pharmaceutics

Supplementary Material S1: Configuration file and script containing information on the grid box centers and sizes of prepared receptors and selected drugs.

Shell script

```
#! /bin/bash

for f in *.pdbqt; do
  b=`basename $f .pdbqt`
  echo Processing ligand $b
  mkdir -p $b
  vina --config conf.txt --ligand $f --out ${b}/out.pdbqt --log ${b}/log.txt
done
```

Configuration files (i.e content of conf.txt) for the different docking simulations

```
receptor        =       5h6v_only.pdbqt

center_x        =       -8.522
center_y        =       3.178
center_z        =       -14.473

size_x          =       12
size_y          =       10
size_z          =       17
```

```
receptor        =       5k8t_only.pdbqt

center_x        =       115.969
center_y        =       2.824
center_z        =       64.433

size_x          =       14
size_y          =       19
size_z          =       14
```

receptor = 5kqs_only.pdbqt

center_x = 52.145
center_y = 10.164
center_z = -2.722

size_x = 15
size_y = 15
size_z = 12

receptor = 5mrk_only.pdbqt

center_x = 18.216
center_y = 7.699
center_z = 4.793

size_x = 13
size_y = 18
size_z = 15

receptor = 5u04_only.pdbqt

center_x = 25.036
center_y = 68.817
center_z = 103.577

size_x = 12
size_y = 16
size_z = 16

receptor = 5ulp_only.pdbqt

center_x = -2.874
center_y = -1.66
center_z = 26.51

size_x = 15
size_y = 17
size_z = 16

Supplementary Material S2: The modifications made on the ligand refinement ready-made script for the induced fit simulations in PELE.

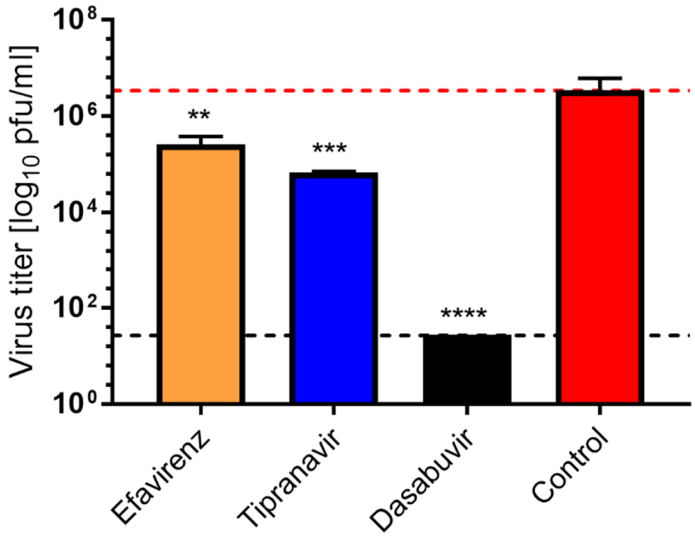
```
pele &
    het Chain:ID & #The chain and identification of the drug
    pdbmodel yes &
    init_min yes &
    steric_tr 500 &
    steered 1 &
    waitfor 5 &
    task &
        show bind_ene 1 &
        spawn point 1 xyz lt n & #xyz are the specific binding coordinates; n was lowered depending on the drug position at the start of the simulation
        if random 1 gt 0.5 then tra_r 0.6 else tra_r 0.3 endif &
        if random 2 gt 0.5 then rot_r 0.25 else rot_r 0.05 endif &
        exit steps gt 100 &
    end_task &
    tries 50 &
    temp 4000 &
    anmfreq 1 &
    spfreq 1 &
    mifreq 1 &
    wrfreq 1 &
    sprad 5.0 &
    lcom_con 0.01 &
    side &
        randomize yes &
        iter 1 &
        verbose no &
        failsafe no &
    sideend &
    path traj_ &
    min &
        rmsg 0.04 &
        nbup yes &
        gbup yes &
        alphaup yes &
    minimend &
    mirad 60 &
    caconst 0.5 &
    rem_bulk_mov 3 &
```

```
anm_eig_freq 100000 &
anm_altm_freq 10 &
anm_altm_type 4 &
lanmanm neig 6 &
lanmanm mode 5 &
lanmanm move_ca 0.8 &
lanmanm mix_modes 0.80 &
lanmmin &
        mxitn 100 &
        iter 1 &
        rmsg 0.04 &
        nbup yes &
        alphaup no &
  minimend
```

