University of Zimbabwe, School of Medicine

UZCHS-CTRC

Saving Lives Through Innovative Research Strategies

Contraceptive Hormone Induced Changes - CHIC

INNOVATION IN HIV PREVENTION RESEARCH WORKSHOP

Cresta Lodge, Harare

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Background

- Approx. 210 million hormonal contraceptive users globally, 35 million on injectable DMPA
- DMPA use is common in Sub Saharan Africa, a region host to >70% of global HIV burden
- Approx. 15% of the 2.2 million Zimbabwean women on modern contraceptives use DMPA
- Epidemiologic & Laboratory studies: possible association between DMPA use and increased HIV acquisition risk but findings have not been consistent

We therefore sought to investigate the biological plausibility of the observed increased HIV acquisition risk by measuring the number of HIV target cells in female genital tract and T-cell responsivity to stimulation

Untangling the mixed data on HC-HIV

Two parallel approaches :

Objective:
To assess the impact of contraceptive methods on the numbers and activation status of immune cells in the genital tract and frequency of cytokine producing T-Cells in peripheral blood following polyclonal stimulation ex vivo

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  cervical HIV target cells compared to baseline after 3 months of use.
- DMPA use decreases T cell activation to polyclonal stimulation as measured by Cytotoxic T-Lymphocyte Associated Protein–4 expression

Study Methods

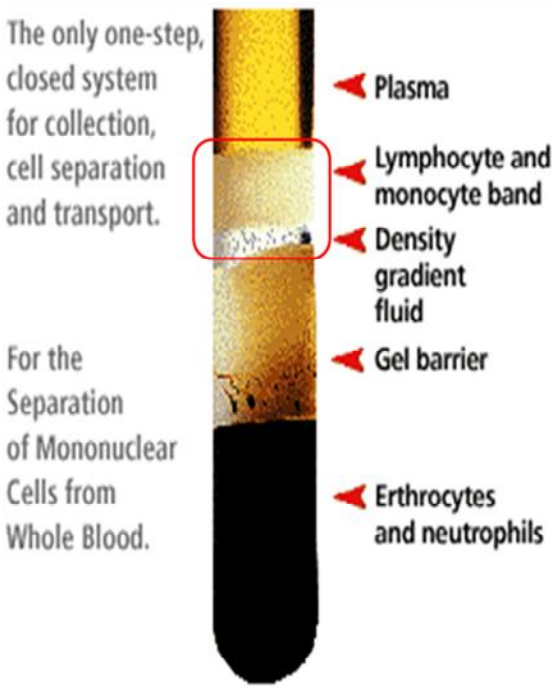
- **234** Healthy Women Ages 18-34 in Harare. (Median age- 27.7yrs)
  - HIV negative
  - Free of STIs (GC, CT, *Trichomonas*, active HSV)
- No recent exogenous hormone use
  - No hormonal or intrauterine contraceptives for >30 days
  - No DMPA for >10 months
  - All in follicular phase of menstrual cycle (day 1-14) and not bleeding
  - **Confirmed objectively by UPLC-MS/MS at each visit**
- Contraception (started immediately after baseline sampling*)
  - **Injectables**: DMPA-**43**, Net-EN-**41**, MPA/E2-**36**
  - **Implants**: LNG - **36** and ENG - **37**
  - **IUD**: copper - **41**)
- Immune cell populations from **PBMCs** and **cervical cytobrushes** were quantified by flow cytometry

