New Insights into Posttranslational Modifications and Host Partners of Influenza Virus

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Due to the small size of viral genomes, viruses in general rely on cellular proteins to complete their replication cycle. Furthermore, posttranslational modifications of viral and cellular factors greatly expand the diversity of the functions of the cellular and viral factors. Molecular and cellular biology of these processes have just begun to be understood. To this end, we performed several RNAi library screening to identify cellular proteins, which may serve as either positive or negative factors for viral replication. The most prominent examples of negative factors are the ubiquitin machinery that polyubiquitinates various viral proteins, leading to their degradation by proteosomes. This mechanism accounts for a majority of regulatory pathways to modulate viral replication. On the other hand, we have found another group of E3 ubiquitin ligases that primarily monoubiquitinate viral proteins and are positively involved in various steps of viral replication. Examples include ITCH ligase, which is involved in the ubiquitination of M1 protein and release of virion RNA from the endosome during virus "uncoating", and a newly identified ligase involved in the ubiquitination of NP protein, thereby enhancing its RNA-binding activity. Its RNA-enhancing activity was abolished by treating it with de-ubiquitinases. An additional type of cellular factors is the normal transcription factors that complex with viral RNA-dependent RNA polymerase. These factors utilize very similar functional subdomains for RNA- and DNA-dependent transcription factors, suggesting that the virus can convert cellular transcription machinery into an RNA-transcribing or -replicating machine. An example of this category is the transcription factor DR1 and another SUMOylation-regulated transcription factor. These various features will be highlighted in my talk to illustrate how viruses usurp cellular factors for its own replication.