

# The way to a virus' 'heart' is through its enzymes

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The arrival of bluetongue virus (BTV) in the UK last year posed a major threat to the economy and the increasing temperatures of our changing climate mean it is here to stay. If we are to fight this disease, which has had a major impact on farming already, we must discover how it works. A review published in the August issue of the *Journal of General Virology* outlines our current understanding of the "heart" of the virus, which may help us to develop antiviral therapies to treat many human pathogens.

Bluetongue disease is transmitted to ruminant animals like cows when they are bitten by a midge carrying the virus. It is endemic in tropical and subtropical countries and represents a major economic threat in many parts of the world. Until recently, outbreaks in European countries have been sporadic and relatively rare but since 1998 outbreaks of bluetongue in mainland Europe have been common events, moving steadily northwards.

In September 2007 the virus reached the UK where it has become a major threat to farming. Because of the seriousness of the animal disease caused by bluetongue virus, it has been a subject of intense molecular study for the last three decades and is now one of the best understood viruses at the molecular and structural levels.

"Replication of the viral genome is the 'heart' of a virus," said Professor Polly Roy from the London School of Hygiene and Tropical Medicine. "It is the key process that allows establishment of infection."

Understanding the fundamental processes of how bluetongue virus initiates and sustains infection will help us determine the best way to prevent and control bluetongue disease."

When bluetongue virus enters animal cells, infection is initiated through a process which requires a number of enzymes to work together. We know this thanks to a range of research methods including the use of genetically engineered proteins and by looking at the 3D structure of the enzymes. Now that it is possible to synthesise the structures that allow replication of the virus in the lab, scientists will be able to examine the effects of viral mutations on replication. Recently a DNA-based system has been developed that will provide breakthrough experimental techniques of relevance to many viruses that infect humans and animals. It will also pave the way for the development of a highly safe and successful vaccine against bluetongue disease.

"Viruses depend on the cells they infect for certain functions that enable them to exist. This dependence limits the number of possible targets for the development of antiviral therapy," said Professor Roy. "Bluetongue virus uses unique viral enzymes to replicate. At the Roy laboratory we have been using bluetongue as a model system to study detailed molecular processes for many years. This contributes to a better understanding of other similar RNA genome viruses, such as rotavirus, which are also responsible for a large burden of disease in humans."

"The knowledge accumulated through this work will have an impact on the fundamental understanding of the structure-function relationships underpinning bluetongue virus replication," said Professor Roy. "It will also contribute to the understanding of viral replication in general and help us to understand the very essence of infection process of viruses. Understanding the fundamental biological processes of virus replication is the best route to achieving effective control of the diseases caused by the virus, in a way that is both clinically effective and safe."

Source: Society for General Microbiology

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