Laboratory cell preparation

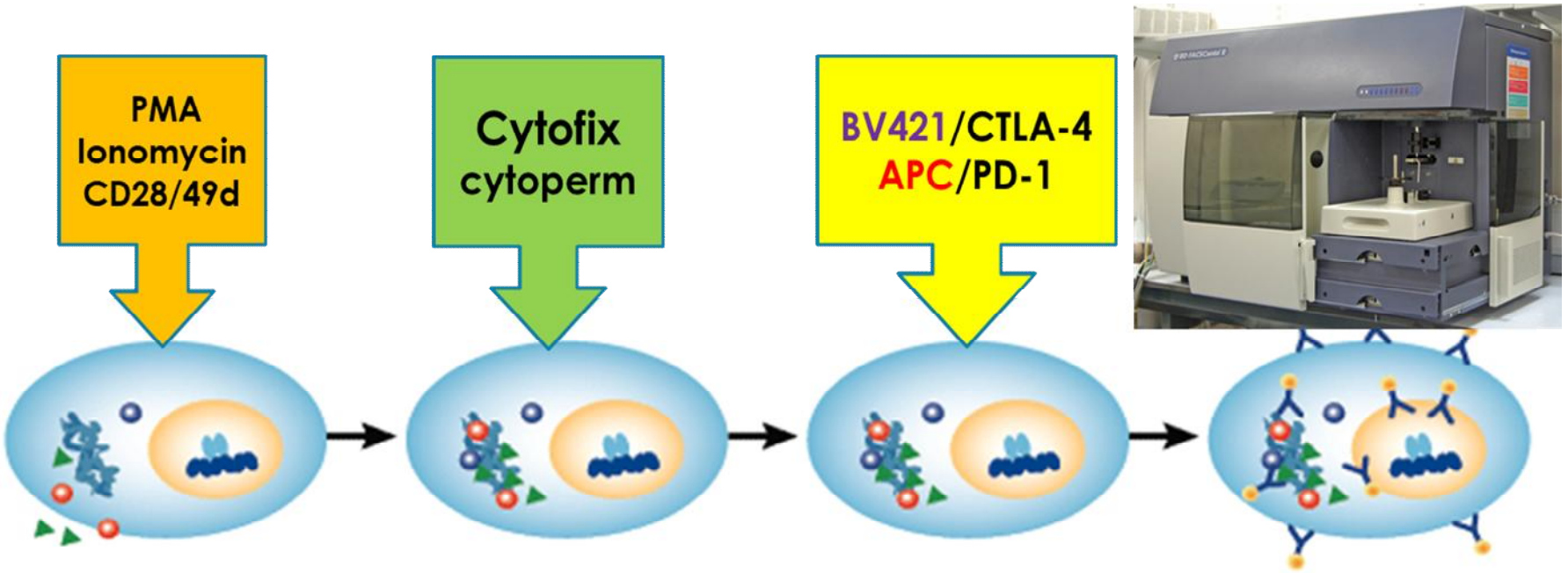
Empty CPT Tubes

Blood filled CPT tubes

After Centrifugation



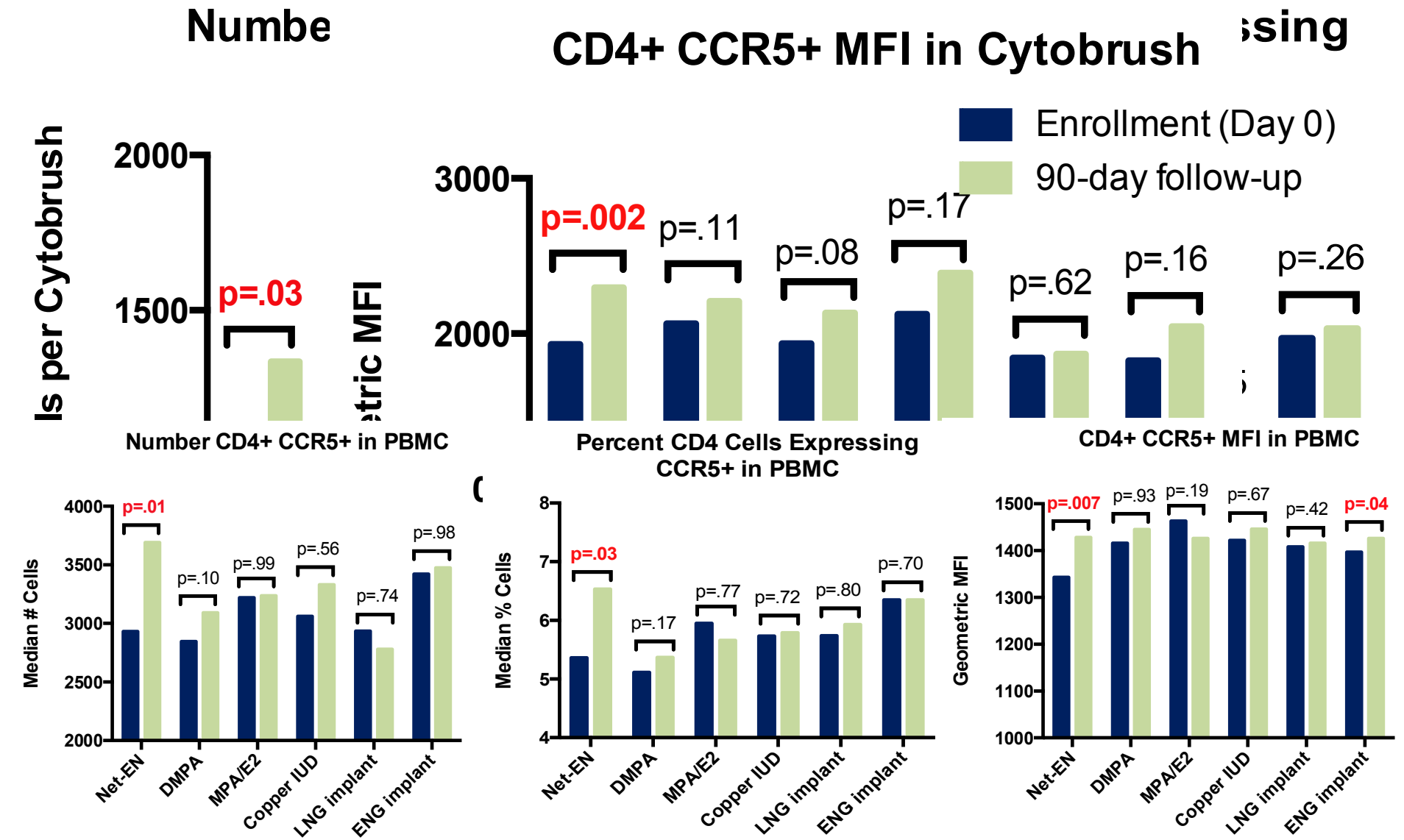
Intracellular staining and Flowcytometry



