DOI 10.18699/SBB-2022-065

3D-MAGs – spatial conformations of individual microbial genomes reconstructed from Hi-C metagenomes

Revel-Muroz A.[1]*, Sobolev A.[1], Solovyev M.[2], Vasiliev P.[1, 3], Ulianov S.[1, 2], Ivanova V.[1], Tyakht A.[1]

[1] *Institute of Gene Biology, RAS, Moscow, Russia*

[2] *Lomonosov Moscow State University, Moscow, Russia*

[3] *Research Centre for Medical Genetics, Moscow, Russia*

* *revelanastasia@gmail.com*

Key words: Hi-C, metagenomics, spatial conformation of genome, microbiome, contact map, regulation of expression, 3D genome, chromosome interaction domain (CID)

Motivation and Aim: High-throughput metagenomic sequencing of a microbiome sample coupled with adequate bioinformatic analysis allows reconstructing information about multiple microbial genomes from a single sample. Termed MAGs (metagenome-assembled genomes), each of such approximations represents an unordered sets of contigs. Augmentation of metagenomics with chromosome conformation capture (Hi-C metagenomics) yields Hi-C MAGs that can outperform ordinary MAGs, particularly in terms of completeness and contamination, as well as align the contigs into a chromosome-level scaffold. By reconstructing chromosome contact maps of a MAG similarly as it is commonly done for single eukaryotes, it is possible to evaluate the 3D organization of the microorganism. However, such analysis is yet to be conducted systematically and compared with other layers of genomic information.

Methods and Algorithms: Here we propose the concept of a 3D-MAG – spatial structure of a single microbial genome reconstructed from Hi-C metagenome. We investigated the substantiality of the concept on novel experimental data from 3 types of microbiomes of varying diversity – fermented beverages (low diversity), gut microbiome (medium diversity) and thermophilic community from a hot spring (high diversity). Hi-C MAGs were obtained using a recently developed pipeline [1]. For each high-quality Hi-C MAG, its contact map was generated and aligned. 3D genomes were compared with published metatranscriptomic data of related species.

Results: 8 samples were processed and at least 3 high-quality 3D-MAGs were received in each community. Most 3D-MAGs were associated with species, whose spatial structure has not been studied yet. We discovered the second diagonal on the contact map of *Lactobacillus brevis*, which is similar to its relative *Bacillus subtilis.* In addition to bacteria, the archaeal 3D genome was also studied. We found an off-centered second diagonal and loops on a contact map of *Thermofilum uzonense*. For a number of 3D-MAGs, the relationship between gene expression and CIDs (chromatin interaction domains) boundaries was confirmed. For one of the major human gut microorganisms *Alistipes finegoldii* we compared the genome spatial structure at two time points to find differences in chromatin conformation related to the boundaries of the CIDs in the region of highly expressed genes. The change might be linked to altered gene expression of the microorganism.

Conclusion: Reconstruction of 3D-MAGs using Hi-C metagenomics provides information of the chromosome structure of individual species in various metagenomic

communities. Linking it to other omics-derived information about the microbe provides insights into temporal dynamics of gene regulation *in vivo*. Large scale Hi-C metagenomics profiling involving 3D-MAGs can deepen our understanding of the relation between spatial and functional organization of microorganisms

Acknowledgements: This work was supported by the Russian Science Foundation (No. 19-74-10092).

References

1. Ivanova V. et al. Hi-C Metagenomics in the ICU: Exploring Clinically Relevant Features of Gut Microbiome in Chronically Critically Ill Patients. *Front Microbiol*. 2022;12:770323. doi: 10.3389/fmicb.2021.770323.