

Progesterone Increases are Associated With HIV Susceptibility Factors in Women

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HIV susceptibility due to progesterone

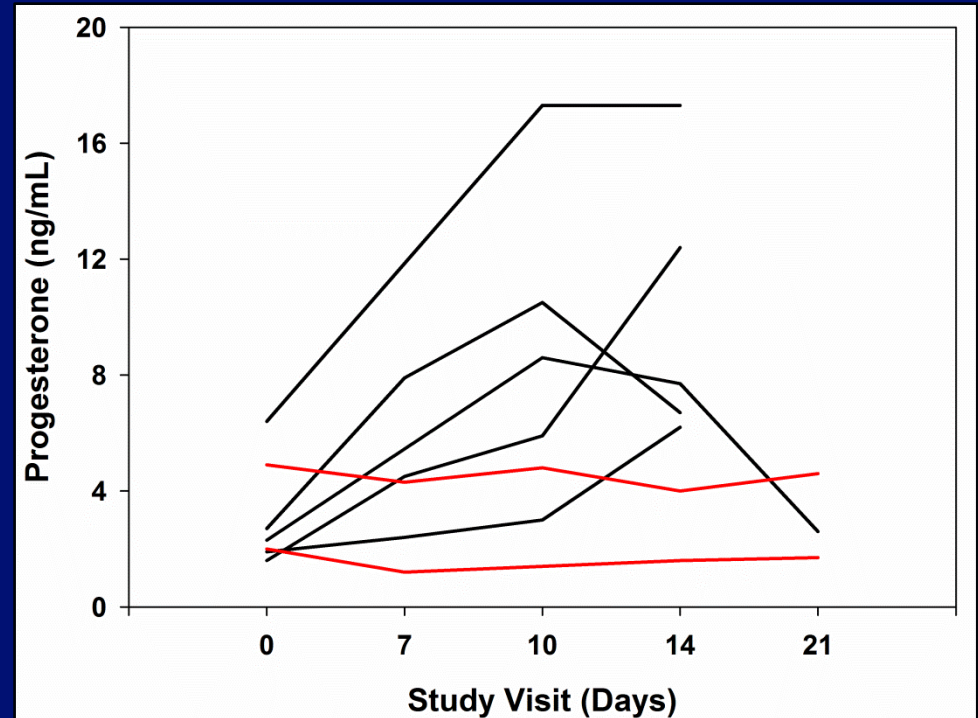
- **Association between HIV risk and exogenous progesterone usage**
 - Polis CB and Curtis KM. 2013. *Lancet Infect Dis*
 - Ralph LJ *et al.* 2015. *Lancet Infect Dis*
 - Morrison CS *et al.* 2015. *PLoS Med*
- **Association between SHIV infection and endogenous progesterone levels in macaques**
 - Vishwanathan SA *et al.* 2011. *J Acquir Immune Defic Syndr*
 - Kersh EN *et al.* 2014. *J Med Primatol*
- **Do increased progesterone levels during the luteal phase increase markers of susceptibility in HIV target cells?**

Study Design

- **7 participants scheduled for 5 study visits in a single menstrual cycle**
 - Approximately days 0, 7, 10, 14, 21 following menses
- **Whole blood collected at each visit**
- **Plasma:**
 - Luminex multiplex assay for Progesterone and Estradiol
- **PBMC:**
 - Stained with antibodies to CD4, CCR5, CD38
 - Stimulated *ex vivo* for 5 hours in presence of golgi inhibitors
 - Stained for intracellular production of TNF α , IL-2 and IFN- γ

