[PS2.41]

Chikungunya virus mobilizes the apoptotic machinery to invade host cells and escape innate immune recognition.

P Krejbich-Trotot*[1], M Denizot[1], JJ Hoarau[1], MC Jaffar-Bandjee[2], T Das[1], P Gasque[1]

[1]GRI, Infection and immunopathology Research Grouping University of La Reunion, St Denis, Ile de la Reunion, France, [2]Biology Microbiology Virology Biochemistry units CHR North Felix Guyon, St Denis, Ile de la Reunion, France

Chikungunya virus (CHIKV) surprised by a massive re-emerging outbreak in Indian Ocean, reaching Europe in 2007 and with exceptional pathologies in infants and elderly. Although CHIKV was recently shown to persist in tissue macrophages, we argued that robust antiviral mechanisms, including apoptosis, are essential to ward-off the acute infection. We herein tested the capacity of CHIKV to mobilize the apoptotic machinery on HeLa cells as well as primary fibroblasts and making use of several inhibitors of caspases, cell blebbing and engulfment of the apoptotic blebs by neighbouring cells. CHIKV triggered apoptosis through intrinsic and extrinsic pathways. Bystander apoptosis was also evidenced in neighbouring cells in a caspase 8-dependent manner. Remarkably, CHIKV hiding into apoptotic blebs was able to infect surrounding cells. In HeLa cells, these events were inhibited specifically by zVAD-fmk, DEVD-cho (caspases inhibitors), blebbistatin, Y-27632, genistein, annexin-V and cytochalasin B (inhibitors of blebbing and engulfment). These CHIKV-apoptotic blebs were also capable of infecting macrophages (primary cultures, MM6- and THP1-PMA differentiated cells) otherwise refractory to infection by CHIKV alone. Remarkably, viral replication in macrophages did not yield a pro-inflammatory response. We herein describe a novel infectious mechanism by which CHIKV invades host cells and controls the innate immune anti-viral response.

Keywords: chikungunya alphavirus, apoptosis, macrophages, persistence