Molecular insight into the mechanism of peroxisome degradation via autophagy in land plants

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Since plants cannot escape from undesired environmental change, they have developed flexible and sophisticated strategies to counteract against the stresses. Organelles' functions support plant cellular homeostasis. Under environmental changes, organelles flexibly rearrange their metabolisms, morphology, and positions to adopt the change inside and outside cells. Peroxisome, which is one of the organelles, is ubiquitous in eukaryotic cells. Peroxisomes contain metabolic pathways including fatty acid degradation and polyamine biosynthesis. Besides, plant peroxisomes are involved in photorespiration and biosynthesis of phytohormones auxin and jasmonate. These functions are essential for organisms' life.

Because peroxisomal metabolisms contain several oxidases and produce hydrogen peroxide (H_2O_2), peroxisomes are exposed to H_2O_2 and gradually oxidized and subsequently disordered. Therefore, the quality control system of peroxisomes is necessary to keep cells healthy. In the previous studies, applicants demonstrated that oxidized peroxisomes are selectively recognized and eliminated by autophagy, and this process had a pivotal role in the peroxisomal homeostasis. The selective autophagy targeting peroxisomes is called pexophagy. Although the molecular mechanism of pexophagy is well studied in yeasts and mammalian cells, the knowledge in plants is still a little. However, the analysis on autophagy mutants in plants have shown that the degradation of peroxisomes via autophagy occurs more frequently than that of other organelles, such as mitochondria, indicating that the importance of the quality control of peroxisomes in plants and this is a characteristic of plant peroxisomes.

The primary objective of this project is to understand the molecular mechanisms underlying the pexophagy in plants. Our recent study using the autophagosome-visualized transgenic plants and the pexophagy mutants strongly suggested that the initiation and the development of autophagosome membrane proceed in a different manner from those of yeast and mammals. Indeed, several autophagy-related genes are not conserved in the plant genome, implicating the plant-specific regulation of autophagy/pexophagy. Therefore, we plan to address the following questions by the proposed project:

- How and at where is the formation of the autophagosome membrane initiated in the cell?
- In what order do pexophagy-related factors contribute to the formation of autophagosome?
- How much impact does pexophagy have in plant development?

Based on the forward genetics approach, we have isolated several mutants which exhibit abnormal peroxisome degradation, and subsequently identified pexophagy-related genes. The proposed plan addresses the questions using the pexophagy mutants and transgenic plants which is designed to access subcellular localization, protein-protein interaction and the roles of pexophagy-related proteins. Two model plants, a higher plant (*Arabidopsis thaliana*) and a liverwort (*Marchantia polymorpha*), are adopted in the proposed project to accelerate the speed of the research and to understand basal strategy underlying the mechanism of peroxisome homeostasis in land plants.

Although there are differences among the regulation in each organism, autophagy is a universal system in eukaryotes. The process of autophagosome formation is involved not only in pexophagy but also other types of autophagy. The knowledge obtained from the proposed project together with that from other organisms can provide a wider vision of strategies how autophagy is controlled among eukaryotes, including humans and also crops.