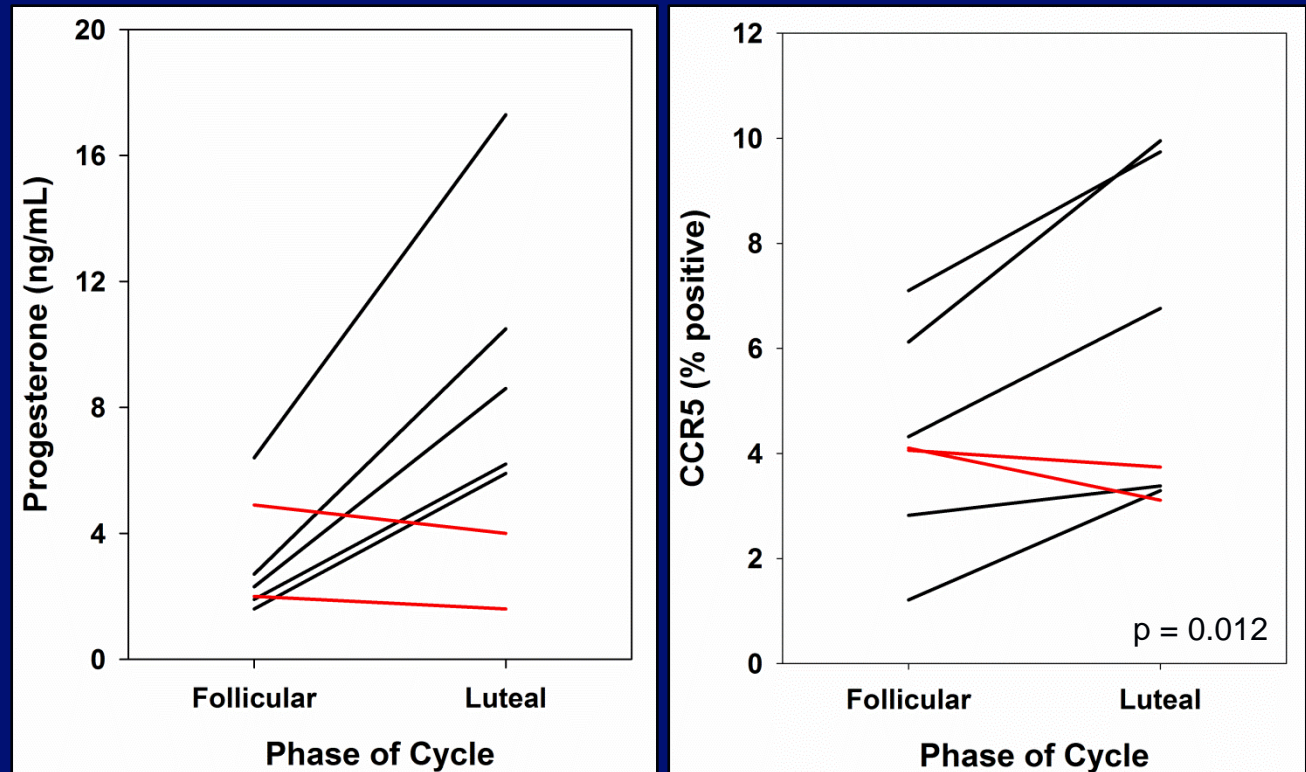
Progesterone rises during the luteal phase

- **Women completed 28 total visits**
 - 1 woman – 5 visits
 - 5 women – 4 visits
 - 1 woman – 3 visits
- **No detectable sustained rise in progesterone in 2 of 7 women (red)**



