T16-040
T16-123

Tohoku University's Invention

Cargo-specific degraders using selective autophagy

Degradation and clearance of disease related intracellular targets by autophagy

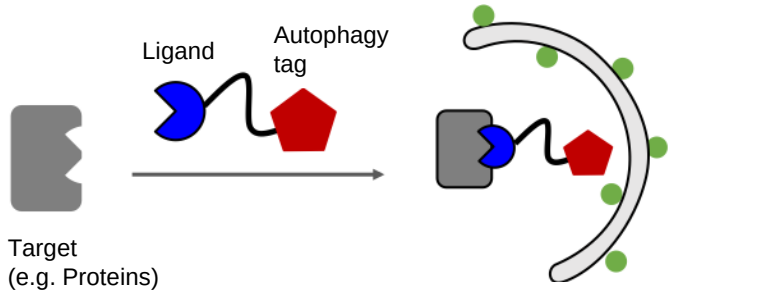
Introduction

Autophagy is a intracellular degradation mechanism and is related to a large scale of diseases, e.g. neurodegenerative disease, cancer and metabolic disease. It is a promising approach in drug discovery.

By now, current technologies cannot selectively trigger autophagy targeting specific proteins. This invention established a system to introduce autophagy embracing the target of interest (See the figure below).

PROTAC, a targeted protein degradation technology, is existent but it is a ubiquitin-proteasome system, thus the scope of targeted proteins are limited to soluble intracellular ones. Meanwhile, this invention's system is suitable for aggregated proteins, organelles and pathogens, etc.

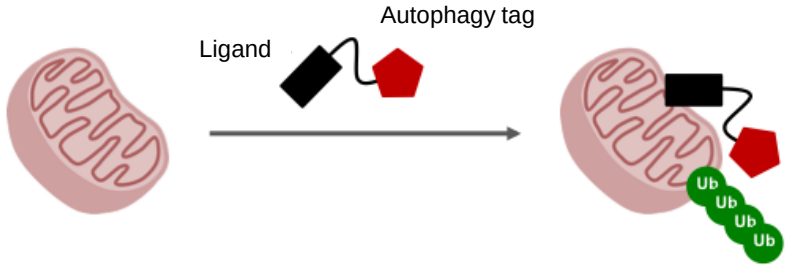
This invention: AUTACs (Autophagy-targeting chimeras)

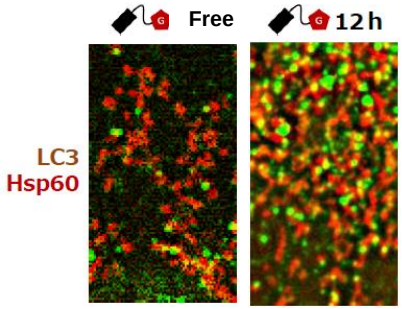


*Please refer to this article:
Takahashi et al., Molecular Cell, (2019), 76, p1-14.

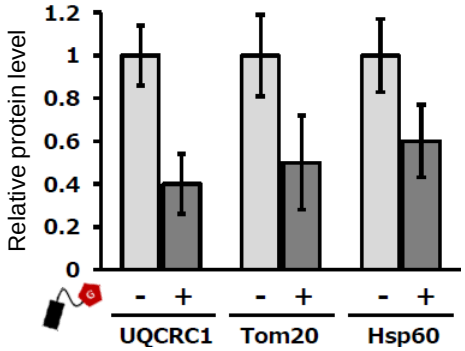
Degradation of fragmented mitochondria by autophagy

［Opal knockdown conditions］





LC3：Autophagy marker
Hsp60：Mitochondria
(Merge of these two shows degradation (yellow))



Mitochondrial protein levels are significantly reduced when autophagy occurs.
→ It implies the fragmented mitochondria are degradated.

Patent Data Sheet

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