Understanding the Viral and Host Transmission Fitness Factors Associated with Different Routes of HIV-1 Subtype B Transmission

Yiying Zhang[1], Eric Arts[1]
[1]Microbiology & Immunology, Schulich School of Medicine & Dentistry,
Western University, London, ON, Canada

Schulich MEDICINE & DENTISTRY

Western

Background

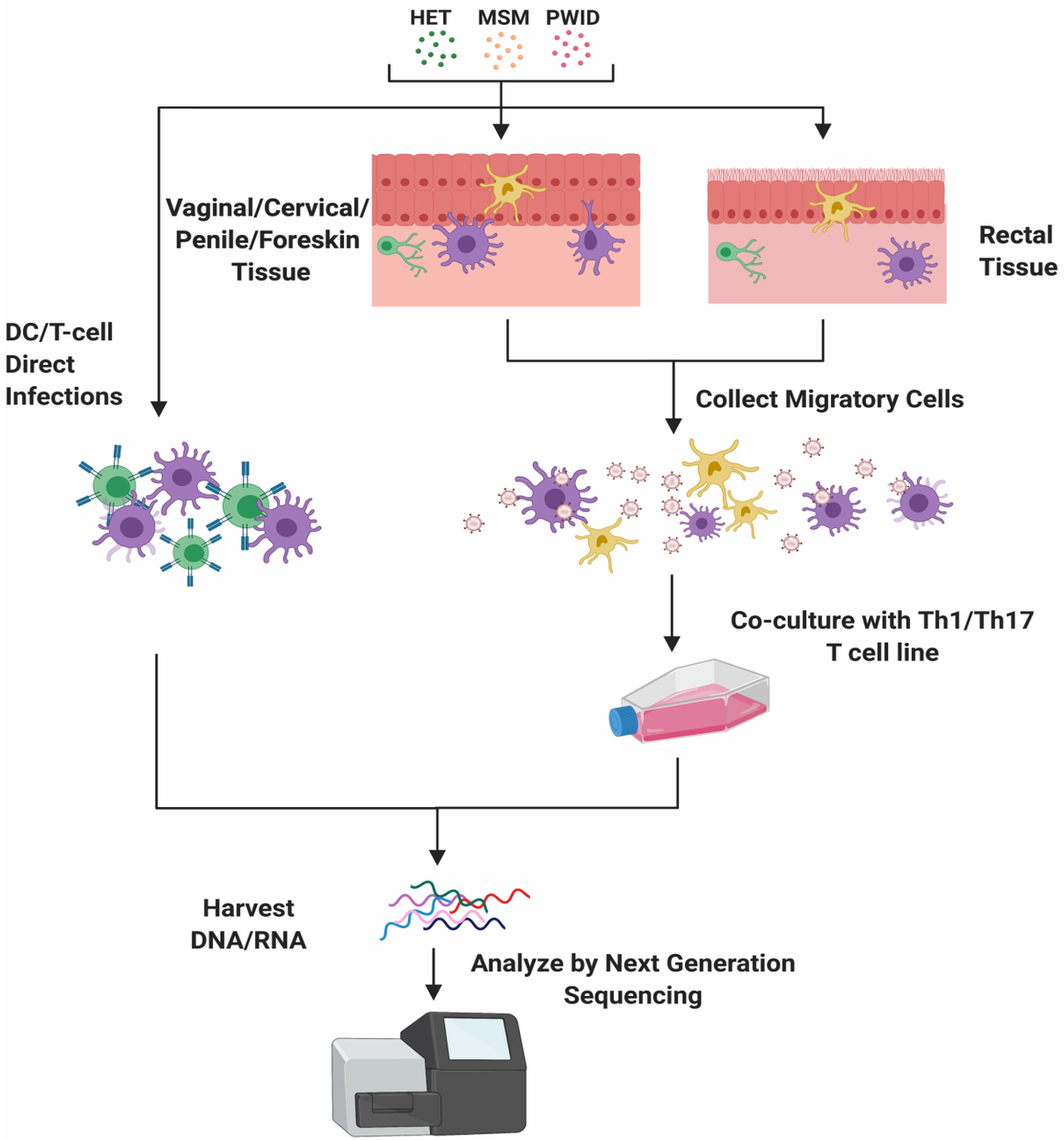
- HIV-1 transmission modes can be divided into mucosa contact and blood contact.
  - Mucosa contact includes heterosexual contact (HET) and men who had sex with men (MSM).
  - Blood contact includes people who inject drugs (PWID) and people who received contaminated blood transfusions (CBT).
- Transmission bottleneck exists during HIV-1 transmission. Virus overcomes transmission bottleneck and establishes systematic infection in the host is defined as transmitted/founder (T/F) virus.
- Specific traits that allow for successful transmission have not been identified clearly.