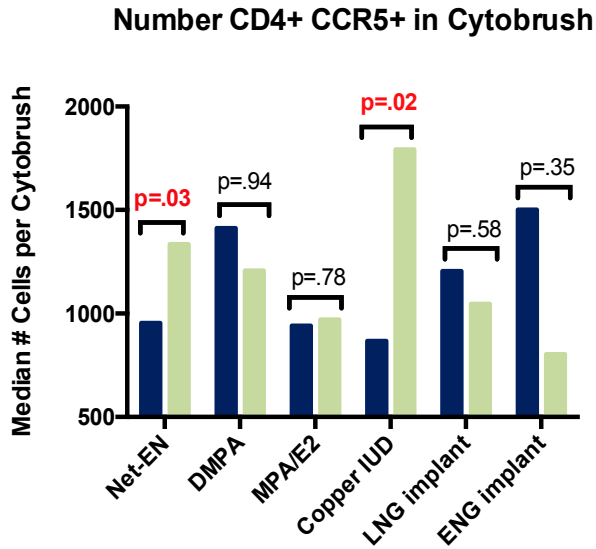
CD4+, CD8+, CD69+.
CCR5, TNF-α, IFN-Ɣ,
IL-4
IL-13

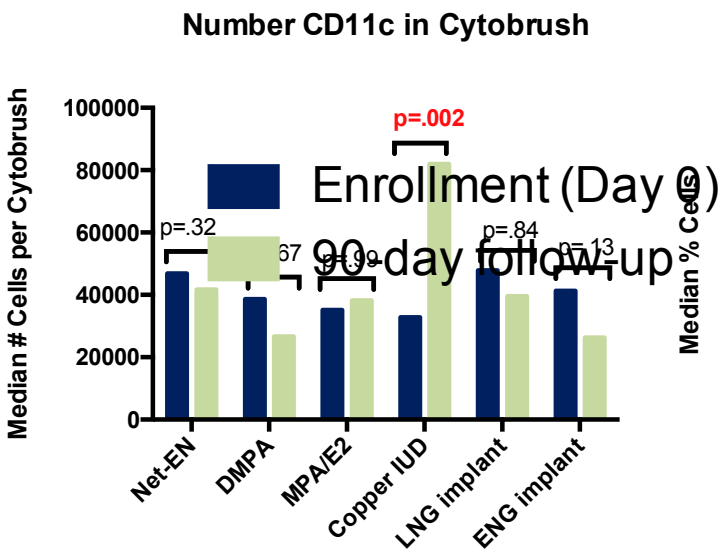
Results

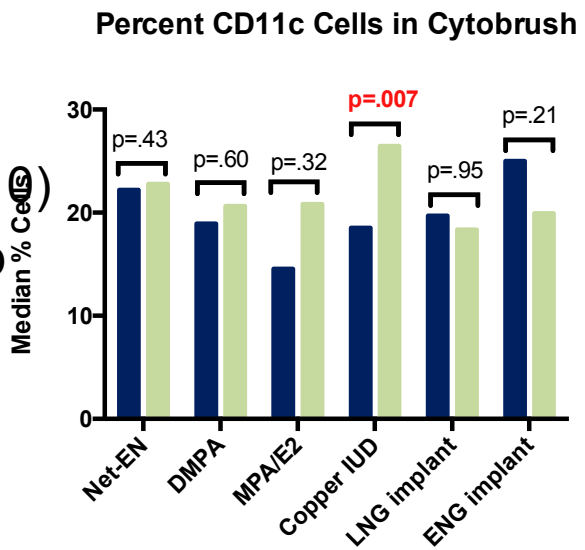
Net-EN Use Associated with Local and Systemic Increases in HIV-Target Cells



