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Comparative Analysis of Mycobateriophage Minor Tail Protein Carbohydrate Binding Module Polymorphism and Host Range

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Mycobacteriophages are divided into clusters, based on overall nucleotide sequence homology. Within a given cluster, significant sequence variation is uncommon. Conversely, areas of strong nucleotide sequence homology between phages from different clusters are atypical. An intriguing example of cross-cluster homology was found in the cluster N Mycobacteriophage Andies through BLASTn analysis against the PhagesDB phage collection. Gene 20 of phage Andies and gene 21 of the cluster P phage Fishburne share a small segment of homology. In both, these genes code for a minor tail protein.   
  
Further investigation indicated that this small shared segment of homology is likely the result of genetic recombination between different phages. Phamerator analysis revealed the region to be intragenic, within the genes, as opposed to encompassing the entire gene or larger regions of the genome. This is analogous to dissecting an automobile, inserting a slice from another model of automobile, fusing these together and producing a novel functional automobile. It is implausible that the parts, or in this case the protein domains or motifs, would align correctly to produce a functional product. The recombinant minor tail protein gene 20 of phage Andies is functional; otherwise Andies would be unable to infect host cells. HHPred analysis showed this homologous region to match the carbohydrate binding module (CBM) of hyaluronate lyase with 98.7% probability. Interestingly, sequence homology to this specific CBM was found in the minor tail proteins of phages from a broad range of clusters. However, the specific amino acid sequence of the CBMs differs greatly between clusters.   
  
This suggests that malleability in the CBMs allows for conservative amino acid substitution, thereby retaining function despite alterations in CBM primary structure. The consistent appearance of this specific CBM across phage clusters may warrant its classification as a conserved domain. These CBMs presumably aid phages during attachment to their bacterial hosts. Given that each cluster has its own unique CBM amino acid sequence, it was intriguing to investigate whether differences in the CBM amino acid sequences affect the phage’s host range. To explore this, RasMol was used to produce 2D images of conformational models for the CBMs of various phages, and Expresso was used to determine structural homology. These bioinformatic softwares facilitated both sequence-based and structure-based comparisons of CBMs across phages from different clusters. The minor tail protein CBMs of 22 phages from 10 clusters/subclusters were analyzed. Infectivity data from 10 host strains considered together with CBM analysis showed that differences in the carbohydrate binding module does influence phage host range.