Viruses knowledge unlocked by new metagenomics technologies

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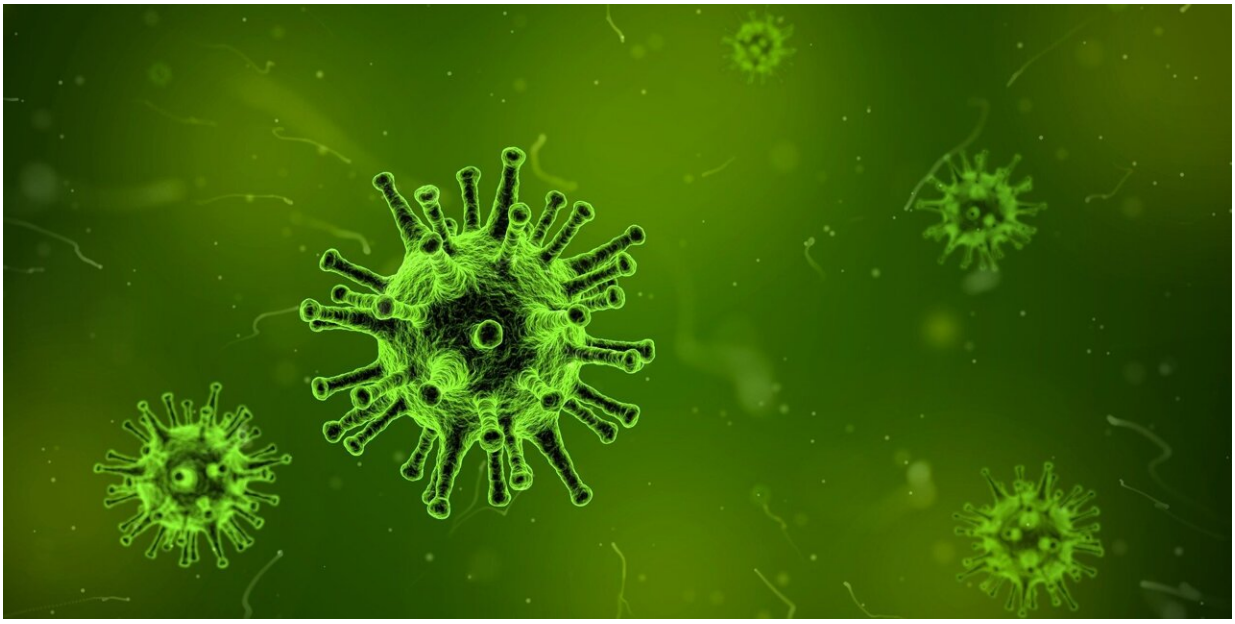

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Metagenomic sequencing techniques allows the study of microbiomes from all sorts of habitats, and using this to explore phages (bacteriophage genomes integrated into the circular bacterial chromosome) has expanded knowledge of viruses that integrate into bacterial genomes and how they benefit their hosts.

Flinders University Ph.D. candidate Laura Inglis—part of the Flinders

Accelerator for Microbiome Exploration (FAME) lab, an interdisciplinary research group at Flinders University's College of Science and Engineering—has outlined the advantages in her new research published on transforming phages.

The paper, "How Metagenomics Has Transformed Our Understanding of Bacteriophages in Microbiome Research," by Laura Inglis and Robert Edwards, has been published in the journal *Microorganisms*.

"The microbiome is an essential part of most ecosystems, but it has been especially difficult to study microbiomes from all sorts of habitats," says Ms Inglis. "Metagenomic sequencing changes this. It is especially useful for finding phages from many different environmental conditions, but many genomes are added to databases without the inclusion of comprehensive metadata.

"Being able to automatically sort these sequences into an environmental ontology would allow for these sequences to be useful in future projects, but we need considerably more high-quality data to determine how best to sort these sequences."

The increasing number of sequences uploaded to online databases has both pros and cons. It means that more data is available for use but curating such a vast amount of data is becoming unmanageable.

"There are many challenges with curating metagenomes but the use of machine learning for automatic curation could alleviate some of the problems," explains Ms Inglis.

Phages play significant roles in the microbiomes of many species and in different environments. They can protect their host from deadly infections, and give their host access to beneficial genes such as antimicrobial resistance or toxin production—but the way phages

interact with their host changes depending on the environment.

"Several factors influence whether bacteriophages choose lysis or lysogeny and several different hypotheses attempt to explain why some environments have higher rates of lysis or lysogeny," says Ms Inglis.

Many studies have examined phages in different environments and conditions but only look at a few different environments or conditions at a time. Ms Inglis says that taking advantage of the large number of metagenomes online could allow for a larger study examining the rates of lysis and lysogeny across many different environments at once—but she acknowledges that issues with curating the genomes need to be fixed first.

Researchers have conducted many studies on phages from various environments, and developed hypotheses regarding what factors influence survival strategies, such as the lytic/lysogenic decision, although much more needs to be learned about how prophages interact with their hosts under different conditions.

"Learning more about metagenomes and prophages could provide many insights into human and environmental health, and obtaining a better understanding of what a healthy microbiome should be may enable us to detect changes more quickly or accurately in microbiomes that could be a sign of disease," says Ms Inglis.

One issue with using open-access metagenomic data is that sequences added to databases often have little to no metadata to work with, so finding enough sequences can be difficult. Many metagenomes have been manually curated but this is a time-consuming process and relies heavily on the uploader to be accurate and thorough when filling in metadata fields and the curators to be working with the same ontologies.

Using algorithms to automatically sort metagenomes based on either the taxonomic profile or the functional profile may be a viable solution to the issues with manually curated metagenomes, but it requires that the algorithm is trained on carefully curated datasets and using the most informative profile possible in order to minimize errors.

Ms Inglis' paper on gut microbiome is one of one of seven recent papers from Flinders University's FAME lab, with the interdisciplinary research group providing access to microbiome and metagenomics resources that help accelerate microbiome research.

Other significant recent publications from the FAME lab include Vijini Mallawaarachchi's research on a new bioinformatics tool to assemble genomes from multi-bacterial genome data; Ph.D. student Lias research on microbial functions to coral health (with fellow Ph.D. student Bhavya Papudeshi) and her review of the ecophysiology of a single coral species in the current environmental conditions of Caribbean coral reefs; and Ph.D. student Susie Grigson about how to use advanced maths and computer science with biology to help understand microbes and what they are doing.

The FAME lab was created by Robert Edwards, Matthew Flinders Fellow in Bioinformatics who coordinates the computational analysis of DNA sequences associated with the microbiome, along with Elizabeth Dinsdale, Matthew Flinders Fellow in Marine Biology, whose research uses genomics to investigate the biodiversity and ecology of microbes and viruses on coral reefs, kelp forest and shark epidermis.

More information: Laura K. Inglis et al, How Metagenomics Has Transformed Our Understanding of Bacteriophages in Microbiome Research, *Microorganisms* (2022). DOI: 10.3390/microorganisms10081671

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