Memory T Cell Activation in the Second Trimester Prior to Preeclampsia Onset

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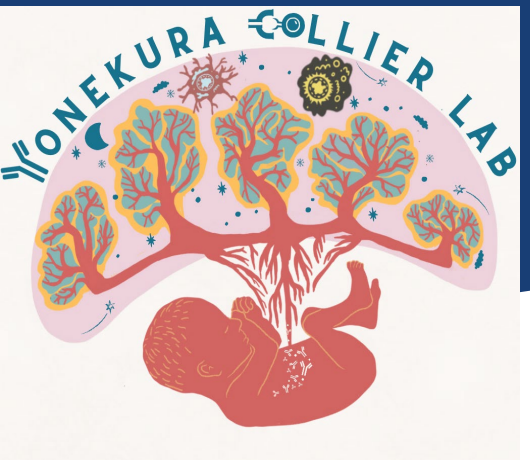

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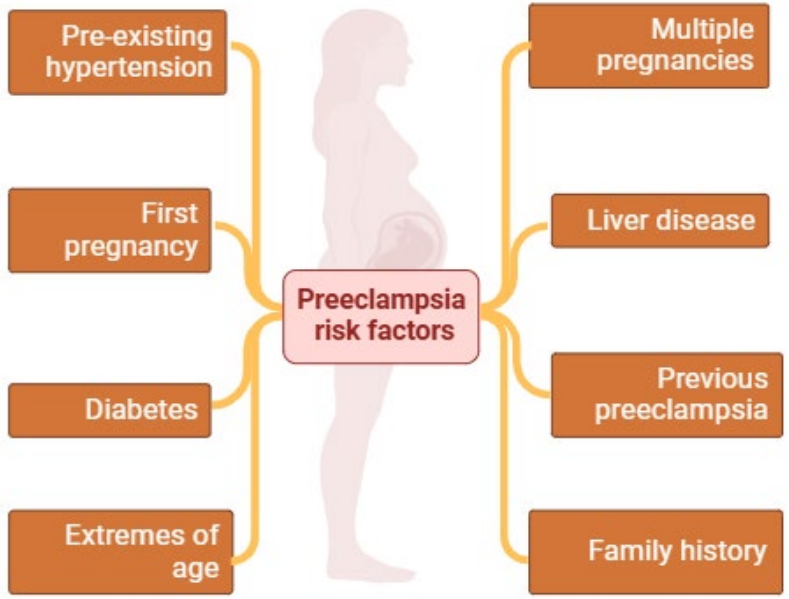
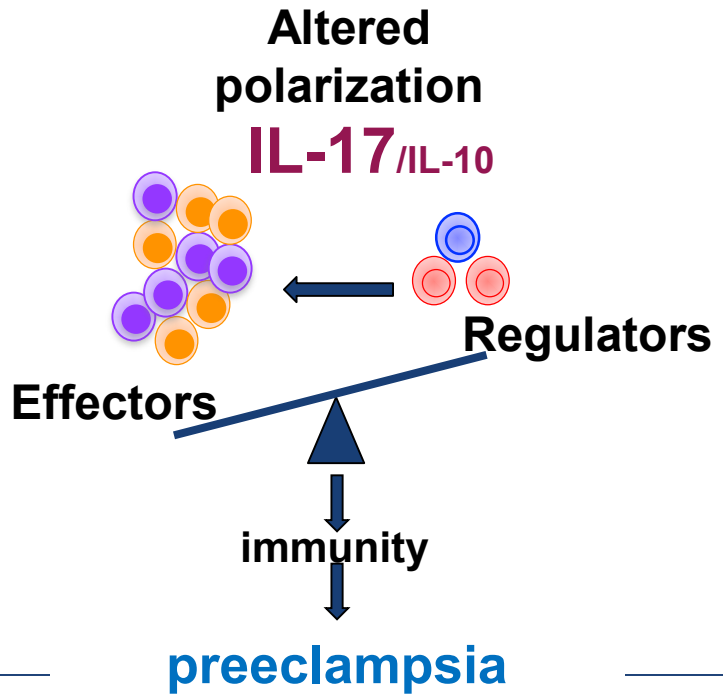
Preeclampsia (PE)

