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A New Mouse Model of HIV in Pregnancy: the *EcoHIV Pregnancy Model*

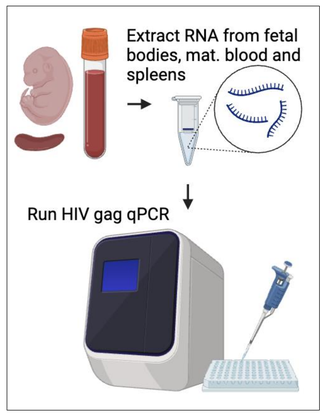
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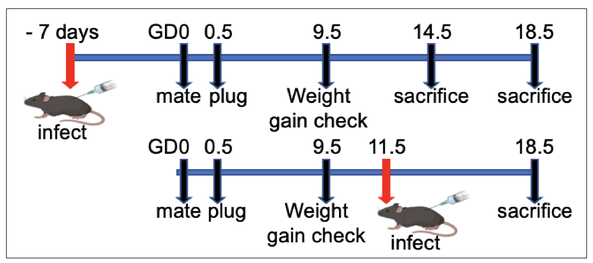
BACKGROUND

- 1.3 million women living with HIV become pregnant each year – with untreated HIV infection during pregnancy poses risks to both maternal and child health[1]
- Developing a reliable mouse model of HIV during pregnancy could provide mechanistic insights into the adverse maternal and fetal outcomes associated with HIV infection
- **EcoHIV** is a chimeric ecotropic HIV virus that has been modified by replacing the coding region of gp120 with gp80 from *murine leukemia virus* to allow infection in mouse immune cells [2,3]
- Here we present a new mouse model of EcoHIV infection in pregnancy

METHODS



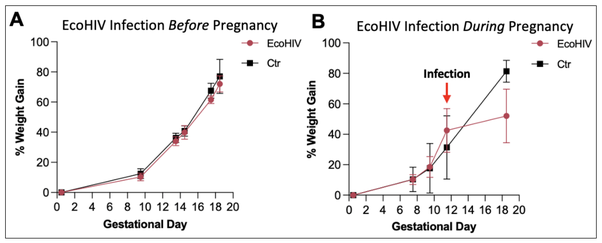
- RNA was extracted from maternal blood, spleens, and fetal bodies
- The gag gene served as a marker for HIV/EcoHIV presence (quantified by RT-qPCR
- Absolute gag levels were calculated using plasmid standards
- Samples were considered positive if their gag expression exceeded the control detection limit



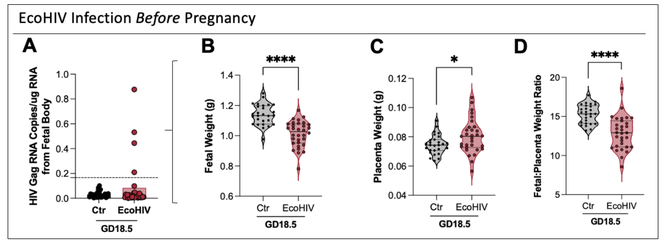
Experimental Design of EcoHIV Infection in Pregnancy (A) Infection Before Pregnancy: Mice received PBS or 2.5×10⁶ pg/mL EcoHIV via IP injection, then mated one week later. (B) Infection During Pregnancy: Pregnant mice were IV injected with saline (control) or 2.5×10⁶ pg/mL EcoHIV on GD11.5.

EcoHIV pregnancy mouse model parallels clinical findings of fetal growth restriction, placental insufficiency, and ~10% vertical transmission rate. Maternal EcoHIV infection associated with fetal brain inflammation.

