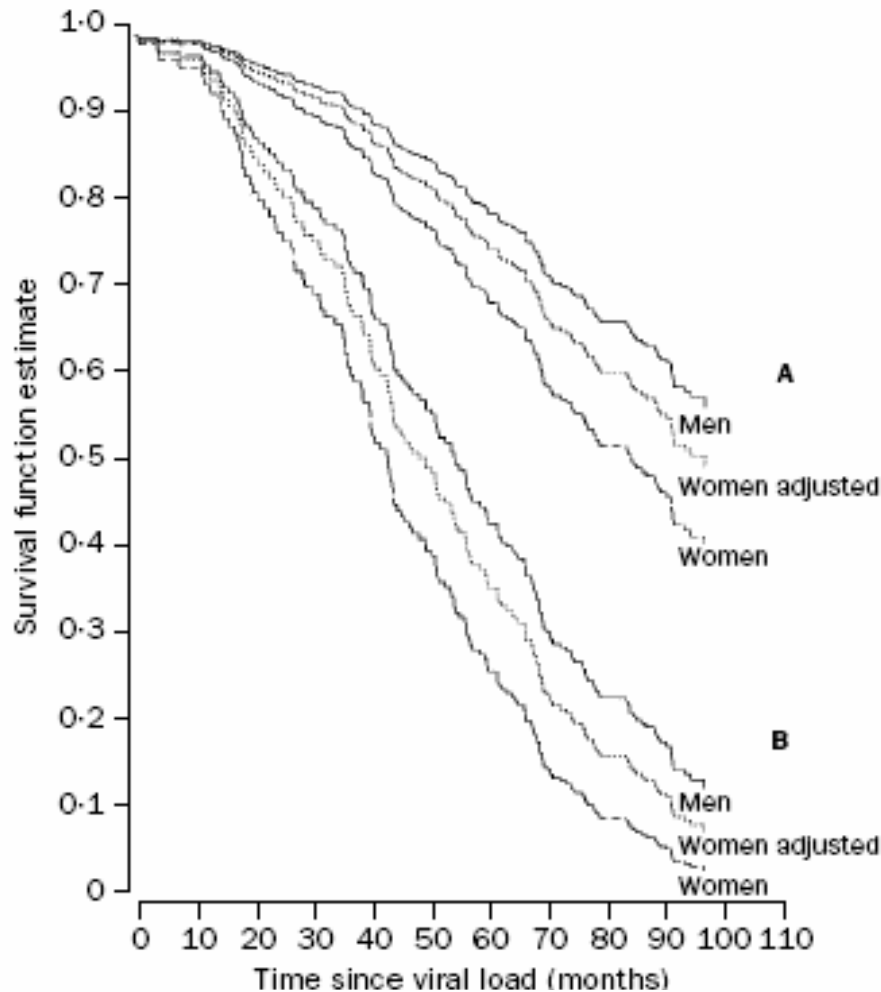


# **TLR-mediated pDC responses to HIV-1 ligands**

**Judy Chang, PhD**

# Differences between women and men

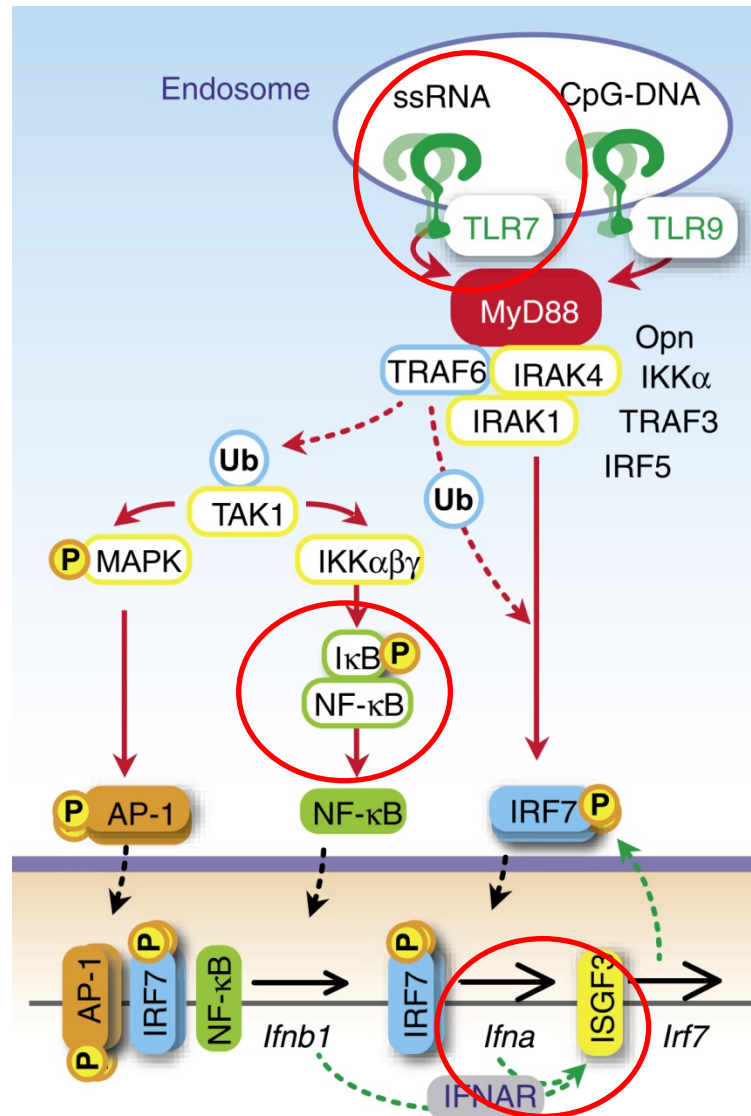


- HIV-1–infected women tend to have lower viral loads early in HIV-1 infection
- However, women progress faster to AIDS for a given viral load than men

	Pattern A	Pattern B
Men	CD4 400, VL 6000	CD4 100, VL 40 000
Women	CD4 400, VL 6000	CD4 100, VL 40 000
Women adjusted	CD4 400, VL 3000	CD4 100, VL 20 000

