SIgN Immunology Seminar

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Mechanisms in the Formation of Alphavirus Replication Structures

Host
Dr Lisa Ng
Singapore Immunology Network, A*Star

Date
Friday,
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Time
2:00pm – 2:45pm

Venue
SIgN Seminar Room
Immunos Building
Level 4
Biopolis

Similarly to all known positive-sense RNA viruses, alphaviruses replicate their genome in association with modified intracellular membranes. Alphavirus replication sites consist of numerous bulb-shaped membrane invaginations, also known as spherules, which contain the viral double-stranded replication intermediates. We have devised a novel, efficient trans-replication system, which allows us to dissect the requirements for spherule formation. In this system, replication proteins and templates are expressed in mammalian cell from separate plasmids permitting easy manipulation. To detect spherules and study their properties in transfected cells, we use correlative light and electron microscopy (CLEM). The results indicate that in addition to the replication proteins, the presence of a replication template and active polymerase are required for spherule biogenesis. The role of the other enzymatic activities of the replicase in this process is under on-going investigation and will be presented.

Secondly, by using different sizes of replication templates, we have shown that the template length plays an active role in defining the size of the spherule: Shorter templates generate much smaller spherules than those observed during the replication of full-length viral templates. A combination of different template sizes also yields different classes of spherules sizes in the same cell. Thus, the formation of alphavirus spherules clearly differs from that of brome mosaic virus or flock house virus, for which the spherule formation either does not depend on viral RNA at all, or where the length of the RNA does not influence the size of the spherules, respectively. Our work highlights both fundamental similarities as well as important differences in the processes that lead to the modified membrane compartments in cells infected by distinct groups of positive-sense RNA viruses.