【Grant-in-Aid for Scientific Research(S)】
Biological Sciences (Agricultural sciences)

Title of Project : Elucidation of Aging Regulatory Mechanisms Related to Mitochondrial Function and Identification of Anti-Aging Food Factors

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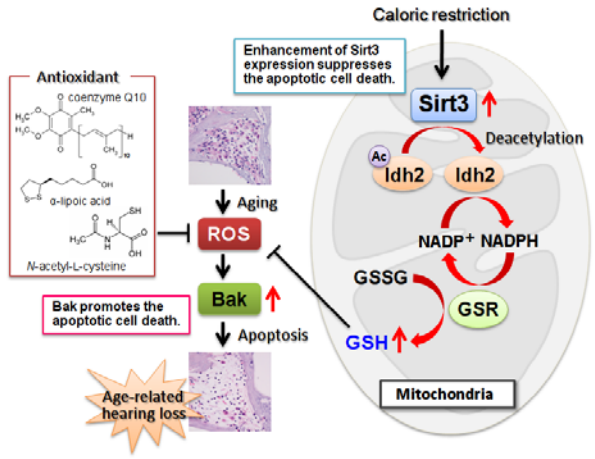
Research Area : Food Science
Keyword : Aging regulatory mechanism, Mitochondria, Anti-aging food factor

【Purpose and Background of the Research】

Age-related hearing loss, known as presbycusis, is a universal feature of mammalian aging and is the most common sensory disorder in the elderly population. We previously provided three essential findings for understanding the regulatory mechanism of age-related hearing loss. (i) The mitochondrial pro-apoptotic factor Bak mediates age-related apoptotic cell death in the cochlea. (ii) Age-related hearing loss is promoted by oxidative stress and is suppressed by antioxidants. (iii) The mitochondrial deacetylase Sirt3 mediates reduction of oxidative damage and prevention of age-related hearing loss under caloric restriction.

In this research project, we focus on the regulatory mechanism of apoptotic cell death mediated by Bak and Sirt3. There are the following major objectives:

1) Identification of novel pathways in age-related hearing loss and caloric restriction.
2) Identification of novel anti-aging food factors and elucidation of their action to Bak, Sirt3 and other regulatory factors.



【Research Methods】

1) We plan to analyze the other regulatory factors that work on downstream pathway of Sirt3 and the mitochondrial apoptotic-related factors that coordinately function with Bak. To achieve this purpose, we will make use of gene-expression analysis and molecular interaction analysis and Sirt3 deacetylation analysis of several knockout mice.
2) To identify anti-aging food factors, we plan to perform interaction screening between food factors and target regulatory factors such as Bak and Sirt3 and to evaluate the effect of identified food factors on age-related hearing loss. Moreover, the action mechanism of anti-aging food factors to target factors will be analyzed by using structural biological methodology.

【Expected Research Achievements and Scientific Significance】

The molecular mechanism of age-related hearing loss and caloric restriction would contribute to understanding the mammalian aging mechanism and would provide new insights into anti-aging research fields. In addition, anti-aging food factors are expected to decrease the incidence rate of age-related hearing loss in the elderly population.

【Publications Relevant to the Project】

・ Someya, S., Tanokura, M., et al. Age-related hearing loss in C57BL/6J mice is mediated by Bak-dependent mitochondrial apoptosis. *Proc Natl Acad Sci USA* 106, 19432-19437 (2009).
・ Someya, S., Tanokura, M., et al. Sirt3 mediates reduction of oxidative damage and prevention of age-related hearing loss under caloric restriction. *Cell* 143, 802-812 (2010).

【Term of Project】 FY2011-2015

【Budget Allocation】 166,300 Thousand Yen

【Homepage Address and Other Contact Information】

http://
fesb.ch.a.u-tokyo.ac.jp/english/index.html