Expression of HIV coreceptor CCR5 increases during the luteal phase

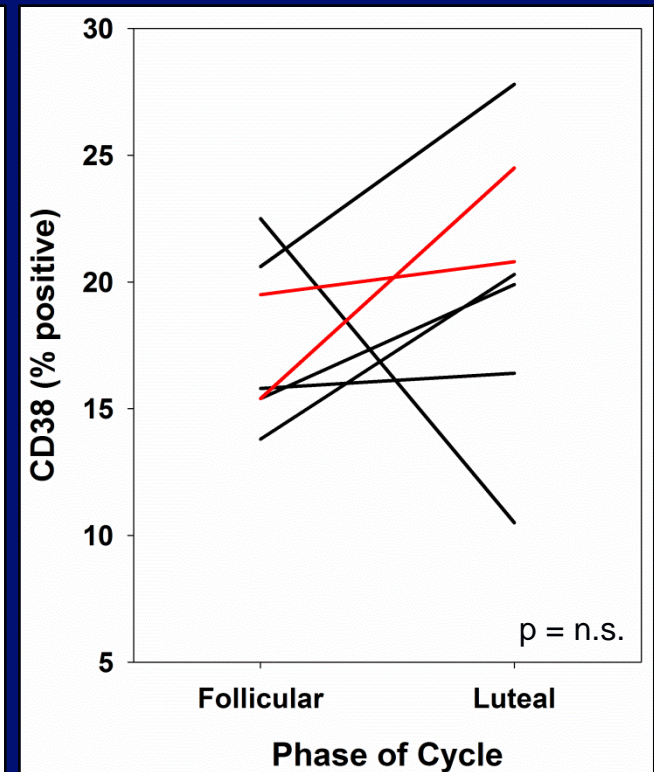
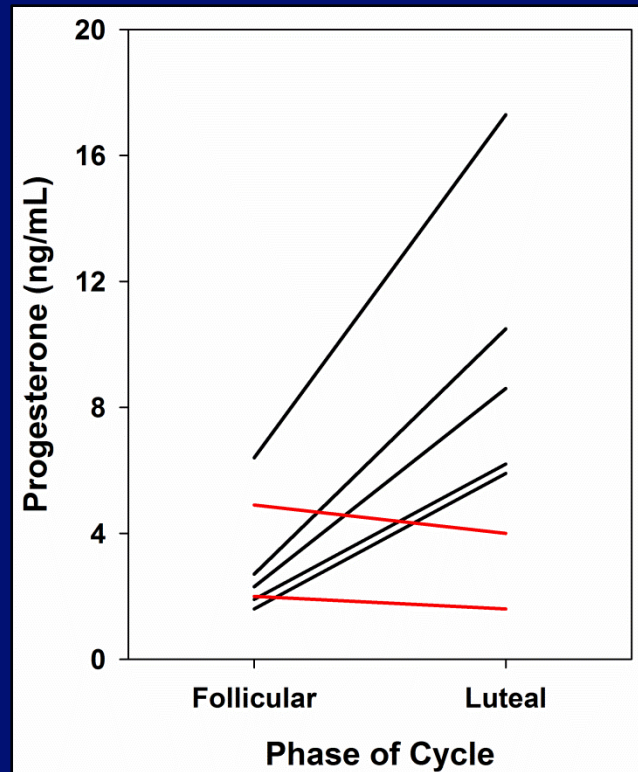
- CCR5
Expression:
%CD4+ cells
expressing
CCR5



- Proportion of CD4+ T cells expressing CCR5 increased during the luteal phase of the menstrual cycle

Expression of cell activation markers on HIV target cells increases during the luteal phase

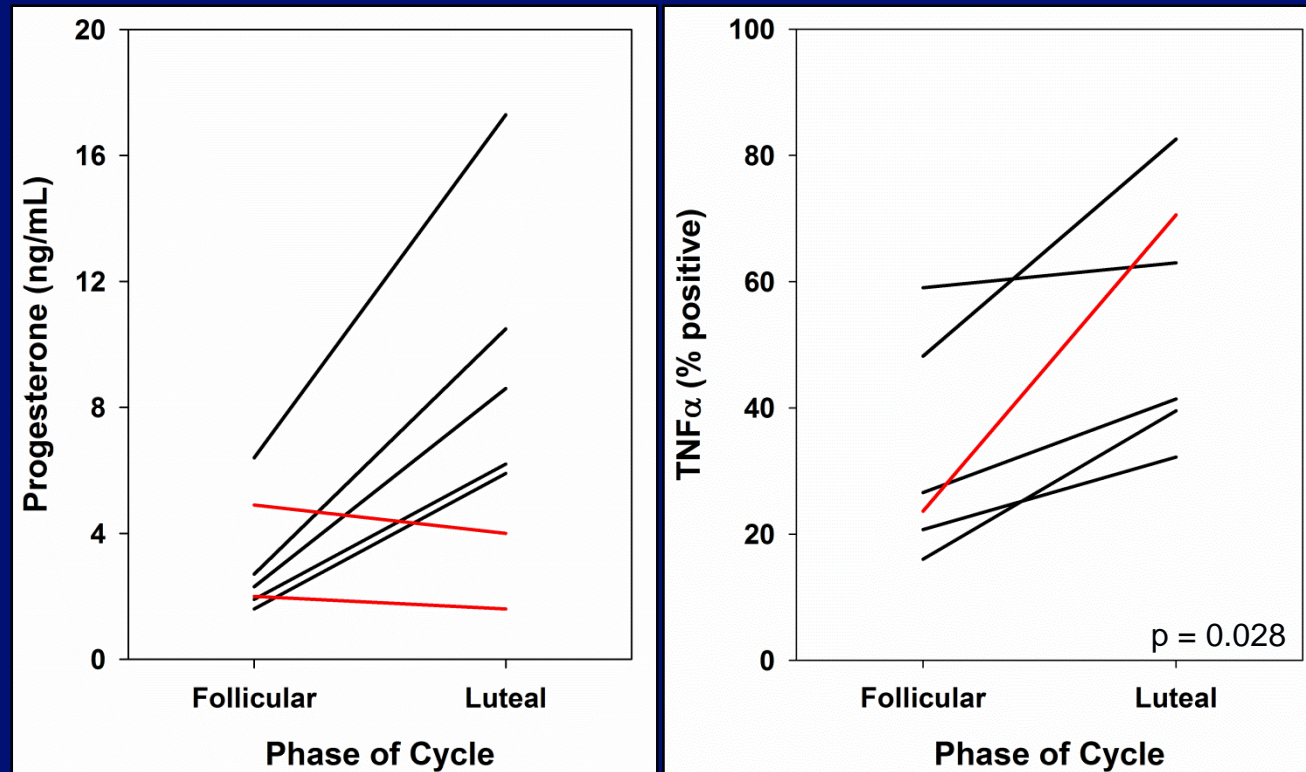
- CD38
Expression:
%CD4+ cells
expressing
CD38



