

## ORT.33 - Repurposing Annita® drug against ZIKV infection on Human Placenta and Cervix cells

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**Introduction:** Drug repurposing is the promptest way to obtain an effective drug during a global public health emergency as the spread of Zika virus that is associated with the congenital syndrome. Why the virus reaches the fetus is still unclear, however the placenta represents an important route of transmission, since the virus was detected *in vivo* and *in vitro* human and murine placenta. The fetal infection may occur by passing the virus through spaces created by lesions or inflammation that may break the placental barrier. Another hypothesis is that the virus crosses the placenta through infection of host cells, being possible the transmission of ZIKV to the fetus occur from sexual transmission. Despite the emerging severity caused by the ZIKV infection, there still no specific treatment for this disease. The antiparasitic and antiviral drug Annita® already approved through the Food and Drug Administration and safe for pediatric use and for administration in pregnant women, being included in category B, could have activity against ZIKV due to broad aspect and affordable price.

**Objective:** With this in mind our group evaluated the antiviral effect this drug in chorionic cells of primary culture human placenta and in cervix human cells, two important targets of infection, in comparing to Vero cells from African green monkey and C6/36 cells from *Aedes albopictus*.

**Methodology:** The antiviral effect was assessed by immunofluorescence, Plaque assay and RT-qPCR in cultures infected with ZIKV and treated with non-toxic concentrations of the drug for 48h.

**Results:** Previous results using Vero cultures showed antiviral effect of drug only when the treatment was performed after the adsorption step. This treatment scheme revealed a dose-dependent reduction of infection in chorionic cells at 79% at the concentration of 50 µg/mL. Interestingly, in the cervix cells, at the concentration of 12 µg/mL already had a 95% of infection reduction. The EC<sub>50</sub> values were 23±5µg/mL for chorionic cells and 6±0.4µg/mL for cervix cells. Analyzing the reduction of infectious particles, the concentration of 25 µg/mL in the chorionic cells and 12 µg/mL in the cervix cells inhibited 100% of the progeny. In addition, the quantification of viral RNA copies/mL in the supernatant of the treated cultures with 50 µg/mL showed a reduction of 93% in chorionic cells and 87% in cervix cell cultures. However, in cells of the ZIKV-infected C6/36 mosquito line, the treatment did not reduce the number of infectious particles in the cultures supernatant, suggesting that the activity of this drug is related to the response of the host cells.

**Conclusion:** The Annita® drug demonstrated good antiviral activity, which may be related to host cell response. Studies aimed at reusing drugs should be encouraged because they accelerate the discovery of drugs for the treatment of ZIKV infection, especially for infected pregnant women.

**Keywords:** Annita® drug; Antiviral effect; Zika virus