

Enrichment of Bacterial Virulence Factors in Bacteriophages

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Virulence

Virulence Defined

The capacity of a microorganism to proliferate despite host defenses

Influences on Virulence

- Number of microorganisms
- Composition of the mobile genetic reservoir
- Location of niche
- Host immune capabilities

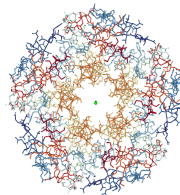
Bacterial Virulence Factors Increase Pathogenesis

Examples of Virulence Factors

- Increased fitness for nutrients
- Host immunity resistance
- Toxin secretion

Diseases from Virulence Factors

Cholera, dysentery, botulism, and food poisoning



PDB Structure of Cholera Toxin

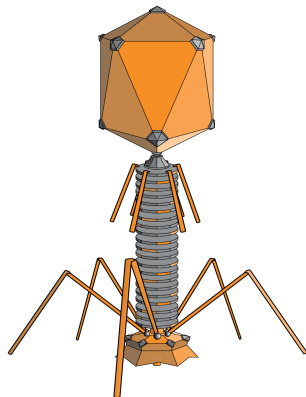
Bacteriophages as a Genetic Reservoir of Virulence Factors Genes

Bacteriophages (Phages)

DNA viruses that infect bacteria

Phages and Pathology

Virulence Factors that cause cholera, dysentery, botulism, and food poisoning are carried on phage elements.



Novick, Richard, Plasmid (2003)

Objective

Characterize the abundance of bacterial virulence factors in phages

Data

Virulence Protein Databases

- VFDB
Chen, Lihong, et al. Nucleic Acids Research (2005)
- PatricVF
Wattam, AR, et al. Nucleic Acids Research (2017)

Virulence HMMs

- pFam
Bateman, Alex, et al. Nucleic Acids Research (2004)
- pVOG
Grazziotin, AL, et al. Nucleic Acids Research (2016)

Phage Protein Database



Methods

Sequence Annotation Methods

BLAST vs **HMM**

Normalizing By Gene Count

Hit Percentage = P

Hit Count = HC

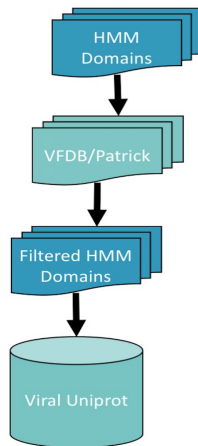
Gene Count = GC

$$P = HC/GC$$

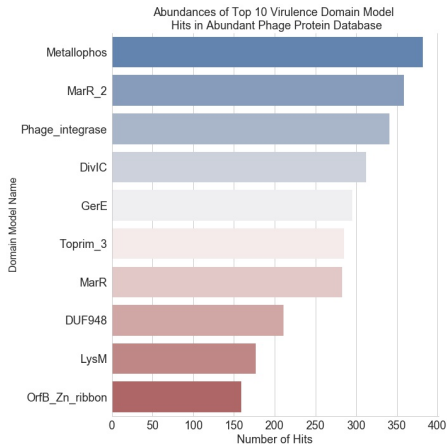
Filtering By Phage Abundance

Streptococcus phage:

