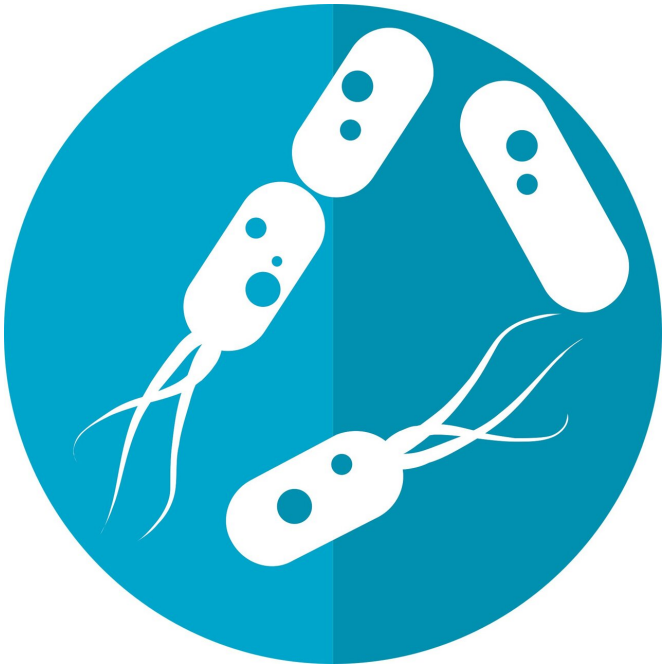
Metagenomic analyses used to identify changes in the gut microbiome after spinal cord injury

12 May 2021



Credit: Pixabay/CC0 Public Domain

Using metagenomic sequencing, researchers have identified changes in populations of bacteria and viruses that occur after spinal cord injuries in mice. The novel metagenomic data sets, presented in *mSystems*, an open-access journal of the American Society for Microbiology, provide new information on the taxonomy and function of diverse microbes, including viruses. This information may help to better predict how spinal cord injury-induced changes in the microbiome influence systemic and neurological outcomes after traumatic spinal cord injury.

"This is the first study that has applied metagenomics to characterize gut dysbiosis after spinal cord injury," said principal study investigator Phillip Popovich, Ph.D., Professor and Chair of the Department of Neuroscience and Executive Director of the Belford Center for Spinal Cord Injury at the Ohio State University (OSU). "A lot of people are interested in understanding the gut microbiome because of its potential impact on a host of comorbidities that affect people with spinal cord injury, including metabolic disease, cardiovascular dysfunction, decreased immune function, fatigue and mental health issues. There is a lot of literature in other fields that implicate the gut microbiome in the onset or progression of these comorbidities."

"We were able to show spinal cord injury dependent effects on a number of different bacteria and viruses—some increase, some decrease and some are virtually depleted by the injury," said Matthew Sullivan, Ph.D., Professor, Department of Microbiology and Founding Director of OSU's Center of Microbiome Science and co-senior author of the study. "And because we used cutting-edge genome-resolved metagenomics and viromics, we were able to do more than determine how spinal cord injury affects the number and composition of gut bacteria. That is what gene targeting sequencing techniques like 16s rRNA sequencing are good at doing. By comparison, metagenomic sequencing allows us to simultaneously evaluate how spinal cord injury affects bacteria, archaea, fungi and viruses and then begin to predict the functional consequences associated with these changes in the microbial ecosystem of the gut."

Applying metagenomics to study mammalian microbiome is still a relatively new approach, but these techniques have long been used to understand microbial diversity in the oceans. In fact, Dr. Sullivan has been using these techniques to determine the impact that viruses found in the ocean have on global biogeochemistry.

In the new study, the researchers performed spinal cord injuries on the 4th thoracic spine (T4) or 10th thoracic spine (T10) in mice and then compared their results to mice receiving sham injuries (i.e., spinal surgeries without spinal cord injury). They collected fecal samples at baseline and three weeks post injury (or surgery) and then performed metagenomic analyses. The researchers found that after spinal cord injury, the relative abundance of several beneficial bacteria decreased, while potentially pathogenic bacteria increased. They also found that functionally, microbial genes encoding proteins for tryptophan, vitamin B6, and folate biosynthesis, essential pathways for central nervous system function, were reduced after spinal cord injury. Viruses of beneficial bacterial hosts decreased, while viruses of pathogenic bacterial hosts increased after spinal cord injury.

"Spinal cord injuries occur at different spinal cord levels, and the level at which an injury occurs will have distinct effects on the gut and the microbiome," said Dr. Popovich. Indeed, the researchers found that although the microbiomes and viromes were changed in all mice with spinal cord injuries, some of these changes were notably enhanced in mice with higher level spinal injury.

Though a pilot study and not yet in humans, the findings provide first steps for developing therapies and treatments. For example, Lactobacillus johnsonii, which was decreased in mice after spinal cord injury, was a primary source of lactocepin which is an anti-inflammatory bacterial protease that is essential for proper immune function. Thus, replacing Lactobacillus johnsonii using custom-made probiotics could help to boost immune responses and reverse the infectious complications that plague people with spinal cord injuries.

Provided by American Society for Microbiology