Dengue Virus Modulates Secretion And Post-Translational Modifications Of Alpha-Enolase in HepG2 Cells.

Higa, L.M. 1; Curi, B.M. 1; Zingali, R.B. 2; Da Poian A.T 1

1Dep de Bioquímica Médica, IBqM-UFRJ, RJ; 2Unidade de Espectrometria de Massas e Proteômica - UFRJ

Introduction: Haemostatic dysfunction is a common feature in the severe forms of the dengue diseases. Previously, our group used a proteomic approach to study the effects of dengue virus (DENV) infection on protein secretion from HepG2 hepatic cells. We showed that DENV infection alters the secretion of several proteins including alpha-enolase (ENO1). Recently, ENO1 was described as a plasminogen receptor that modulates its activation. In this work, we study the effects of DENV infection on the modulation of alpha-enolase in HepG2 cells.

Material and Methods: ENO1 secretion was analyzed by indirect ELISA. To assess cell viability, we performed trypan blue and LDH activity assays. Western Blot were used to inquire ENO1 intracellular content. Two-dimensional gels western blots were used to analyze ENO1 isoforms. Results: Our data show that ENO1 secretion correlates with viral load in a dose-dependent manner. However, DENV infection does not affect the ENO1 intracellular content. Cell viability was not affected by DENV up to 24h post-infection. Two-dimensional Western blots indicates that ENO1 presents 5 isoforms with different isoelectric points indicating post-translational modifications. Comparative analysis showed that the distribution of these isoforms differs between control and infected cells. Conclusions: The infection of HepG2 cells by DENV leads to an increase in alpha-enolase secretion which is dose-dependent but it has no effect on ENO1 intracellular content. Our data also suggests that DENV infection ENO1 modulates post-translational modifications. In our future investigations, we will study the effects of ENO1 secreted by infected and control cells on plasminogen activation. Discussion: The increase of ENO1 secretion by infected cells might be associated with fibrinolysis impairment through plasminogen activation promoting haemostatic dysfunction and playing an important role in dengue pathogenesis.

Key Words: Alpha-Enolase ; Dengue Virus ; Secretion ; Post-Translational Modifications
Financial Support: CNPq and FAPERJ