



► This small algal organism (coccolithophore) is surrounded by a skeleton (cocosphere) of calcium carbonate plates (coccoliths).

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Survival of the fattest

There are 10^{31} viruses in our oceans. Placed end to end, they'd stretch for 200 million light years (about 60 galaxies away) and would have a combined mass equivalent to around a million blue whales. Yet we know surprisingly little about what they do. Mike Allen and Willie Wilson describe their work on one fascinating family, the coccolithoviruses.

Viruses are like lubricants in the Earth system's engine room, and their role in transforming planktonic cells into dissolved material means they are crucial to global biogeochemical cycling – the pathways that all elements and molecules move along in an ongoing cycle, passing through both living things and inorganic processes.

Coccolithophores are some of the most abundant and widespread organisms in the oceans. These photosynthetic microscopic algae form the base of the oceans' food chain and play a major role in the global carbon cycle, drawing down vast volumes of carbon dioxide from the atmosphere.

They use this carbon to build hard chalk-like shells of calcium carbonate. *Emiliana huxleyi* is the most numerous coccolithophore in our oceans, and satellite observations often show massive blooms that grow rapidly before abruptly disappearing. Until recently, the mechanisms of *Emiliana huxleyi* bloom disintegration were poorly understood, but most scientists now accept that viruses play an important part in these sudden crashes.

Analysis of these viruses' genetic make-up revealed large double-stranded DNA viruses with genomes of approximately 410,000 base pairs. These viruses belong to the newly-created genus *Coccolithovirus*. When researchers sequenced the genes of the type species, EhV-86, they discovered a circular genome with 407,339 base pairs, making it the largest algal virus ever sequenced.

This giant of the viral world revealed a truly mysterious genome, full of genes of unknown function. Yet the few genes whose function we did know were baffling. Along with the usual suspects, the genes that code for common proteins and enzymes, was a pathway that codes for the production of sphingolipids.

Sphingolipids are an important class of lipid, a type of fatty acid. We know they are used for cellular signalling and recognition. Yet the viral pathway's origin was a mystery until very recently. Newly-available data from a project aiming to sequence the genome of *Emiliana huxleyi* showed that the mysterious metabolic pathway came from closer to home than we ever imagined.

It turns out the virus has stolen a near-complete pathway for the production of sphingolipids from its host. It's long been known that viruses can pick up the odd gene or two from their hosts, but this is the first known case of one helping itself to genes controlling the production of multiple enzymes from a metabolic pathway.

This isn't the first time the giant

coccolithovirus's quirky nature has attracted attention. Its complex interaction with the coccolithophores has revealed new insights on the constant and ongoing arms race between hosts and their viruses.

Red queens and Cheshire cats

The Red Queen's race in Lewis Carroll's *Alice's Adventures in Wonderland* is a common metaphor for the evolutionary arms race: 'It takes all the running you can do to stay in the same place.' In an interesting take on the Red Queen hypothesis, this novel system has spawned what has been dubbed the 'Cheshire Cat' escape strategy, after the disappearing antics of another famous character in the same book.

Emiliana huxleyi seems to use an intriguing strategy to avoid viral infection – it switches to an entirely different state in its life cycle so that an attacking virus can't get a foothold. By completely changing its physical appearance it makes itself impenetrable to infection. The algae's later phase is calcified, or covered in chalky armour plates, and is susceptible to infection, but its earlier non-calcified stage is unrecognisable to the coccolithovirus, so it resists infection.

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It turns out that the host doesn't have things all its own way, though. Indeed, the virus seems to have other tricks up its sleeve. In what could be the ultimate insult, it looks like the virus may actually use the host's own sphingolipid pathway against it.

Our research has shown that during a natural algal bloom, the expression of *Emiliana huxleyi*'s normal sphingolipid pathway is almost totally replaced by the virally-encoded pathway. When the virus infects a coccolithophore, it quickly turns on this sphingolipid pathway and expresses it to a level two orders of magnitude greater than the normal *Emiliana huxleyi* pathway.

Unfortunately, we still have only limited information on this virus-host system, so we can only speculate on why the virus produces sphingolipids. There are a few clues – for example, we know that the virus disrupts cell signalling and keeps the infected host healthy as

long as possible. Sphingolipids are known to be important in a wide variety of cellular processes. It's not implausible that the hijacked pathway may even be linked to the victim's 'Cheshire Cat' escape strategy, and that it may stop it switching to the earlier, infection-resistant phase in its life cycle.

Another of our theories is that sphingolipids are used to form 'lipid rafts' to help the virus escape from the algal cells. Or the sphingolipids may even help disrupt programmed cell death by manipulating signalling pathways. Programmed cell death (PCD) is the process by which cells 'commit suicide' in a controlled and orderly manner. If infected cells can kill themselves, they can limit the spread of the virus. We know that sphingolipids play a role in PCD, so the hijacked virally-encoded sphingolipid pathway could help prevent the pathway from activating and so let the virus keep spreading.

Whatever the reason it was originally acquired, the virally-encoded sphingolipid pathway is probably crucial to a successful infection, since the virus throws a lot of resources at keeping it turned on and active. We call it 'survival of the fattest' between the host and the virus – the winner is decided by who can manipulate sphingolipid production more effectively.

The coccolithophore-coccolithovirus system is truly remarkable. The more we discover, the more we realise how little we know about it. But crucially, we are generating ideas and concepts that are being applied to totally unrelated systems. The theories we're

proposing have attracted interest from a whole new field of evolutionary researchers.

Last year marked the 150th anniversary of the publication of Darwin's seminal work *On the Origin of Species*, from which the phrase 'the survival of the fittest' was born. Research into this novel marine host-virus system is providing crucial insights into many of Darwin's evolutionary theories. It's a shame that Darwin isn't around to see this research; one can only imagine what he would make of this amazing virus system (whose host takes part of its name from his most ardent supporter, TH Huxley) where the survival of the fittest could depend on the survival of the fattest.

MORE INFORMATION

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