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Abstract

Exploitation of Host Factors and Cellular Pathways by Tombusviruses for the Biogenesis of the Viral Replication Organelles †

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Abstract: Plus-stranded RNA viruses recruit cellular vesicles and co-opt cellular proteins involved in cellular metabolism and lipid biosynthesis to build viral replicase complexes (VRCs) within the large viral replication compartments. We use tombusviruses (TBSV), which are small (+)RNA viruses, as model plant viruses to study virus replication, recombination, and virus–host interactions using yeast (Saccharomyces cerevisiae) as a surrogate host. Several systematic genome-wide screens and global proteomic and lipidomic approaches have led to the identification of ~500 host proteins/genes that are implicated in TBSV replication. We characterized the role of two-dozen co-opted host proteins, sterols, and phosphatidylethanolamine in tombusvirus VRC assembly and viral RNA synthesis. We provide evidence on the critical roles of phosphoinositides and co-opted membrane-shaping proteins in VRC formation. We also present data that tombusviruses hijack the glycolytic and fermentation pathways to obtain ATP, which is required for the biogenesis of the replication compartment. Finally, we show evidence that TBSV usurps COPII and endosomal vesicles to form a unique microenvironment involving peroxisomes and endoplasmic reticulum (ER) to support viral replication. These new insights highlight the amazingly complex nature of virus-host interactions.

Keywords: virus-host interaction; genomics; proteomics; lipidomics; host factors; virus replication; RNA virus; TBSV; yeast