

Quarterly Newsletter: Fall 2022



The Future of Phage Research



New ProxiMeta applications enable studies on fecal microbiota transplantation and phage-host association.

New technology, recently published in [Nature Biotechnology](#), allows us to reconstruct metagenomes, linking plasmids, phages, and mobile AMR genes to their microbial hosts without culturing. Discover how this method works [here](#) or check out our posters below.

Culture-Free Phage Genome Reconstruction and Host Assignment in Microbial Communities Using Proximity-Ligation (Hi-C) Sequencing

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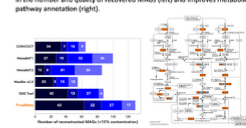
Summary

Proximity-guided metagenomics employs proximity ligation technology to deconvolve metagenomes.

- Method starts from high-throughput chromosome conformation capture (Hi-C, Hi-C).
- Formaldehyde crosslinking of intact microbiome samples traps DNA that is proximal in physical space inside cells.
- Proximity ligation joins nearby DNA molecules, creating chimeric junctions that can be sequenced.
- Paired sequence reads connect contigs that originated inside the same cell.

Using the proximity signal between contigs, we can reconstruct high-quality MAGs of microbes, viruses, and plasmids and connect mobile elements to their hosts.

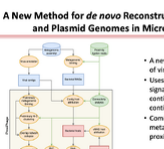
Proximity-guided metagenomics outperforms conventional binning methods in the number and quality of recovered MAGs (left) and improves metabolic pathway annotation (right).



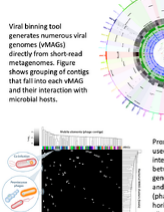
A New Method for *de novo* Reconstruction of Phage and Plasmid Genomes in Microbiomes

- A new pipeline for binning all viral and plasmid MAGs.
- Uses physical interaction signal between host contigs, virus and plasmid contigs, and intra-virus.
- Combines conventional metagenome binning with proximity ligation data.

Viral binning tool generates numerous viral genomes (vMAGs) directly from short-read metagenomes. Figure shows grouping of contigs that fall into each vMAG and their interaction with microbial hosts.



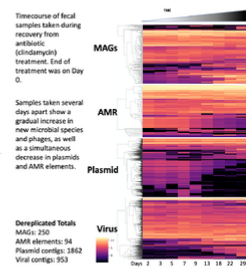
Proximity signal is also used to measure the interaction strength between microbial genomes (vertical axis) and mobile elements (phage shown here, horizontal axis). This allows viral host range identification.



Understanding Mobile Element Dynamics in Complex Microbial Communities

Timecourse of fecal samples taken during recovery from antibiotic (clindamycin) treatment. End of treatment was on Day 0.


Samples taken several days apart show a gradual increase in new microbial species and phages, as well as a simultaneous decrease in plasmids and AMR elements.



Deeplicated Totals:
MAGs: 292
AMR elements: 94
Plasmid contigs: 282
Viral contigs: 953

Application Note

Viral genome reconstruction and host attribution



The metagenome analysis described here is enabled through the ProxiMeta™ service platform from Phase Genomics

Proximity ligation sequencing reveals dynamics of phage-host and plasmid-host interactions during engraftment in intestinal microbiota transplantation for *Clostridium difficile* infection

Anna Orntoft, Christopher Kelly, Benjamin Paul, Tom Lambert, Alexander Khorram

Phase Genomics, Seattle, WA 98101

Summary

Proximity ligation sequencing applied to a time course of fecal samples from a cohort of patients enrolled in a clinical trial using BMT for recurrent *C. diff* infection.

Proximity ligation links phages to their microbial hosts

Crosslinking of intact microbiome samples traps DNA located in the same cell and paired sequence reads reconstruct microbial genomes and mobile elements (plasmids/phages/ARGs).

Phages can occupy multiple microbial hosts after transplantation.

Phage abundance can be positively or negatively correlated with that of the host.

Genome-resolved metagenomics and mobile element tracking during engraftment

Patients carry multidrug resistant organisms before transplant, identified without culture

Proximity ligation sequencing shows multidrug resistant *E. coli* and *Klebsiella* strains in patient gut at baseline.

Plasmid-come (red) and genomically-encoded (blue) AMR genes are identified and associated with their hosts.

In both cases, numerous phages are identified in situ which infect these multidrug resistant hosts.

AMR genes are mobilized during engraftment

Large numbers of stress-response and AMR genes are transferred between microbes during engraftment.

In many cases these mobile genes are found in the patient baseline, but not the donor.

Even after successful treatment, these genes can be transferred and maintained in the newly engrafted healthy microbiome.

Application Note: Viral genome reconstruction and host attribution

The metagenome analysis described here is available through the PhageMeta™ service platform from Phase Genomics

Prefer Podcasts?

Discover new startups, research, and tech through interviews with leading researchers and founders in the genomics industry.

Bacteria Breakthroughs

Watch this Fall's [Genome Startup Day](#) event, featuring startup founders and researchers exploring the burgeoning field of phage research.



Phase Genomics has also made appearances in popular podcast series such as [MendelsPod](#) and [Beyond Biotech](#), covering advancements in phage research technology and new developments in [oncology](#).

Recent Research



Chromosome-level genome assembly for the Aldabra giant tortoise enables insights into the genetic health of a threatened population



Chromosome-Level Genome Assembly of *Trichoderma cornudamae* Using Hi-C Data



Integration of multi-omics data reveals cis-regulatory variants that are associated with phenotypic differentiation of eastern from western pigs



The reference genome of the
Vernal Pool Tadpole Shrimp,
Lepidurus packardii



Chromosome scale genome
assemblies and annotations for Poales
species *Carex cristatella*, *Carex scoparia*,
Juncus effusus and *Juncus inflexus*



Localization of Epigenetic
Markers in *Leishmania*
Chromatin



High quality, chromosome-scale genome assemblies: comparisons of three *Diaphorina citri* (Asian citrus psyllid) geographic populations



The clove (*Syzygium aromaticum*) genome provides insights into the eugenol biosynthesis pathway

MORE PAPERS

Catch us at a Conference

We are looking forward to upcoming events celebrating the achievements researchers have been making around the globe. Phase Genomics is dedicated to making our presence at these events as safe as possible and will be adapting to the most recent safety guidelines and regulations.

Association for Molecular Pathology – Phoenix, AZ (Nov 1-5)

Global Metagenomics Conference – Miami Beach, FL (Nov 18-21)

Plant and Animal Genome Conference – San Diego, CA (Jan 13-18)

Have a project in mind?

Contact Us

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