Objectives

- Determine the transmission fitness of HIV-1 subtype B transmitted/founder (T/F) viruses from different transmission modes by *in vitro* competitions on cell lines and human tissues.
- Analyze the contribution of possible phenotypic factors to HIV-1 subtype B viruses transmission fitness.

Methods

In vitro Competition

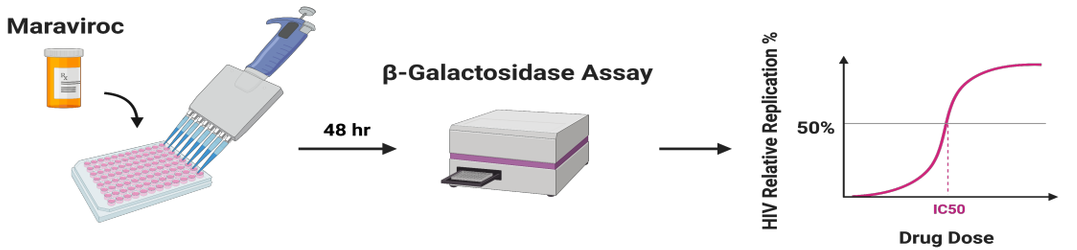


Multi-virus Competition Strategy of T/F Viruses

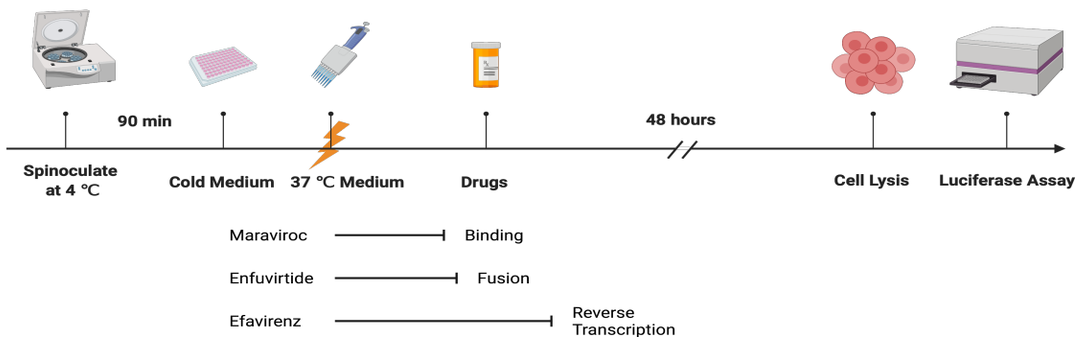
Group	T/F Viruses				
A	B19	40	41	78	1
B	82	37	B4	B7	79
C	B19	40	41	B7	79
D	B19	40	41	82	37
E	78	1	B4	B7	79
F	78	1	82	37	B4
G	B19	40	41	B4	82
		PWID	HET	MSM	

