

公益財団法人 セコム科学技術振興財団
研究成果報告書

研究課題名

オートファジー機構を応用したスマート・エイジング対策法の開発

Development of anti-aging method against autophagy machinery

研究期間

平成25年 4月 ～ 平成29年 3月

報告年月

平成29年 6月

研究代表者

東京医科歯科大学 難治疾患研究所 教授

清水 重臣

Tokyo Medical and Dental University, Medical Research Institute, Professor
Shigeomi Shimizu

Abstract

It is a crucial problem how we postpone healthy life expectancy. The aging research has been performed from various aspects, including cellular senescence, DNA damage, epigenetics, and so on. Among them, autophagy is one of the crucial cellular events to regulate aging. This is because various geriatric diseases occur via the gradual accumulation of damaged proteins/organelles inside cells during aging. Autophagy is capable to degrade these waste products and maintain homeostasis. In this research project, we examined the involvement of autophagy in aging, developed molecular markers of aging applying autophagy, and developed small therapeutic compounds for geriatric diseases.

In the study examining the involvement of autophagy in aging, we found the weak autophagy activity in aged cells. We also developed molecular markers to detect age-related loss of autophagy activity. We identified PPM1D as an age-regulation molecule. The lack of this molecule facilitates aging. We also found that decrease of alternative autophagy activity should be the cause of Alzheimer dementia.

We developed fluorescent probe to monitor possible cell aging, but failed to identify any serum biomarker to detect tissue aging. In the study developing small therapeutic compounds for geriatric diseases, we have established a high-throughput assay system that can monitor excessive autophagy. Using this assay, we screened a low-molecular weight compound library and natural compound library and successfully identified anti-cancer compounds, anti-polyglutamine Disease compounds, and anti-Alzheimer dementia compounds. We also identified natural compounds for metabolic disease.

We would like to optimize our compounds against anti-geriatric diseases for clinical use, especially focusing on anti-Alzheimer dementia compounds. Because this autophagy-related study concerning geriatric disease is a pioneer work and because autophagy is useful for longevity, we would like to continue autophagy-related aging study.