Modifications In The HepG2 Cells Protein Synthesis Machinery Caused By Dengue2 Virus Infection

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Dengue virus (DV) propagation relies on the host cell translational machinery but induced changes in the host cell protein synthesis are unknown. We analyzed transcriptional profiles of hepatoma cells, HepG2 after 48 hours of infection with DV and genes involved in the protein synthesis machinery were selected. To certificate these results, a temporal microarray was analyzed using 6, 24 or 48 hours post infection. Significant inhibition of transcription of the essential genes eIF4A, eIF2B2, involved in cap-dependent initiation of translation, and eEF1A and eEFIG, involved in elongation, was found, accordingly to previous data that show that DV protein synthesis does not rely in cap-dependent protein synthesis, thus, we are currently analyzing other genes. In order to verify microarray data and to assay transcription of these genes during progression of infection quantitative real-time reverse transcription-PCR analysis was used (6, 24 or 48 post infection). Surprisingly at earlier times of infection transcription of these genes was not altered, but down regulated after 24 hours of infection. To confirm the status of protein translation the state of phosphorylation of p70S6 kinase and 4EBP1 was assayed. At short-term infection (6 hours) DV infection maintains these two proteins active but progression of infection leads to dephosphorylation. The global expression of 4EBP1 and p70S6 kinase was observed too, and the pool of these proteins weren't modificated. The results suggest that DV protein synthesis sustains activation of the cap-dependent machinery at early stages of infection and progression of infection switches protein synthesis to a cap-independent process.

Key words: Protein synthesis, Dengue, viral infection

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