Investigation of Cell Death Induced by Yellow Fever Virus

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Flaviviruses cause diseases like Yellow fever and Dengue. These arboviruses have a particular importance for public health in South America, Central America and Asiatic southeast. Virus-induced cell death is related to a cytopathological consequence of an infection by flaviviruses, *in vivo* or *in vitro*. During programmed cell death, some cellular mechanisms occur, such as phosphatidylserine (PS) exposure and DNA condensation. If the programmed cell death type 1 (Apoptosis) is activated, it occurs DNA fragmentation, caspases activation and release of messengers of the apoptotic pathways. Once the mitochondrial pathway is activated, loss of mitochondrial membrane potential ($?\psi_m$) occurs and caspase-9 is activated by release of pro-apoptotic messengers through the voltage-dependent anion channel (VDAC). The process by which Yellow Fever virus (YFV) induces cell death remains not clearly understood. Here, we investigate the YF-induced cell death process. With this aim, we infected Vero cells with YFV using a multiplicity of infection (MOI) 1. To follow the process induced by infection, we analyzed the cell viability, the PS exposure and the $?\psi_m$ through fluorescence microscopy, using LIVE/DEAD cell viability kit assay, Fluorescein(FITC)–annexinV conjugate and $Dioc_6$, respectively. We also analyzed the DNA condensation by the nuclear dye Hoechst 33342 through fluorescence microscopy. Cell death is observed on the fifth day of infection with PS exposure and nuclear condensation, characterizing a programmed cell death. We also observed loss of $?\psi_m$, suggesting that the apoptotic mitochondrial pathway is being activated, contributing partially for the cell death process induced by these flaviviruses.

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