

MS11-1-1 Fantastic bacteriophages and where to find them

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A. Butler¹

¹Durham University - Durham (United Kingdom)

Abstract

Viruses are highly diverse, sophisticated infectious agents that replicate solely inside living organisms by exploiting host cell metabolic machinery. The virosphere is comprised of all viruses that are found in the environment and therefore presents high degrees of genetic diversity. The Horizon 2020 Virus-X—Viral Metagenomics for Innovation Value—project was established in 2016 with a central aim to better understand genetic diversity amongst viruses found in extreme natural environments like geothermal springs. These insights could then be utilised to develop novel gene products for uses in a wide range of biotechnological applications, including novel therapeutics and molecular diagnostics.

The project established a highly intertwined and collaborative pipeline, which covered the initial retrieval of viral metagenomes and processing using bioinformatics to protein characterisation and progression onto innovation. This unique approach allowed for the careful selection of target genes, with the greatest potential for innovation, to be taken forward for functional and structural characterisation. These were a combination of non-structural viral proteins, where their functions were largely understood; as well as those with uncharacterised properties, allowing for the discovery of new functionalities. The structures of many of these proteins have been successfully determined experimentally using X-ray crystallography. Protein structure determination proved complementary to bioinformatics, and thus a total of 97 proteins have been thoroughly characterised including robust lytic enzymes from thermophilic bacteriophages. Here, I will present the structure of one of these phage lytic enzymes, which was solved using an integrative approach of standard crystallographic phasing techniques alongside structure prediction models generated from artificial intelligence systems such as AlphaFold.