WNV replicates in the human testis ex vivo

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Résumé

Several viruses have been found in the human testis and some of them, such as Zika virus (ZIKV) or Ebola virus (EBOV), are able to persist and be sexually transmitted long after systemic clearance. West Nile virus (WNV), Dengue virus (DENV) and Japanese Encephalitis virus (JEV) are emerging flaviviruses closely related to ZIKV. Therefore, we aimed to assess their potential to infect the human testis and persist in testicular germ cells, a reservoir for ZIKV.

To this end, we used our original organotypic culture model of human testis, consisting in small explants derived from post-mortem testis maintained in air/medium culture for 10 days (Matusali et al., JCI, 2018; Roulet et al., Human reprod, 2006). By RT-qPCR and plaque assay, we demonstrated that WNV productively replicates in the human testis ex vivo, producing infectious viral particles over the 10 days of culture. In contrast, DENV2 only transiently infected the testis at low level, whereas JEV consistently failed to replicate. RNAscope in situ hybridization demonstrated WNV infection both in the interstitial tissue and within the seminiferous tubules, suggesting a possible tropism for testicular germ cells. We showed that the testicular germ cell line Tcam-2, which has spermatogonia characteristics, is permissive to WNV replication in vitro. In the testis explants, WNV infection induced an antiviral-oriented innate response dominated by the induction of interferon-stimulated genes (ISG) but no interferon upregulation or pro-inflammatory response, as previously observed upon ZIKV infection. In accordance with the replication curve, DENV only triggered a transient antiviral response and JEV did not induce any response. Despite significant replication and innate immune response, WNV infection had no major effect on tissue structure over time culture ex vivo but its impact on steroidogenesis remains to be assessed.

These results show that WNV replicates in human testis explants and infects both the interstitial and seminiferous tubules compartments, which could lead to viral release in semen. We will next assess the ability of this emerging virus to infect and persist in testicular germ cells and affect testis functions ex vivo.

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