Copper IUD Use Associated with Local Increases in HIV-Target Cells

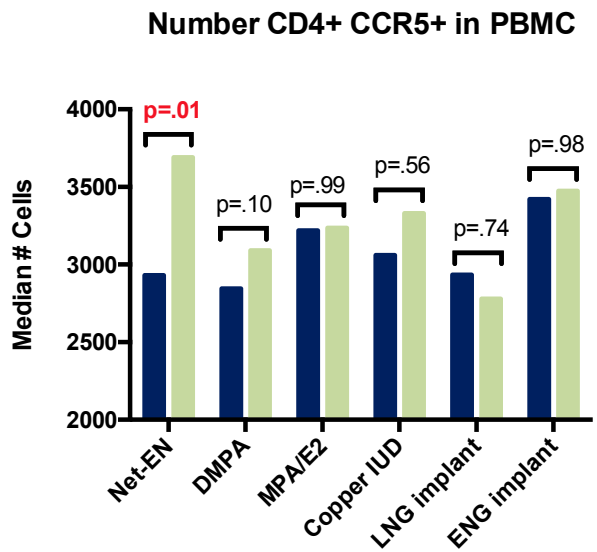


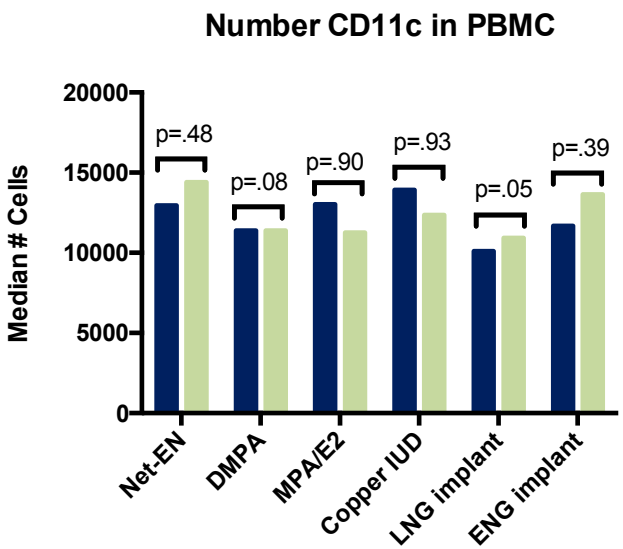


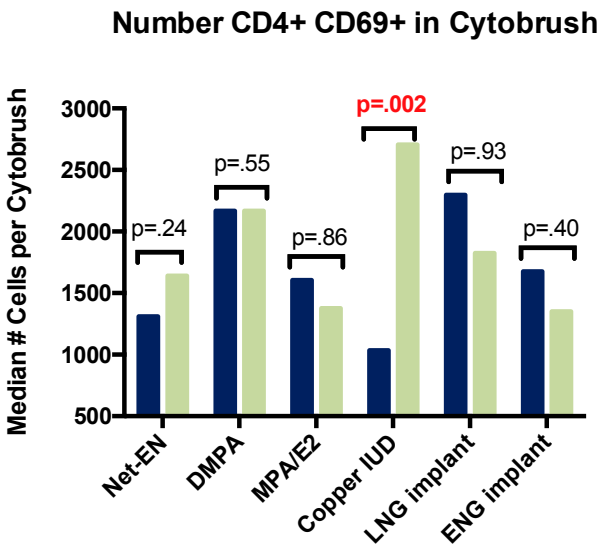


Enrollment (Day 0)

