Detecting viral genomes by using CRISPR adaptive immunological memory

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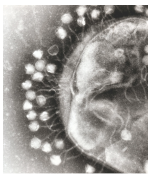
Introduction

- About 10^{31} viruses exist on Earth
- They involved the evolution of cellular organism via horizontal gene transfer



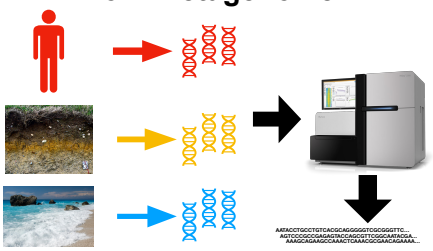
Reference phage genome is limited

- 2292 complete phage genomes are recorded in NCBI

To understand the evolution of viruses, we need more sequences

Problem

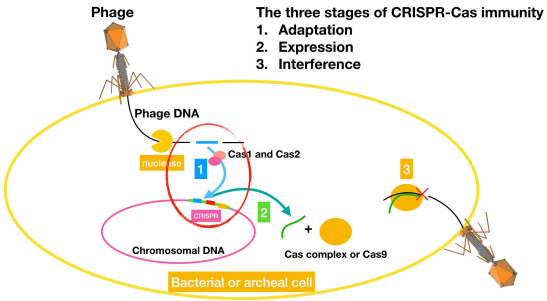
How do we discover phage genome sequences from metagenome?



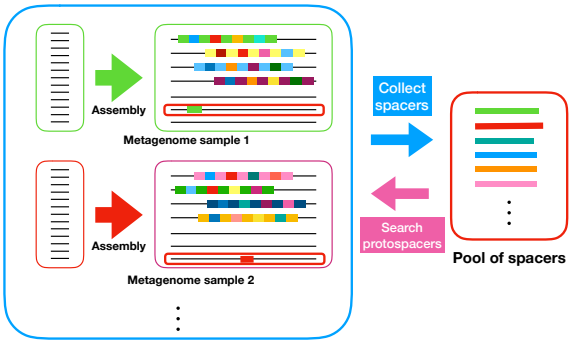
Challenges

1. Phage genomes are highly diverse
2. There is no marker genes
3. Reference sequence is limited

We utilize CRISPR, prokaryotic adaptive immunological memory.



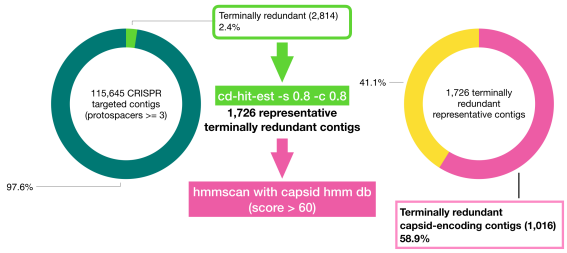
Method



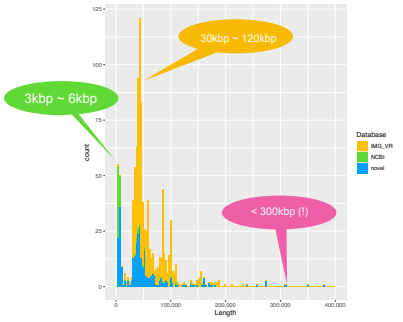
Analyzed 511 human gut metagenome (9.8Tbp)

Result

Total 463,248 unique CRISPR spacers
133,358 (28.8%) protospacers

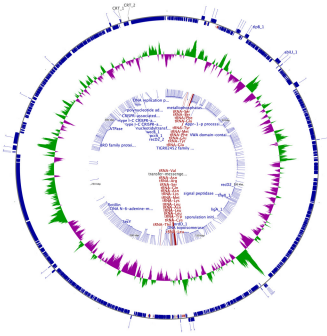


Discovered 298 novel viral genomes



Distribution of the genome length

A case-study: CRISPR-Cas encoding large phage

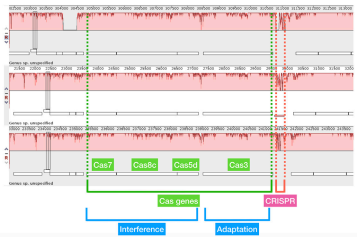


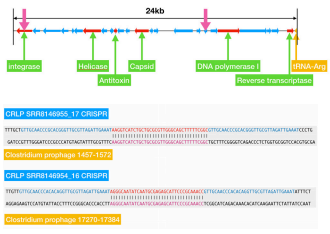
Features

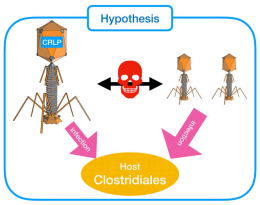
- Genome length: 349,676
- Number of ORFs: 364
- Discovered from 3 independent samples
- 8~12 protospacers
- The genome is positively circular
- Predicted host is Clostridiales order, Clostridium sp. AM09-51 (ANI=98.78%)

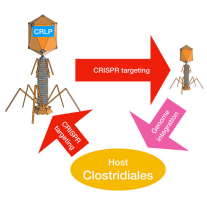
Notable genes

- DNA polymerase III alpha and beta subunits
- N6 adenine methyltransferase
- tRNA and tmRNA
- Capsids
- Typel Cas genes and CRISPR









Next

- Detection of non-terminally redundant viral genomes
- Detection of RNA phages
- Construction of a database for viral genomes and protein families