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Structure Reveals Mechanisms of Viral Suppressors that Intercept a CRISPR RNA-Guided Surveillance Complex

Genetic conflict between viruses and their hosts drives evolution and genetic innovation. Prokaryotes evolved CRISPR-mediated adaptive immune systems for protection from viral infection, and viruses have evolved diverse anti-CRISPR (Acr) proteins that subvert these immune systems. The adaptive immune system in Pseudomonas aeruginosa (type I-F) relies on a 350 kDa CRISPR RNA (crRNA)-guided surveillance complex (Csy complex) to bind foreign DNA and recruit a trans-acting nuclease for target degradation. Here, we report that the cryo-electron microscopy (cryo-EM) structure of the Csy complex bound to two different Acr proteins, AcrF1 and AcrF2, at an average resolution of 3.4 A˚. The structure explains the molecular mechanism for immune system suppression, and structure-guided mutations show that the Acr proteins bind to residues essential for crRNA-mediated detection of DNA. Collectively, these data provide a snapshot of an ongoing molecular arms race between viral suppressors and the immune system they target.

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