Project title: Marine viruses: important players in global warming?

Project code:

Host institution: University of Warwick

Theme: ‘omics and biogeochemical cycles

Key words: Carbon fixation, bacteriophage, marine environment, global warming

Supervisory team (including institution & email address):
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Project Highlights:
- Isolation and sequencing of cyanophages from different oceanic provinces
- CO₂ fixation rates of *Synechococcus* cells infected with different cyanophage isolates
- Functional characterisation of host and phage carbon metabolism proteins

Overview:
Cells of the major marine cyanobacterial genera *Synechococcus* and *Prochlorococcus* are numerically the most abundant phototrophs on Earth. These organisms are responsible for up to 90% of primary production in various oceanic regions, with their numbers likely increasing in the future, so are vital to understanding the functioning of, and controls on, the global carbon cycle which is intrinsically linked to global warming. Their co-occurring viruses (cyanophages) are known to be equally widespread in their distribution. However, cyanophages are unique compared to other phages, because they maintain copies of photosynthetic genes within their genomes and likely play a direct role in modulating the fixation of CO₂ and the production of the oxygen that we breathe (1).

 Whilst it is clear that the photosynthetic ability of *Synechococcus* is maintained during phage infection, there is no direct evidence that CO₂ fixation is maintained. Our preliminary data demonstrates that cyanophage infection causes a decrease in host CO₂ fixation, the magnitude of which varies in different phage. We hypothesise that variation in cyanophage-encoded homologues of bacterial genes, that alter host metabolism and are designated as Auxiliary Metabolic Genes (AMGs), cause this difference. This research project will thus focus on the frequency of AMGs in cyanophage isolates from different environmental niches with the aim to understand how AMGs provide cyanophage with a fitness advantage in a specific environment. This will be complemented by functional characterisation of cyanophage AMGs specifically involved in carbon metabolism, to determine their physiological role and how they may alter host CO₂ fixation capacity.

![Figure 1: Proposed mechanism of phage encoded proteins to alter the flow of carbon(2)](image)

CP12 is thought to inhibit the Calvin cycle, with phage-encoded transaldolase shunting carbon towards fructose-6-phosphate, whilst G6PDH and 6PGDH increase flux through the pentose phosphate pathway. This will result in increased NADPH production, and ribose-5-phosphate for DNA biosynthesis.
Methodology: This PhD Project aims to answer the key question: How do CO₂ fixation rates vary in globally important primary producers, *Synechococcus* and *Prochlorococcus*, infected by cyanophages. The successful applicant will isolate and analyse a range of cyanophages to determine their ability to alter host CO₂ fixation. Furthermore, gain a mechanistic understanding of this by determining the function of specific genes. This project is multidisciplinary in that it encompasses both traditional microbiology, molecular biology and bioinformatics, with supervisors in both the Medical School and Life Sciences. Methods will include: High throughput sequencing of cyanophage isolates, bioinformatic analysis of bacteriophage genomes, construction of *Synechococcus* mutants, protein over expression and enzyme assays.

Training and skills: CENTA students are required to complete 45 days training throughout their PhD including a 10 day placement. In the first year, students will be trained as a single cohort on environmental science, research methods and core skills. Throughout the PhD, training will progress from core skills sets to master classes specific to the student's projects and themes. More specifically, this PhD project will offer the student a unique opportunity to learn cutting edge genomics skills, alongside advanced bioinformatics analysis of bacteriophage genomes. This will be combined with the opportunity to isolate a range of novel cyanophages and experience of modern molecular/biochemical techniques including mutant construction, enzyme assays, protein over-expression.

Partners and collaboration (including CASE): The Millard and Scanlan groups have pioneered work on marine cyanophages and their picocyanobacterial hosts. Current research in their groups is funded by the Natural Environmental Research Council, The Leverhulme Trust and BBSRC. Further details on their research activities can be found via the links below:

Dr Millard group: [http://www2.warwick.ac.uk/fac/med/research/tsm/microinfect/staff/millardlab](http://www2.warwick.ac.uk/fac/med/research/tsm/microinfect/staff/millardlab)

Prof. Scanlan group: [http://www2.warwick.ac.uk/fac/sci/lifesci/research/marinemicro](http://www2.warwick.ac.uk/fac/sci/lifesci/research/marinemicro)

Possible timeline:

**Year 1:**
- Isolation of cyanophages from different oceanic provinces
- Construction of *Synechococcus* mutants to express phage AMGs
- CO₂ fixation rates of *Synechococcus* cells infected with different cyanophage isolates

**Year 2:**
- Genome sequencing and bioinformatic analysis of genomes
- Over expression of selected AMGs in *E. coli*
- CO₂ fixation rates of *Synechococcus* mutants

**Year 3:**
- CO₂ fixation rates of *Synechococcus* mutants infected with specific cyanophages.
- Functional characterisation of AMGs expressed in *E. coli*
- Enzyme Assays

Further reading:


Further details:

Potential applicants are encouraged to contact: Andrew Millard ([a.d.millard@warwick.ac.uk](mailto:a.d.millard@warwick.ac.uk))