Review of: "Discovery of a Novel Inhibitor for Chikungunya Virus"

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Potential competing interests: The author(s) declared that no potential competing interests exist.

Ana C. Puh et.al screened 36 compounds using a replicon system and ultimately identified 3-methyltoxoflavin (3-MT) with activity against CHIKV using cell assays (EC50 200 nM) on Huh-7 cells, but no activity on Vero 76 cells. They have additionally screened 3-methyltoxoflavin against a panel of viruses and showed that it also inhibits yellow fever virus (IC50 370 nM, SI=3.2 in Huh-7 cells).

Major revision

1. Many viruses including EEE, MERS etc in supplementary also contain conserved cysteine residues. How can 3-MT specifically block infections of CHIKV and yellow fever virus?
2. Replicon is not involved expression of structural proteins (E1/2). How can Replicon-based antiviral assay screen out 3-MT targeting on folding and assembly of the E1 and E2 envelope glycoproteins.
3. Information about “Primary CPE and secondary VYR assays for viruses” is not enough.
4. Data calculation of CC50 = 6.2 ± 5.5 μM of 3-MT (Figure 1C) should be re-evaluated.
5. How can 3-MT inhibiting CHIKV infection cell type-specifically?