

Abstract:

RNA is subject to a wide array of post-transcriptional modifications. 2'-O-methylation is an essential intrinsic modification of RNA. It affects the structure and reactivity of the molecule as well as its function. 2'-O-methylation is highly conserved, present in all three domains of life. Viral RNA uses this modification to mimic the host and evade detection by the immune system. There are two main mechanisms, through which viral 2'-O-methylated RNA does this. The first is evading detection by a pattern recognition receptor from the RIG-I-like receptor family Mda5. Mda5 is capable of detecting unmethylated RNA and recognising it as non-self, thus initiating an immune response. The second mechanism the evasion and restriction of an effector molecule IFIT. IFIT proteins are capable of detecting the absence of 2'-O-methylation on viral RNAs and inhibiting their translation. They do this by interfering with the formation of the ternary complex, an essential member of ribosomal formation. Using viral 2'-O-methylation as a target for therapy, it is possible to develop attenuated vaccines.

Keywords: viral RNA, RNA modifications, 2'-O-methylation, Mda5, IFIT, RIG-I-like receptors, epitranscriptomics, WNV, JEV