Arboviruses are an emerging public health threat yet currently there are limited vaccines and no effective antiviral therapies targeting these pathogens. Recent outbreaks of Zika virus (ZIKV) in the Americas have highlighted the urgent need to develop these antivirals to treat at-risk populations such as pregnant women and children. One avenue for anti-arbovirus drug development is to repurpose known, approved, and pregnancy-friendly drugs that have antiviral potential to be used on these vulnerable individuals. We addressed the antiviral activity of several pregnancy-friendly drugs as well as known antiviral compounds; interestingly, we found that Atovaquone, a hydroxynaphthoquinone, FDA Pregnancy Category C drug used for the treatment and prevention of Pneumocystis jirovecii pneumonia (PCP) and parasitic infections such as malaria, inhibited ZIKV and chikungunya virus (CHIKV) replication in vitro. To date, antiviral activity of this drug has not been described. We proposed Atovaquone as a potential anti-Zika virus (ZIKV) candidate given its structural proximity to ubiquinone (Coenzyme Q) and therefore active role in de novo pyrimidine synthesis.

**PURPOSE**
- To find anti-Zika virus activity in “pregnancy-friendly” existent drugs.

**METHODS**

- Atovaquone + DMSO
- Incubate for 24h at 37°C
- Fix & Stain with Anti-Flavivirus Envelope Protein Antibody (4G2)
- Zika NIH 293T, Vero cells
- Ugandan ZIKV
- Brazilian ZIKV
- Atovaquone inhibits ZIKV at early stages of viral cycle
- Uridine rescues ZIKV infection

**RESULTS**

- Atovaquone inhibits ZIKV
- Atovaquone inhibits CHIKV
- Atovaquone inhibits Zika virion production in animal & human cells
- Atovaquone inhibits CHIKV

**CONCLUSIONS**

- Our findings reveal that Atovaquone has antiviral activity against ZIKV and CHIKV and this has the potential to be translated in the clinical setting into an attractive candidate for the treatment of arbovirus infections in vulnerable populations such as pregnant women and children.
- In addition to its role in inhibiting mitochondrial membrane potential, Atovaquone likely inhibits pyrimidine biosynthesis by competing with ubiquinone (Coenzyme Q) which is a substrate of DHO dehydrogenase enzyme, functioning through the depletion of cellular nucleotides.
- Studies are underway to address this mechanism and to determine the potential broad-spectrum antiviral activity of Atovaquone in vitro and in vivo.