



# Modeling Zika virus tissue tropism in rhesus macaques to define the risk of donor derived transmission

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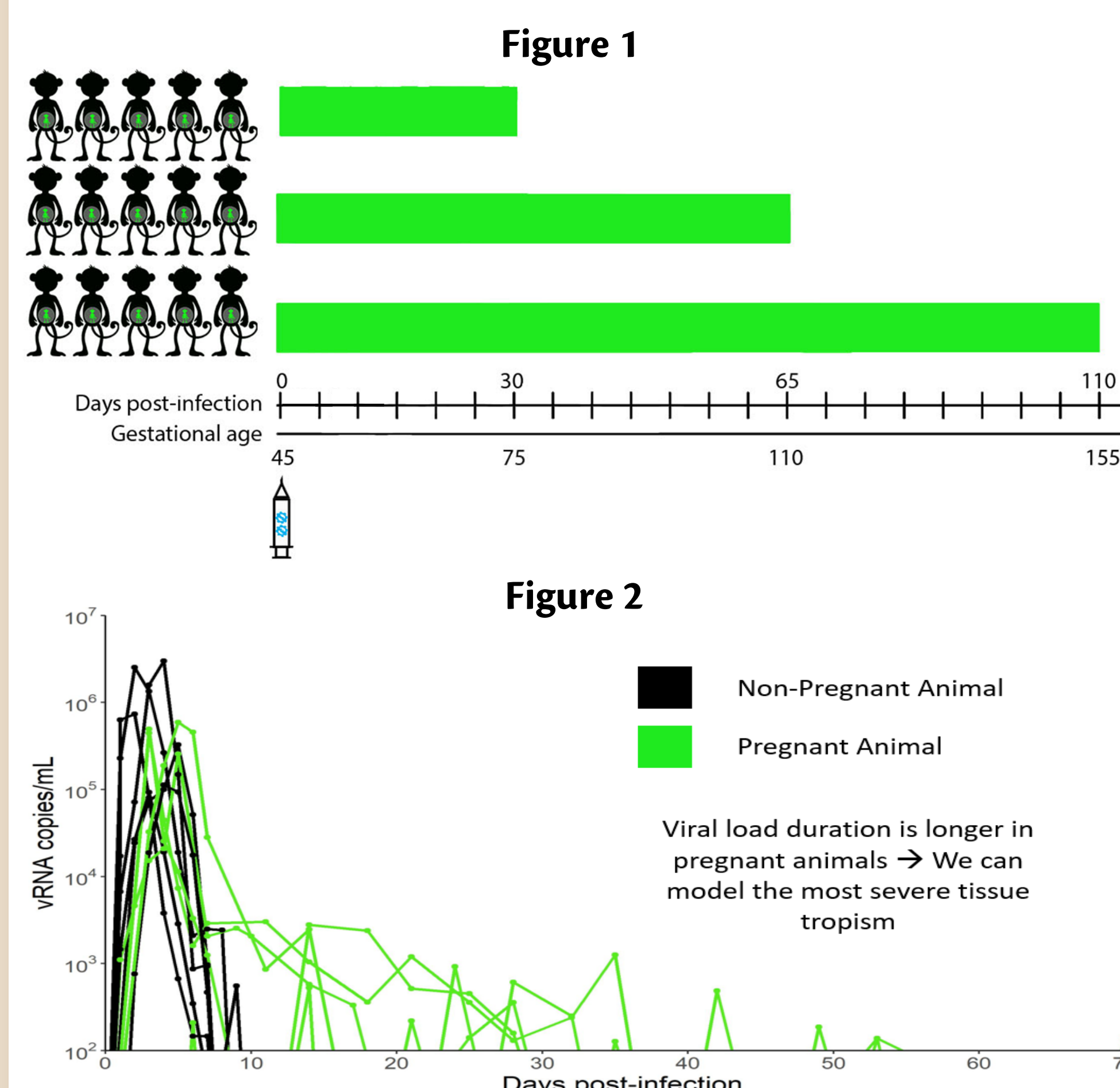
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## BACKGROUND

- In 2016 the World Health Organization declared the spread of Zika virus (ZIKV) in the Americas a public health emergency.
- It is unclear how ZIKV infection may be transmitted from donor to recipient in solid organ transplants.
- Travelers from areas with active ZIKV outbreaks often disqualified or delayed organ and tissue donation abilities for fear of donor-derived ZIKV infection → increases discrepancy between number of donors and number of waitlisted recipients
- We aim to define ZIKV tissue tropism and the risk of donor derived transmission to hopefully maintain a larger donor pool in ZIKV endemic regions.