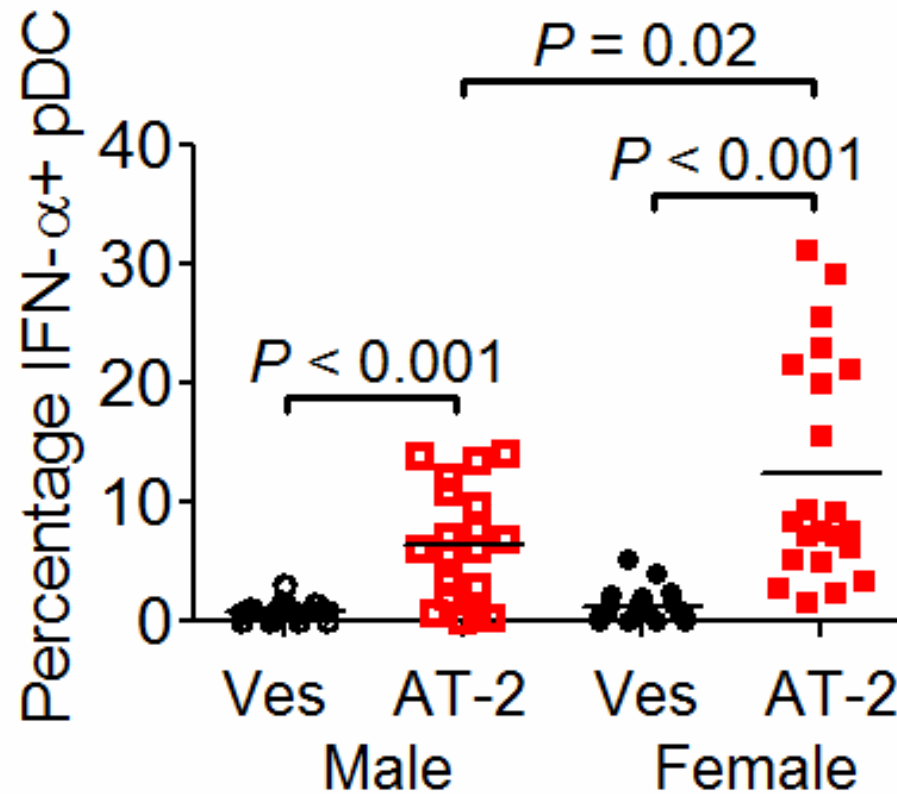
Farzadegan et al. Lancet 1998

# TLR7/8/9 signaling pathway

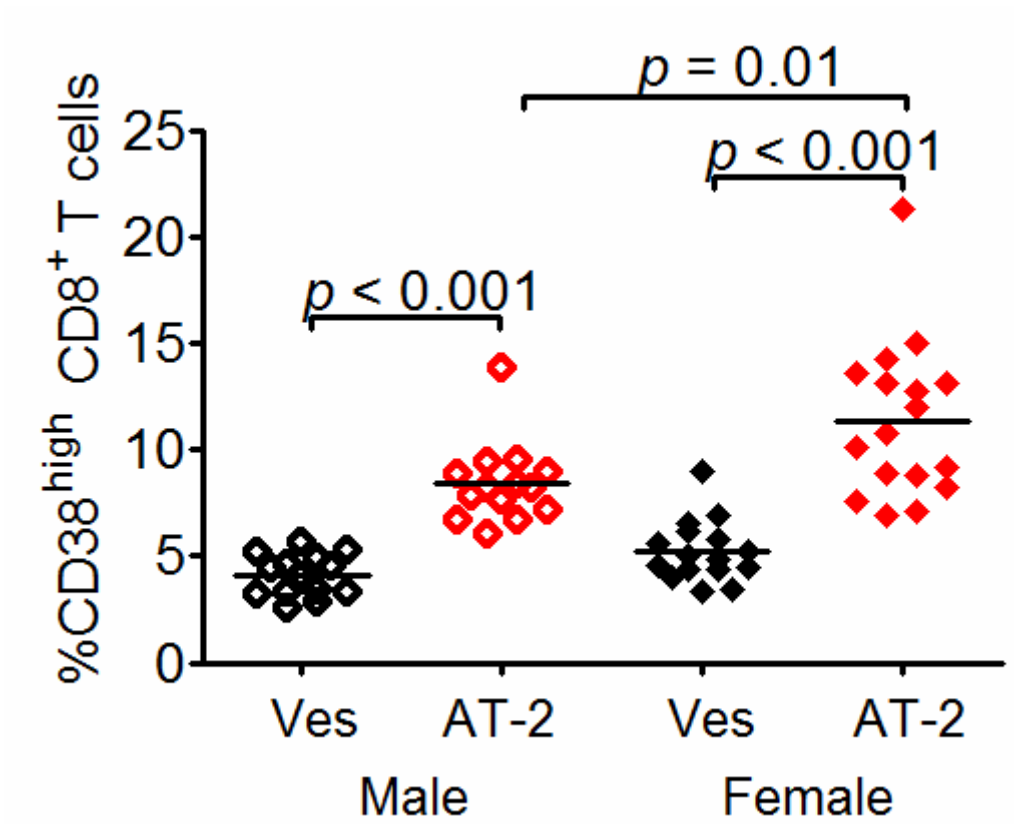


