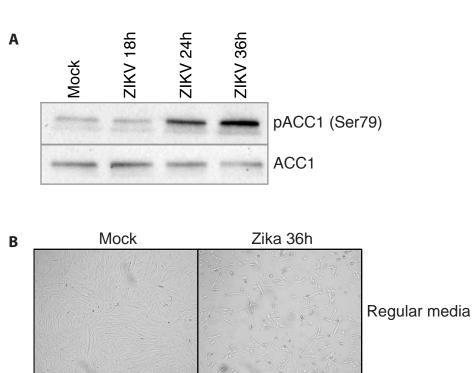


## Supplementary Figure 1. *Related to Figure 1.* Glycolytic metabolism is actively reprogrammed by ZIKV infection.

(A) HFF-1 cells were mock-infected, infected by ZIKV (MOI=3), or infected by UV-inactivated ZIKV for 36 hours and glucose consumption and lactate production were measured at 36 hours post-infection. Data are represented as mean +/- s.d.
(B) HFF-1 cells were labeled with U-13C glucose and metabolites were extracted 18, 24, and 36 hours post-ZIKV infection and analyzed via LC-MS/MS to determine fractional contribution into glycolytic

intermediates. n.m. indicates that the metabolite was not measured. n.c. indicates that there was no change in the fractional contribution for that metabolite between conditions.

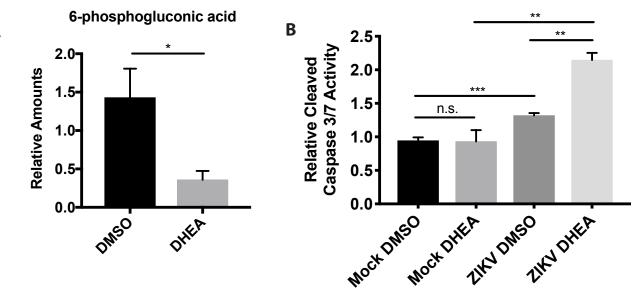


250 μM adenine + uridine

## Supplementary Figure 2. Related to Figure 3.

(A) HFF-1 cells mock-infected or infected with ZIKV for 18, 24, or 36 hours were lysed and Western

(B) HFF-1 cells were mock-infected or infected with ZIKV and cultured in regular media or media containing 250  $\mu$ M adenine and uridine for 36 hours. Light microscopy images are shown in the figure. Scale bar, 20  $\mu$ M.



## Supplementary Figure 3. Related to Figure 4.

(A) C6/36 cells were treated with 50uM DHEA and 6-phosphogluconate levels were measured by LC-MS metabolomics to confirm reduction of G6PD activity.
(B) Cleaved caspase 3/7 activity was measured in C6/36 cells following treatment of DMSO or with DMSO or DHEA (50uM) and mock-infection or ZIKV-infection for 48 hours. Data are represented as mean +/- s.d.