Genome integrity sensing by the broad-spectrum Hachiman antiphage defense complex

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Presenter : Chia-Yi Lin **Date/Time** : 2025/02/20 15:10-16:00

Commentator : Ching-Hao Teng Ph.D. **Location** : Room 601, Med College Building

Background

Bacteriophage infections pose a threat to bacterial survival, often resulting in cell lysis. In response, bacteria have evolved a variety of antiphage defense mechanisms. One such phage defense system is Hachiman, which encodes two gene loci: HamA and HamB. HamA is a previously uncharacterized protein, whereas HamB is a Ski2-like helicase. Although Hachiman is found in more than 5% of prokaryotic genomes, its molecular mechanism remains poorly understood.

Objective

To understand how the Hachiman system protects bacteria from phage infections.

Results

First, the authors demonstrate that Hachiman protects bacteria against diverse bacteriophages by inhibiting phage progeny production and degrading both phage and host DNA during infection. This phenomenon is known as abortive infection, which induces programmed cell death before phage release, thereby protecting the entire bacterial population from infection. Next, cryo-electron microscopy (Cryo-EM) analysis reveals that HamAB forms a stable complex, with its structural integrity being critical for antiphage activity. Biochemical characterization shows that HamB functions as a DNA helicase and ATPase, preferentially recognizing 3’ single-stranded DNA (ssDNA), while HamA acts as an effector nuclease to degrade the DNA. Notably, induced DNA damage alone can activate HamAB, indicating that in addition to phage defense, Hachiman may function as a genome surveillance system. Furthermore, structural analysis of HamB in complex with DNA reveals that HamB undergoes conformational changes upon binding with DNA, which disrupts the HamAB interface and activates the HamA nuclease. Structural analysis of HamA*B (an inactive HamA mutant) with plasmid DNA suggests that there is a binding form of HamAB that exists in an inactive state. The authors propose a model in which HamAB scans the DNA in this inactive state; once it detects ssDNA caused by DNA damage or phage presence, ATP hydrolysis by HamB induces structural rearrangements, activating HamA to degrade DNA and initiate abortive infection.

Conclusion

Hachiman is a nuclease-helicase complex that provides protection against bacteriophages through indiscriminate DNA degradation. Through structural and biochemical analyses, the authors proposed a mechanism for Hachiman's immunity. However, some questions still remain to be addressed.