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Sewing Up the Gaps in Phage Research with Thimble

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Non-tuberculosis mycobacteria (NTMs) are challenging antibiotic resistant pathogens that pose significant hurdles for treatment, particularly in immunocompromised individuals. Mycobacteriophages (phages), viruses that infect and kill mycobacteria, offer a potential alternative to traditional antibiotics. Pathogenic NTMs, including *Mycobacterium abscessus*, are closely related to non-pathogenic *M. smegmatis* which serves as a comparable fast-growing host for the isolation and characterization of therapeutically relevant mycobacteriophage. Novel mycobacteriophage Thimble was isolated from strawberry garden soil from Hampden, ME, using *M. smegmatis* mc2155. Thimble forms pinpoint turbid plaques and initial experiments indicate that Thimble may be able to form lysogens. This is supported by the presence of a tyrosine integrase, gp54, which facilitates integration of the phage genome into the bacterial host genome. Gp57 encodes a helix-turn-helix DNA binding domain and is potentially an immunity repressor. Thimble is a *Siphoviridae* phage belonging to Cluster E with a genome that is 71,466 bp in length with a GC content of 63.1%. Thimble encodes 134 protein-coding genes and two tRNAs. Thimble exhibits genome organization that is consistent with the synteny of a *Siphoviridae* phage, encoding structural genes on the left arm and DNA replication genes on the right arm. Analysis of the Thimble genome identified that gp39 encodes an Lsr2-like DNA binding protein. In *M. tuberculosis* and *M. smegmatis*, this protein acts as a transcriptional regulator. Additional research is needed to confirm that Thimble can form lysogens and to determine if Thimble’s gp39 can perform Lsr-2-like regulatory functions. Thimble’s ability to infect *M. smegmatis* makes it a candidate for further investigation in phage therapy, particularly for multidrug-resistant mycobacterial infections.