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Minor Tail Protein Differences in Cluster A3 Mycobacteriophages May Contribute to Expanded Host Range

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Mycobacteriophage LarryKay was isolated on *Mycobacterium smegmatis* in the Fall of 2020 as part of the SEA-PHAGES program at The College of St. Scholastica. Genome sequencing revealed a 50916 bp genome belonging to the A3 subcluster. Preliminary genome annotation identified 87 protein coding genes and 3 tRNAs. LarryKay is member of the same subcluster TNguyen7, another A3 subcluster mycobacteriophage isolated at our school. TNguyen7 is unique, in that it, along with its close relative Isca, are known to infect *Mycobacterium abscessus*, a relative of *M. smegmatis*. This host range makes TNguyen7 and Isca potential agents in phage therapy against the potentially pathogenic *M. abscessus* which also expresses significant antibiotic resistant phenotypes. We hypothesize that differences in minor tail proteins account for the varying ability to infect *M. abscessus*. We performed Gepard dotplot and protein modeling analyses in order to elucidate possible sequence and structural differences in A3 minor tail proteins. Dotplots comparing the first 5000 bases of sequence of select A3 phages which contain putative minor tail proteins indicated a general strong degree of sequence similarity between the phages with the exception of genes in pham 54270 (gene #4 in draft LarryKay annotation) and pham 54417 (gene #33 in draft LarryKay annotation). Preliminary protein modeling of the minor tail proteins in LarryKay TNguyen7 using the software Phyre2 revealed overall 3-dimensional structural similarities between LarryKay and TNguyen7, with the exception of pham 54417. We are awaiting modeling results for pham 54270 sequences. We hypothesize these differences in minor tail proteins may driving the expanded host range of some cluster A3 phages.