Investigating the cervicovaginal mucus barrier properties of women with bacterial vaginosis

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Mucus is a barrier to pathogens

Mucus coats entry points

Highly adhesive and viscoelastic

Mucus can sterically and adhesively block pathogens

1. Iwasaki, A., Nat Rev Immunol. 2010
2. Sanders et al., AJRCCM, 2000
3. Cone, R.A., Mucosal Immunology, 1999
Cervicovaginal Mucus (CVM)

- Mucus is secreted by endocervix
- Expelled into vaginal compartment through cervical os
- Mixes with: vaginal transudate, exfoliated epithelial cells, bacterial secretions
- In FRT, mucus lining is ~10 µm thick
- CVM is home to microbiota that can produce enzymes to modulate it
- Enzymes can degrade barrier properties of CVM
The vaginal microbiota varies among women

- **Lactobacilli** dominated:
  - Near monomicrobial *Lactobacilli*
  - pH < 4.0

- Polymicrobial culture/Bacterial Vaginosis (BV):
  - Overgrowth of many different mostly gram-negative species
  - pH > 4.5
  - Recurrence rate >50% within 12 months
  - BV incidence rate **29.2%** in the US
  - BV increased risk of HIV acquisition by **60%**
  - Risk factor for adverse obstetric outcomes, PID, acquisition/transmission of STIs
Methods

• Donor Mucus
  Undiluted CVM can be obtained from self-administered collection device
• mCherry fluorescently labeled HIV

• Quantitative Microscopy Technique
  - Multiple Particle Tracking (MPT)
  - Obtain x, y positional data over time
  - Calculate Mean-Square Displacement (MSD)
HIV is diffusive in polymicrobial CVM

*Lactobacillus*-dominated

Polymicrobial/BV
HIV is diffusive in polymicrobial CVM

Polymicrobial/BV

Lactobacillus-dominated

Distance Traveled

<MSD> (µm²)

Time Scale (s)

Water

Polymicrobial/BV

Lactobacillus-dominated
HIV is diffusive in CVM even after antibiotic treatment

- BV is treated with course of antibiotics (Metronidazole, Clindamycin, Tinidazole)
- 1 month after treatment, HIV is still diffusive in CVM
CVM barrier properties similar between women with symptomatic and asymptomatic BV

- **Symptomatic** - presented at a clinic for treatment
- **Asymptomatic** - self-reported “healthy” and without vaginal symptoms
- HIV diffusion was similar between these two groups
HIV diffusion correlated with pH and lactic acid concentration

- HIV diffusion correlated with higher pH (>4.5)
- *Lactobacillus* make lactic acid
- Higher % lactic acid correlates with HIV trapping
Future Directions

• Mechanisms by which BV-associated bacteria degrade CVM barrier properties

• Prospective clinical study to understand how Depo-Provera may modulate the microbiota thus effecting the CVM barrier properties
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