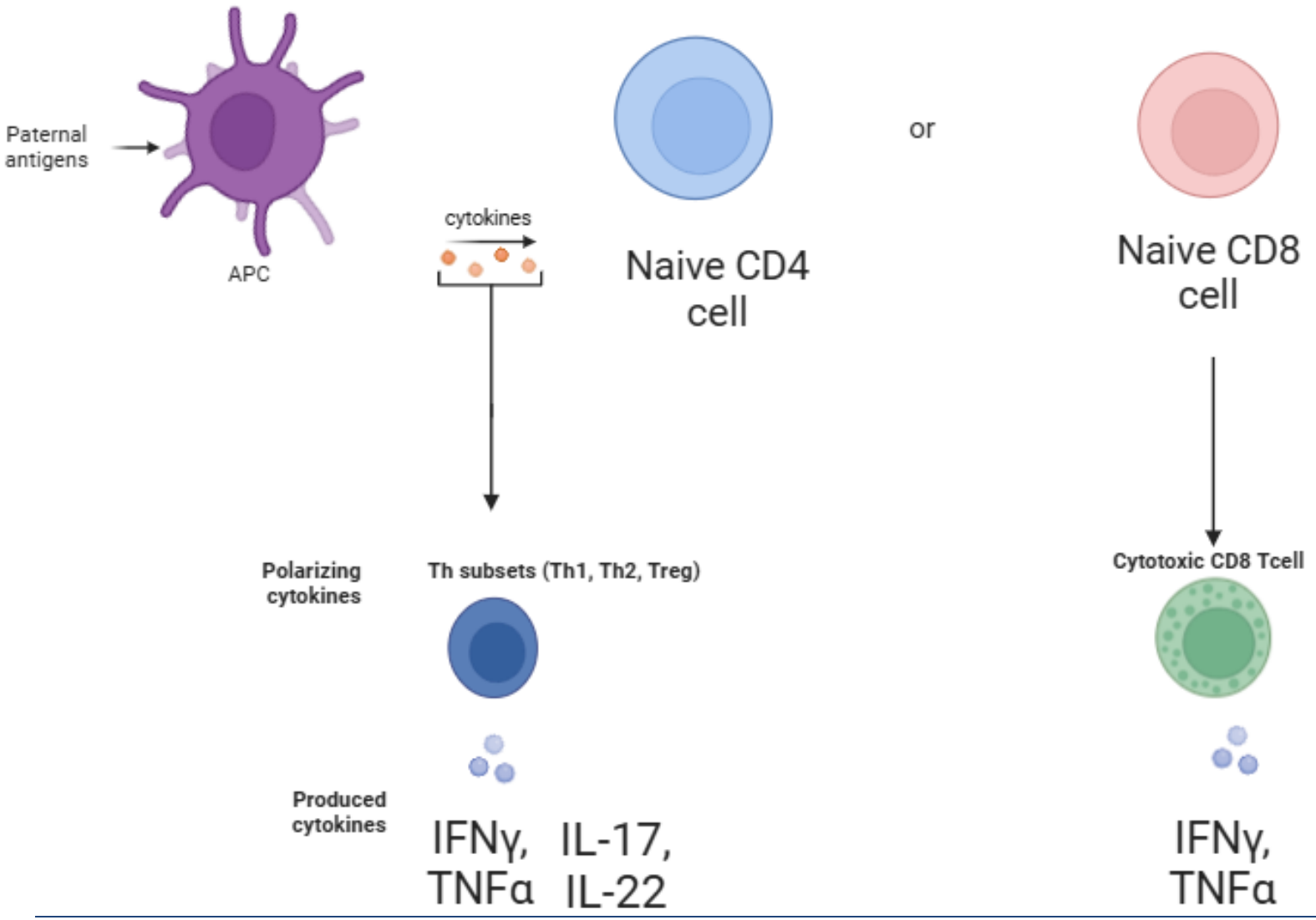
- New onset hypertension occurring at 20 weeks or more of gestation
- 4-10% pregnancies affected
- High morbidity and mortality
- Limited treatment options
- Prior research suggest an immune component to PE
- Spectrum-- Severe features brief review (include box 3)





