Inflammasome signaling pathways exert antiviral effect against chikungunya virus in human dermal fibroblasts

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Résumé

Arboviruses represent an emerging threat to human. They are transmitted to vertebrates by the bite of infected arthropods. Early transmission to vertebrates is initiated by skin puncture and deposition of virus in this organ. Events at the bite site remain largely unknown. Here we report that Chikungunya virus (CHIKV), and West Nile virus (WNV) despite belonging to distinct viral families, elicit a common antiviral signature in primary human dermal fibroblasts attesting for the upregulation of interferon signalling pathways and leading to an enhanced expression of IFN-β, interleukines and chemokines. Remarkably, both WNV and CHIKV enhance IL-1β genes expression and induce maturation of caspase-1, indicating the capacity of these pathogens to elicit activation of the inflammasome program in resident skin cells. In this study we also demonstrate that the inflammasome AIM2 sensor is upregulated in infected fibroblasts. Interestingly, AIM2 RNAi silencing interferes with CHIKV- and WNV-induced IL-1β upregulation. Further analysis demonstrated that activation of the inflammasome limits chikungunya virus replication in human dermal fibroblasts. Together, these results indicate that dermal fibroblasts contribute to the pro-inflammatory and anti-viral microenvironment created at the skin level in the early stages of interaction with arboviruses.

Mots-Clés: Arbovirus, flavivirus, alphavirus, dengue, chikungunya, West Nile virus, fibroblast, inflammasome, AIM2, IL, 1β

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