Abstract

the Alzheimer's disease (AD) is very important The investigation of mechanisms involved in because of the high prevalence of this disease. In this study, the unfold proteins response (UPR) mechanism in the endoplasmic reticulum (ER) during accumulation of amyloid beta (Aβ), with emphasis on the role of transcriptional activator factor 4 (ATF4) was investigated. ATF4 is activated by permanent ER stress and the accumulation of Aβ-deficient proteins and Tau fibrils. ATF4 induces the increase of cell chaperons to refolding of proteins, inhibit translation and restore homeostasis. With extension of damages, ATF4 induces the transcription of the CCAAT-enhancer-binding protein homologous protein (CHOP) gene and then activates apoptosis and mediates nerve cell removal. The aim of this study was to investigate the relationship between expression of ATF4 factor and age in the AD model of fruit fly (*Drosophila melanogaster*) induced by Aβ. After mating the virgin female flies OK107-Gal4, GMR-Gal4 and elav-Gal4 with male flies of UAS-Aβ42, the first generation were examined. The confirmation of induction of Aβ mutation in first-generation fruit flies was proved by morphological (GMR-Gal4-UAS-Aβ42), behavioral (OK107-Gal4-UAS-Aβ42) and molecular (elav-Gal4-UAS-Aβ42) analysis. The first-generation flies were located at 18 °C for first 10 days in order to downregulate the expression of Aβ expression, and then they were located in the normal temperature (24 °C) for next 20 and 30 days in order to evaluate aging process. Then, the analysis of genes expression was performed using Real-time PCR with three replications for all ages at target time points. It was found that the temperature 18 °C reduced the expression of human Aβ in flies, and the highest toxicity was observed after a decade by placing flies at normal temperature. On the other hand, the amount of ATF4 expression was controlled by lowering the temperature and its expression increased in the 20th and 30th days compared to the cold period. In the end, it is suggested that the ATF4 gene will be targeted to develop new therapeutic strategies for AD associated with age. Also, various expressions of the elav Gal4 gene with the aging process in the fruit flies as well as other important genes involved in end-stage UPRs, such as CHOP, should be examined.

Key words: Amyloid beta, Alzheimer, ATF4, D.melanogaster, Aging

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Graduate School

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Department of Biology

The Thesis submitted for the Degree of Master of Science (In the Field of Genetics)

Title:

Evaluation of relationship between age and ATF4 expression in *Drosophila melanogaster* Alzheimer model

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Summer 2018