Collier et al. Reprod Sci. 2023

CD4 and CD8 Effector Cells in Pregnancy

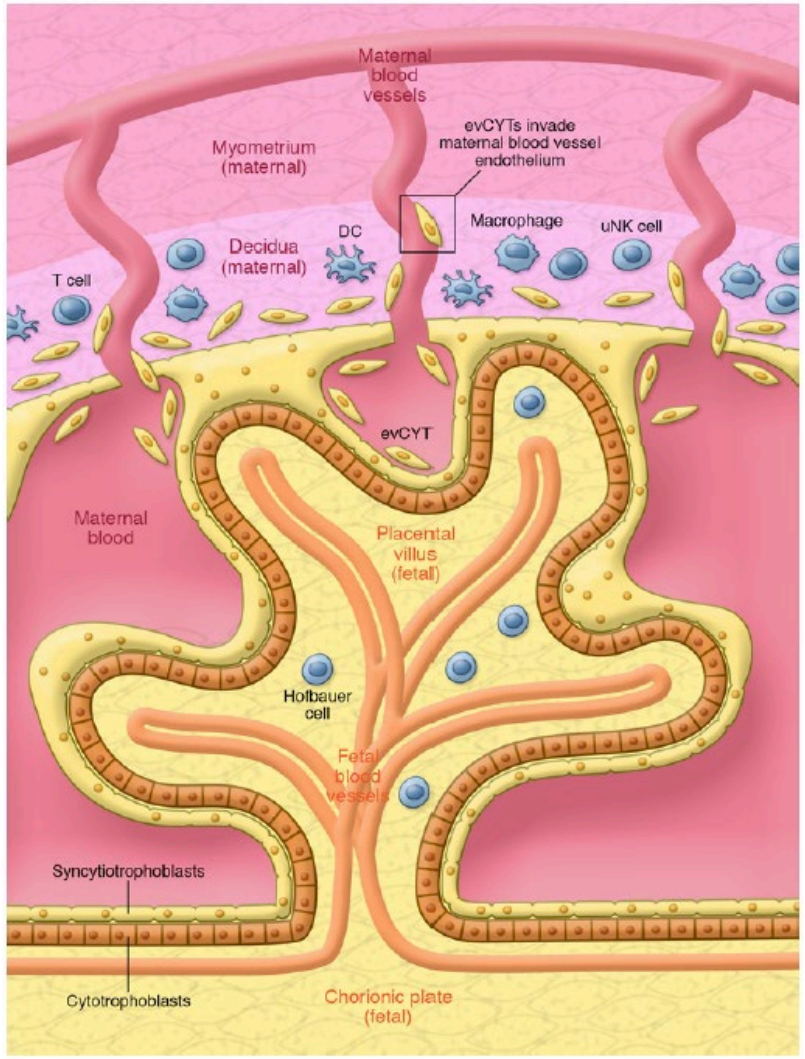


Naive T cells differentiate into effectors once exposed to antigen and polarizing cytokines

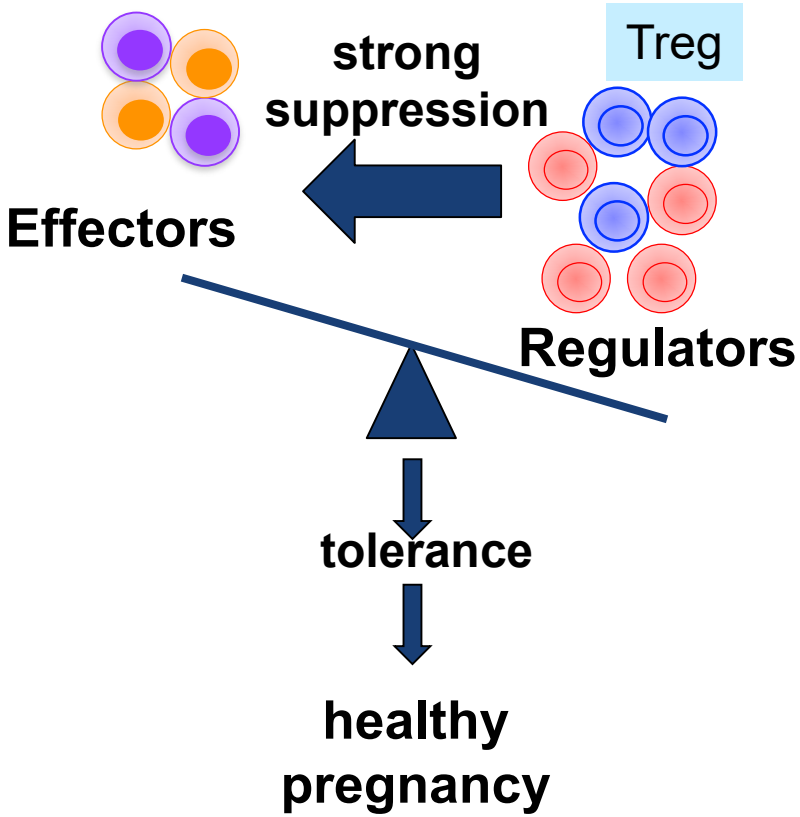
Memory T cells of different lineages are identified by CD45RO+

