

SUSCEPTIBILITY OF MAMMALIAN CELLS TO DENGUE VIRUS INFECTION

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Abstract

Dengue virus (DENV) is a single positive stranded RNA virus belonging to the family Flaviviridae, genus Flavivirus. There are four different dengue viruses from DENV-1 to DENV-4. Despite decades of study, it is still not clear as to whether the viruses interact with susceptible cells in the same way, or whether there are virus specific or even strain specific interactions. 12 different dengue viruses including 4 laboratory adapted strains, 4 strains isolated from dengue hemorrhagic fever patients and 4 strains isolated from dengue fever patients were used. This study aimed to determine whether there are virus or strain specific alterations in the dengue virus: host cell interaction. To determine if there are virus specific changes in the dengue virus: host cell interaction, it is necessary to have high and equal infection of cells. Initial experiments to assess DENV infection under conditions of antibody dependent enhancement of infection showed that clinical isolates were not able to infect U937 cells and only poorly infected K562 cells. Subsequent experiments were undertaken under conditions of direct infection, using HEK293T and LLC-MK₂ cells. Under conditions of direct infection, LLC-MK₂ cells, but not HEK293T cells showed a roughly equal degree of infection for all 12 viruses (75±10%). Therefore LLC-MK₂ cells were infected separately with all 12 viruses and proteins were analyzed by MALDI-TOF and significance determined by Principle component analysis (PCA). The PCA analysis showed significantly different proteomic profiles for each sample. In a further analysis, a partial proteome profile was determined for three laboratory adapted viruses (DENV-1, DENV-2 and DENV-4) using GeLC-MS/MS. A total of 549 different proteins were identified as significantly differentially expressed (p-value < 0.05). Compared with mock-infection, 81 proteins were significantly down-regulated in DENV infection whereas 13 proteins were significantly up regulated in DENV infection. These results showed that strain is a significant mediator of the DENV: host cell interaction, and a number of proteins whose expression is regulated in the infection process were identified.