Baccala et al. Nat Med 2007

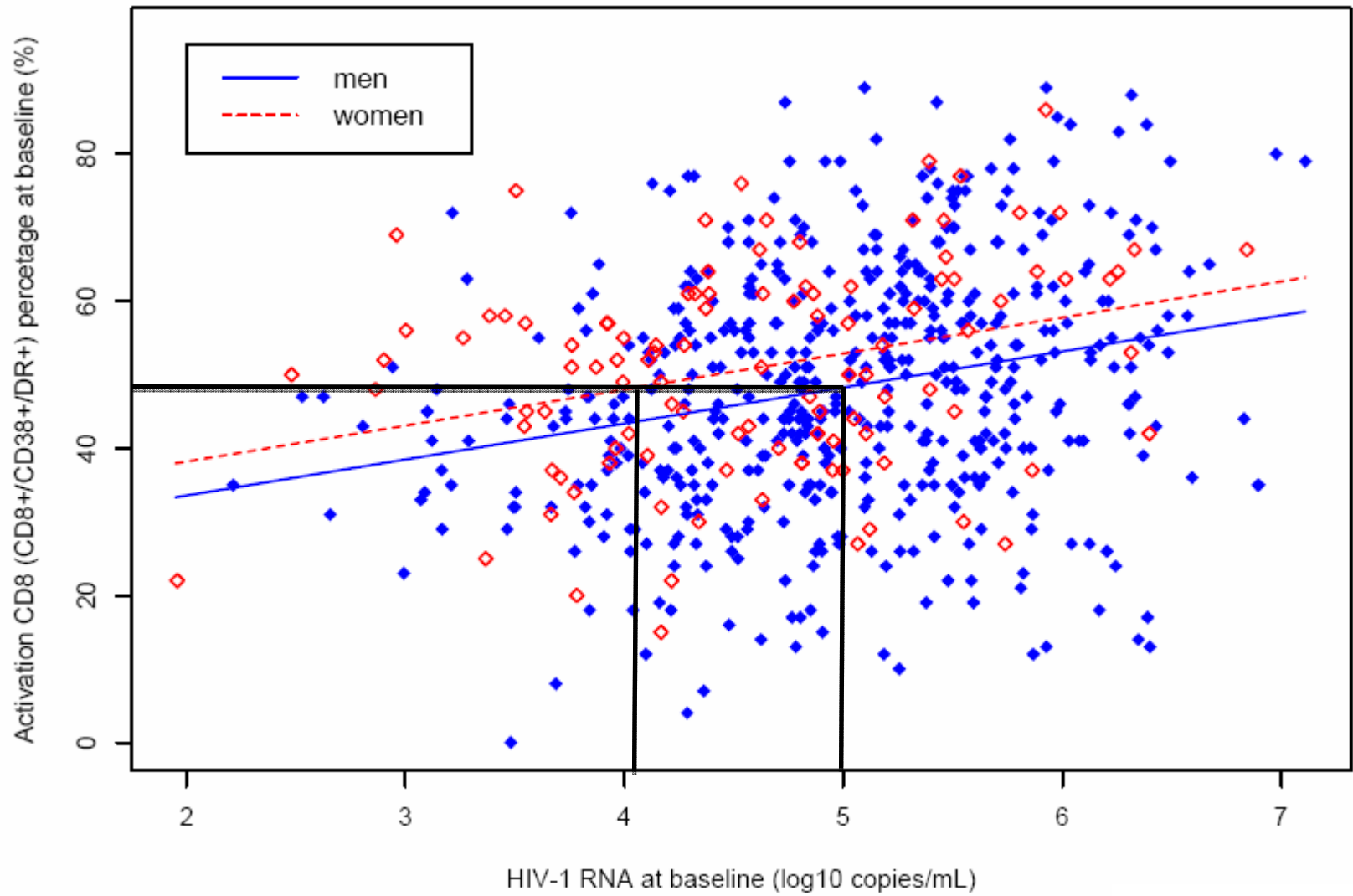
# pDCs of females produce more IFN- $\alpha$ than pDCs from males



