Culture-free discovery and host-attribution of viruses, plasmids, and ARGs in metagenomes using proximity ligation (Hi-C) technology.

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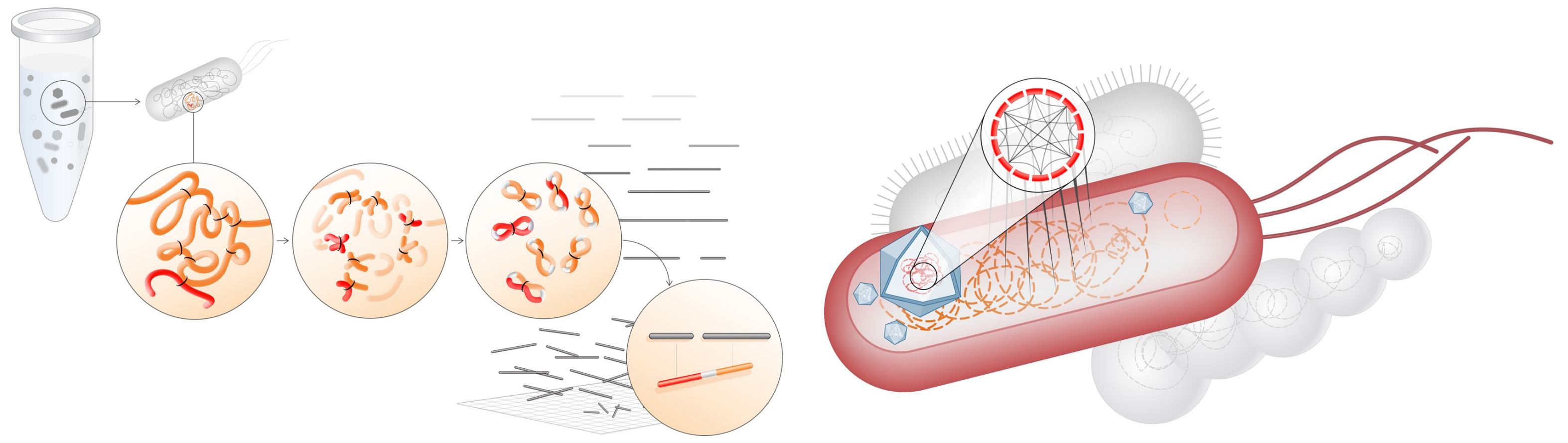
*Put the
little hands
pic here?

