ASPIRIN USE IMPACTS T CELL TRAFFICKING AND CORRELATES WITH LOWER HIV TARGET CELLS AT THE GENITAL MUCOSA

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The authors do not have conflict of interest to declare

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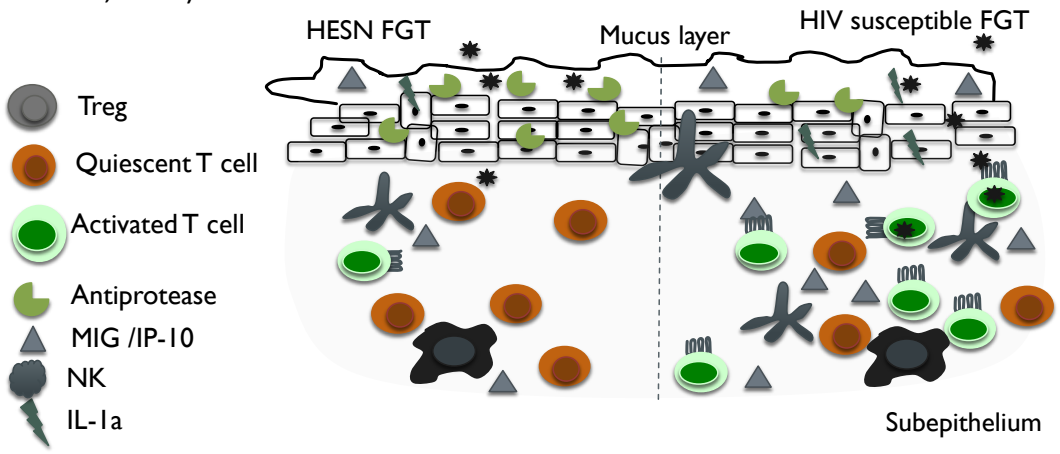
Introduction

- In Africa, women are **twice as likely** as men to be infected by HIV during unprotected vaginal intercourse.

- Despite being at high risk of HIV infection, some individuals remain HIV negative (**HESN**).

- We have associated this natural protection to HIV with a unique immune phenotype called **Immune Quiescence**. This is defined by a lower level of baseline T cell immune activation, lower level of inflammatory cytokines at the genital tract, and higher level of regulatory T cells in the blood (Card and al, 2013).



- To **mimic** this unique immune phenotype among susceptible women, we gave a daily dose of **aspirin (81mg)** to healthy women.

- Aspirin (ASA):
  - Non-steroidal anti-inflammatory drug;
  - Use daily for the prevention of cardiac diseases
  - Widely accessible, safe record, affordable and community accepted .

- In a pilot study, we showed that daily use of **ASA, results in a 39% decrease in the proportion of HIV target cells** at the female genital tract.

Gap in knowledge:
Is the decrease of genital HIV target cells observed among those taking aspirin is due to a local decrease of immune activation or changes in cell trafficking?

Methods and Participants' Description

Hypothesis: Daily use of ASA will decreased the trafficking of activated T cell at the female genital tract.

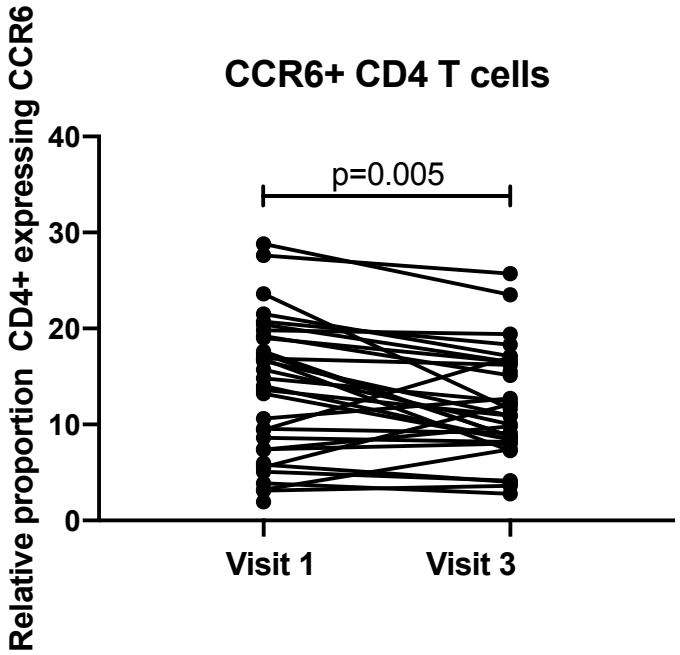
Study design:

