

**Figure S1: validation of BAX mitochondrial localization as a marker of apoptosis.** A549 cells were treated with TNF/CHX for 16h and co-immunolabeled with anti-BAX Ab and anti-mitochondria Ab (mito), or anti cytochrome c Ab (cyt c) (**A**): Immunodetection of BAX and mitochondrial colocalization, (**B**) Immunodetection of BAX is associated with cytosolic cytochrome-c in apoptotic cells.



**Figure S2: Alphavirus RRV induces early and massive apoptosis compared to Zika virus.** Vero cells were infected with Ross River virus (RRV) or with ZIKV at an MOI of 1 for 72 hours and analysed for (**A**) caspase 3/7 activity, (**B**) cell viability assay (MTT) and (**C**) released LDH activity in cell supernatants. Values represent the mean and SD for one experiment. (\*\* p<0.01; \*\*\* p<0.001, \*\*\*\* p<0.0001, ns = not significant).



**Figure S3:** **ZIKV-PF13 does not cause significant activation of apoptosis until late in infection in U251MG cells*.*** U251MG cells were infected with ZIKV PF13 (clinical isolate) at MOI of 1 for 96h*.* (**A**) Percentage of U251MG cells infected immunostained with anti-BAX antibody were determined at 24, 48 and 96 hpi. (**B**) The infectious viral particles were collected from infected cell culture supernatants during 96 hours post infection and titrated.



**Figure S4:** **ZIKV-MR766 does not cause significant activation of apoptosis until late in infection and ZIKV-MR766 is able to control cell death.** A549 cells were infected with MR766MC at MOI of 1 and during 96h. The percentage of A549 infected cells immunostained with anti-BAX antibody at 24, 48 and 72 hpi (**A**). The infectious virus was collected in supernatant of infected cells at 24, 48, 72 and 96 hpi for titration (PFU assay) (**B**). A549 cells were infected with MR766MC at MOI of 1 for 8 hours and treated with TNFα/CHX 2 hours before infection (2hbi) or 2 hours post infection (2hpi). Percentage of A549 cells immunostained with anti-BAX antibody (**C**). Values represent the mean and standard deviation of three independent experiments (\*\*\*\* p<0,0001, ns: not significant).



**Figure S5:** **A549 cells transiently expressing a ZIKV-MR766 replicon are protected against cell death by apoptosis*.*** A549 cells were transfected with amplicons of ISA methods to generate replicon for ZIKV-MR766 or with pEGFP-N1. 48h after transfection A549 cells were treated with Etoposide for 16 h. Percentage of A549 cells immunostained with BAX antibody were monitored. Values represent the mean and standard deviation of three independent experiments (\*\* p<0,01, ns: not significant).