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2024 SEA Symposium Abstract

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Exploring the cytotoxicity and essentiality of gene products encoded by F1 mycobacteriophage NormanBulbieJr

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Bacteriophages represent important sources of novel gene functions. Most genes encoded by phages cannot be assigned a function through bioinformatic methods, and for most phages, even genes with functional predictions have not yet been experimentally characterized. In the SEA-GENES project, arrayed phage genome libraries are constructed and deployed in systematic overexpression screens to identify from the thousands of uncharacterized gene phamilies, those gene products that can confer some effect on the host bacterium, *Mycobacterium smegmatis*.   
  
   
  
Here, we provide the results of a genome-wide overexpression screen, identifying gene products encoded by Cluster F1 mycobacteriophage NormanBulbieJr (NBJ) that can inhibit mycobacterial growth. We identified 34 cytotoxic gene products encoded by NBJ, including 24 whose overproduction resulted in severe reduction or abolition of host growth. We describe a comparative analysis between NBJ and previously screened Cluster F1 mycobacteriophage Girr, revealing good behavioral agreement between shared gene phamilies and identifying conserved growth inhibitors. Because we know this subset of genes encoded by NBJ are likely interacting with the host to mediate these toxic effects, it is important to next determine if they are essential to phage replication. We are in the process of assaying a subset of genes identified as toxic in a deletion analysis using Bacteriophage Recombineering of Electroporated DNA (BRED) to understand their essentiality for phage replication. Through the combination of our overexpression screen results and the data collected from our BRED deletion analysis, we aim to better understand NBJ phage gene function.