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Poster #100: Balancing of immune activation and suppression by N4-like Pseudomonas aeruginosa phages.

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Signaling-based anti-bacteriophage systems such as CBASS and Thoeris synthesize infection-triggered nucleotide signals that activate anti-phage effectors. However, the phage features sensed by these systems and the mechanisms phages use to evade signaling immunity remain poorly understood. Here, studying clinically relevant N4-like Pseudomonas aeruginosa phages from the Migulavirinae family, we show that closely related phages encode subtle allelic variation in side tail fiber proteins that determine sensitivity to type II Thoeris. In parallel, these same phages encode an "anti-defense hotspot"that contains three adjacent genes, each sufficient to facilitate phage evasion of both CBASS and Thoeris defenses, counter balancing the activating proteins. Comparative analysis of this anti-signaling hotspot across the broader family of related N4-like phages uncovered a new Thoeris anti-defense RyRTad protein that sponges NAD-derived molecules (e.g. gcADPR) and exhibits sequence and structural similarity to a poorly characterized nucleotide-binding region of the human ryanodine receptor. Together, these findings reveal how the balance between immune activation and antagonism shifts phage outcomes and reveal a surprising similarity between a phage molecular sponge and a human ryanodine receptor.

Reference #1

Reference #2

Reference #3

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