Laboratory of Macromolecular Structure

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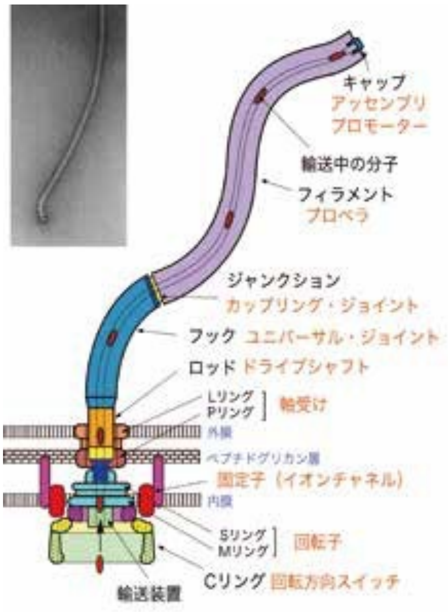
In living organisms, molecular machines made up of biomacromolecules play essential roles in various chemical reactions and biological functions to maintain life. Unlike artificial machines, biological molecular machines function with high precision but with high flexibility. The flagellar system and protein transport system of bacteria are typical examples of biomolecular machines. We study the molecular mechanisms of function and formation of such biomolecular machines through 3D structural analysis and reconstruction of molecular machines.

Elucidation of molecular mechanisms of flagellar formation and rotation.

The flagellum, a locomotive organelle of bacteria, is the first rotational system discovered in living organisms. At the base of the flagellum, there is a motor about 45 nm in diameter made up of many protein molecules. The motor is driven by the proton or sodium ion influx across the cell membrane. The proton motor rotates at about 300 rps and the sodium ion motor at 1500 rps. The motor can rotate in reverse direction, and the rotation direction is switched by a signal from the chemotaxis sensor. Thereby, bacteria change the swimming direction. The molecular mechanism of rotation is obscure, although it is thought that torque is generated by the interaction of the stator and rotor coupled with the ion flow through the stator, a membrane protein complex. Interestingly, the stator is frequently replaced while the motor is rotating, and ion transmission begins when it is assembled into the motor. However, the molecular mechanisms of stator association/dissociation coupled with on/off of ion transmission are unknown. To solve these mysteries, we are working on structural and functional analysis of the proteins that compose the chemotaxis sensor, rotor, and stator, as well as their complexes.

Structure and function of the bacterial protein transport system

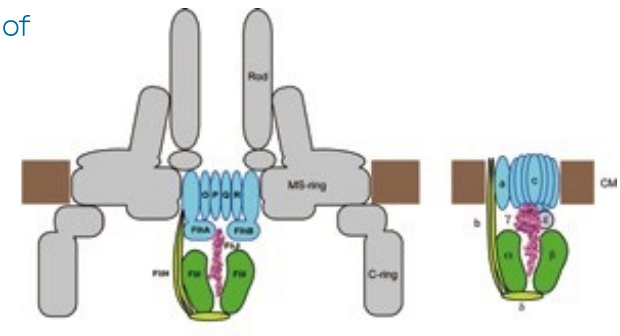
The bacterial flagellum is constructed on the outside of the bacterium, and therefore the flagellar proteins synthesized inside the cell must be transported to the outside of the cell. A transport device is located at the base of the flagellum to select only flagellar proteins and deliver them to the outside of the cell at the right time. The transport system not only transports the proteins, but also switches the type of the flagellar proteins according to the formation status of the flagellum and regulates the expression of the flagellar proteins. This transporter is a member of the type III secretion system used by pathogenic bacteria to deliver virulence factor proteins directly to host cells during infection. Therefore, both systems are thought to share a common working mechanism. Although the molecular mechanism of transport is unknown, we have revealed that the transport apparatus has an ATPase unit structurally similar to FoF1-ATP synthase, which has a rotational molecular mechanism.



細菌べん毛の電子顕微鏡写真と模式図

Structure and function of bacterial fimbriae

Porphyromonas gingivalis, a major periodontal pathogen, have at least two types of Type V fimbriae for biofilm formation and adhesion to host cells. We are conducting structural analysis and reconstruction experiments to elucidate the molecular mechanism of fimbriae formation and adhesion.



べん毛蛋白質輸送装置（左）とF_0F_1-ATP合成酵素（右）の模式図

As is the case with the workings of biomolecular machines, there are many things in the world that seem to be understood but really are not. Please think carefully about what you do not understand. A new world will open up to you.

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