APOPTOSIS INDUCED BY DENGUE-2 VIRUS: INVESTIGATION OF MITOCHONDRIAL PATHWAY

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Flaviviruses cause diseases like Dengue and Yellow fever. These viruses are transmitted by mosquitoes mainly in South America, Central America and Asiatic southeast, where they have a particular importance for public health. Virus-induced apoptosis is known as a consequence of an infection by flaviviruses. During apoptosis, some cellular mechanisms occur, such as activation of messengers of the apoptotic pathways. Once the mitochondrial pathway is activated, loss of mitochondrial membrane potential (?ψ_m) and release of pro-apoptotic messengers through the voltage-dependent anion channel (VDAC) occur. The process by which Dengue virus induces apoptosis remains not clearly understood. Here, we investigate the Dengue-induced apoptosis process. With this aim, we infected Vero cells with DENV2 and analyzed the DNA fragmentation by TUNEL and the effect of the pancaspases inhibitor BAF. We also analyzed the ?ψ_m through fluorescence microscopy. Apoptosis is observed on the fifth day of infection with loss of ?ψ_m. We also investigated the importance of the mitochondrial pathway by VDAC inhibition. We also observed that viral RNA replication is controlled by an understood mechanism. Our real time rt-PCR results showed an increased viral RNA replication rate from the fourth day, explaining the infection effects observed only from the fifth day post infection. The present data show that Dengue virus is able to induce apoptosis from the fifth day of infection and that the mitochondrial pathway is activated, contributing partially for the cell death process induced by these flaviviruses.

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