The Role of Inhibitor of Apoptosis in Fat Body Remodeling in *Drosophila melanogaster*

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The precise regulation of programmed cell death (PCD) is critical for homeostasis and development. In contrast to necrotic cell death, which results from disease or injury, PCD removes abnormal cells and eliminates obsolete tissues. The metamorphosis of *Drosophila melanogaster* from the larval to the adult form results in rapid (~8 days) destruction of many larval tissues by PCD. This is regulated by the steroid, 20-hydroxyecdysone (ecdysone)\(^1\). A high titer ecdysone pulse at the end of larval development induces puparium formation (the beginning of metamorphosis) and larval midgut destruction. A second pulse, ~10 h later, induces the prepupal-pupal transition and larval salivary gland cell death. These larval tissues are destroyed by a PCD mechanism, known as autophagy, characterized by the formation of intracellular cytoplasmic vesicles.

Autophagy of larval tissues is initiated by up-regulation of the cell death activator genes *reaper* (*rpr*) and *head involution defective* (*hid*). Down-regulation of the antiapoptotic genes *Inhibitors of Apoptosis* (*diap1* and *diap2*) occurs at the same time as the up-regulation of the proapoptotic genes. While DIAP2 functions in innate immunity and resistance to gram-negative bacterial infection, DIAP1 has a key role in cell survival\(^2\). DIAP1 regulates PCD by inactivating caspases while *rpr* and *hid* suppress *diap1* to initiate histolysis of most larval tissues. A unique exception is the developmental fate of the larval fat body, which is refractory to cell death and instead undergoes remodeling from an organized tissue to separated individual cells. The larval fat cells persist 3-4 days after eclosion of the adult and are then replaced by sheets of adult fat body.

While the timing of fat body remodeling is ecdysone-dependent, its genetic regulation still needs to be elucidated. Ectopic expression of *diap1* in fat body represses its destruction in the adult fruit fly, suggesting that IAPs may be involved in fat body remodeling\(^3\). I hypothesize that, during larval salivary gland histolysis fat tissue is refractive to PCD due to upregulation of *diap1*. To test this hypothesis, I am constructing a temporal profile of *diap1* expression in fat body via quantitative real-time PCR. Additionally, to investigate if *diap1* is necessary for fat body remodeling, I am studying fat body development in tissue specific loss-of-function *diap1* animals.