Supplementary Table S1. PDB accession numbers indicated by target-location

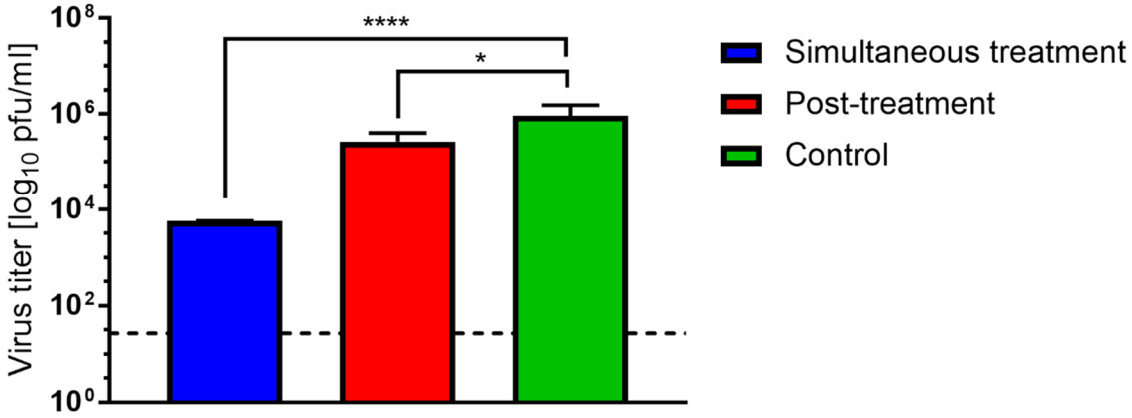
HCV Polymerase-Active Site	Dengue Polymerase-Active Site	HCV Protease-Active site
2AWZ	5HMY	3SU3
2AX0	5HMZ	3SUD
2AX1	5HN0	
3FQK		
3FQL		
3G86		
3H5S		
3H5U		
3H59		
4MIA		
4MK7		
4MK8		
4MK9		
4MKA		
4MKB		
5W2E		

Supplementary Figure S1: Inhibitory effect of efavirenz, tipranavir, and dasabuvir on ZIKV growth in Vero cells in a post-treatment assay.



Dasabuvir, efavirenz, and tipranavir (i.e., drugs that inhibited ZIKV in a simultaneous treatment assay) were further used in a post-treatment antiviral study. The potency of these compounds to inhibit ZIKV 2 hours post-infection was assayed in Vero cells. The cells were infected with ZIKV (strain MR-766) at multiplicity of infection = 0.1. After two hours, the medium containing virus was removed and replaced with a fresh medium containing the tested compounds at concentration of 50 µM. DMSO was added to virus-infected cells as a negative control at a concentration corresponding to a dilution of the initial drug–DMSO stock (at a maximal final concentration of 0.5% (vol/vol)). After 48 h of incubation, culture media were harvested and subjected to plaque assay. Horizontal dashed black line indicates the minimum detectable threshold of 1.44 $\log_{10}$ PFU.ml^{-1}. Horizontal dashed red line indicates the mean titer of the control. Data were analyzed using Student's t-test (GraphPad Prism, version 7.04); **, $p < 0.01$; ***, $p < 0.001$; ****, $p < 0.0001$.

Supplementary Figure S2: Inhibitory effect of a reference compound (7-deaza-2′-C-methyladenosine) on ZIKV growth in Vero cells.



7-deaza-2′-*C*-methyladenosine was used at the concentration of 50 µM as a reference compound in our antiviral assays. The potency of 7-deaza-2′-*C*-methyladenosine to inhibit ZIKV in Vero cells was investigated in a simultaneous assay, and 2 hours post-infection assay. The cells were infected with ZIKV (strain MR-766) at multiplicity of infection = 0.1. In case of simultaneous treatment, culture medium containing 7-deaza-2′-*C*-methyladenosine at concentration of 50 µM was simultaneously added to the cell monolayers. In case of post-treatment, the medium containing virus was removed at 2 hours post-infection and replaced with a fresh medium containing 7-deaza-2′-*C*-methyladenosine at concentration of 50 µM. DMSO was added simultaneously to virus-infected cells as a negative control at a concentration corresponding to a dilution of the initial drug–DMSO stock (at a maximal final concentration of 0.5% (vol/vol)). After 48 h post-infection, culture media were harvested and subjected to plaque assay. Horizontal dashed black line indicates the minimum detectable threshold of 1.44 $\log_{10}$ PFU.ml^{-1}. Data were analyzed using Student's t-test (GraphPad Prism, version 7.04); *, $p < 0.05$; ****, $p < 0.0001$.