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O0999 Different IFN type I signature and sensitivity in WNV L1- or USUV-infected human dendritic cells

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Background: Dendritic cells (DCs) are an important cell type during infection by multiple mosquito-borne flaviviruses, including West Nile virus (WNV) and USUTU virus (USUV). Despite this, the interplay between these viruses and DCs remains poorly defined. In order to gain new insights into the ability of these viruses to induce the innate immune response, we evaluated and compared the induction of type I IFNs expression in immature and mature DCs upon WNV L1 and USUV infection.

Materials/methods: We evaluated the single-growth curve replication of WNVs and USUV and the type I IFN response after WNV L1 and USUV infection at different MOI of monocyte-derived dendritic cells collected from 12 healthy donors. Aliquots of the cells were collected at the time of virus adsorption and at 4, 8, 12, 24, 48, 72 h p.i. WNV L1 and USUV titers and mRNA levels of type I IFN subtypes were determined using real-time RT-PCR. The levels of IFN alpha subtype released by USUV- and WNV L1-infected DCs were evaluated using ELISA. The antiviral activity of IFN-α and IFN-β against USUV and WNV L1 at 48 h p.i. in the A549 cell line was also examined.

Results: The results showed that the USUV replication peak began earlier than that of WNV L1. We observed that IFN alpha subtype levels were detectable in USUV-infected immature DCs and not in those infected with WNV L1. Moreover, we observed a different type I IFN signature between WNV L1 and USUV infected DCs: gene expression of type I IFNs (IFN-α subtypes and IFN-β) was reduced and delayed in WNV L1-infected immature DCs than that induced by USUV at all the MOI analyzed. Furthermore, we found that pretreatment of A549 cells with type I IFN significantly reduced USUV and WNV L1 replication, but the USUV yield reduction was higher than that recorded for WNV L1.

Conclusions: USUV induces a higher activation of IFN-associated antiviral immune response and is more sensitive to types I IFN than WNVL1. Thus, the rare association of USUV with human diseases could be due to the inability of the virus to evade IFN-associated innate immunity.