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論　文　内　容　の　要　旨

〔　題　　名　〕

Structure of the Flagellar Filament of *Salmonella* FljB and Its Difference from the FliC Filament

（サルモネラ菌におけるFljBとFliCの鞭毛繊維の構造比較）

学位申請者　當間頌子

Salmonella typhimurium (*S. typhimurium*) cells swim by rotating peritrichous flagella distributed over the cell surface, a process driven by rotary motors at the base of the flagella, which is powered by proton influx through the stator complexes spanning the inner membrane. To understand the function of flagella that works as nanomachine, I have studied the structure of the flagellar filament at sub-nm resolution. The flagellar filament grows as long as 15 μm but the diameter is only 230 Å. The tubular structure of the filament is formed by 11 protofilaments, which is an assembly of a single protein, flagellin. Flagellin is composed of four domains, D0, D1, D2, and D3, from the inner to outer radius of the filament. Domains D0 and D1 form the inner core of the filament, and domains D2 and D3 form the projection on the filament surface. *S. typhimurium* switches its flagellin expression between two distinct phases, FliC and FljB. The phase change may be just to escape from the host immune response by changing the antibody recognition domain D3 on the filament surface. However, the difference between the structures of the FljB and FliC filaments may still have some other functional implications. To better understand the importance of this phase variation, I set out to solve the structure of FljB filament at near atomic level to compare the structural and functional differences between FljB and FliC filaments.

In the studies described herein, I report the structure of FljB filament at 7.5 Å resolution obtained by electron cryomicroscopy and helical image analysis. Interestingly, the FljB filament has different orientation of D3 compared to that of FliC. I built a homology model of FljB from the atomic model of FliC, refined it with the density map of the FljB filament, and superposed it with the structure of FliC to compare the two structures. The overall positions and orientations of domains D0, D1, and D2 and their intersubunit packing interactions do not differ substantially between FljB and FliC. However, the D3 domains on the filament surface show distinct orientations between the two. Functional studies indicate that this translates into faster swimming speed of cells with the FljB filaments compared with FliC in highly viscos media.

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論文審査の結果の要旨及び担当者

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論文審査の結果の要旨

申請者は、サルモネラ菌の運動器官であるべん毛を構成する2種類のフラジェリンのうち、構造未知のFljBべん毛繊維の立体構造とらせん型プロペラとしての機能を解析し、構造既知のFliCべん毛繊維の構造や機能と比較することにより両者の違いを明らかにした。

低温電子顕微鏡法によりFljBべん毛繊維の立体構造を８Å分解能で解析し、FliCべん毛繊維とのドメイン配置の違いを明らかにした。そして、らせん型プロペラとしての機能の違いも計測することにより、サルモネラ菌が宿主免疫系から逃れるためだけではなく、これら2種類のべん毛繊維を使い分ける理由とその仕組みに手掛かりを得た。また、FljB分子の結晶化に最適なフラグメントを設計し、大量発現・精製してＸ線結晶構造解析も行った。これらの成果は博士号の学位授与にふさわしいと判断するものである。