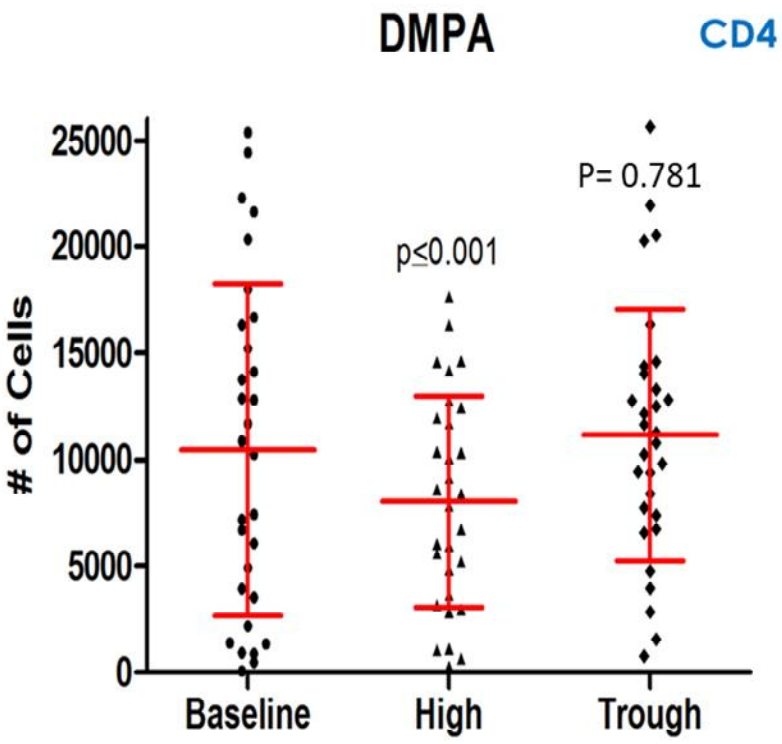
90-day follow-up

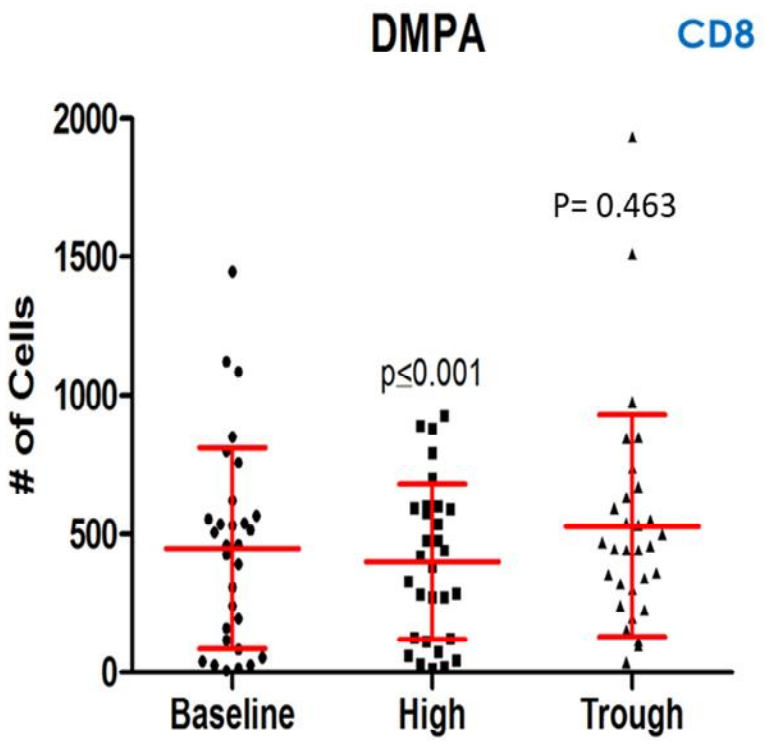




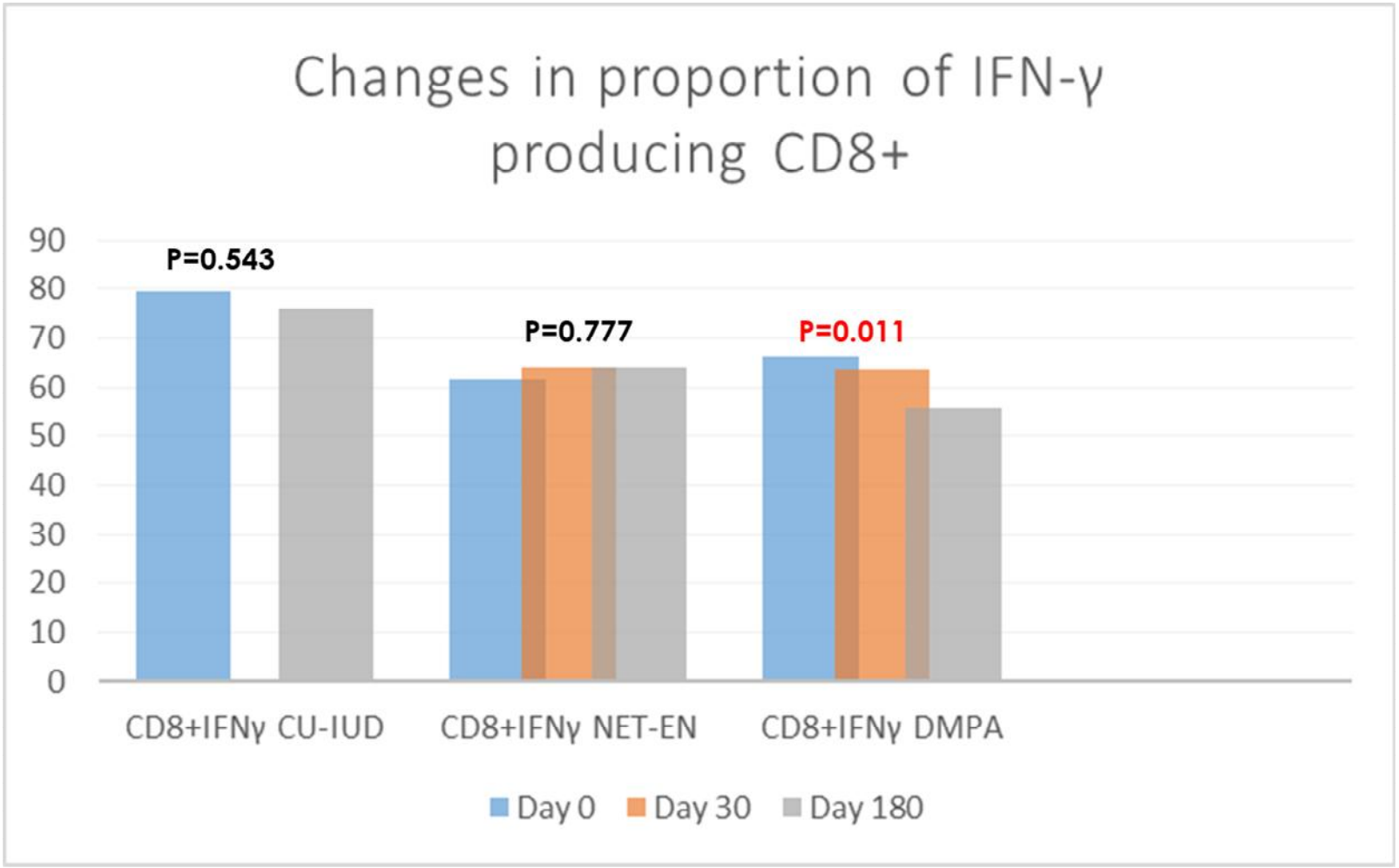


DMPA reduced T-Cell responsivity to polyclonal stimulation at steady state levels as measured by CTLA-4 expression





DMPA depletes proportion of CD8+IFN-Y+ cells following polyclonal stimulation



What is a reasonable level of risk

No increased risk of HIV acquisition

Increased risk of HIV acquisition

Conclusions

- Net-En and not DMPA is associated with increased CCR5 and CD69 on CD4+ cells in peripheral blood and female genital tract.
- CU-IUD is associated with increased CCR5 and CD69 on CD4+ cells in female genital tract
- DMPA, at high serum concentrations is associated with decreased T-cell responsivity to polyclonal stimulation
- DMPA is associated with decreased frequency of CD8+IFN-Ɣ+ cells in PBMCs following polyclonal stimulation

Thank you

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- UZCHS-CTRC Clinic and Lab Teams

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