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Investigation of Potential Genes Influencing Host Specificity in Cluster AZ1 and EH Phages

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Bacteriophages are obligate parasites that can infect a variety of bacterial hosts. However, much is still unknown concerning phage host-range specificity. This study investigated the role of genetics in host specificity; specifically, genes thought to correlate with isolation host were examined. Two clusters, AZ1 and EH, were chosen for analysis as separate case study groups based on a knowledge gap identified in a prior study that indicated that phages in these clusters share close functional relationships but did not explore host-specific differences. This study specifically compares the genomes of phages with respect to their isolation hosts to evaluate for the presence of shared genes considered relevant to host-phage interactions based on previous research. Eight phages were selected from each cluster through stratified random sampling: four AZ1 phages infecting *Arthrobacter atrocyaneus*, four AZ1 phages infecting *A. globiformis*, four EH phages infecting *Microbacterium foliorum*, and four EH phages infecting *M. sp*. Network phylogeny analysis supported the genetic closeness of intra-host phages, defined as intra-cluster phages infecting the same host. Gene content similarity (GCS) analysis of phages revealed a general trend of higher GCS between intra-host phages. However, EH phages infecting *M. foliorum* were an exception, with an average GCS value that was not statistically different from the average GCS between EH phages infecting different hosts (p-value = 0.57). Prior research postulated that receptor binding proteins (RBPs) and endolysins were important for host-range specificity. Intra-host comparison of pham patterns was conducted to analyze putative regions modulating host-specificity. AZ1 phages exhibited synteny in their minor tail regions and endolysin genes, and EH phages exhibited synteny in a potential RBP region. EH phages Percival (infecting *M. foliorum*) and IAmGroot (infecting *M. sp*.) shared more synteny than with other intra-host phages. These findings provide evidence for the importance of investigating gene determinants of host-specificity to streamline bacteriophage host-range identification.