Summary

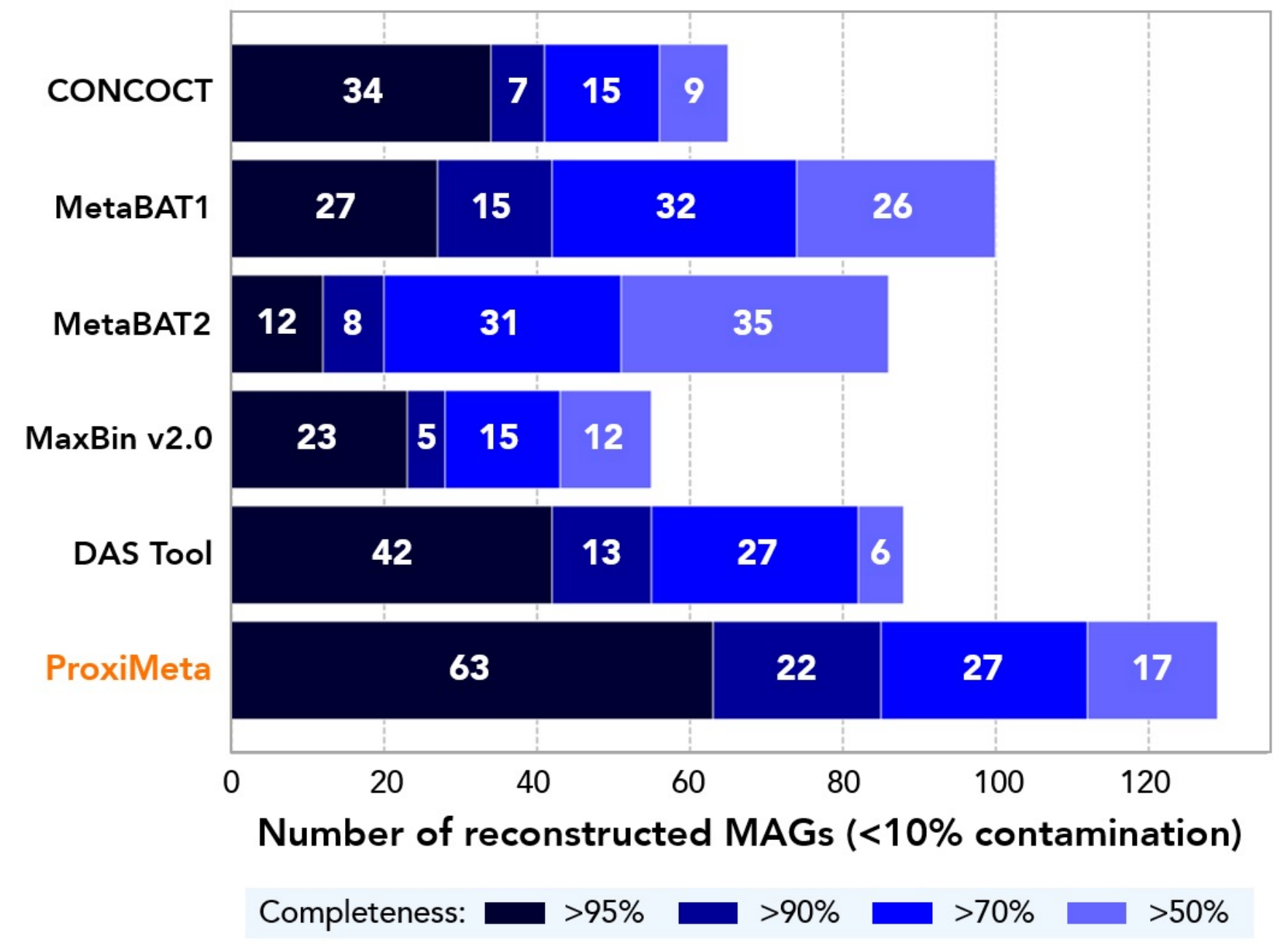
Proximity-guided metagenomics employs proximity ligation technology to deconvolve metagenomes.

