The good, the bad, and the cleaved: 14-3-3η in viral battles

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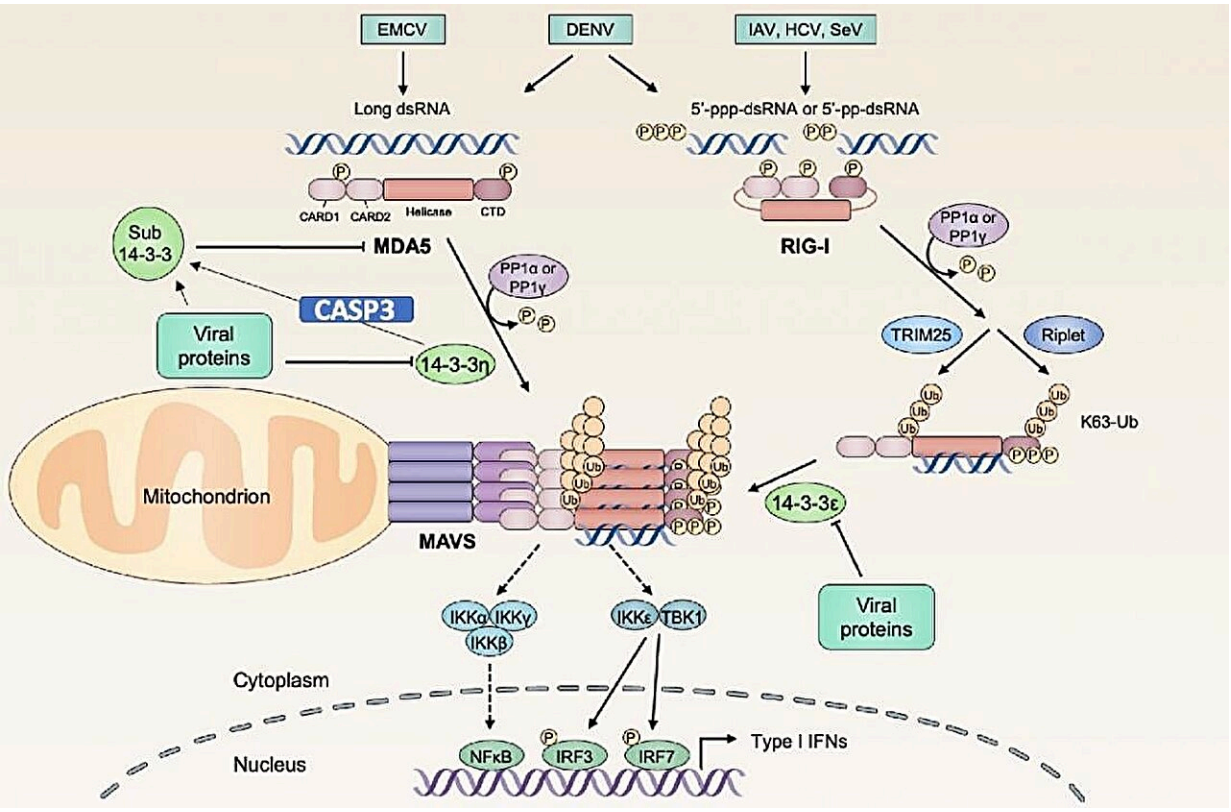

Illustration of the proposed model during viral infection. Credit: National Taiwan University

Scientists from NTU have made a discovery about a protein named 14-3-3η, revealing its complex role in the host's defense against RNA viruses.

Initially, 14-3-3η acts as a crucial ally in the immune response. It works with another protein called MDA5 to detect and alert the immune system about the presence of RNA viruses. This early warning system is essential for mounting a swift and effective defense.

However, the story doesn't end there. Under certain circumstances, 14-3-3η can be cleaved by an enzyme known as Caspase-3, transforming it into a new form that counteracts its original function. This newly generated version of 14-3-3η can actually inhibit MDA5's activity, potentially limiting the immune response.

The paper is published in the journal *PLOS Pathogens*.

This dynamic interplay between 14-3-3η's dual roles is crucial for maintaining a delicate balance. The host needs to be able to effectively fight off infections, but it also needs to prevent excessive inflammation, which can be harmful. 14-3-3η helps to regulate this process, ensuring that the immune response is appropriate and controlled.

Unfortunately, some RNA viruses have evolved strategies to exploit 14-3-3η's dual nature. They can manipulate the body's signaling pathways to favor the production of the inhibitory form of 14-3-3η, allowing them to evade detection and potentially establish infection.

This new understanding of 14-3-3η's role in viral infections opens up exciting possibilities for therapeutic intervention. In conclusion, the discovery of 14-3-3η dual roles in the immune response against RNA viruses provides valuable insights into the complex interplay between the host and the pathogen.

By targeting the mechanisms that regulate 14-3-3η, researchers may be able to develop novel strategies to enhance the immune response against RNA viruses. Additionally, understanding how viruses manipulate

14-3-3η could lead to the development of antiviral agents that disrupt these viral tactics.

More information: Yun-Jui Chan et al, Temporal regulation of MDA5 inactivation by Caspase-3 dependent cleavage of 14-3-3η, *PLOS Pathogens* (2024). DOI: 10.1371/journal.ppat.1012287

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