# TLR7 stimulation associated with immune activation



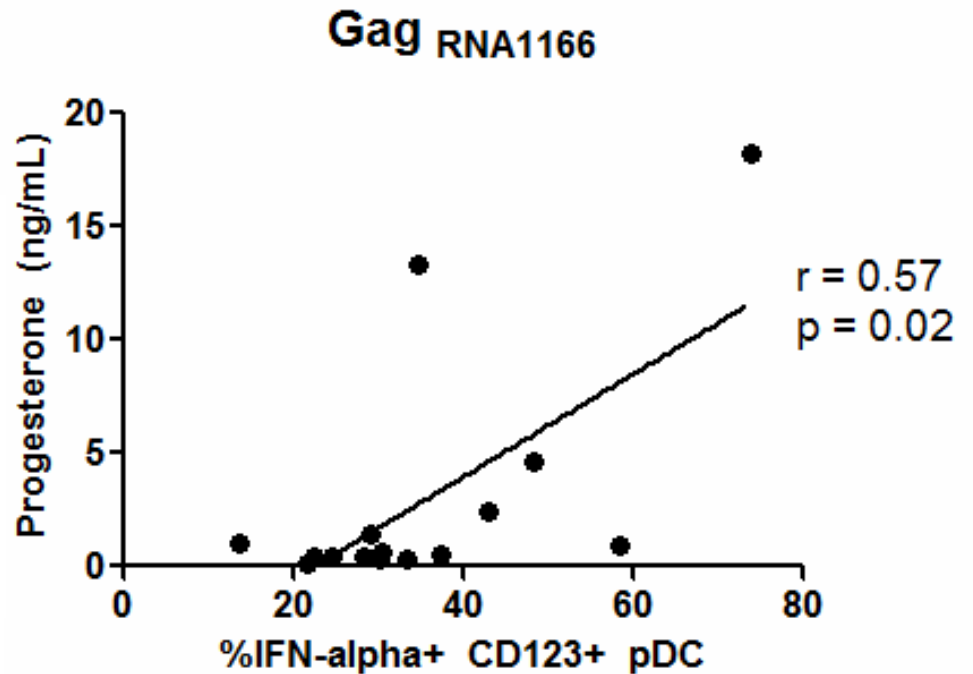
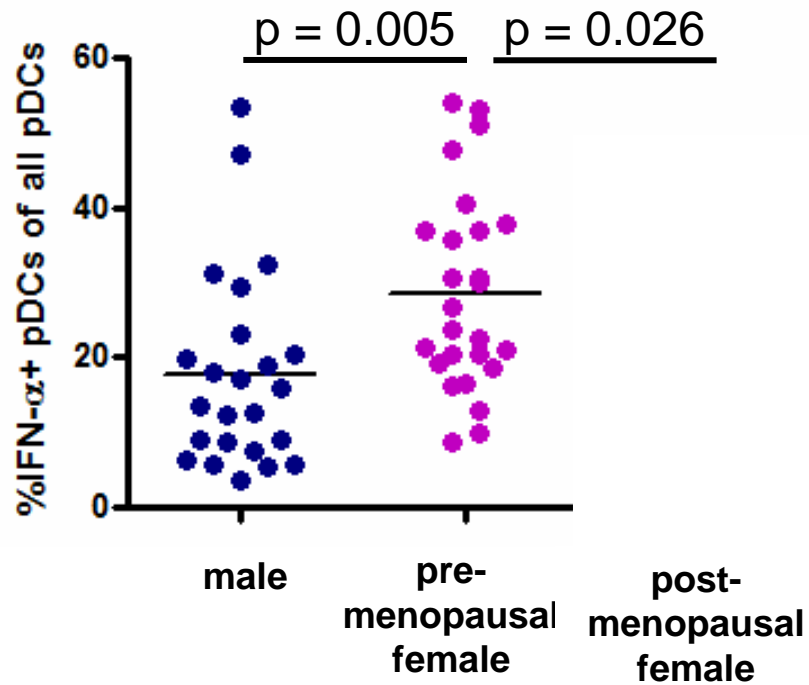
# Difference in male/female immune activation observed in HIV chronic infection



