Structural Basis of ribosome binding, manipulation, translocation, and initiation of protein synthesis by a viral internal ribosome entry site RNA

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Technology description

Summary

Background In eukaryotic cells, protein synthesis on the majority of mRNA’s occurs via a process in which a modified nucleotide “cap” (5’-cap) is recognized by proteins that then lead to the initiation of translation by placing the ribosome on the mRNA. An alternative mechanism, discovered in the early 1990’s, bypasses the need for a 5’-cap and many of the associated initiation protein factors (dispensing with all in some cases). These RNAs are known as internal ribosome entry sites (IRES) and are found in many pathogenic viruses, including many positive stranded ssRNA viruses. IRESes display a surprising diversity of sequence, secondary structure, and cofactor requirements, which has complicated efforts to understand their structure and mechanism. IRES RNA sequences are critical for infection of many pathogenic viruses including hepatitis C & A, poliovirus, foot-and-mouth-disease virus, encaphalomyocarditis virus and HIV (among others). The Dicistroviridae family of ssRNA viruses only infect invertebrates and are not human pathogens; however, they do include a number of viruses that in some way cause an economic threat, or are found to be potentially economically interesting to the shellfish industry and agricultural industry. Taura syndrome virus is one of the more devastating pathogens affecting the shrimp farming industry worldwide. Another member of Dicistroviridae, Solenopsis invicta, is being used for fire ant pest control. Technology Dr. Jeffrey Kieft and colleagues at the University of Colorado have determined the complete three-dimensional crystal structure of the internal ribosome entry RNA site (IRES) from a member of the Dicistroviridae family. With the first complete three-dimensional structure of an IRES RNA solved (Science 314, p. 1450, and Costantino et al, submitted), this is the first of its kind and allows for further investigations into the mechanism by which the IRES operates, at a level of detail not before possible. Use and knowledge of the structure may prove invaluable in efforts to design novel antiviral drug targets or more novel bio-solutions addressing the taura syndrome disease in shrimp caused by Dicistroviridae virus.

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