Cellular RNA Helicase Facilitates Retroviral Genome Packaging

December 12, 2011

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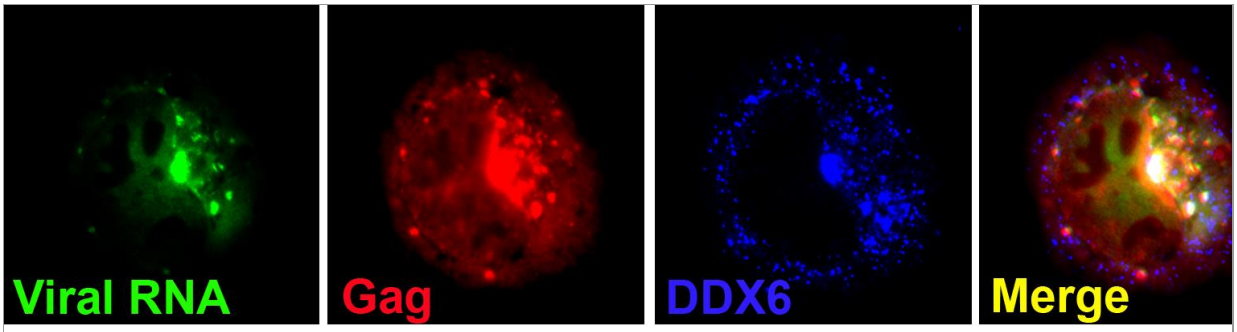
Despite their notoriety for disseminating disease (such as AIDS), retroviruses are also being explored as gene delivery agents because they are highly effective at inserting exogenous genetic material into host cell genomes. For example, a group of retroviruses called foamy viruses are of interest as gene delivery agents. A potential limitation of this approach is that retroviruses appear to be restricted in the amount of genetic material they can package. Recent work by staff scientist Dr. Shuyuarn Yu and colleagues in the Division of Basic Sciences sheds new light on the factors that affect RNA packaging during retrovirus assembly.

Yu *et al.* focused their investigation on cellular proteins that affect foamy virus assembly, as viral determinants of retrovirus assembly are already well characterized. They used siRNA to knock down gene expression of six target proteins. These proteins participate in RNA metabolism and are found within P bodies and stress granules (sites where mRNAs are degraded or sequestered for later translation). Proteins associated with these sites have been previously implicated in both viral replication and inhibition. The authors found that siRNA knockdown of the RNA helicase DDX6 had the greatest impact on foamy virus infectivity by reducing titers 33-fold. They then demonstrated that this reduction in infectivity was associated with less RNA in virus particles. However, microscopy of fluorescently labeled viral components in cells lacking DDX6 showed that these components do not require DDX6 for localization to virus assembly sites. In contrast, 15-25% of endogenous DDX6 was observed to relocate from P bodies to virus assembly sites following foamy virus infection. Yu *et al.* also showed that the contribution of DDX6 to foamy virus assembly was independent of entry, uncoating or integration, but dependent upon DDX6's ability to both metabolize ATP and unwind RNA. The authors thus propose that DDX6 may facilitate the unwinding of viral RNA for retrovirus packaging. They are currently in the process of defining the interactions between DDX6 and foamy virus RNA, which may ultimately pave the way for improvements in retroviral gene delivery.

Yu SF, Lujan P, Jackson DL, Emerman M, Linial ML. 2011. The DEAD-box RNA helicase DDX6 is required for efficient encapsidation of a retroviral genome. *PLoS Pathogens* 7:e1002303.



Shuyuarn Yu

The cellular RNA helicase DDX6, which facilitates the packaging of RNA genomes into foamy virus particles, co-localizes with viral RNA and the viral capsid protein Gag at virus assembly sites in infected cells.