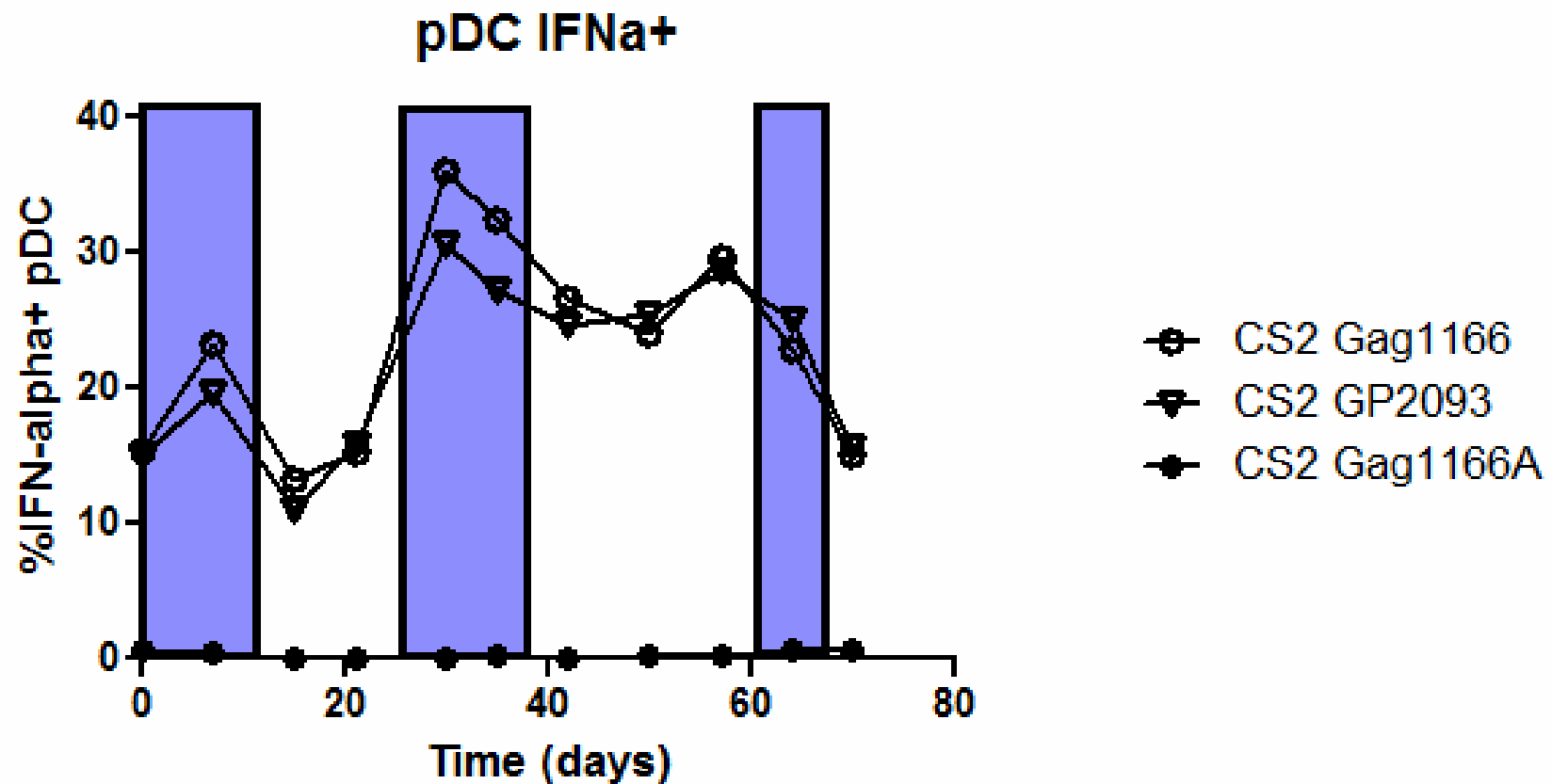
Meier/Chang et al. Nat Med 2009

What factors could explain  
higher pDC IFN $\alpha$  in women?