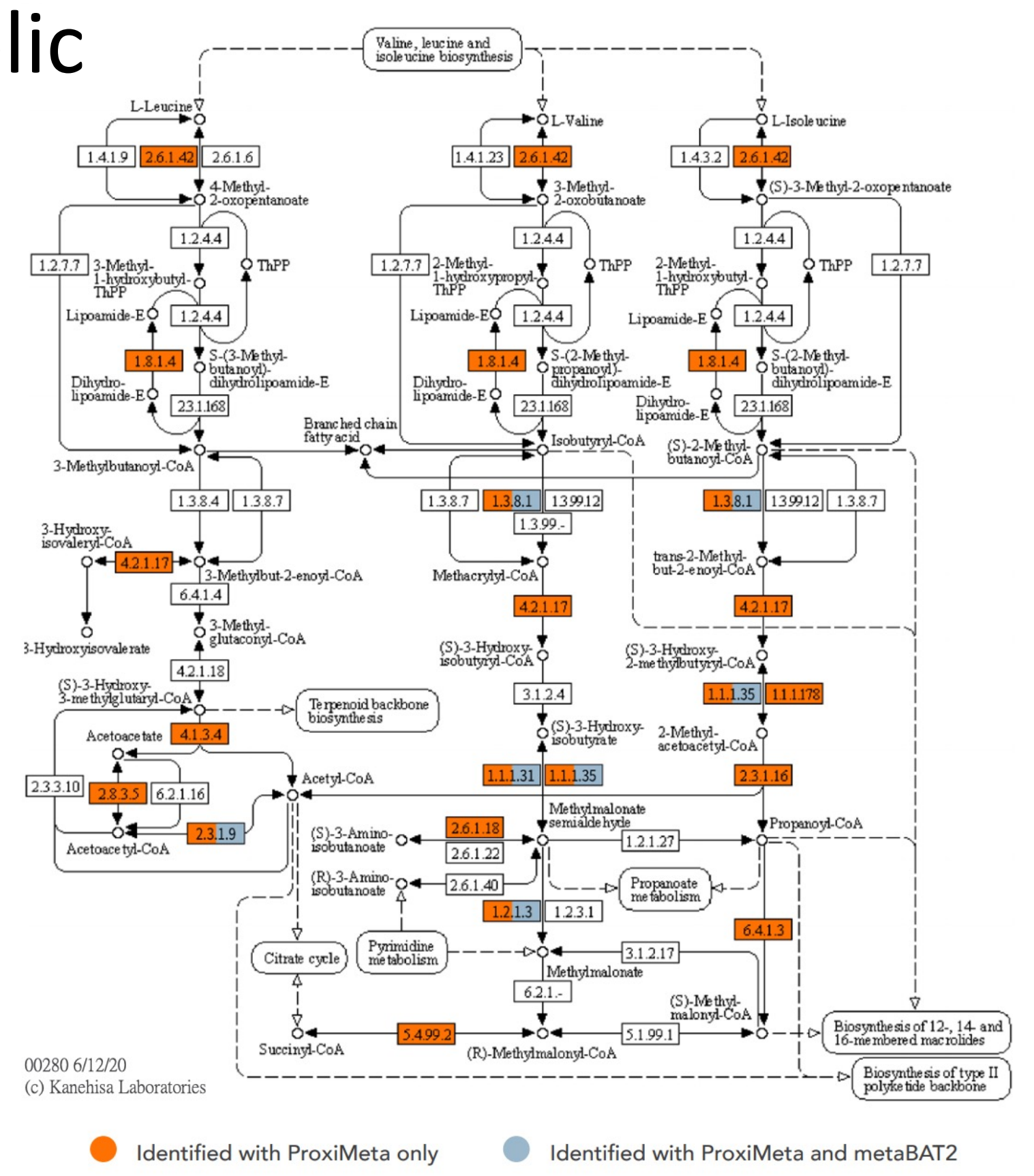
- Method stems from high-throughput chromosome conformation capture (aka 3C, Hi-C)
- Formaldehyde crosslinking of intact microbiome samples traps DNA that is proximal in physical space inside cells
- Proximity ligation joins nearby DNA molecules, creating chimeric junctions that can be sequenced.
- Paired sequence reads connect contigs that originated inside the same cell.



