学位論文抄録
(Abstract of Thesis)

A AAA ATPase Cdc48 with a cofactor Ubx2 facilitates ubiquitylation of a mitochondrial fusion-promoting factor Fzo1 for proteasomal degradation

(Cdc48-Ubx2複合体はミトコンドリア融合誘導因子Fzo1のプロテアソーム分解のためのユビキチン化を促進する)

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Abstract of the Thesis

Background and Purpose:

Functionality of mitochondria is pivotal for the cells which is maintained by continuous fusion and fission events. Mitochondrial fusion is regulated by two different ubiquitylations of an outer membrane protein Fzo1. One ubiquitylation of Fzo1 promotes fusion, which is removed by a deubiquitylating enzyme Ubp12. This fusion-competent ubiquitylation precedes the other ubiquitylation, which leads to Fzo1 degradation. The degradation-signaling ubiquitylation is removed by deubiquitylating enzyme Ubp2. Mitochondrial fusion was inhibited in yeast mutant strains of a multi-functional AAA protein, Cdc48. Various functions of Cdc48 are controlled by corresponding adaptor proteins. A previous study in our lab revealed that two Cdc48 adaptors, Ubp3 and Ubx2, were involved in the fusion process and in Fzo1 turnover, respectively. The purpose of this research is to reveal specific roles of Ubx2 in the regulation of Fzo1 turnover.

Methods:

Turnover of Fzo1 was analyzed by cycloheximide chase experiments followed by the western blotting. The interactions between Fzo1, Ubx2, and Cdc48 were tested by co-immunoprecipitation assay. In order to assess ubiquitylation status of Fzo1, cells were treated with a proteasome inhibitor, MG132, and subsequent immunoprecipitation and the western blotting were performed.

Results:

In this study, we showed that Ubx2 directly interacted with Cdc48 and Fzo1. Moreover, the amount of Cdc48 co-immunoprecipitated with Fzo1 has reduced in the absence of Ubx2. Also we demonstrated that Cdc48-Ubx2 complex facilitated ubiquitylation of Fzo1 for promoting the degradation process by ubiquitin proteasome system. In addition, we also found Cdc48-Ubx2 directly interacted with Ubp2. Furthermore, amount of Cdc48 interacted with Ubp2 has reduced in Δ*ubx2* strain suggesting Ubp2 as one of potential substrate of Cdc48-Ubx2 complex.

Conclusion:

In this study we conclude that the Cdc48-Ubx2 complex regulates Fzo1 turnover by modulating ubiquitylation status of the Fzo1.