

TITLE: EXTRINSIC REGULATION MEDIATED BY IL-22 AND TNF- α AND ITS IMPLICATIONS TO DEVELOPMENT OF CELL INJURY MECHANISMS IN LIVER DAMAGE OF HUMAN FATAL CASES INFECTED BY YELLOW FEVER VIRUS

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Yellow fever (YF) is a febrile hemorrhagic disease caused by the yellow fever virus (YFV). The disease is endemic in forest areas of Africa and Latin America, leading to epizootic diseases in monkeys which constitute the YFV reservoir. YFV is an arbovirus transmitted by mosquitoes of the *Haemagogus*, *Sabethes* and *Aedes* genus, the *Aedes* presents mainly in urban areas, highlighting the risk of reintroduction of this virus in the urban area. The virus infection, IL-22, and TNF- α cytokines act in a kinetic way polarizing a Th22 immune response which in other studies showed to provide high regeneration factor on hepatocytes injured, but no studies related about their effects on liver damage caused by YFV in humans. Thus, the study aims to quantify the IL-22 and TNF- α expression in hepatitis yellow fever in humans. For that, this study analyzed 21 samples of human liver of YF fatal cases. The cytokines IL-22 and TNF- α were immunolabeled by the biotin-Streptavidin-peroxidase method. Statistical analysis, we used the one-way ANOVA testing, Turkey pos-test, and Pearson correlation coefficient using the *GraphPad Prism 5.0* program, we considered a significance level of 5% ($p \leq 0.05$). The results showed a wide expression of IL-22 and TNF- α in the liver parenchyma, mainly in the midzonal when compared to control. Finally, this is the first study to demonstrate which the response mediated by IL-22, the cytokine characterized by signature Th22 profile could impacting directly on Kupffer cell activity since the synergistic effect observed in TNF- α implies the formation of an inflammatory cascade which can result in the necrosis and apoptosis development.

Keywords: Yellow Fever, Physiopathology, Cytokines.

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