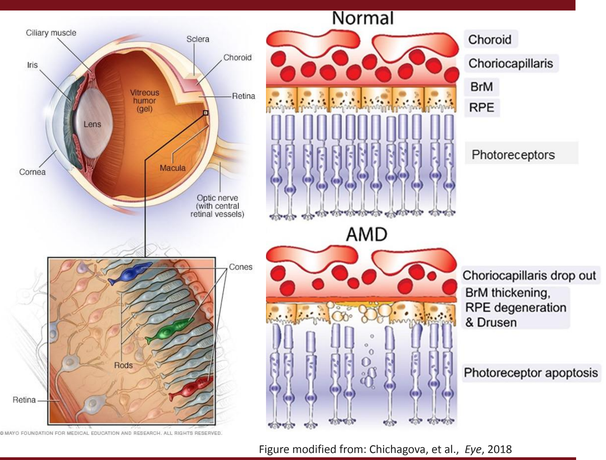
INTRODUCTION

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. Therefore, we tested the **hypothesis** that defects in mitochondrial fission and fusion lead to an accumulation of damaged mitochondria in AMD RPE.

Significance:

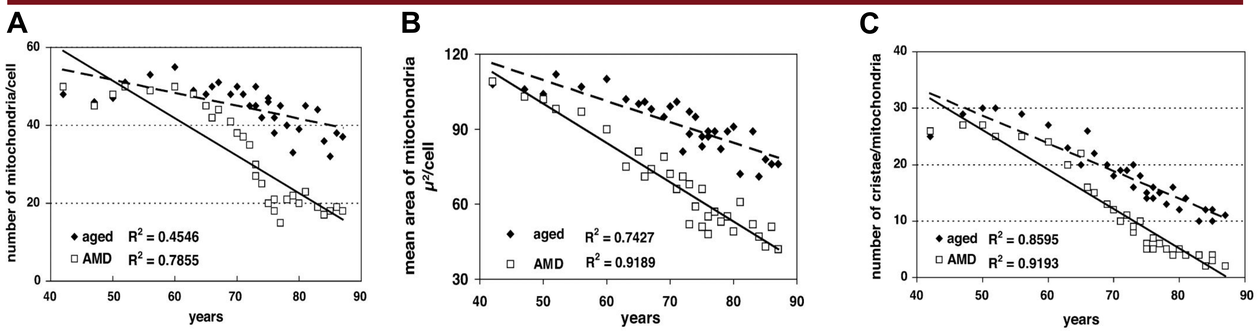
- AMD is the leading cause of irreversible blindness in developed countries [1]
- 30% of individuals age 75-85 have AMD [1]
  Estimate of individuals with AMD
  - 2020: 196 Million
  - 2040: 288 Million
- No FDA approved treatment for dry-AMD [2]



