



University of zabol

Graduate school

Faculty of science

Department of Biology

**The Thesis submitted for the Degree of M.Sc
(in the field of Genetic)**

Title:

**Study of human ApoE gene effect on expression level of marf
and drp-1 genes using transgenic Drosophila melanogaster**

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Abstract

Alzheimer's disease is the most common neurodegenerative disease in the world. One of the most important risk factors for Alzheimer's is aging. Alzheimer's disease is generally divided into sporadic and familial categories, with about 10% of cases being autosomal dominant. Alzheimer's disease slowly destroys memory and thinking, a point mutation in the amyloid beta precursor, and proteins pericillin 1 and 2 accumulate tau protein bundles in neurons. Decreased glucose metabolism is also seen in patients. Apolipoprotein E is a plasma glycoprotein that can be one of the genetic risk factors for late-onset Alzheimer's disease. This gene has three isoforms including E2, E3, and E4, the E4 isoform being more frequent in individuals with Alzheimer's disease, a single or hereditary type with a higher incidence of age, which affects amyloid accumulation and clearance. Beta and its effect on beta amyloid deposition are involved in the development of Alzheimer's disease. Despite the understandable advances in the study of the pathogenic mechanism of this gene, its precise cellular and molecular mechanism has not yet been elucidated. . Since the role of mitochondria in the development of neurodegenerative diseases has been confirmed, the present study sought to determine the involvement of mitochondria in neurological disorders mediated by APOE by modeling this disease in *Drosophila melanogaster*. *Drosophila* is a suitable model to investigate the functional principles of the neural circuitry and the GAL4-UAS system is an efficient tool in this model. And the glia expressing the central nervous system were used. Larval olfactory learning test was performed to investigate the effect of Apolipoprotein gene expression on larval memory and ethanol sensitivity behavioral test in adult fly. Biochemical tests of Lipid Profile, Cu ++, Zn in brain tissue extracts were also evaluated. Using qReal Time PCR technique, expression of two DRP-1 MARF genes involved in mitochondrial dynamics regulation was measured in brain tissue. In the olfactory learning test, E4 larvae showed decreased memory in both neurons and glia compared to the control group. MARF gene expression increased in UAS-ApoE4 / +; Elav Gal4 / +. DRP-1 gene increased expression in UAS ApoE4 / +; Elav Gal4 / +. There were no significant changes in the Ethanol Sensitivity test. Cholesterol levels in E3 and E4 isoforms were significantly increased in both neurons and glia. Due to decreased fusion protein and increase in fission protein, it impaired mitochondrial dynamics. E3 isoforms affect the level of mitochondrial dynamics and decrease MARF expression, thereby reducing fusion and E4 isoforms increase MARF expression, which needs further investigation. E4 isoform increased DRP-1 expression and consequently increased mitochondrial fission, whereas fission decreased in E3 isoform. E4 causes oxidative stress, increases lipid levels and thereby decreases memory.

Keyword: *Apolipoprotein, drp-1 gene, marf gene, Drosophila Melanogaster, Oxidative Stress*