DDX3X

The DEAD-box RNA helicase DDX3X promotes translation initiation and associates with stress granules. A range of diverse viruses produce proteins that target DDX3X, including hepatitis C, dengue, vaccinia, and influenza A. The interaction of some of these viral proteins with DDX3X has been shown to affect antiviral intracellular signaling, but it is unknown whether and how viral proteins impact the biochemical activities of DDX3X and its physical roles in cells. Here we show that the protein K7 from vaccinia virus, which binds to an intrinsically disordered region in the N-terminus of DDX3X, inhibits RNA helicase and RNA-stimulated ATPase activities, as well as liquid-liquid phase separation of DDX3X in vitro. We demonstrate in HCT 116 cells that K7 inhibits association of DDX3X with stress granules, as well as the formation of aberrant granules induced by expression of DDX3X with a point mutation linked to medulloblastoma and DDX3X syndrome. The results show that targeting of the intrinsically disordered N-terminus is an effective viral strategy to modulate the biochemical functions and subcellular localization of DDX3X. Our findings also have potential therapeutic implications for diseases linked to aberrant DDX3X granule formation [1)].

1)
L Venus S, Tandjigora K, Jankowsky E. The viral protein K7 inhibits biochemical activities and condensate formation by the DEAD-box helicase DDX3X. J Mol Biol. 2023 Jul 28:168217. doi: 10.1016/j.jmb.2023.168217. Epub ahead of print. PMID: 37517790.