TITLE: INFLUENCE OF ROR-γ AND STAT3 IN THE PROCESS OF DIFFERENTIATION AND PLASTICITY OF RESPONSE OF TH17 LYMPHOCYTES IN HEPATIC SAMPLES IN FATAL HUMAN INFECTION BY YELLOW FEVER VIRUS

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ABSTRACT:

The Yellow Fever Virus (YFV) is one of the main examples of the *Flaviviridae* family. It causes yellow fever (YV), a non-contagious infectious disease that remains endemic or enzootic in the tropical forests of the Americas and Africa, periodically causing isolated outbreaks or epidemics with a significant impact on public health. ROR-γ and STAT3 are transcription factors that once activated participate in the host's antiviral immune response and virus-induced inflammatory responses, as well as in the differentiation of effector cells and enough for the secretion of key cytokines. No study was found to demonstrate the influence of these transcription factors on the differentiation and plasticity of Th17 lymphocyte response in hepatic samples in fatal human infection by YFV. Twenty-one human liver samples diagnosed as positive for YFV were used and others five samples were used as negative controls for *Flavivirus* that died from other causes and preserved the liver parenchyma. Expression of ROR-γ and STAT3 *in situ* was based on the Labeled StreptAvidin Biotin Method. Statistical analysis was performed on *GraphPad Prism* 5.0 using one-way ANOVA, Tukey and Pearson's correlation, significance level of 5% ($p \leq 0.05$). Quantitative analysis of IL-6 and TGF-β *in situ* revealed that immunostaining was predominant in the midzonal zone of the hepatic parenchyma in fatal cases of YF compared to the control. Thus, we can observe that this is the first study to characterize the response pattern of Th17 lymphocytes where the two transcription factors may be determinant to trigger the potentiation of the inflammatory process that influences the construction of cellular injury mechanisms responsible for aggravating in fatal cases affected by both YFV and midzonal zone necrosis and hepatocyte apoptosis.

Keywords: Yellow Fever, physiopathology, ROR-γ, STAT3.

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