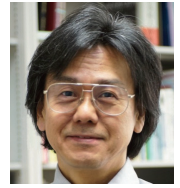




CryoEM structures of bacterial flagellar motor useful for designing anti-bacterial drugs and rotary nanodevices

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Abstract

The recent progress in electron cryomicroscopy (cryoEM) and single particle image analysis has made it possible for the structure determination of biological macromolecules to be carried out from a small amount of solution sample as small as a few μg . Now the data collection throughput is as high as 30,000 cryoEM images per day so that collection of a few thousands cryoEM images needed for structural analysis can be completed within a few hours. The structure-based drug screening that pharmaceutical companies are keen to carry out can be done very efficiently. We utilized this technology to determine the structures of multiple rings of the bacterial flagellar motor, and they revealed the mechanisms of torque transmission by the rotor ring and nearly zero friction of bushing for energy-efficient high-speed rotation of the motor.

Background & Results

Because the mechanisms of life in the living organisms are driven by dynamic networks of biological macromolecules based on 3D structures, the structural information is essential for our mechanistic understanding of life. Many bacteria, such as *Salmonella*, have a motile organelle called the flagellum, composed of a long helical filament as a propeller and a rotary motor, to swim around to find favorable environments for their survival. The structure of the rotary motor had been elusive, and the mechanisms of torque generation-transmission and friction-less high-speed rotation of the drive shaft inside the bushing remained unknown.

By the recent progress in cryoEM with automated high-throughput data collection, it is now possible for structural analysis to reach atomic resolution within a relatively short period of time. This allowed the structure of the flagellar motor to be determined at near atomic resolution. The structure of the rotor ring called the MS ring has shown that it is composed of 34 subunits of FlIF protein in two different conformations, generating a complex structure made of disks and cylinder with three different, 34-fold, 23-fold, and 11-fold rotational symmetries. The bushing called the LP ring is made of 26 subunits of FlIH and FlIL, forming an intricate network of long anti-parallel β -strands to build the solid wall of the hollow cylinder as a bushing. The inner surface of the LP ring is charged both positively and negatively and closely faces the negatively charged outer surface of the drive shaft to realize nearly zero friction for energy-efficient high-speed rotation of the motor by well-balanced electrostatic forces.

Significance of the research and Future perspective

The structural information of the bacterial flagellar motor at atomic level will be useful for future engineering applications, such as a design principle of highly energy efficient self-assembling nanodevices, as well as the basis for the development of anti-bacterial drugs.

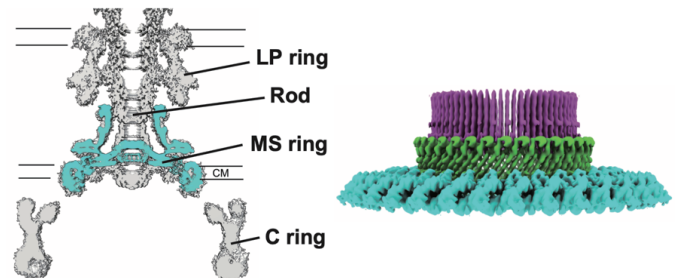


Fig. 1 Entire structure of the bacterial flagellar basal body spanning the inner and outer membranes as a nanoscale rotary motor (left) and high-resolution density map of the rotor S ring (right).

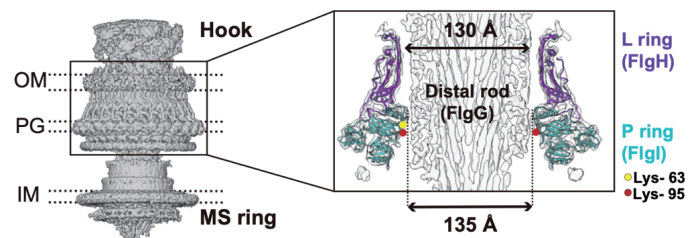


Fig. 2 High-resolution structures of the bacterial flagellar basal body (left) and its bushing LP ring (right).

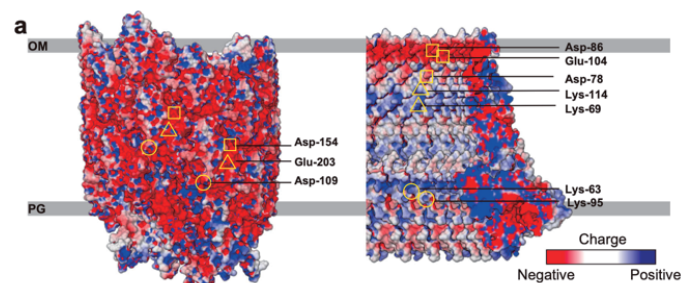


Fig. 3 Electrostatic potential distributions on the surfaces of the drive shaft (left) and the bushing LP ring (right).

Patent

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Keyword

Kawamoto, Akihiro; Miyata, Tomoko; Makino, Fumiaki et al. Native flagellar MS ring is formed by 34 subunits with 23-fold and 11-fold subsymmetries. *Nature Communications*. 2021; 12: 4223. doi: 10.1038/s41467-021-24507-9.

Yamaguchi, Tomoko; Makino, Fumiaki; Miyata, Tomoko et al. Structure of the molecular bushing of the bacterial flagellar motor. *Nature Communications*. 2021; 12: 4456. doi: 10.1038/s41467-021-24715-3.

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electron cryomicroscopy, single particle image analysis, structural analysis of biological macromolecules, protein nanomachine, bacterial flagellar motor