

## **Abstract**

A degree of dementia or oblivion occurs in many living organisms including humans. This phenomenon is associated with aging. Many of the central nervous degenerative diseases such as Alzheimer's causes mental decline at later stages of age. Alzheimer's disease is the most common cause of dementia in the elderlies with more than 15 million affected people around the world. Several environmental and genetic factors cause brain cell death. In this study, we investigate the effect of E4 isoform of human APOE gene in the central nervous system of the vinegar fly (*Drosophila melanogaster*), focusing on possible changes in the metabolism of fats and the function of neurons in memory and learning processes. For this purpose, the transgenic *Drosophila* of UAS-hAPOE4 and UAS-hAPOE3, which have E3 and E4 isoforms of the human gene APOE in their genome, were used. Using the Gal4/UAS system, appropriate driver stocks such as elav-Gal4 Repo-Gal4 and OK107-Gal4 the APOE gene was expressed in neurons, Glial cells, and mushroom bodies. To confirm the existence of the human APOE4 gene in the genome of the flies, the genomic DNA was extracted and by making use of allele specific PCR (AS PCR) the presence of this gene was confirmed. The APOE4 and APOE3 expressing flies underwent behavioral and biochemical studies. The behavioral tests performed on larvae and adult stage of flies' life. APOE transgenic flies showed some degree of oblivion in both stages of life, both in the larval stage and in the puberty stage. A standard biochemical test was conducted to measure the triglyceride (TG) and cholesterol levels in the brain homogenate of the flies. A remarkable decrease in the level of TG and cholesterol in APOE expressing flies were evident when compared to control flies.

**Keywords:** Dementia, Neurodegeneration, Lipid profile, human APOE4 gene, AS PCR.



*University of Zabol  
Graduate School  
Faculty of Scienses  
Department of Biology*

The Thesis Submitted for the Award of M.Sc.  
Degree in Genetics

Title:

To investigate mechanism of action for APOE4-mediated  
neurotoxicity: A transgenic Drosophila model

Supervisor:

*Dr. Mohammad Haddadi*

By

*Elahe Yalame*

January 2018