Genera abundance greater than 30



HMM Hit Distribution



MarR

Domain involved in antibiotic resistance

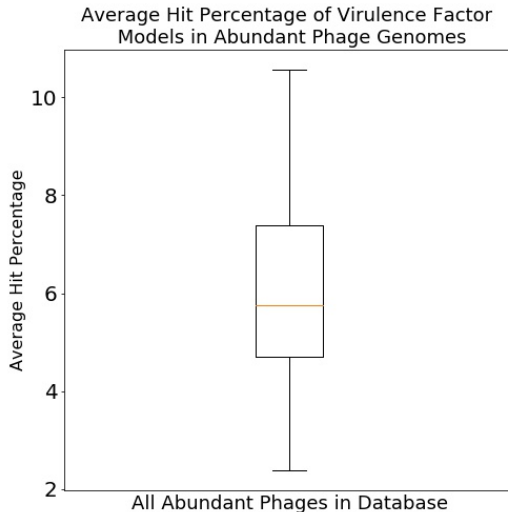
DivIC

Part of sporulation process

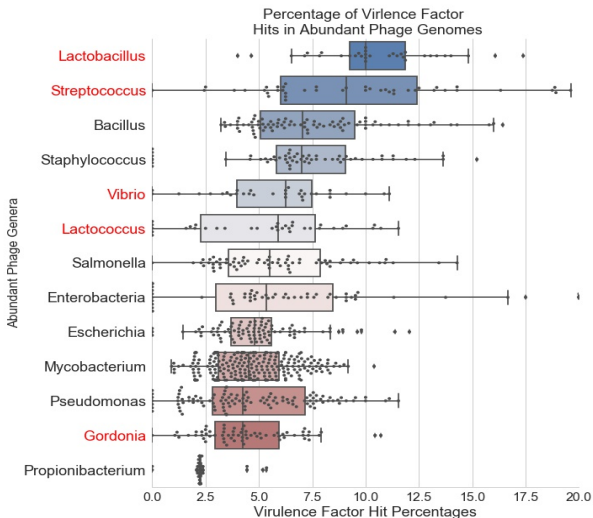
LysM

General peptidoglycan function

Distribution of Hit Percentage in All Phages



Abundant Phage Distributions by Genera Name

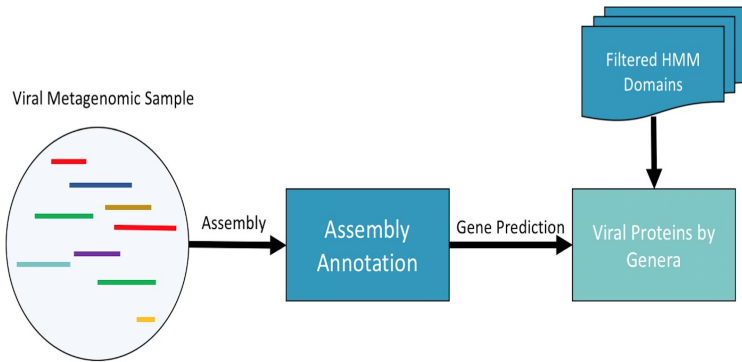


Clinical Data and Methodology

Clinical Data Sources

- Virome from Cystic Fibrosis Patients
PRJNA39545
- Virome from *Clostridium difficile* Patients
PRJEB22784

Clinical Data Pipeline



Cystic Fibrosis Virome Results

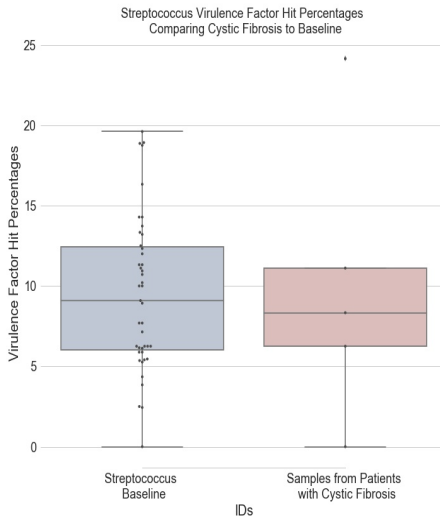
Abundant Annotated Genera (>20 Contigs)

- Streptococcus Phage
- Enterobacteria Phage
- Staphylococcus Phage

Nonparametric Testing

H_0 : Samples == Baseline

$p = 0.487$



Clostridium difficile Virome Results

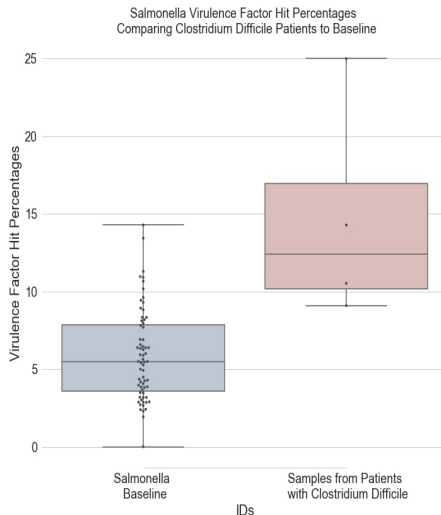
Abundant Annotated Genera (>20 Contigs)

- Salmonella Phage
- Pseudomonas Phage
- Escherichia Phage
- Enterobacteria Phage

Unequal Variance Parametric Testing

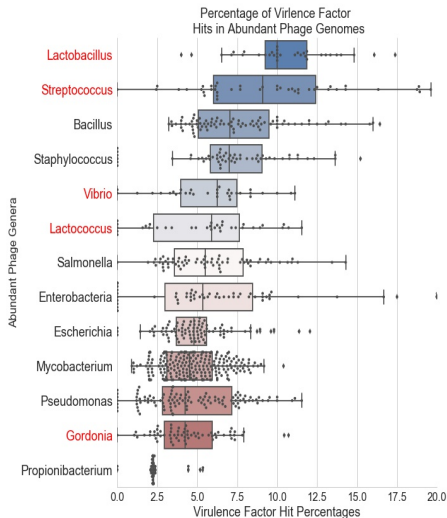
H_o : Samples == Baseline

$p = 0.09$



Concluding Remarks

Virulence Factor Abundance



Clinical Virulence Distribution

Trending enrichment of virulence hits in Salmonella phages in patients with *Clostridium difficile* infections

Research in Progress

Application to Non-Tuberculosis *Mycobacterium* infections in Cystic Fibrosis patients

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Questions?

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