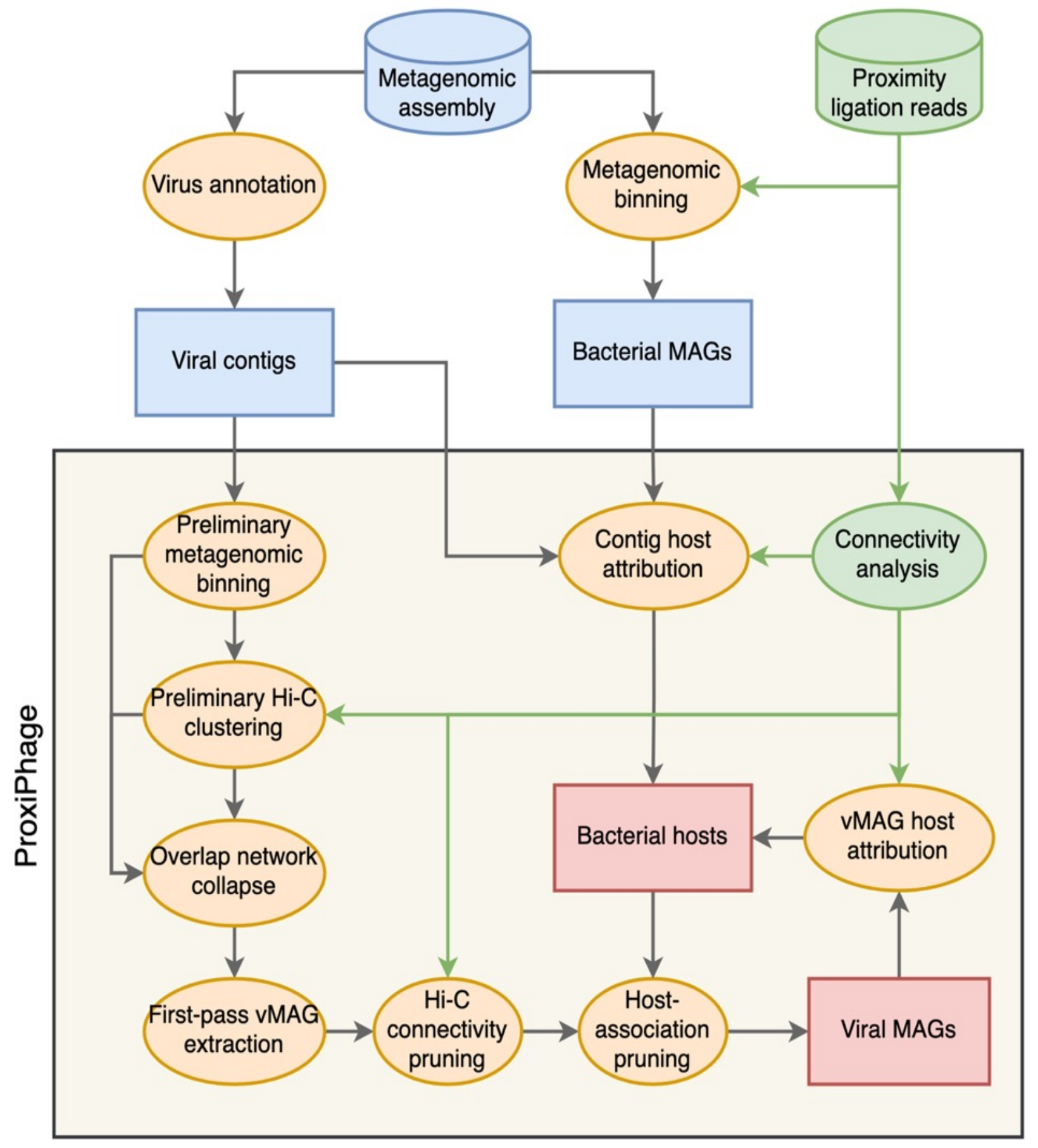
Using the proximity signal between contigs, we can reconstruct high-quality MAGs of microbes, viruses, and plasmids and connect mobile elements to their hosts.

