# A study on the amyloid toxicity in Alzheimer's disease model of APPL-Gal4 Drosophila eye

**Pratap G.K.**
Mangalore University
**Manjula Shantaram** ( manjula59@gmail.com )
Mangalore University

**Method Article**

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# Abstract

Alzheimer's disease (AD) is one of the most prevalent neurodegenerative disorders. The pathogenesis involves two hallmarks: amyloid-beta aggregation (Aβ) and neurofibrillary tangles (NFTs). This has incited the use of animal models to mirror the disease. The fruit fly, *Drosophila melanogaster* has garnered considerable attention as an organism to recapitulate human disorders. *Drosophilaisusedas novel genetic tools* for studying cellular aspects and behavioural and physiological traits of human neurodegenerative diseases. Here, authors use the *Drosophila* model in understanding AD pathology and the insights were gained in drug discovery for AD therapy


# Introduction

Alzheimer's disease (AD) is one of the most prevalent neurodegenerative disorders. The pathogenesis involves two hallmarks: amyloid-betaaggregation (Aβ) and neurofibrillary tangles (NFTs). This has incited the use of animal models to mirror the disease. The fruit fly, *Drosophila melanogaster* has garnered considerable attention as an organism to recapitulate human disorders. *Drosophilaisusedas novel genetic tools* for studying not only cellular aspects but alsobehavioural andphysiological traits of human neurodegenerative diseases. Here, authors use the *Drosophila* model in understanding AD pathology and the insights were gained in drug discovery for AD therapy[1].

Nearly 75% of human genes linked with the disease have a *Drosophila* ortholog, hence *Drosophila* is theultimate model to study neurodegenerative diseases [2].*D. melanogaster*eye has a red-brown colour caused by the presence of two pigments, pteridines (red),ommochromes (brown) and it contains a set of mechano-sensory bristles, which are to be found at the anterior vertex of each ommatidium[3]. It consists of eight(8) photoreceptor cells and support cells. The AD model amenability of the Gal4/UAS targeted system allows misexpression of foreign genes along the spatiotemporal axes in the developing*Drosophila* eye. AD model system in *Drosophila* eye increased the levels of human amyloid-beta (Aβ42) which was mis-expressed in the differentiating retinal neurons of the developing fly retina using a Glass Multiple Repeat Gal4 driver[4]. The transgenic flies model exhibited strong neurodegeneration in the fly retina and resultedin reduced eye size.

### Objectives

To study Aβ toxicity in Alzheimer's disease model of APPL-Gal4 eye

# Materials And Methods

1. Transgenic APPL-Gal4 model (45 days' old)
2. Control model Wild type Drosophila (Oregon K)
3. APPL-Gal-4 flies' eyes were observed under SEM(SEM images showed a distinct pattern of eye degeneration in the eye context)

4. Histopathology: The flies were anaesthetised, fixed in Carnoy's fixativeat4°C overnight. After the fixation of the flies' heads, the fly sample was dehydrated in alcohol (40-100%) and the heads were embedded in paraffin wax. Sections of 4µm thick heads were stained with H-E stain[5]. The stained fly sections were observed under a light microscope (Olympus) for neuroanatomical studies to confirm the internal morphology of the flies' eye sections, which showed loss of bristle, disrupted ommatidial reduced eye size and photoreceptor abnormalities in the eye.

# Results/ Observations

Control eye **(Wild type; A)-** No disruption in eye morphology and no loss of corneal lenses (ommatidia) **(B)**Transgenic APPL-GAL4 eye when Aβ expressed in eye tissue showing loss of eye morphology and corneal lenses. Using an eye specific GAL4 driver, the AD gene was expressed in the eye. The AD model eye was compared with the normal(Wild type Drosophila)eye, the degenerative eye can show disruption of ommatidial structure, reduced size, and loss of pigmentation**(Fig.1)**[6]

The eye phenotypes influencedby abnormal expression of Aβ42 in the developing eye were aggravated by *sra* overexpression. The overexpressing of Aβ42 in the adult eye has severely distorted nerve tissue as a result of neurodegeneration. Overexpression of *sra* alone resulted in a slightly rougheye compared with that of the control eye. Overexpression of *sra* in Aβ42-expressing flies exacerbated the rough-eye phenotype (H-J) for this reason we used APPL-Gal4 fly models for AD.

# Conclusion

The *Drosophila melanogaster* is one of the best model to study human disorders. There are currently different Drosophila models for neurodegenerative diseases studies including Huntington's disease, parkinson's disease, motor neuron disease, and AD. There are many distinct fly models for a range of neurodegenerative diseases; we focus on select studies from models of APPL-Gal4. These fly models, providing understanding into Aβ expressed in eye tissue, studying the eye morphology, corneal lenses, mechanisms and pathways, as a foundation for translational and therapeutic research.