- Proportion of CD4+ T cells expressing CD38 increased in 6 of 7 women during the luteal phase of the menstrual cycle

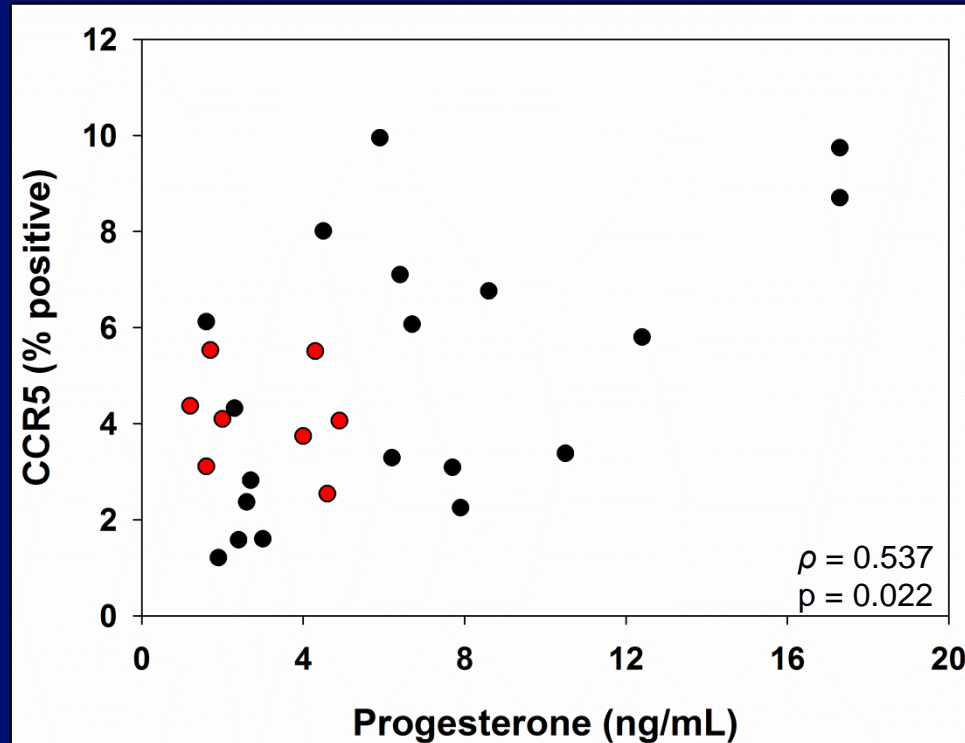
Responsiveness of HIV target cells to stimulation increases during the luteal phase

