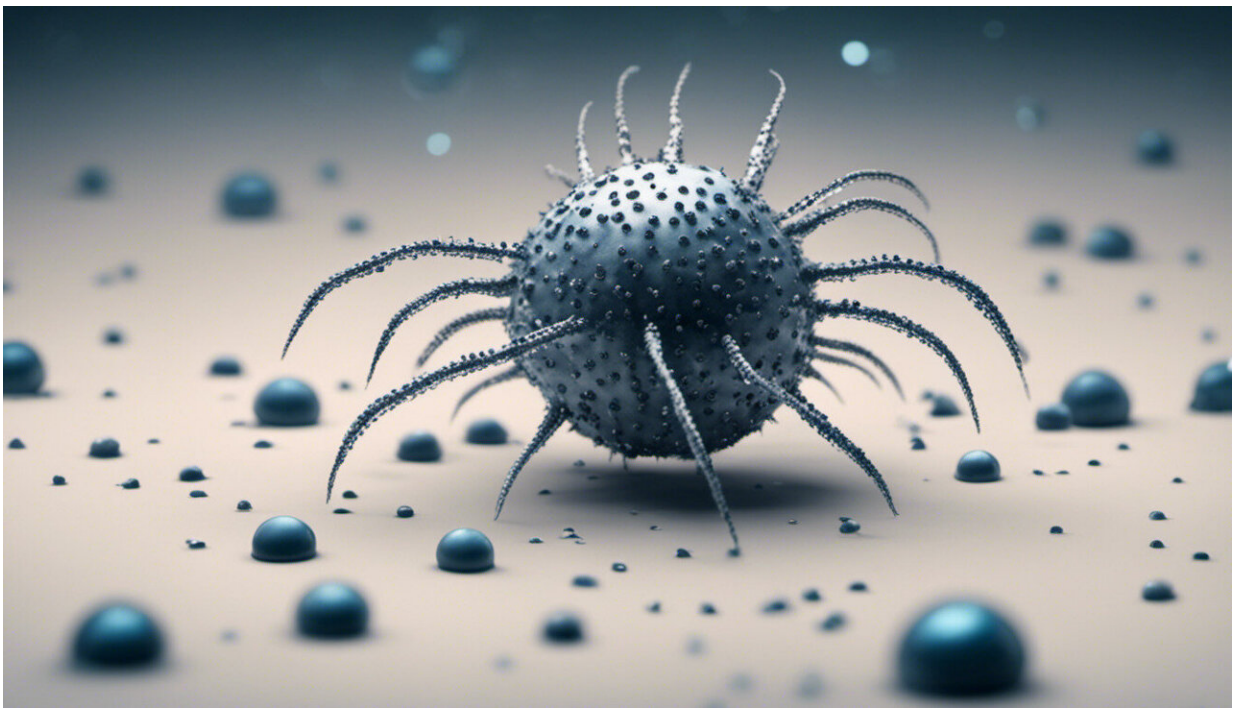
Surprising enzymes found in giant ocean viruses

June 5 2019



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A new study led by researchers at Woods Hole Oceanographic Institution (WHOI) and Swansea University Medical School furthers our knowledge of viruses—in the sea and on land— and their potential to cause life-threatening illnesses. Their findings, which examine newly-identified genes carried by mysterious "giant" viruses, could represent

potential new drug targets for giant viruses linked to human diseases. The work published this week in *Proceedings of the National Academy of Sciences*.

An international team of researchers team searched more than 8,000 virus genomes and found that many newly-discovered giant viruses contain multiple genes for a type of enzyme called cytochrome P450. P450 enzymes are common in animals, plants and bacteria, but finding them in new viruses is unexpected. Prior to the giant viruses, it was never considered that viruses would have these genes.

"This is an extremely interesting finding," says biologist John Stegeman, senior author of the paper and the director of the Woods Hole Center for Oceans and Human Health at WHOI. "In animals, P450 enzymes metabolize drugs, make steroid hormones, and defend against pollutants. We have yet to find out what they are doing in these viruses, but for sure they are unique, unlike P450s in any other organism."

P450 enzymes, which constitute one of the largest enzyme superfamilies known, may also have major implications for understanding chemical effects both in the sea and in human disease processes.

"We know some giant viruses may be linked to some forms of pneumonia, so gaining a better understanding of them will help us to develop ways of tackling those viruses," explains David Lamb, lead author from Swansea University Medical School in Wales, who was working on the research while at WHOI on a Fulbright Scholarship.

"The P450s could represent drug targets for giant viruses thought to contribute to some pneumonias," says Stegeman.

Finding P450 genes and enzymes in diverse viruses opens a new window on the evolution of these important enzymes, which may help in

understanding the biology and the origin of the giant viruses themselves, which currently is unknown, and hotly debated, Stegeman says.

Viruses are the most numerous biological 'entities' on Earth, though giant viruses were not known until 2003, when a virus large enough to be seen with a light microscope was discovered. More than 1,000 genes were identified in that first giant virus; by comparison, the influenza virus has 14 genes. Since then, additional giant viruses with many more genes, and more P450s, have been found worldwide, some with nearly 3,000 genes. Increasingly, giant viruses are being found in the oceans, including in the deep sea.

More information: On the occurrence of cytochrome P450 in viruses, *Proceedings of the National Academy of Sciences* (2019). DOI: 10.1073/pnas.1901080116 , www.pnas.org/content/early/2019/06/04/1901080116

Provided by Woods Hole Oceanographic Institution