

[Core laboratory]

Laboratory of Innovational Biology

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Living organisms adapt to their environment by evolving their shapes and forms in a wide variety of ways. In the Laboratory of Innovational Biology, we are pursuing our goal to understand "the mechanisms underlying the formation of various 'shapes' of life," such as "how 'shapes' are formed," "how differences in 'shapes' are generated," and "how 'shapes' evolve".

Based on a tremendous number of studies to date, considerable progress in understanding the mechanisms by which the properties of each cell are determined during the developmental process has been made. However, how the final "shape" is achieved after the cell properties are determined is still largely unknown.

Insects boast more than one million species, and the diversity of their "shapes" is outstanding, making them suitable organisms for studying the mechanism of "shape-making." Among these, a fruit fly *Drosophila melanogaster* is one of the most ideal organisms because you can change the activity of any gene at any time in any cell as you like, and there are tools to visualize the expression and localization of various genes and proteins in real-time while they are alive. In our laboratory, we are mainly studying the following subjects using *Drosophila* with an evolutionary perspective.

(1) Molecular Mechanisms of Adult Leg Shape Formation

Insects have evolved a variety of appendages such as legs, antennae, and mouth parts, which originally had the same morphology. In addition, appendages usually consist of several segments along the proximodistal axis, and the number and shape of the segments vary greatly depending on the type of appendage or among insect species. We are studying the "shaping" mechanism of the adult leg of *Drosophila* by using live imaging to continuously observe the formation of the leg. Recent our studies have revealed that surprising morphological changes of cells and formation of unexpected structures occur transiently during the formation of the final "shape." Through understanding the mechanism underlying the "shape" formation of the adult leg in *Drosophila*, we aim to understand the molecular mechanism of "shape-making" of organisms and how it changes to produce differences in "shape" among appendages and insect species, thereby challenging elucidate the mysteries of the formation, diversification, and evolution of "shapes."

(2) Mechanism of Body Shape Regulation by Extracellular Matrix
Insects are organisms with exoskeletons, and their bodies are covered by an extracellular matrix called the cuticle. The cuticle is composed of chitin fibers and various proteins called

cuticular proteins, which are secreted from epidermal cells. Insect body shapes varies greatly from round to highly elongated, and our recent studies have revealed that the properties of the cuticle, which are determined by cuticular proteins, play an important role in determining insect body shape. Through these studies, we will elucidate how the shape of an organism is controlled by substances secreted outside the cell, rather than by the cell itself.

(3) Molecular Mechanism Creating the "cut here line" on the Cuticle

The cuticle that covers the surface of arthropods, including insects, not only serves as an exoskeleton but also protects the body from environments. For this reason, the cuticle is a rigid structure. However, because of the cuticle rigidity, arthropods must molt or eclose to grow their body during the post-embryonic development or change their shapes by metamorphosis, respectively. During molt or eclosion, a new cuticle is formed and an old one is shed. At this time, the old cuticle is not broken randomly but always cleaved in a pre-defined line. In other words, some kind of "cut here line" is formed during cuticle formation. We are trying to clarify how the "cut here line" is formed, how its position is determined, and what the structure of the cuticle is to function as a "cut here line". Because the "cut here line" on the cuticle is the most basic and essential property for survival not only in insects but also in all arthropods, and because each arthropod has its own characteristic position of the "cut here line", we are trying to deepen our understanding of the evolution of not only insects but also arthropods generally as a whole through the study of the "cut here line."



Fig. 1. Legs of various insects.



Fig. 2. Shaping process of an adult leg observed by live imaging.



Fig. 4. Eclosion of *Drosophila*



Fig. 3. Various cuticular protein mutants (wild-type at the center).