Disordered protein controls formation and stability of the bacterial flagellar hook

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Video Abstract

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Abstract

The bacterial flagellum is one of the most amazing structures in biology. The whip-like appendage rotates as many as 300 times per second, allowing bacteria to swim around. That speed is thanks to a powerful internal motor, and a strong hook that acts as a universal joint and transmits torque. Scientists know a lot about how these machines work, but there are still important questions, like how hook proteins function. Now, researchers at the Okinawa Institute of Science and Technology and their collaborators have identified a surprisingly important role for a disordered segment of the hook protein. The biologists first noticed that many bacterial species share a 40- to 60-residue section of their rod and hook proteins. This part lacks structure and is considered intrinsically disordered, but it might, in its flexibility, be essential. The team named this peptide ID-Rod-Stretch since it was conserved in length in the rod protein, but varied in the hook protein. To identify which parts of ID-Rod-Stretch are important for hook function, the researchers mutated the fully and partially conserved residues in *Salmonella*, both individually, and as a group. When expressed in bacteria, they found that swapping out lysine 32 with an alanine left 90 percent of cells without any flagella, and the remaining 10 percent had only one or two, compared to the typical 12. The other point mutations had minor effects, and the strain with all mutations had no flagella at all. Interestingly, the K32 mutant strain made twice as much hook protein, suggesting the lysine is important for hook assembly. To discover other possible functions of the hook protein, the team then mutated residues in a five-amino-acid sliding window. This revealed the importance of many sections of ID-Rod-Stretch, except for the middle and very C-terminal end. Finally, the scientists investigated the hook protein in *Campylobacter*, which has 20 more residues in its ID-Rod-Stretch than *Salmonella*. When they deleted the segment, they saw that cells had a much harder time swimming, and many of their flagella had broken off. The results demonstrate that despite its disorder, ID-Rod-Stretch is critical for flagellar formation and stability. As a result, the disordered segment may be a good target for new drugs that fight bacterial infections, especially *Campylobacter*, which uses its flagella to move and secrete toxins.