



Quarterly Newsletter: Summer 2023



Focusing in on phage research

Unraveling microbial mysteries

Our understanding of virus and microbe interactions is changing as we develop better tools to explore the microbiome. In this recent **Nature Microbiology** publication, researchers use ProxiMeta Hi-C to link viral interactions between distant microbes in a deep-sea hydrothermal mat, revealing surprising interactions across microbe domains.

Read the article [here](#) »



Constructing the next biggest tool in microbial research

One year ago, we started a [global-scale project](#) with funding from the Gates Foundation and the NIH to catalog bacteriophages in human gut and wastewater

samples. Today, we have captured over 67,000 phage-host interactions using these samples that came in from around the world. With this database, we aim to develop new therapeutics, a surveillance system for microbial threats, and more. Stay tuned for further updates and applications involving this project!

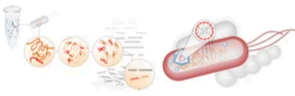
Building a large-scale database of phage-host interactions using culture-free phage genome reconstruction and host assignment with Proximity-Ligation (Hi-C) Sequencing

Sam Bryson¹, Jonas Grove¹, Zach Sisson¹, Benjamin Auch¹, Steven Eacker¹, Hayley Mangelson¹, Shawn Sullivan¹, Ivan Liachko¹

1. Phase Genomics, Seattle, WA 98109

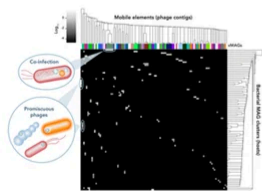
Proximity-Ligation Sequencing

Proximity-guided metagenomics employs proximity ligation technology to deconvolve metagenomes. The proximity signal between contigs enables reconstruction of high-quality MAGs for microbes, viruses, and plasmids and identifies connections between mobile elements and their hosts.



The method originates from high-throughput chromosome conformation capture (3C, Hi-C) technique

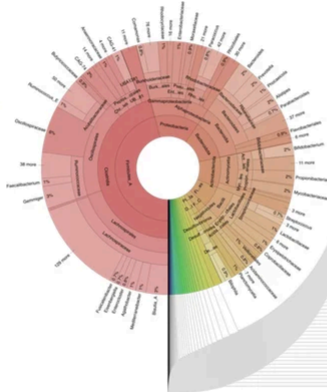
- DNA that is physically proximal is connected by formaldehyde crosslinking within intact cells.
- Nearby DNA molecules are joined by proximity ligation, creating chimeric junctions that are prepared for sequencing.
- Sequences that originate from the same cell are connected by paired-end reads.



The proximity signal is used to determine the interaction strength between microbial genomes (vertical axis) and mobile elements (phage shown here, horizontal axis). This allows confident identification of a viral hosts.

Expanding the diversity of known phage-host interactions


67,431 phage genomes assigned to 2,428 microbial genera



Host Rank	Host Taxa
Phylum	73
Class	151
Order	352
Family	776
Genus	2,428
Species	4,284

Proximity-guided metagenomics significantly improves our knowledge of diverse phage-host interactions over culture-based methods that are strongly biased to a limited number of microorganisms. For example, the INPHARED database, a curated set of reference phage genomes, is highly biased towards specific microbial genera – only 30 different bacterial host genera account for ~75% of the phage genomes.

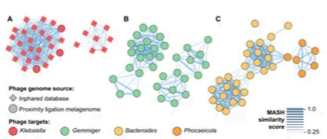
662 Proximity-ligation metagenomes





Sample collection has focused on environments that harbor phage-host interactions with potential for development of therapeutics and combating the spread of antimicrobial resistance.

Clustering of phage genomes based on shared k-mer composition

- Clusters of (A) *Klebsiella* phages identified with culture and proximity-based methods.
- Clusters of novel (B) *Gemmiger* phages and (C) similar *Bacteroides* and *Phocaeicola* phages identified through proximity-guided metagenomics.



Application Note: Metagenome analysis including viral genome reconstruction and host attribution described here is available through the ProxiMeta™ service platform from Phase Genomics

Recent publications

- Catch me if you can: capturing microbial community transformation by extracellular DNA using Hi-C sequencing (read [here](#) »)
- A chromosome-scale genome assembly of the grape powdery mildew pathogen *Erysiphe necator* reveals its genomic architecture and previously unknown features of its biology (read [here](#) »)
- The soil-borne white root rot pathogen *Rosellinia necatrix* expresses antimicrobial proteins during host colonization (read [here](#) »)

MORE PAPERS

Catch us at a conference

Phase Genomics is on the road! Look for us at these upcoming conferences:

[Evergreen International Phage Meeting](#)

Olympia, WA (Aug 6-11)

[Cancer Genomics Consortium](#)

Saint Louis, MO (Aug 13-16)

[American Society of Human Genetics](#)

Washington, DC (Nov 1-5)

[Association for Molecular Pathology](#)

Salt Lake City, UT (Nov 14-18)

Have a project in mind?

Contact Us

Phase Genomics, 1617 8th Ave N, Seattle, Washington 98109, United States, 833-742-7436

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