# Hormone associated immune effect

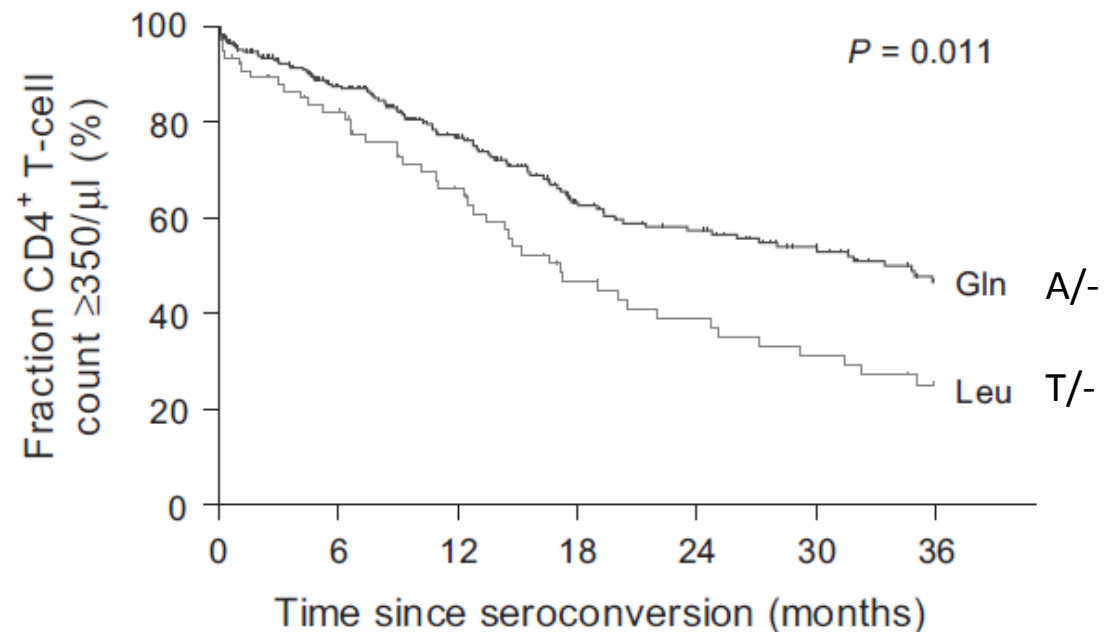
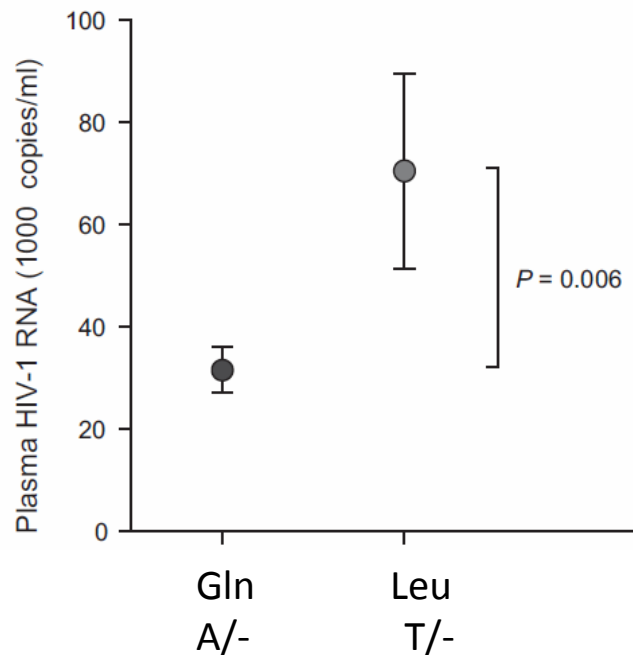


