Project number　52

Characterization of different types of cellular senescence

［1］Research group
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Expenditure report of research funds：
Consumables 100,000 YEN

［2］Research setup

Healthy aging and longevity in humans are modulated by a combination of genetic and non-genetic factors. As longevity exhibits high heritability, insights into the genetic factors may improve our present understanding of mechanisms responsible for promoting health and reduce the risk of diseases. However, only a few genes and genetic loci have been identified for this trait and, therefore, the study of longevity genes warrants further investigations. It is estimated that about 25% of the variation in human life span is determined by genetics, but which genes, and how they contribute to longevity, are not well understood. A few of the common variations (called polymorphisms) associated with long lifespans are found in the APOE, FOXO3, and CETP genes, but they are not found in all individuals with exceptional longevity. It is likely that variants in multiple genes, some of which are unidentified, act together to contribute to a long life. Therefore, there is a need to identify and characterize more human longevity genes to discover gender and tissue specific aging patterns that were previously unrecognized.

We have recently identified a novel regulator of human oxidative stress response, Oxidative stress-responsive serine-rich protein 1 (OSER1), which extends lifespan and enhances stress response via antioxidative properties by maintaining mitochondrial morphology and functional integrity (Song et al under revision).

OSER1 in silkworms and human cells showed nuclear localization in the unstimulated conditions. Most cellular processes are carried out by protein complexes, but whether OSER1 interacts and form complex with other cytosolic proteins or regulate nuclear processes to regulate mitochondria functions is yet unknown. To better understand the function of OSER1 and, which biological pathway(s) it is part of, we characterized human OSER1 containing complexes. We used plasmids containing GFP-tagged OSER1, which were transfected and overexpress in U2OS cells.

［3］Research outcomes

（3－1）Results

Dr Yasui's group identified several interesting OSER1 interacting proteins. These results are currently being followed up in Dr Rasmussen's group by cellular and biochemical assays dependent on the nature of the protein complex.

（3－2）Future perspectives

The results will provide better understanding of the role of OSER1-mediated redox biology in healthy aging. This project will increase our understanding of the human oxidative stress response and how it affects lifespan, healthspan, and reproduction.

［4］List of research achievements

Song J, Li Z, Zhou L, Chen X, Sew WQG, Herranz H, Ye Z, Olsen JV, Li Y, Nygaard M, Christensen K, Tong X, Bohr VA, Rasmussen LJ, Dai F. FOXO-regulated OSER1 reduces oxidative stress and extends lifespan in multiple species. Nat Commun. 2024. In revision.