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Bacteriophages possessing Cas4 family exonucleases infect hosts with primarily type I CRISPR immunity

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Cas4 family exonucleases are of curious abundance among bacteriophages in Actinobacteria, being noted in dozens of phams and myriads of clusters, including EG and Microbacterium phage Fregley with a high probability. The presence and function of these proteins in bacteriophages is not well understood, and is only recently being identified. Phages possessing Cas4 exonucleases span a handful of hosts, predominantly Mycobacterium, Arthrobacter, Streptomyces, and Microbacterium. This study examined the distribution of hosts among a sample of clusters possessing Cas4. Hosts were compared to determine whether type II CRISPR morphology was selective for the Cas4 exonuclease in bacteriophages. Interestingly, among the most conserved hosts throughout the 24 phams studied, type I systems were more common, and there was little similarity between the Cas proteins of different hosts. Thus it can be assumed Cas4 exonucleases are not limited to phages infecting hosts with type II CRISPR systems, and their function may be more varied between hosts. The presence of hosts with phages lacking Cas4 proteins in the Actinobacteria database imply that other host features may determine the presence or absence of Cas4 exonucleases in bacteriophages.