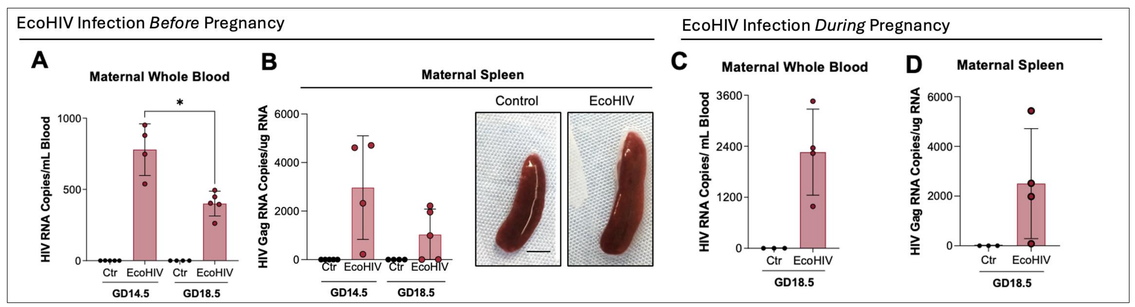
RESULTS



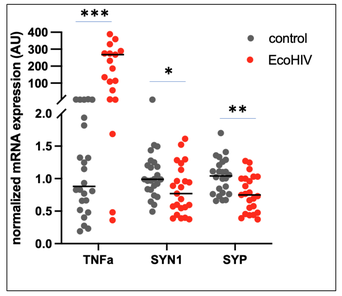
Maternal weight progression as % increase from plug detection is shown for EcoHIV-infected (red) & control (black) mice infected before pregnancy (A) or on GD11.5 (B, red arrow). Data are means ± SD, with significant effects for treatment in (A) (p=0.04) and treatment × time in (B) (p=0.01) by ANOVA.



Lower fetal weight, higher placenta weight, and lower placental efficiency observed at E18.5 in mice infected with EcoHIV as compared to controls. This parallels clinical data recorded in pre-ART era.[4]
N= 32-34/ group. Statistical comparisons via t-test. * p-value <0.05, ** p-value <0.01, *** p-value<0.001.



Elevated gag RNA levels in maternal whole blood (A, C) **and spleen** (B, D) were measured at GD14.5 or GD18.5 in mice infected with EcoHIV (red) before or during pregnancy, compared to uninfected controls (black). Data are shown as individual dots with median ± interquartile range, and statistical comparisons were made using the Mann-Whitney test. Picture shows spleen enlargement with EcoHIV infection.



Maternal EcoHIV infection is associated with evidence of neuroinflammation and neurotoxicity in fetal brain in the absence of fetal infection. mRNA of TNFa, synapsin1 (SYN1), and synaptophysin (SYP) assessed in fetal brain at E14.5. N= 24 fetuses/group. Statistical comparisons via t-test. * p-value <0.05, ** p-value <0.01, *** p-value<0.001.

CONCLUSION

- The EcoHIV pregnancy model represents the first mouse pregnancy model that includes HIV infection
- *In utero* EcoHIV exposure was associated with fetal growth restriction and placental insufficiency even in the absence of fetal infection, paralleling clinical findings.
- The larger placenta size and overall decreased efficiency could potentially mean a compensatory mechanism is at play – further investigation required
- Evidence of fetal brain inflammation and neurotoxicity with maternal EcoHIV infection, in the absence of fetal infection.

ACKNOWLEDGEMENTS

CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada
UNIVERSITY OF TORONTO
UHN

REFERENCES

1. HIV and AIDS - StatPearls - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK534860/. **2.** Potash MJ, Chao W, Bentsman G,et al. A mouse model for study of systemicHIV-1 infection, antiviral immune responses, and neuroinvasiveness. Proc. Natl Acad. Sci. USA. 102:3760 (2005). **3.** Chao-Jiang Gu, Alejandra Borjabad, Eran Hadas et al. EcoHIV infection of mice establishes latent viral reservoirs in T cells and active viral reservoirs in macrophages that are sufficient for induction of neurocognitive impairment https://doi.org/10.1371/journal.ppat.1007061 (2018) **4.** Morphological aspects of the placenta in HIV pregnancies - ScienceDirect.https://www.sciencedirect.com/science/article/abs/pii/0143400488900070?via%3Dihu