Laboratory of Cell Biology

Graduate School of Science

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The body of a complex multicellular organism is formed through systematic assembly of many different cells. Therefore, the "life" of an organism depends on the integration of diverse functions exerted by these cells. For example, cells determine their own destinies by exchanging information among themselves. However, it is still elusive how cells perform their amazing functions.

Our laboratory is interested in how cells function in the development of animal tissues and organs according to genetic programs. We are challenging this question using *Drosophila*, in which whole varieties of genetic tools and comprehensive genomic and chromosomal information are available.

Chirality of cells makes the animal body left-right asymmetric

Even in animals that are left-right symmetrical in appearance, their internal organs are often left-right asymmetrical. A good example is the left-right asymmetry of human internal organs. The mechanisms underlying the formation of such left-right asymmetries are evolutionarily diverse and largely unknown in invertebrates.

Drosophila is an ideal laboratory animal for studying the formation of left-right asymmetry, because of its genetically determined and clear left-right asymmetry. Our laboratory uses the *Drosophila* melanogaster to study the mechanisms by which left-right asymmetry is formed. We have revealed for the first time that cells exhibit chirality (the property that the mirror image does not overlap with its original), which is the basis to form the left-right asymmetry of the body. We searched for mutants that reverse the left-right asymmetry of the gastrointestinal tract, and found that various genes required for the left-right asymmetric development of this organ.

In addition, we have succeeded in identifying genes that invert (mirror) cellular chirality and the left-right asymmetric organs. We are currently investigating the mechanism of left-right asymmetric tissue deformation caused by cellular chirality by computer simulation of tissues composed of three-dimensional model cells that exhibit cellular chirality. In addition, we are elucidating the molecular mechanism how cellular chirality is formed in *Drosophila* macrophages.

Intercellular signaling via cell-to-cell contact-Notch signaling pathway

Cell-to-cell communication is essential for development and homeostasis in multicellular animals. The exchange of information between cells is the basis for the orderly behavior of cells. In recent years, great progress has been made in our understanding of the mechanisms of cell-to-cell communication. However, many mysteries remain unsolved. Receptor proteins on the surface of the plasma membrane are responsible for the reception of information between cells. These are proteins that "receive" information, called as receptors.

Notch is a receptor protein that presented at the plasma membrane. Proteins that sends information from the neighboring cells to Notch, designated as ligands, are also transmembrane proteins. Therefore, Notch receives information only when direct cell-cell contact exists between signal sending and receiving cells. This mechanism allows intercellular communication to occur through cell-cell contact. This signaling pathway is called Notch signaling pathway, which functions in a variety of cell-fate decisions and morphogenesis. Therefore, abnormalities in Notch signaling are known to cause of various human diseases, including cancers. We are studying the mechanism of Notch signaling and its regulation in *Drosophila*.

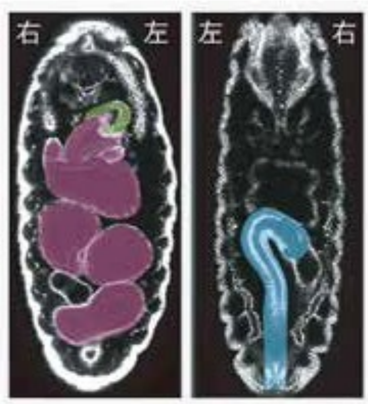

Figure 1.
The digestive tract of a *Drosophila* embryo (parts in green, purple, and blue) is left-right asymmetric. The left panel shows a ventral view, and the right panel shows a dorsal view/

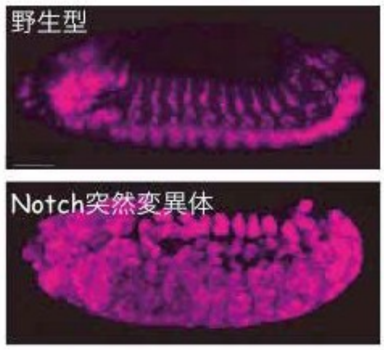

Figure 2.
The nervous system of a wild-type *Drosophila* embryo (purple) is a ladder-like nervous system; in the embryo carrying a mutant of the gene encoding the Notch receptor, cell-to-cell communication is dysfunctional and cell differentiation is disrupted. As a result, all cells that are normally epidermal are converted to neural cells.

There is still a lot of uncharted territories in biology. In other words, there is still a lot of fun waiting for us.

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