CDB SEMINAR

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National Institute of Biological Sciences, Beijing

Wednesday, Sept 30, 2009

16:00~17:00 A7F Seminar Room

## *C. ELEGANS* AS A MODEL SYSTEM TO STUDY AUTOPHAGY

**Summary**

Autophagy, the primary intracellular catabolic mechanism for degradation of cytosol or damaged organelles, involves the formation of a double membrane structure, called the autophagosome, which engulfs a portion of the cytoplasm and/or organelles and delivers them to the lysosome for degradation. A basal constitutive level of autophagy has been shown to be required for removing diffuse aggregate-prone proteins and loss of autophagy activity leads to intracellular accumulation of polyubiquitinated protein aggregates, particularly in neurons or hepatocytes. Whether and how the autophagic machinery selectively recognizes and degrades preferential substrates during animal development remains largely unexplained.

Germ P granules are a specialized type of protein aggregate that are maternally contributed and are found exclusively in germ cells in *C. elegans*. During the early embryonic divisions that generate germ blastomeres, some P granules are left in the cytoplasm destined for the somatic daughter cell and these are quickly disassembled and/or degraded. We demonstrated that aggregate-prone P granule components PGL-1 and PGL-3 that remain in somatic cells are selectively degraded by autophagy. In autophagy mutants, PGL-1 and PGL-3 failed to be removed and formed granules in somatic cells (termed PGL granules). We further showed that the formation and degradation of PGL granules requires the activity of *sepa-1*. In *sepa-1* mutants, PGL granule components are diffusely distributed in the cytoplasm and fail to be eliminated. SEPA-1 forms protein aggregates and is also a preferential target of autophagy. SEPA-1 directly binds to PGL-3 and also to the autophagy protein LGG-1/Atg8. Thus, SEPA-1 functions as a bridging molecule in mediating the specific recognition and degradation of PGL granule components by autophagy.

The wealth of knowledge about *C. elegans* developmental biology, including its invariant cell lineage and the availability of powerful experimental tools such as genetic screens for assembling genes into pathways, make the degradation of PGL granules and SEPA-1 aggregates by autophagy a good model for dissecting the autophagic machinery and also for studying selective autophagic degradation of protein aggregates.

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