Alternative Translation Mode for Proteins in C6/36 Cells Infected by the Dengue 2 Viruses

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Background/Objective

The eukaryotic translation initiation factor 4E-binding protein (eIF4EBP) is usually phosphorylated in response to various signals, resulting in its dissociation from eukaryotic translation initiation factor 4E (eIF4E) to activate cap-dependent mRNA translation. However, eIF4E-BP has been reported to shut-down host total proteins in many virus infections, including that infected by the dengue virus.

Method

A nonradioactive measurement using puromycin followed by western blot was used to investigate the efficiency of total protein translation in C6/36 cells with Dengue 2 virus (DENV2). In addition, we demonstrated the effect of eIF4EBP on protein translation either through gene knockdown with dsRNA or dephosphorylation with treatment of rapamycin. RT-PCR and quantitative RT-PCR were used for detection of glutathione S transferase (GST) and other genes at RNA level.

Result

In this study, we demonstrated that DENV2 elicits trivial change in amount of eIF4EBP at 24 hpi in C6/36 mosquito cells in which eIF4EBP was significantly hypophosphorylated. As a result it is believed that DENV2-induced eIF4EBP hypophosphorylation reduced cap-dependent translation, resulting in shut-down of many host proteins, hypothetically due to increased formation of an eIF4E-BP/eIF4E complex. However, our results revealed some host genes, especially those are involved in helping cell survival, are up-regulated in response to DENV2 infection. Glutathione S transferase (GST) is one example that and is frequently up-regulated in C6/36 cells with DENV2 infection. It seems that translation of this gene did not depend on regulation by eIF4EBP-associated cap-dependent translation in DENV2- infected mosquito cells which usually survive the infection.

Conclusion

The present finding implied that the GST gene may translate via alternative translation machinery which is cap-independent. This unique mechanism eventually continues translation for specifically pro-survival proteins even the cap-dependent translation machinery has been shut down in virus-infected cells.