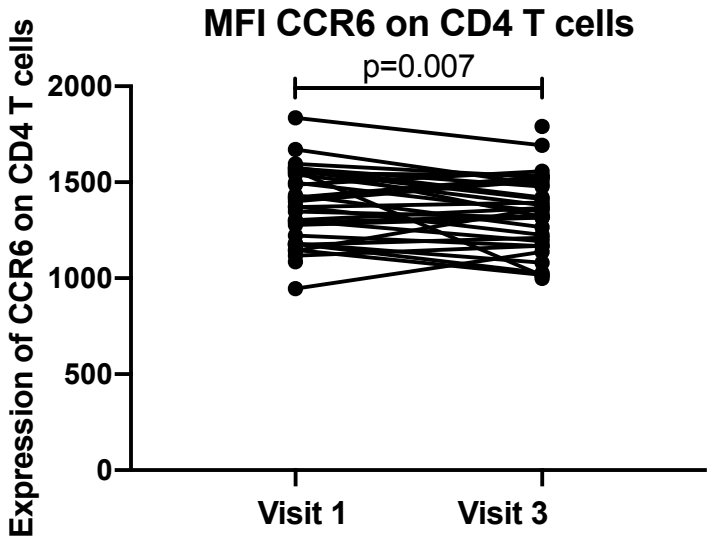
- Thirty-six HIV uninfected women were enrolled for this study.
- Participants were asked to take 81mg of ASA each day for six weeks.
- Blood was taken at baseline (Visit 1 - V1) and six weeks later (Visit 3 – V3).
- Flow cytometry was performed on PBMC.
- Trafficking markers measured: CCR5 (for migration to genital mucosa), CXCR3 (for tissue and lung) , CD103 (general tracking to mucosa), CCR6 (gut), CD25 (activation), CD29 (β1).

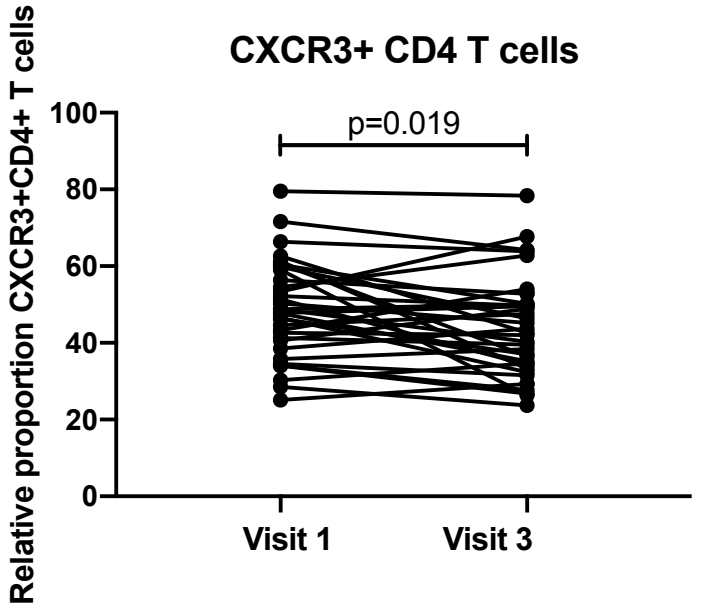
Sociodemographic characteristics of the participants

General Characteristics	
Age (mean [SD])	32 [8.0]
Douching (n(%))	21 (55.3)
Contraception	
No Hormonal Contraception (n(%))	12 (31.6)
Depot/DMPA (n(%))	21 (55.3)
Oral HC (n(%))	2 (5.2)
Regular Partner	
Yes (n(%))	30 (78.9)
No (n(%))	4 (10.5)
Not Disclosed (n(%))	4 (10.5)
Times sexual intercourse with regular partner in last 7 days (mean [SD])	1.19 [1.1]
Used condom with regular partner in the last 7 days (n(%))	5 (13.2)

Results







- After 6 weeks on ASA we observed **lower proportion of CD4+ T cells expressing CCR6 and CD4+ T cells expressing CXCR3** in the blood.
- The level of CCR6 expressed per CD4+ T cells was **lower** after ASA uptake compared to baseline.
- We did not observed changes in the proportion of CD4+ T cells expressing CCR5 and CD103 in the blood.
- Proportion of Th17 expressing CCR6 was similar between visits.

Discussion/Conclusion

- CCR6 is an important marker for Th17 and Treg activation during inflammation. ASA use was associated with a decreased in bulk CD4+ CCR6+ cells but **did not affect the Th17 cells expressing CCR6**.

- CCR6 is also a marker for activated T cells to migrate to the gut. ASA use was associated with a **decrease in the proportion** of activated T cells that can migrate to the **gut mucosa**.

- ASA use was associated with a **decrease in** the proportion **of CD4+ expressing CXCR3**. CXCR3 is highly expressed on activated Th1 cells and lead to migration of activated T cells to inflamed peripherical tissues and re-entry to lymph node.

- ASA use was associated with a **decrease in the trafficking of activated T cells** to mucosa.
- ASA use is associated with a lower proportion of **HIV target cells at the mucosa**.

Thank you!

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- Lucy Mwangi
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