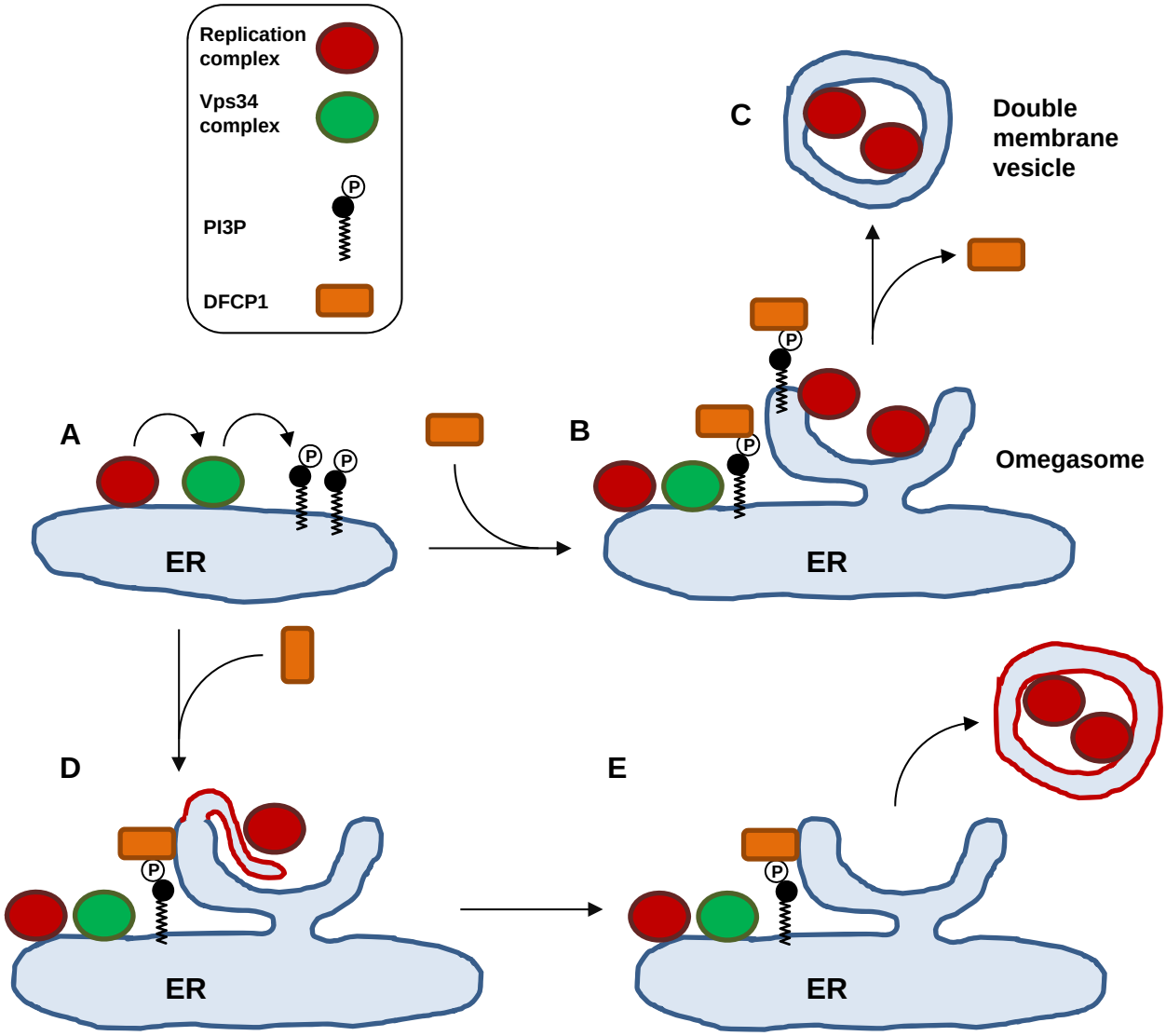

Supplementary Figure S1. Models for the involvement of omegasome formation in the biogenesis of the HCV RNA replication factory. (A) The replication complex, consisting of NS3-NS5B is located on the ER membrane and interacts with the Vps34 complex (consisting of Vps34 together with Vps15, Beclin1 and Atg14L). Vps34 PI3K activity generates a concentration of PI3P at the ER membrane. **(B)** This recruits DFCP1 (via its FYVE domain which interacts with PI3P, and DFCP-1 mediates the formation of cup like protrusions from the ER membrane, referred to as omegasomes). By an unknown mechanism replication complexes become sequestered within these structures. **(C)** Omegasomes pinch off from the ER membrane, forming double membrane vesicles containing the replication complexes, in the process DFCP1 is released back into the cytosol. In an alternative scenario **(D)**, the isolation membrane (in red) forms by extension of the tip of the omegasome, ultimately forming an intact autophagosome which separates from the omegasome **(E).**