# Hormone associated immune effect



# TLR7 and downstream polymorphism

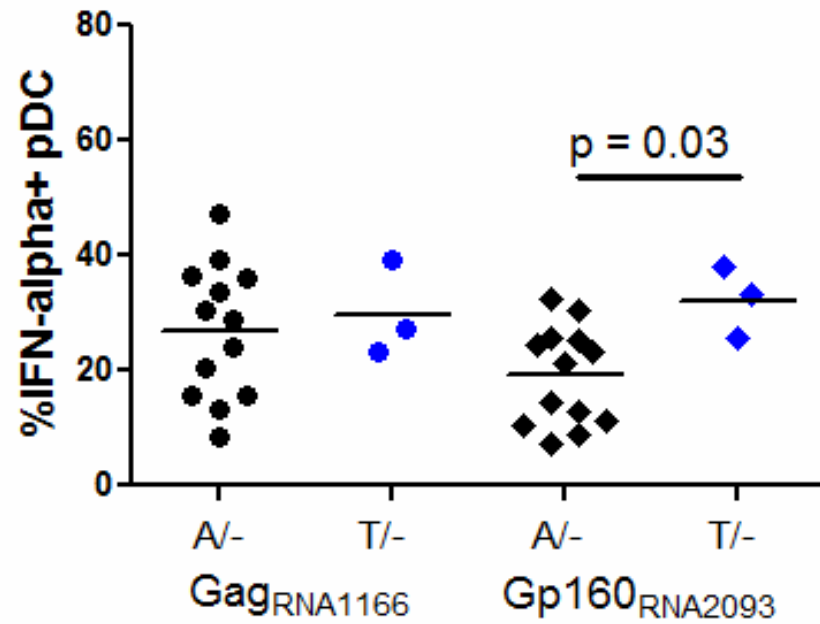
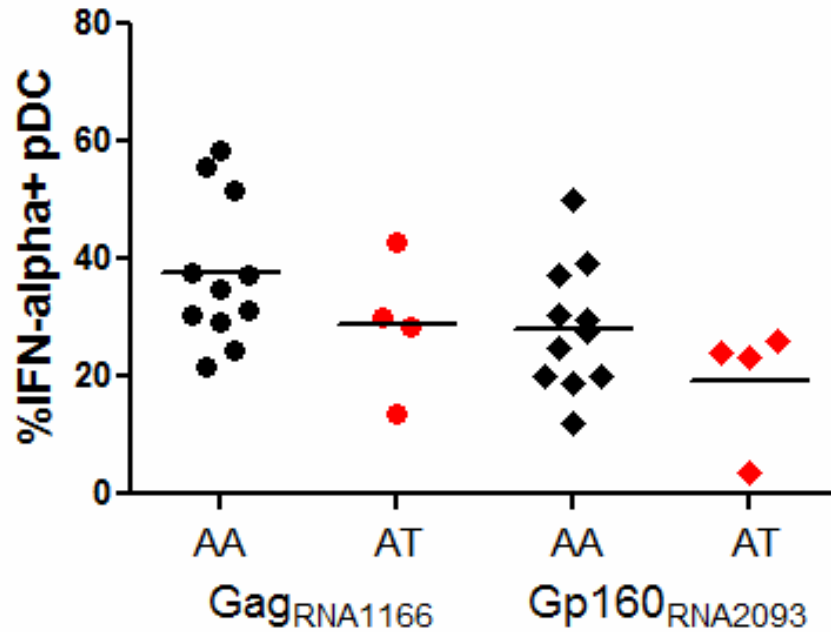
- X-chromosome linked
- HCV infection – *Schott et al. J Hep 2007*
- HIV infection – *Oh et al. AIDS 2009*
  - TLR7 exon3 - C.32A>T



# TLR7 polymorphism

X X  
Female

X Y  
Male



# Conclusion

- Men and women are different
- HIV-1 stimulation via TLR7 induces higher IFN $\alpha$  response in women than in men
- Associated with downstream higher immune activation in women than in men
- Responses may be modulated by hormone levels

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- Men and women are different
- HIV-1 stimulation via TLR7 induces higher IFN $\alpha$  response in women than in men
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- **TLR7 polymorphism in men are associated with higher pDC IFN $\alpha$  production in response to HIV-1**

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