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

Figure modified from: Chichagova, et al., *Eye*, 2018

BACKGROUND



A. Decreased Mitochondrial Number

B. Decreased Surface Area

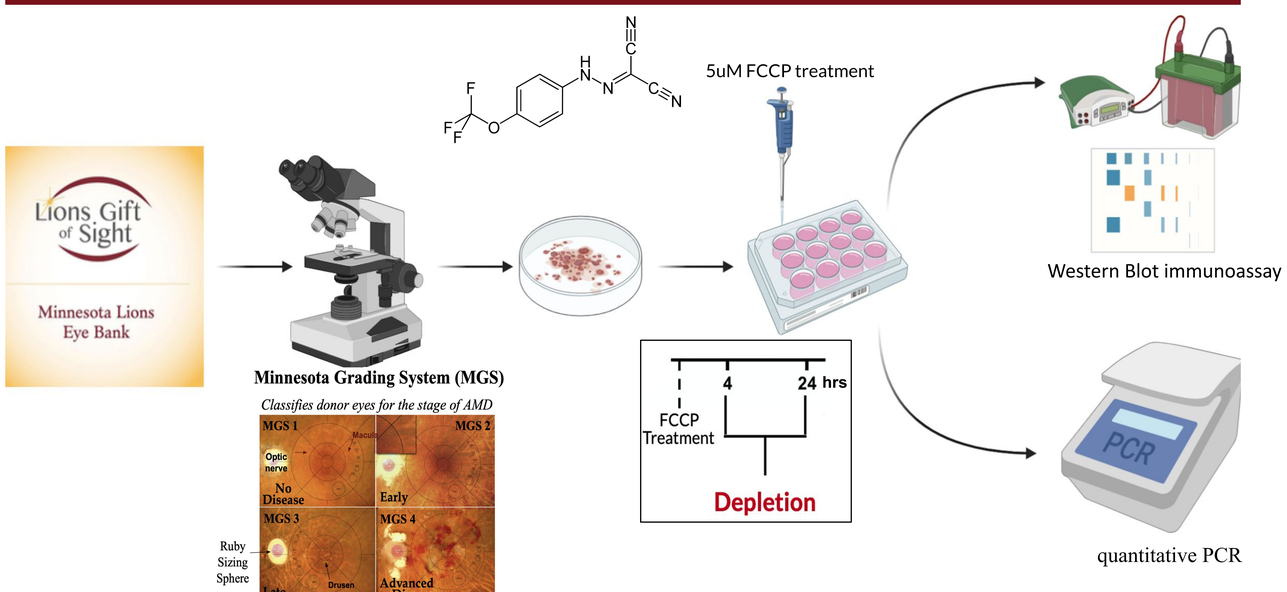
C. Decreased Number of Cristae

D. Increased mtDNA damage

E. FCCP treatment effects on mtDNA

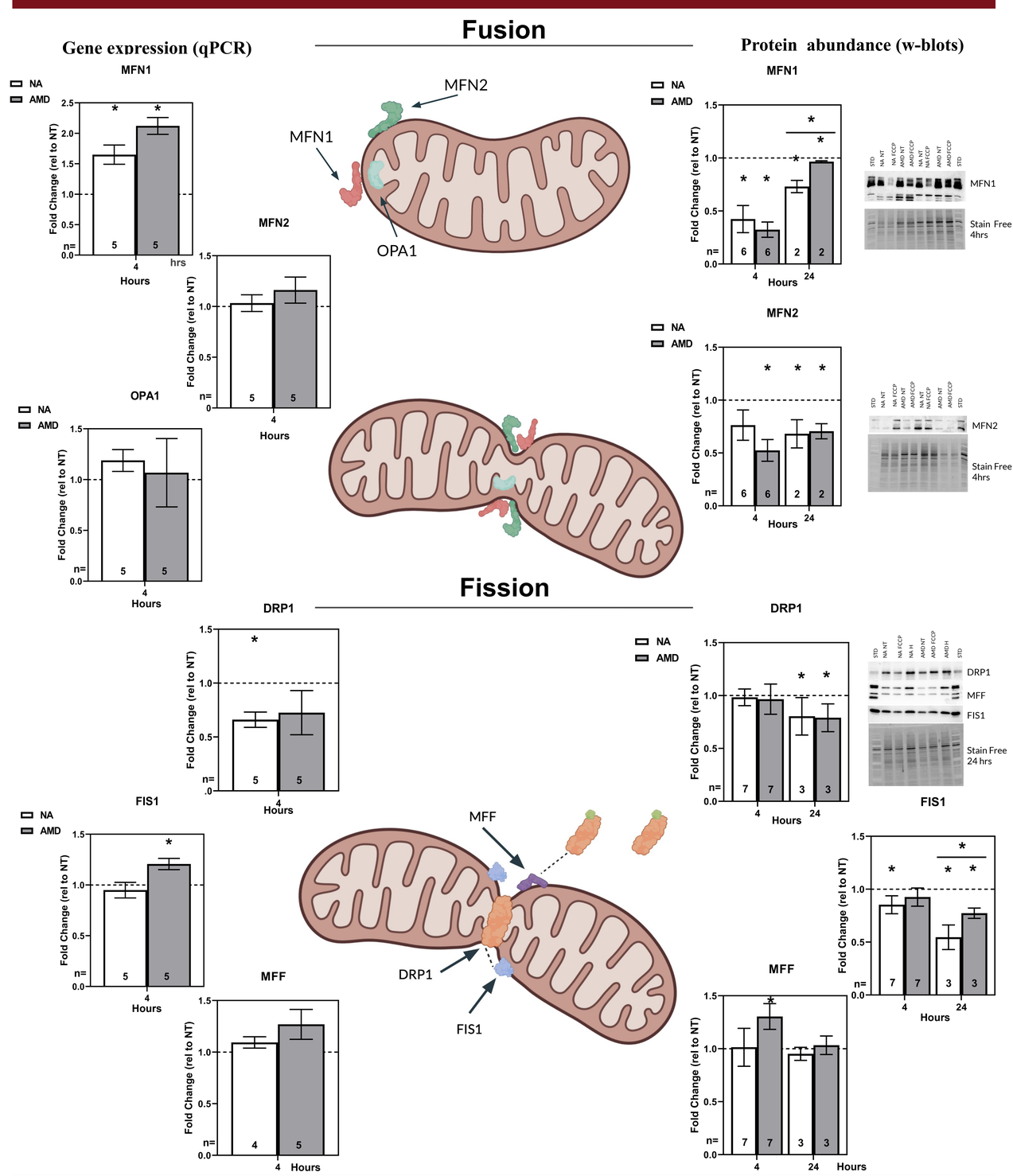
Figures A, B and C: Feher, et al., *Neurobiol Aging*, 2006 ; Figure D: Ferrington, et al., *Exp Eye Res*, 2016 ; Figure E: preliminary data

METHODS



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

RESULTS



SUMMARY and FUTURE DIRECTIONS

- **Protein Abundance**
  - Fission proteins (FIS1 and DRP1) and fusion proteins (MFN1 and MFN2) decrease with FCCP treatment.
  - FIS1 and MFN1 were significantly different when comparing AMD to No AMD
- **Gene Expression**
  - Gene expression of MFN1 increased compared to NT
  - Gene expression of DRP1 decreased compared to NT
- **Future Directions**
  - Investigate Fission and Fusion machinery for recovery time points after washing the FCCP treatment
  - Using similar approach, investigate the mitochondrial biogenesis machinery