# Declarations

### Competing interests

The authors declare no competing interests.

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# Figures

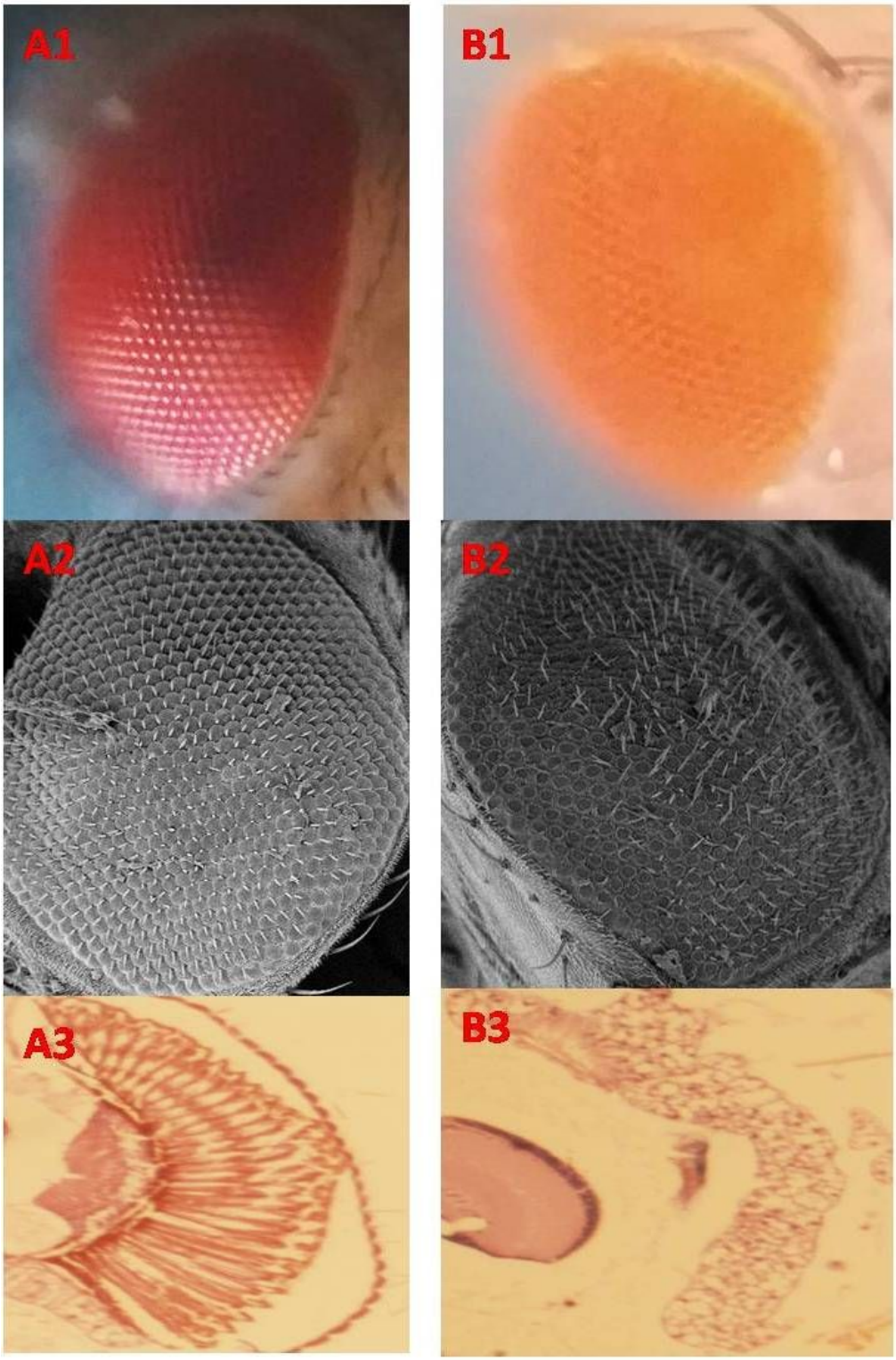


**Figure 1**

Control eye (Wild type; A1 Microscopic image A2: SEM image and A3 Histopathology)- No disruption in eye morphology and no loss of corneal lenses (ommatidia).Transgenic APPL-GAL4 eye(B1 Microscopic image B2: SEM image and B3 Histopathology), when Aβ expressed in eye tissue, showed loss of eye morphology and corneal lenses(B2 and B3).