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「ウイルス遺伝子操作技術の進展と応用」

1．New Parallels in Positive Strand RNA Virus, Retrovirus and dsRNA Virus Replication

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All positive strand RNA viruses replicate their RNA on host membranes in association with vesicles or other membrane alterations, but the nature and function of this membrane association and organization of the replication complex have been poorly understood.

Brome mosaic virus（BMV），in the alphavirus-like superfamily, encodes two interacting RNA replication proteins：1a, with helicase-like and RNA capping domains, and 2a polymerase. We find that BMV 1a, 2a polymerase and a specific cis-acting replication signal recapitulate the functions of Gag, Pol and RNA packaging signals in retrovirus cores. Prior to RNA replication，1a forms capsid-like spherules that partially bud into the endoplasmic reticulum membrane, sequestering viral positive strand RNA templates. A defined viral RNA signal is necessary and sufficient for this template sequestration. When expressed, 2a polymerase co-localizes in these spherules, which become the sites of viral RNA synthesis and retain（−）RNA templates for（+）RNA synthesis.

Similarly, we find that RNA replication by another, very distinct positive-strand RNA virus, the nodavirus Flock House virus, takes place on mitochondria in association with similar spherular invaginations of the outer mitochondrial membrane.

The results explain many widely conserved features of positive strand RNA virus replication. The similarities revealed bridge retroviruses, positive strand RNA viruses and dsRNA viruses, which also sequester RNA templates, RNA polymerase and often RNA capping functions in a protein shell or core.

These and other features imply that all three virus classes, which all replicate via mRNA intermediates, use related mechanisms for nucleic acid replication and may have evolved from common ancestors.

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