PRESS RELEASE

Exploring The Dynamic Partnership Between FtsZ and ZapA Protein

Researchers explore the structure and molecular basis of the interaction between bacterial cell division-associated proteins FtsZ and ZapA

Cell division in bacteria, the process that allows a single bacterial cell to divide into two, is regulated by the FtsZ protein and FtsZ-associated proteins. ZapA, a FtsZ-associated protein, has gained attention for its dynamic interaction with FtsZ. However, the structural basis of this interaction and their functional coordination remains unclear. In this study, researchers focused on understanding the structure and dynamics of the FtsZ-ZapA complex.

Bacterial cell division, a process wherein a single cell divides to form two identical daughter cells, represents one of the most essential biological processes. Understanding the precise mechanism behind this dynamic process can help in the development of targeted ways to inhibit bacterial proliferation.

The process of cell division involves multiple proteins and their complex interactions. FtsZ protein molecules polymerize to form protofibrils that further associate into a ring-like structure called the Z-ring. Z-ring formation is a crucial step in the cell division process, facilitated by multiple FtsZ-associated proteins. ZapA is one such protein, which is conserved widely among multiple bacterial species and is expressed in significantly high levels. The ZapA protein binds to FtsZ protofilaments, assisting in the formation and maintenance of the Z-ring. However, multiple aspects of bacterial cell division remain unexplored, including the exact structure of the FtsZ-ZapA protein complex and the underlying mechanism of interaction.

While previous studies have characterized these proteins separately, researchers wanted to understand their dynamic interaction. Professor Hiroyoshi Matsumura from the College of Life Sciences, Ritsumeikan University, Japan, had led a previous study published in *Nature Communications* in 2023, titled 'Structures of a FtsZ single protofilament and a double-helical tube in complex with a monobody,' which focused on the structure of FtsZ protofilaments. Building on that work, the researchers sought to understand the dynamic interaction between the FtsZ and ZapA proteins.

Now, in a new study led by Prof. Matsumura, published in *Nature Communications* on July 1, 2025, the researchers have finally been able to gain insights into the cooperative functioning of these two proteins. Dr. Ryo Uehara from Ritsumeikan University, Dr. Takayuki Uchihashi from Nagoya University and ExcCELLs, Dr. Keiichi Namba, Dr. Junso Fujita, and Dr. Kazuki Kasai, all from the University of Osaka, were also involved in this study. *"FtsZ is a potential therapeutic target for bacterial infections. Hence, we wanted to understand how it*

maintains its dynamic nature while interacting with ZapA protein and the overall structure of the complex," says Prof. Matsumura while explaining the main inspiration behind their research.

For the study, FtsZ and ZapA proteins from the bacteria *Klebsiella pneumoniae* were analyzed. The scientists utilized cryo-electron microscopy, a high-resolution microscopy technique, to visualize the three-dimensional structure of FtsZ and ZapA. Next, they used high-speed atomic force microscopy to understand the cooperative interaction between the two proteins.

Their analysis revealed that four units of ZapA protein molecules form the ZapA tetramer, which tethers to FtsZ protofilaments to form an asymmetric ladder-like structure. In this ladder-like arrangement, a single FtsZ filament is precisely held between two parallel FtsZ filaments on one side. On the other side, it is tethered to a double anti-parallel protofilament. "*In an anti-parallel protofilament, the filaments run alongside each other, but the subunits are aligned in opposite directions,"* explains Prof. Matsumura. Thus, ZapA impacts the alignment of the FtsZ filament, which further influences the formation of the Z-ring structure. Furthermore, ZapA and FtsZ were observed to interact extensively over large surface areas, and this contact caused minor structural alterations in FtsZ conformation.

Notably, the team also revealed the existence of electrostatic repulsion within the anti-parallel double filament. This repulsive force is thought to enhance the mobility of FtsZ filaments, enabling them to maintain their dynamic nature without any interference.

The team also captured the real-time dynamics of ZapA-FtsZ interaction. The interaction was found to be dynamic in nature, with repeated binding and dissociation, which helps to maintain the mobility of the filaments. They described the interaction as cooperative binding. *"Once ZapA binds to FtsZ, some structural change is observed. This makes the adjacent FtsZ molecule more accessible for the next ZapA molecule,"* said Prof. Matsumura while explaining the cooperative interaction.

This study has revealed the intricate mechanism of bacterial cell division, paving the way for the development of new antibacterial agents. The study also highlights the synergy between cryo-electron microscopy and high-speed atomic force microscopy, demonstrating how combining these tools can unlock some elusive mysteries at the cellular level. Overall, the findings of this study advance our understanding of this essential biological phenomenon and pave the way for future research in this field.

