GENOME WATCH

Gut metagenomics goes viral

Alan Walker

Interest in the human intestinal microbiota has intensified in recent years, but research has been largely focused on bacteriology. This month's Genome Watch reviews a recent metagenomics study that instead aims to better characterize the viruses that inhabit our guts.

The human gut is populated by a rich and diverse microbiota that has an important role in the maintenance of host health. Although numerous studies have attempted to characterize the bacterial communities of the gut, substantially less attention has been paid to the viruses that are present. Previous studies, surveying just a few faecal samples, have suggested that most identifiable DNA viruses are phages (viruses that infect bacteria) and that many of the RNA viruses are plant viruses¹. However, large-scale studies that simultaneously monitor the viral and bacterial components of the gut microbiota are lacking.

To this end, Reyes *et al.*² recently reported a metagenomic study of the faecal microbiota of four pairs of monozygotic adult twins and their mothers at three separate time points over the course of 1 year. To characterize the virome (that is, the collective viral genomes present in each sample), the authors purified virus-like particles from faecal samples and used shotgun pyrosequencing to generate over 280 Mb of sequence. They also carried out pyrosequencing of 16S ribosomal RNA genes to identify the bacterial communities in the faecal samples.

Comparing their viral data against a custom database containing a broad range of reference sequences, the authors found that ~80% of their reads did not match any known viruses, highlighting our poor understanding of the viral inhabitants of our guts. Most of the reads that did have a match in their database were from prophages or temperate phages, the predicted hosts of which coincided with the predominant bacterial groups detected by the 16S ribosomal RNA gene analysis. These phage populations seemed to be remarkably stable and to persist in individuals over extended periods without major divergence or mutations in the viral genomes. Therefore, phage–bacterium interactions in the distal large intestine are potentially strikingly different to those encountered in some aquatic ecosystems, in which lytic phages seem to be predominant and rapid shifts in bacterial and phage populations occur, driven by predator–prey dynamics.

However, comparative analysis of the viromes from each of the faecal donors showed that these stable viral populations were, to a large extent, specific to the sampled individual, with no significant clustering between co-twins or between twins and their mothers. This is in sharp contrast to previous work focusing on gut bacteria, which has shown that, despite a high degree

of inter-individual variation in faecal bacterial communities, twins and their mothers have a higher degree of similarity to each other than to unrelated individuals³.

The authors then analysed the functions encoded by the virome and those encoded by the microbiome as a whole by comparing their viral reads to total community shotgun reads generated for an earlier study of their twins and mothers cohort³. Only a very low proportion of the viral reads could be assigned a putative function, but on the basis of those that could be classified it seems that the virome is enriched for genes encoding proteins involved in DNA and RNA synthesis and replication, whereas total microbial communities are enriched for genes involved in carbohydrate and nitrogen metabolism. Of particular note, they also identified several new genes in the virome that may confer an advantage to their bacterial hosts.

This work makes a valuable contribution to our overall understanding of the processes that shape the intestinal microbiota, and it illustrates that much remains to be learned about the viruses that inhabit the human gut. It will be of particular interest to further investigate the mainly temperate nature of the virus–bacterium dynamics and, as the authors themselves state, to elucidate whether similar dynamics exist in other regions of the colon in which energy supplies are less limited.

Alan Walker is at the Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, CB10 1SA, UK.
e-mail: microbes@sanger.ac.uk

1. Breitbart, M. *et al.* Viral diversity and dynamics in an infant gut. *Res. Microbiol.* **159**, 367–373 (2008).
2. Reyes, A. *et al.* Viruses in the faecal microbiota of monozygotic twins and their mothers. *Nature* **466**, 334–338 (2010).
3. Turnbaugh, P. J. *et al.* A core gut microbiome in obese and lean twins. *Nature* **457**, 480–484 (2009).

Competing interests statement

The author declares no competing financial interests.