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Poster #11: Protein fusion analysis reveals new phage sponges

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Immune systems in animals, plants, and bacteria often rely on intracellular nucleotide signaling to activate immune responses in response to viral infection. Bacteriophages (phages) can evade these defenses by producing sponge proteins that bind and sequester immune signaling molecules. However, the full arsenal of phage sponges is currently unknown. We found that phage sponge proteins tend to be fused to one another in phage genomes. Exploiting this property, we discovered Sequestin, a previously uncharacterized family of phage proteins that manipulates bacterial immune signaling. Experimental validation revealed that Sequestin inhibits the Thoeris defense system by acting as a nucleotide "sponge"that binds the Thoeris signaling molecule 1″–3′ glycocyclic adenosine diphosphate–ribose (3′cADPR). Structural and mutational analyses explain the molecular basis of signal recognition. Thousands of Sequestin homologs occur in phage genomes, highlighting the abundance and diversity of viral strategies that evade nucleotide-based immunity.

Reference #1

Tal, Hadary et al. ,Structural modeling reveals phage proteins that manipulate bacterial immune signaling

Reference #2

Reference #3

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