Unravelling the Mechanisms of Gene Expression of Hepatitis A Virus

Viruses are pervasive pathogens which infect all forms of life, from bacteria to humans. Even so, viruses are remarkably simple creatures, with some consisting of little more than an RNA genome packaged together with viral proteins. Despite this simplicity, viruses have evolved sophisticated strategies to hijack host machinery. After gaining entry to a suitable host cell, the virus commandeers the cell's protein production machinery and uses it to build new virus proteins. At the same time, the virus suppresses the production of cellular proteins in an effort to prevent the host cell from mounting a defense. By studying how viruses manipulate host resources and machinery, we can identify potential weak points in the virus's replication cycle. In the future, we can use this knowledge to develop better treatment options.

Hepatitis A virus (HAV) is part of a large group of viruses called the picornaviruses, many of which cause severe disease in humans. HAV itself is a leading cause of acute viral hepatitis worldwide, but many aspects of its biology remain unclear. In this proposal, we will investigate HAV gene expression and its importance for viral replication. We will identify which cellular factors assist viral protein production and how they do so. We will also determine whether similar mechanisms are used by closely related animal viruses. This will help us understand which HAV-like animal viruses pose the greatest risk of infecting humans. Finally, we will investigate how the virus regulates its own genes while manipulating those of the host cell. Collectively, this research will expand our understanding of an important human virus and perhaps shed light on fundamental mechanisms of gene expression in human cells.