ORT_07 - Placenta damage caused by Zika virus infection impairs interferon lambda responses

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Introduction: Interferon lambda (IFN-λ1-4) acts as an antiviral and immunological barrier at the placenta, although remains elusive if placenta damages caused by Zika Virus (ZIKV) counterbalances this protective response.

Objective: Here we aim to analyze IFN-λs production in different placenta compartments, and if it is modulated according to placental damage caused by ZIKV.

Methodology: At-term placenta from pregnant women exposed to ZIKV was analyzed by ZIKV PCR detection, presence of chronic inflammations, IFN-λ3 immunofluorescence, and by gene expression of *IFN*s and inflammation-related genes in terminal villi region. Following, we accessed the IFN levels in the culture supernatant of primary extravillous cytotrophoblasts (EVTs) and terminal chorionic villi explants incubated with ZIKV.

Results: Our findings showed that albeit ZIKV PCR cleared mature placenta presented augmented expression of *IFNL2* and *IFNL3* in truncal villi, the ZIKV PCR positive exposed to ZIKV in the first trimester of pregnancy presented a non-effective exacerbate response of types I and III *IFN*s and genes related with inflammation. Besides, placenta with chronic villitis showed impaired *IFNL1-4* expression. EVTs presented augmented IFN-λ1 and IFN-α2 in the presence of ZIKV. Albeit terminal chorionic villi explants do not present an exacerbated response upon ZIKV stimulation, they present relatively higher basal levels of IFN-λ1 and 2-3. The immunofluorescence analysis demonstrates that IFN-λ3 is expressed throughout several placenta structures, mainly in syncytiotrophoblast (STB) and villi mesenchymal cells, but EVT cells, Hoffbauer cells, and maternal leukocytes also expressed IFN-λ3, showing visually diminished expression in the presence of chronic inflammations.

Conclusion: Our data demonstrate that IFN-λs are broadly produced in the placenta and lead to antiviral and effective innate responses, although placenta damages caused by uncontrolled viral replication and placenta chronic inflammations impair the proper response of this key protective factor.

Keywords: Zika virus; Placenta; Type III interferon