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Actin Rearrangement of Brain Endothelial Cells and Its Effect on Tight Junction Proteins during a Dengue Infection

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INTRODUCTION AND AIM

During early infection, viruses such as dengue virus (DENV) and Japanese encephalitis virus can interact and manipulate actin cytoskeleton of host cells, leading to a variety of cellular and molecular alterations. These alterations may affect the molecular structure and morphology of endothelial cells, resulting in blood-brain barrier hyper-permeability and disruption. Our study was aimed to investigate the role of actin in early dengue infection of brain endothelial cells and the effects on tight junction (TJ) proteins, specifically occludin and claudin-5, as the infection progresses.

MATERIAL AND METHODS

A mouse brain endothelial cell (bEnd.3) monolayer was infected with DENV type 1 or 2 at 1.5 multiplicity of infection (MOI) in a time-dependent manner. Cells were incubated with virus for 2, 4, 6, 18 & 24 hours, and 4 & 24 hours for actin and TJ proteins alteration study, respectively. The actin and TJ proteins were then detected using immunofluorescence assay.

RESULTS

Actin thickening was observed as early as 2 hours post-infection (p.i.) with subsequent nuclear localization of actin as the infection progressed. At 4 hours p.i., cytoplasmic diffusion of occludin was observed, but not claudin-5. Significant degradation of claudin-5 was observed at 24 hours p.i. ($p<0.0001$) when cell rounding occurred.

CONCLUSIONS

DENV interacts with actin during early infection and may utilize them as a transport system to the replication site. The retraction of actin resulted in the diffusion of occludin into cytoplasm, and together with claudin-5 degradation, leads to compromised integrity of brain endothelial cells.

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