## METHODS

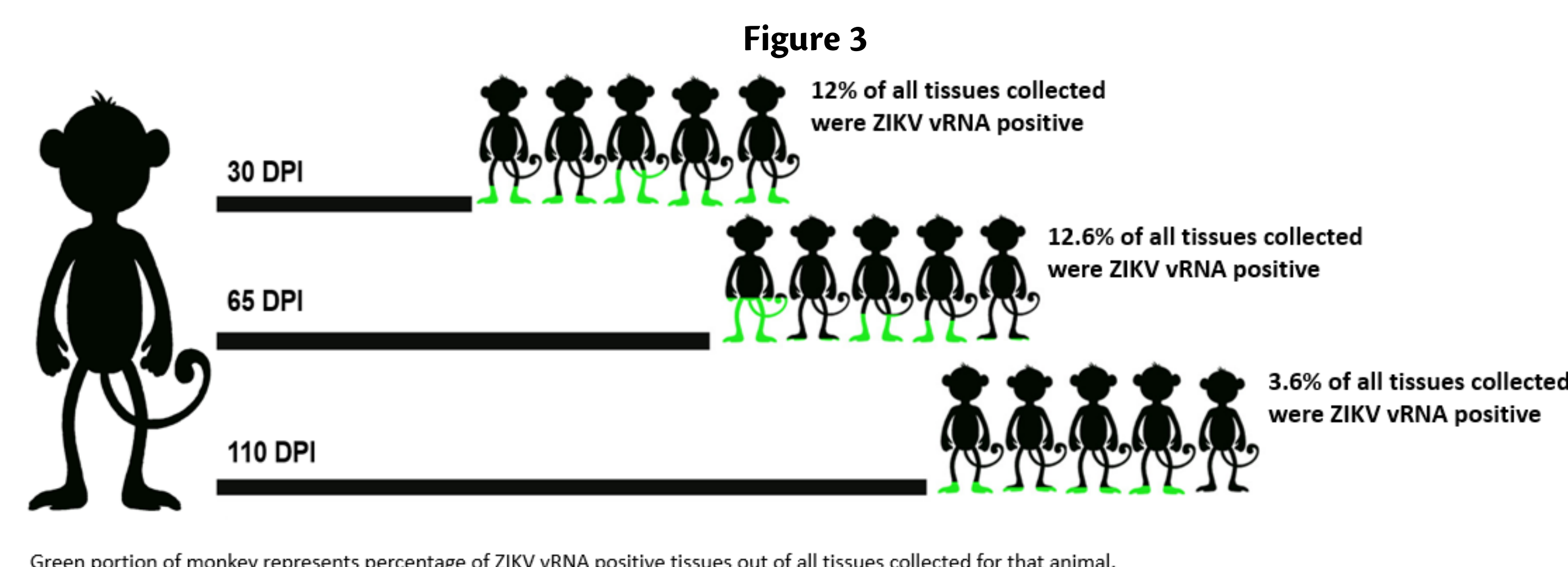
We subcutaneously inoculated 15 Indian-origin rhesus macaques (RMs) with an isolate of ZIKV as seen in Figure 1. All RMs were in mid to early gestation at the time of inoculation. We inoculated pregnant RMs because pregnancy induces longer plasma viremia and we wanted to model the worst-case scenario where a donor may be viremic at the time of organ donation as seen in Figure 2. Animals were euthanized and underwent necropsy at 30, 65 and 110 days post-inoculation. ZIKV viral loads were measured in at least 45 tissues per animal via qRT-PCR.



**ZIKV vRNA is most commonly found in lymph nodes. It is less commonly found in other frequently transplanted organs including the kidney, liver, small bowels, heart, pancreas, and lungs.**

## RESULTS

- Plasma viremia duration >10 days in 13 of 15 RMs
- The percentage of total positive tissues at each timepoint is displayed in Figure 3
- Lymph nodes were the most commonly infected tissue
  - 30 dpi: 63% of ZIKV vRNA positive tissues were lymph nodes
  - 65 dpi: 51% of ZIKV vRNA positive tissues were lymph nodes
  - 110 dpi: 69% of ZIKV vRNA positive tissues were lymph nodes
- Reproductive and maternal/fetal interface tissues were the second-most commonly infected tissues



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## CONCLUSIONS

- ZIKV vRNA is most commonly found within lymph nodes.
  - Lymph nodes included in lung and small bowel transplants → could pose a risk of donor-derived ZIKV transmission
- Virus detection within other commonly transplanted tissues, such as the kidney and blood vessels was much less common.
- Presence of vRNA doesn't necessarily mean infectious virus is present. Future studies will need to address this.
- Donor-derived ZIKV transmission from other commonly transplanted organs, such as the liver, seems unlikely since no vRNA was detected in these organs.

## DATA

The following table displays all maternal tissues and organs that contained ZIKV vRNA upon necropsy, with the exception of immune system tissues. Each column under 30 dpi, 65 dpi, and 110 dpi represents 1 animal, and green squares indicate ZIKV vRNA was found in the listed tissue of that specific animal.

System	Tissue/Organ	Number of Infected Animals		
		30 dpi	65 dpi	110 dpi
Digestive	Colon			
	Jejunum			
	Liver			
Renal	Kidney			
	Bladder			
Reproductive/Maternal Fetal Interface	Amniotic/Chorionic Membrane			
	Uterus			
	Vagina			
Cardiovascular	Endocardium			
	Pericardium			
Circulatory	Femoral Vein			
Connective	Epidermis			
	Fascia Quadriceps			
Musculoskeletal	Cartilage			
	Femur			
	Hand Tendon			
	Hand Nerve			
Nervous	Optic Nerve			
	Sciatic Nerve			
Pulmonary	Bronchus			
	Lung			
Endocrine	Mammary Gland			
	Pancreas			
	Thyroid			