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Genetic Diversity and Phylogenetic Analysis of Cluster P Mycobacteriophage Tyrosine Integrases

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Bacteriophages utilize specific bacterial host genera or strains in their replication cycles. When a temperate phage infects a bacterium, its DNA is integrated into the bacterial genome. This process is facilitated by a phage integrase enzyme, which enables the site-specific recombination of the attachment (attP) site on the phage with the target site (attB) on the bacterium. Phage integrases therefore play key roles in determining the range of bacterial hosts a phage can infect. Integrases could thus serve as tools for identifying bacterial pathogens, determining host range, and bacteriophage phylogenetic studies. Moreover, since phage integrases facilitate site-specific recombination between different DNA sequences, they have the potential to be utilized in gene therapy and cell line manipulation. To enhance our knowledge of phage host range and infection dynamics, it is necessary to investigate the sequence and structural diversity of phage integrases. Phage integrases from all non-draft cluster P members (P1, P2, P3, P4, P5, P6), including phage Gavriela which we isolated and recently annotated were analyzed. A total of 46 integrases were analyzed. All P phages had tyrosine integrases. Maximum likelihood phylograms were constructed using NGPhylogeny.fr and MEGA12. Using Alphafold 2.0, three-dimensional protein folding models were constructed. Inter and intra-subcluster nucleotide and structural differences were observed among the integrases. Further studies are needed across a wider range of temperate phages to determine the impact of integrase gene diversity and structural conservation on bacterial host range, identification, and phage phylogenetic analysis.