Cell-associated HIV transmission: the neglected pathway
Trojan Horse Leukocytes in AIDS Transmission
Anderson DJ, Yunis EJ. NEJM 1983

- T cells and macrophages in semen could transmit HIV
- Intracellular virus is protected from antibodies and antimicrobial proteins
- Cell-to-cell HIV transfer is highly efficient
Questions:

- What are the infectious cells in semen?
- How long do they survive?
- Does CA-HIV have a distinctive genotype?
- What are the molecular events that can be targeted by HIV prevention strategies?
- What are the best in vitro and animal models to study CA-HIV transmission?
- Can CA-HIV transmission be blocked with antibodies, microbicides, ARVs?
In Vitro Tissue Models of Cell-Associated HIV Transmission

- Microscopic studies
- Transcytosis assays
- Explant assays
Adhesion of leukocytes to epithelial cells

D Phillips 1997
Directional HIV shedding towards epithelial surface

Phillips 1997
Macrophage beginning to infiltrate endocervical explant
Macrophages attached to surface of VEC tissue
Macrophages infiltrating VEC stratified squamous epithelium

1 hr
Macrophages have crossed the epithelium and are located in the lamina propria.
JPEG graph of infiltrating cells
TNF-a treated VEC tissue is more permeable to macrophage infiltration

PBS treated control

0.1ug/mL TNF

1ug/mL TNF

10ug/mL TNF
Quantitation of infiltrating cells in TNF-a treated VEC tissue

Total U937 Infiltration of EpiVaginal Tissue

- PBS total
- TNF 0.1ug total
- TNF 1ug total
- TNF 10ug total

- <50um
- 50-100um
- 100-200um
- 200um+
Evidence for cell-associated HIV transmission: in vitro models

- HIV-infected leukocytes are more efficient than free virus at transmitting HIV across polarized epithelial monolayers via transcytosis
  (Tan et al 1993; Chancey et al 2006; Bomsel 1997; VanHerreweghe 2007)

- Both infected cells and free virus infect subepithelial cells in the cervical explant model
  (Collins et al 2000)
Recent In Vitro Studies

• SIV-infected PBMCs crossed the mucosal epithelium of rectal explant tissues and infected target cells.

• HIV-infected PBMCs crossed the mucosal epithelium of human urethral explant tissues and infected subepithelial macrophages
  *Ganor Y et al Mucosal Immunology 2013*
# Summary of Cell-Associated HIV Transmission Models

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