Targeted Project / AY 2023 -2024

How do RNA viruses use RNA structure to control their lifecycles?

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Research area: RNA biochemistry and virology

Project outline:

RNA viruses pack as many functions as possible into small genomes, and have a variety of strategies to do this, such as using overlapping reading frames. As RNA itself can have structural and also catalytic roles, it is likely that, in addition to proteins, RNA viruses also use RNA structures to perform essential functions during the viral lifecycle. There is evidence for this in multiple RNA viruses.

Until recently, however, it has not been possible to study in detail the individual RNA structures formed within a mixture of genomic and subgenomic viral RNAs.

In this project, we plan to study the conserved RNA structures and structural interactions of various flaviviruses. This viral family are enveloped, single-stranded positive sense RNA viruses that usually spread via insect vectors, and that infect a variety of animals, sometimes including humans. Members of the family include the important pathogens Zika, dengue and West Nile viruses. We will study individual RNA structures and RNA-protein interactions using cutting-edge in vitro structural techniques we have developed: in-gel SHAPE (selective 2'OH acylation analysed by primer extension) and XL-SHAPE. Additionally, we will use Zika virus and Nanopore sequencing technology combined with SHAPE to study the RNA structures formed by flaviviruses inside cells. We will then use Zika virus as a model system to study the effects of mutating conserved RNA structures. The project will help us to understand the importance of RNA structures to viral lifecycles, and to identify potential drug targets for the development of pan-flaviviral drugs.

BBSRC DTP main strategic theme: Understanding the rules of life

BBSRC DTP secondary strategic theme: Transformative technologies, Bioscience for an integrated understanding of health