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



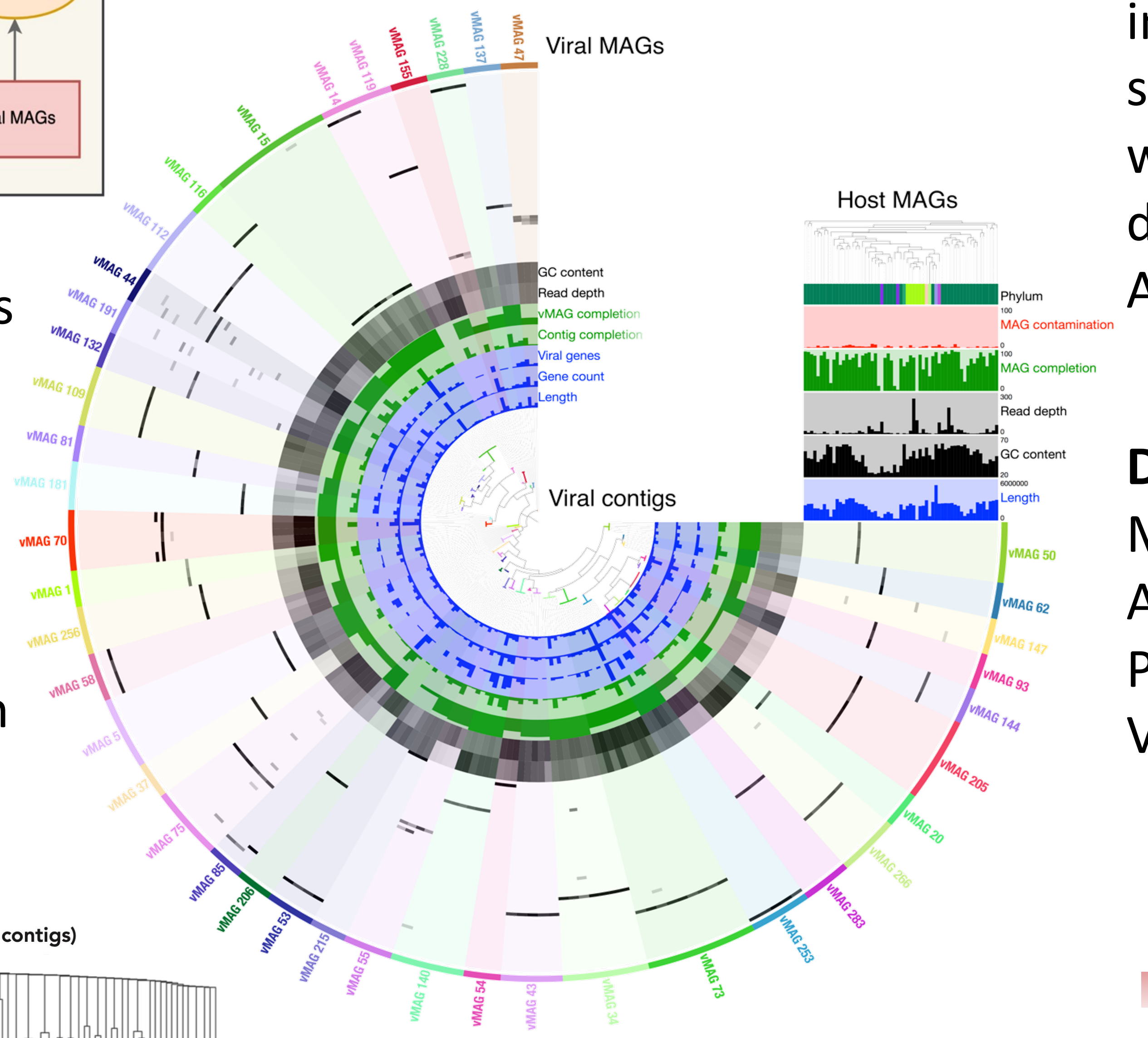


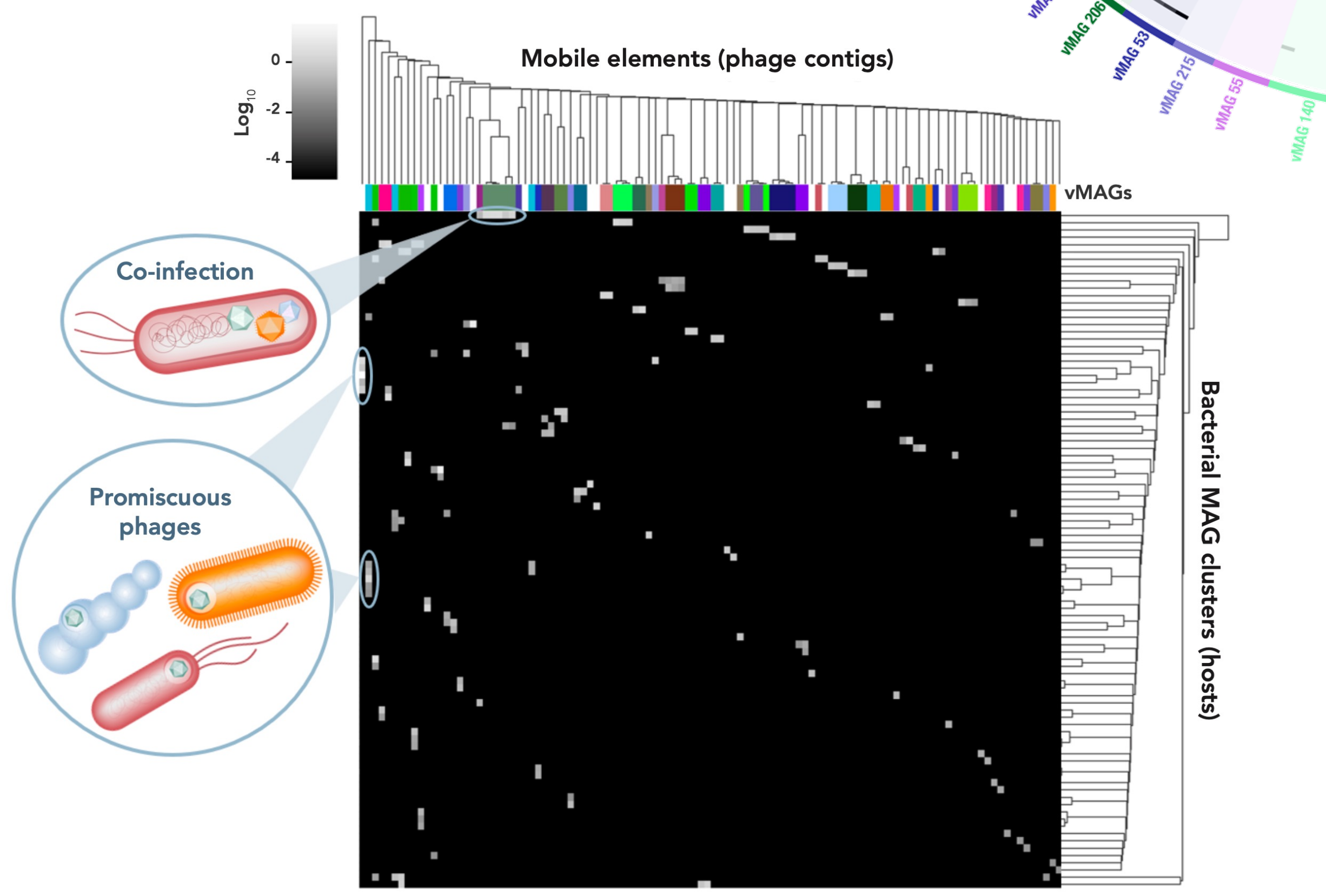
A New Method for *de novo* Reconstruction of Phage and Plasmid Genomes in Microbiomes



- A new pipeline for binning of 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.