Reference

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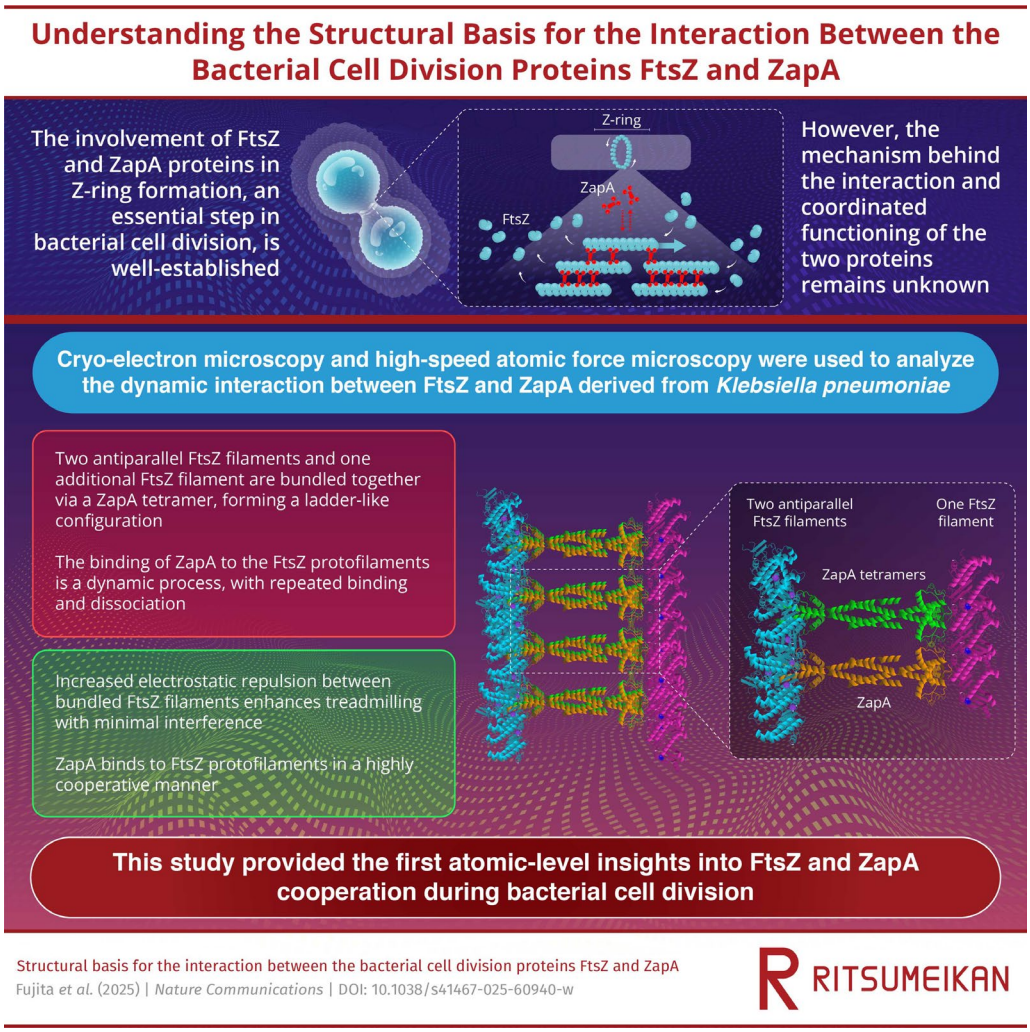

Image title: Behind the scenes of bacterial cell division: Navigating the complexities of FtsZ and ZapA interaction
Image caption: FtsZ and ZapA protein complex plays an important role in bacterial cell division. However, the structure of this complex was elusive. In this study, the researchers focused on the interaction of the two proteins and the structure of the protein complex.
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About Professor Hiroyoshi Matsumura, from Ritsumeikan University, Japan

Professor Hiroyoshi Matsumura completed his Ph.D. in 2000 from the Graduate School of Engineering, University of Osaka, Japan. He is currently a Professor in the College of Life Sciences, Ritsumeikan University and a Ritsumeikan Advanced Research Academy (RARA) Associate Fellow. His expertise lies in various fields, including nano-bioscience, genome biology, molecular biology, structural biochemistry, and biophysics Prof. Matsumura has authored more than 200 research articles.

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