Analysis of the microbiome and virome of a gnotobiotic mouse model by Chromosome Conformation Capture

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Résumé

The gut microbiota houses a complex and diverse microbial community that is crucial for human health. Indeed, the alteration of the composition of bacteria has been associated to various chronic diseases such as inflammatory bowel disease, asthma or obesity. More recently, variations of intestinal viruses, predominated by bacteriophages (phages), have also been associated with dysbiosis, calling for combined studies of both bacterial and viral populations.
Chromosome Conformation Capture (3C) applied to microbial communities is an innovative method to obtain information on both bacterial and viral populations as well as their interactions through DNA collisions. Here, we applied this method and developed the tools to analyze both *in vitro* and longitudinal *in vivo* samples from a group of 12 bacteria stably colonizing the gnotobiotic OMM12 mice model. In addition, we performed deep sequencing *in vitro* and *in vivo* of the total viral fraction to identify the viruses naturally present in this community.

The analysis of data from the 3C method led us to improve the assembly of the 12 bacterial genomes and revealed the precise 3D structures of their chromosomes, providing novel information on the diversity of architecture of non-model bacterial chromosomes and the metabolic activities of these bacteria in the gut environment. In particular, we detected the 3D signature of prophage induction amongst which several formed free particles as confirmed by virome sequencing. This result demonstrates that 3C data can discriminate functional prophages from cryptic ones. The comparison between *in vitro* and *in vivo* data also led to the observation that the gut environment impacted both prophage induction as well as the 3D structure of the bacterial genome. Finally, the temporal stability of bacteria and phage populations was assessed over time as well as the reproducibility of the method.

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Altogether, these data demonstrate that the combination of virome and *in situ* 3C data can reveal the dynamic interactions between phages and bacteria. These results provide a solid base for implementation to further study microbial communities in the gut environment using this gnotobiotic model.

Mots-Clés: Gut microbiota, Chromosome Conformation Capture, Virome, Mouse model, Prophage induction