**Yellow Fever Virus-Induced Mitochondrial Dysfunction: Changes in Mitochondrial Energetic Metabolism and Apoptosis Induction**


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**INTRODUCTION**: 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 related to a cytopathological consequence of an infection in vivo or in vitro. During apoptosis, mitochondrial pathway has been described as a crucial step during viruses-induced apoptosis. Once the mitochondrial pathway is activated, loss of mitochondrial membrane potential ($\Delta \psi_m$) occurs and caspases can be activated, culminating in apoptotic process. Here, we investigate the role of mitochondrial cell death pathway during Yellow Fever Virus (YFV) infection and its consequence to mitochondrial energetic metabolism. **MATERIAL AND METHODS**: We infected Vero cells with YFV using a MOI=1. We analyzed the cell viability using Live/Dead and LDH assay. Apoptosis was analyzed by PhosphatidylSerine (PS) exposure and TUNEL, while the role of mitochondrial pathway was followed by $\Delta \psi_m$ through fluorescence microscopy. The importance of mitochondrial pathway was investigated by Bongkrekic acid, an adenine nucleotide translocator (ANT) inhibitor. The mitochondrial energetic metabolism was studied by oxygraphy. **RESULTS AND DISCUSSION**: Apoptosis was observed after 72 hours post infection (h.p.i.) through TUNEL and PS exposure. The dependence of caspases activation during the apoptosis process was also observed, using z-Vad-fmk, a pancaspase inhibitor. We also observed loss of $\Delta \psi_m$ 72 h.p.i. demonstrating that the apoptotic mitochondrial pathway is being activated and apoptosis is dependent of ANT activity. Oxygraphy results show a slighter increase of routine respiration, but a significant increase of oligomycin-sensitive oxygen consumption at 48 h.p.i., that indicate an increase in oxygen consumption rate coupled to ATP synthesis. **CONCLUSION**: Our results suggest that the mitochondrial pathway is activated, contributing partially for the caspase-dependent cell death process induced by YFV. Our data also suggest changes on mitochondrial energetic metabolism associated to virus infection.

Keywords: Apoptosis, Mitochondrial Pathway, Yellow fever Virus
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