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P1344 Induction of inflammatory response in absence of IFN system activation in human PBMC by ZIKV infection

Francesca Colavita[3], Veronica Bordoni[2], Claudia Caglioti[3], Mirella Biava[3], Concetta Castilletti[3], Licia Bordi[3], Serena Quartu[3], Marco Iannetta[4], Emanuele Nicastri*[4], Giuseppe Ippolito[1], Chiara Agrati[2], Maria Rosaria Capobianchi[3], Eleonora Lalle[3]

[1]INMI "Spallanzani" IRCCS, Department of Epidemiology, Rome, Italy, *[2]INMI "Spallanzani" IRCCS, Cellular Immunology Lab, Rome, Italy*, *[3]INMI "Spallanzani" IRCCS, Laboratory of Virology, Rome, Italy*, *[4]INMI "Spallanzani" IRCCS, Clinical Department, Rome, Italy*

Background: The recent epidemic in the Americas caused by Zika virus (ZIKV), Asian lineage, spurred the research towards a better understanding of how ZIKV infection affect the host immune response. The innate immune response and, in particular the interferon (IFN) system, plays a key role in orchestrating protection against flaviviruses infection. The aim of this study was to evaluate the effects of Asian and East African ZIKV strains infection on the induction of IFN, pro-inflammatory and Th2 cytokines in human PBMC.

Materials/methods: PBMC from 3 donors were exposed for 24, 48 and 72 hours to either MR766 or INMI1 at multiplicity of infection of 0.1 TCID50/mL . Supernatants were collected at each time point. IFN-α and IFN-λ proteins and IL-4, IL-6, IL-8, IL-9, IL-10, IFN-α, TNF- α, were measured by ELISA and by Bio-Plex MagPix System and analyzed with the Bio-Plex Manager respectivelly.

Results: Our results show that ZIKV failed to induce both type I and type III IFN while is able to poorly activate type II IFN, and to produce most pro-inflammatory cytokines such as IL-6, IL-8 and IL-9. In particular, we reported a slight modulation of type II IFN in PBMC exposed to INMI1 strain, but not to MR766, and a complete lack of type I/III IFN induction by both strains, suggesting the ability of ZIKV to evade the IFN system not only inhibiting the antiviral IFN response, but also the IFN production. Moreover, we highlighted a polyfunctional immune activation only in PBMC exposed to INMI1 strain, due to the induction of an inflammatory profile (IL-6, IL-8, TNF-α) and of a Th9 (IL-9) response.

Conclusions: Overall, our data show a different ability of ZIKV Asian strain, with respect to African strain, to activate host immune response that may have pathogenetic implications for virus spread in vivo, including mother-to-child transmission and induction of severe fetal complications, as birth defects and neurological disorders. Further investigation is needed to establish a link between these observations and the correct activation of the immune system in ZIKV infection and to identify different intracellular signals induced by different ZIKV strains, responsible for different cytokine response.