Phenotypic Assays

Entry Inhibitor Sensitivity Assay

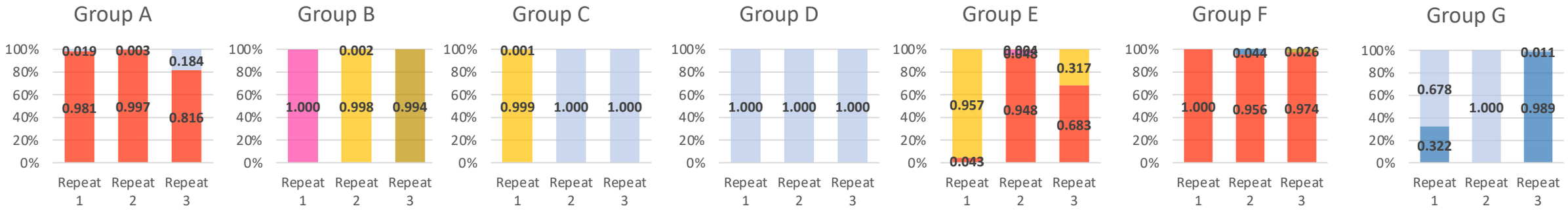


Kinetic Fusion Assay

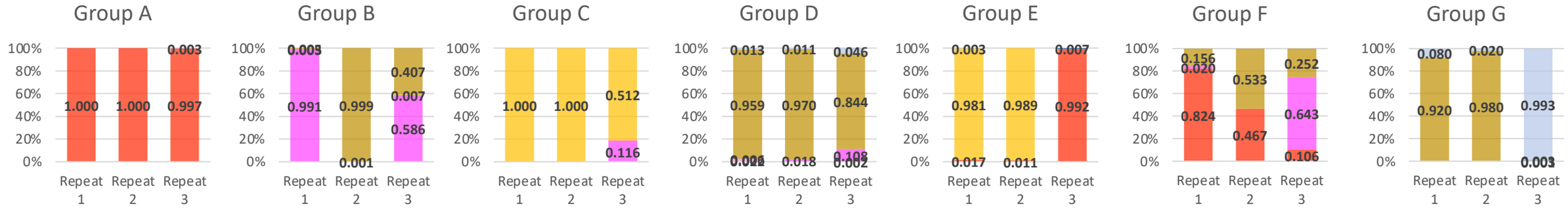


Results

Competition on Th1 Cells

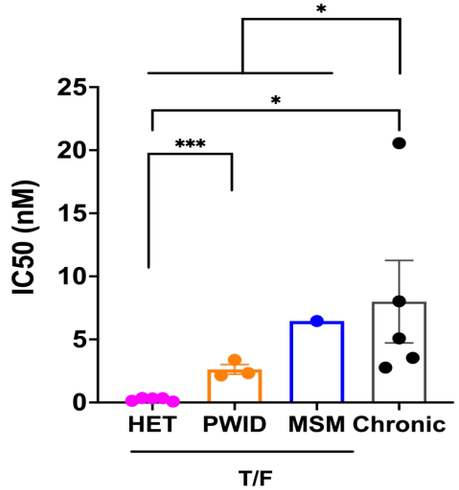


Competition on Th17 Cells

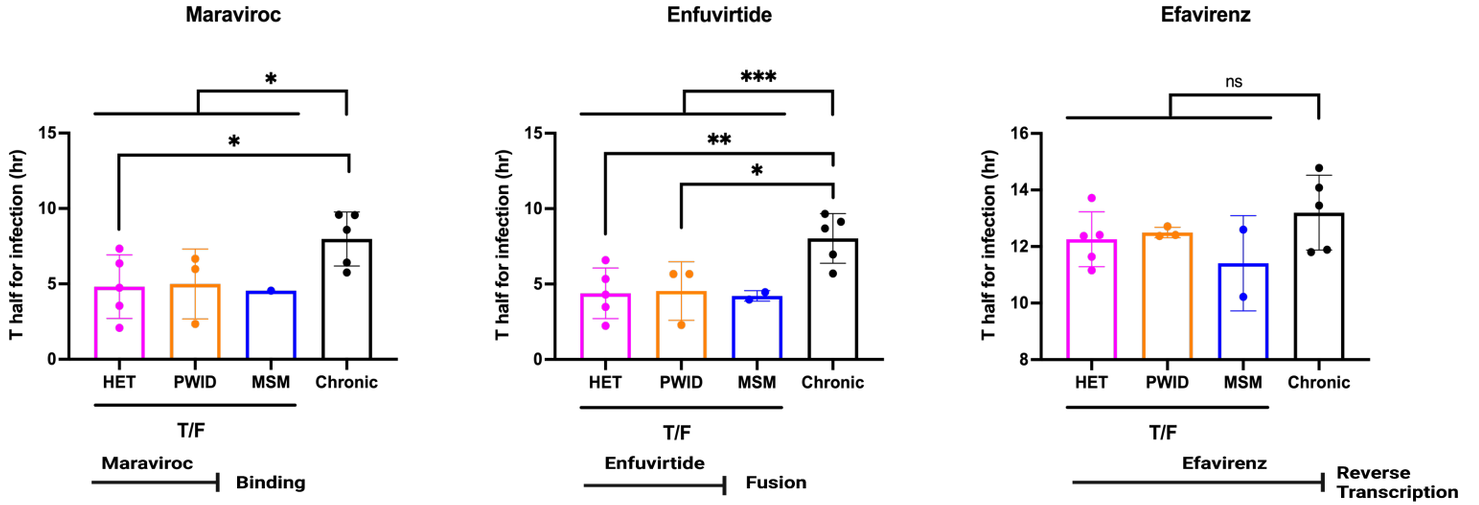


1 40 41 37 B7 78 79 82 B4 B19

Viruses Sensitivity to Maraviroc



Viruses T1/2 against Drugs



Conclusions

- T/F viruses from HET and MSM often outcompete T/F viruses from PWID in T helper type 1 (Th1) cells
- T/F viruses from PWID dominates infection in T helper type 17 (Th17) cells.
- T/F viruses are less resistant to maraviroc and require more stringent CCR5 conformation, especially viruses from HET.
- T/F viruses have faster entry speeds than chronic viruses.

Significance

- This project will establish key viral phenotypes contributing to successful virus transmission to inform the design of a robust and protective anti-HIV vaccine.
- The drugs sensitivity information provided by this project will help the improvement of antiretroviral therapy.

Acknowledgements

- This project is funded by NIH and CIHR.
- Methods schematic were created by BioRender.

National Institutes of Health

CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada