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Characterization of Genome Mosaicism in Cluster E Mycobacteriophages

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Despite their abundance, the evolutionary history of bacteriophages, which are viruses that infect
bacteria, remains subject to speculation as these biological entities commonly exchange
hereditary material. To overcome these challenges, genetically similar phages have been
assigned into distinct groups, termed clusters. However, such allocations are incomplete since
phage genomes are characterized by extensive mosaicism, meaning that their genes have
originated from various viral and bacterial sources, often through horizontal gene transfer.
Cluster E was previously determined to have conserved genomes, exchanging genes with only a
limited number of clusters; however, continued isolation efforts and the subsequent increase of
available sequences render such observations obsolete, leaving the current extent of genome
mosaicism undetermined. Here we attempt to further characterize the inter-and intra-cluster
relationships of Cluster E phages, and identify possible mechanisms that may have enabled the
mosaicism. Qualitative pan-genome studies, which distinguished core and variable genes
exclusive to Cluster E phages or shared with other clusters, revealed that Cluster E genomes
remain highly conserved; yet, the number of shared phams has increased to over 50%, making
the cluster less discrete than previously anticipated. While the factors that enable Cluster E’s
genome mosaicism remain largely unknown, phylogenetic analyses revealed possible evidence
of horizontal gene transfer for various HNH endonuclease phams and concurrent gene
acquisition events for other genes, such as the minor tail proteins. These findings are of
significance since they expand the current knowledge of Cluster E phages, as well as the nature
and complexity of their interactions with other clusters.