- TNF α
Expression:
%CD4+ cells expressing TNF α following 5 hour *ex vivo* stimulation



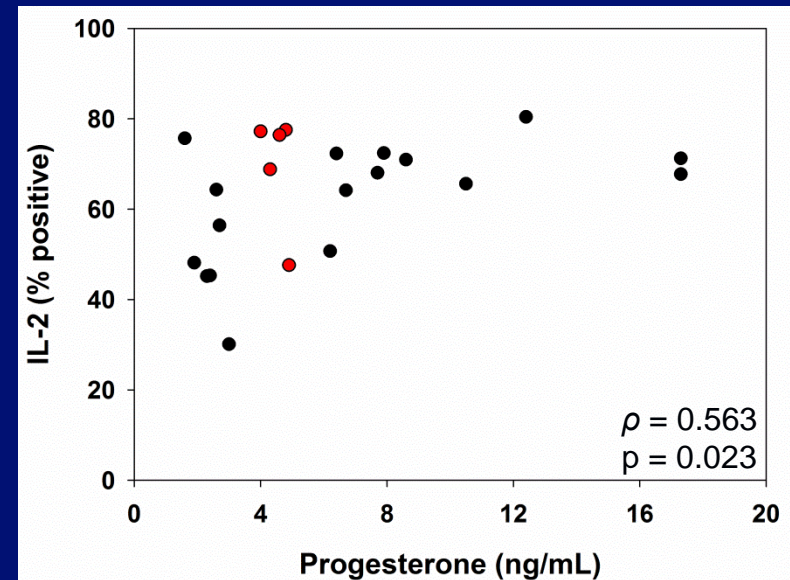
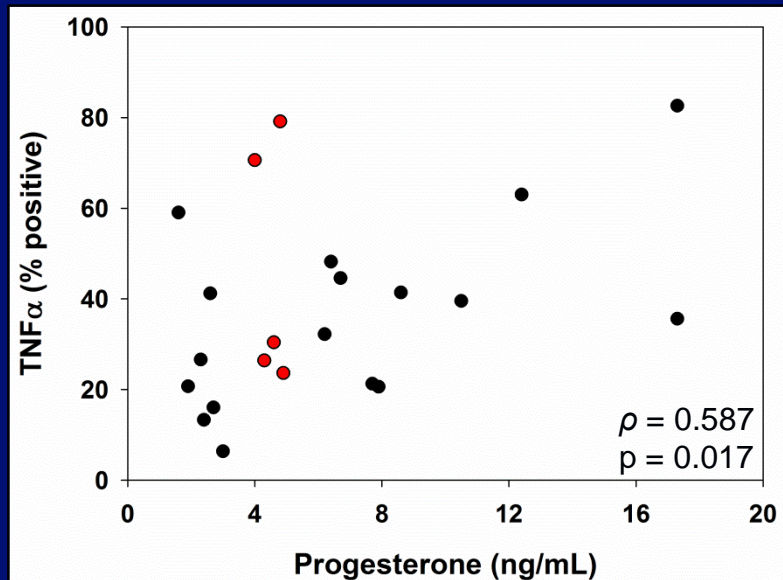
- Proportion of CD4+ T cells able to respond to stimulation increased during the luteal phase of the menstrual cycle

Expression of HIV coreceptor CCR5 increases with increased progesterone



- Proportion of CD4+ T cells expressing CCR5 increased in association with increased progesterone concentrations

Responsiveness of HIV target cells increases with increased progesterone



- Proportion of CD4+ T cells able to respond to *ex vivo* stimulation increased in association with increased progesterone concentrations

Conclusions

- **The proportion of CD4+ T cells expressing the HIV coreceptor CCR5 and responding to *ex vivo* stimulation increased during the luteal phase of the menstrual cycle in association with increased plasma progesterone**
- **HIV target cells in the blood are primed to support viral replication when progesterone concentrations rise during the luteal phase of the menstrual cycle**
- **Future studies will need to examine changes at the surface of the genital mucosa in the presence of progesterone to help identify risks for progestin-based contraceptives**

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