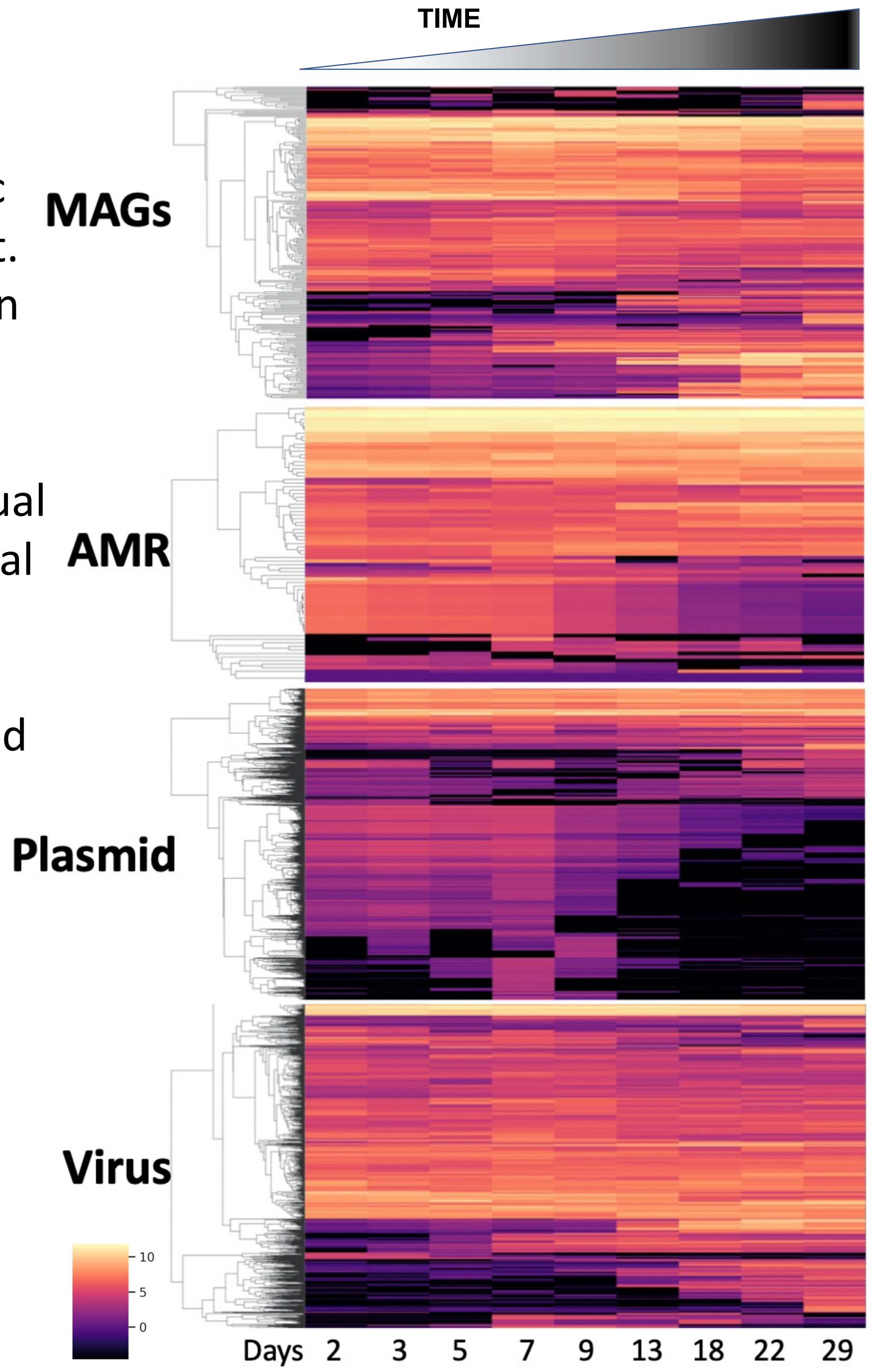


Proximity signal is also used to measure the interaction strength between microbial genomes (vertical axis) and mobile elements (phage shown here, horizontal axis). This allows viral host range identification.

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.



Dereplicated Totals
MAGs: 250
AMR elements: 94
Plasmid contigs: 1862
Viral contigs: 953

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"[Accurate viral genome reconstruction and host assignment with proximity-ligation sequencing](#)"

The metagenome analysis described here is available through the ProxiMeta™ service platform from [Phase Genomics](#)

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