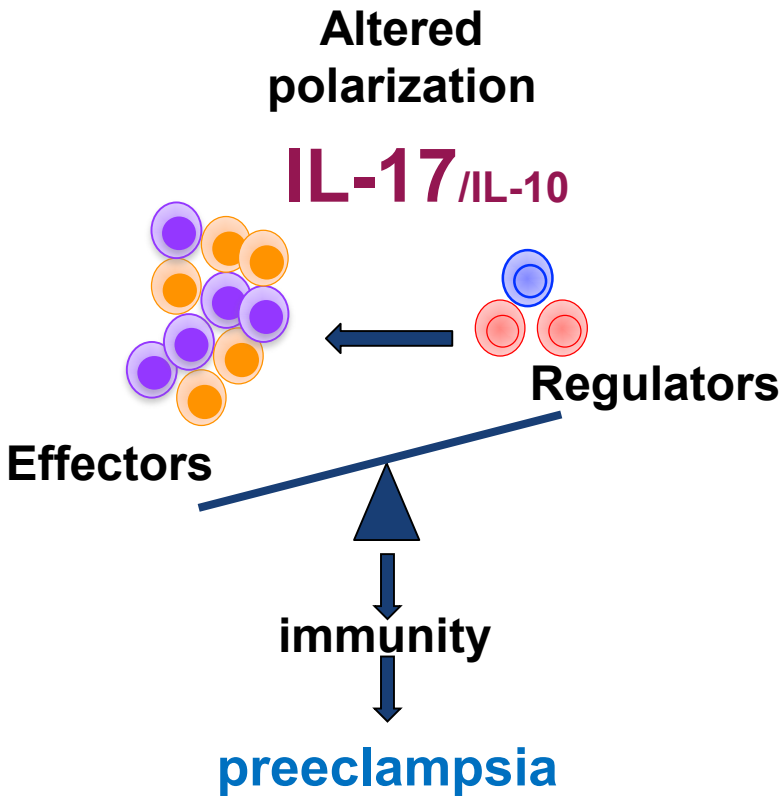
Adapted from Kiefer et al. Front Immunol. 2019

Pregnancy presents a significant challenge to the maternal immune system



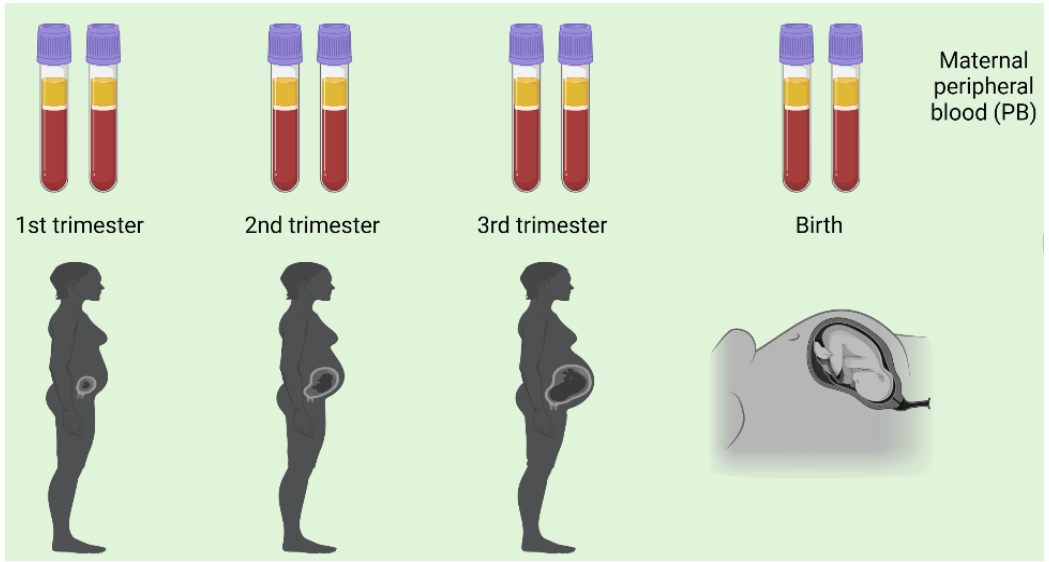
CD8 and CD4 effector T cells

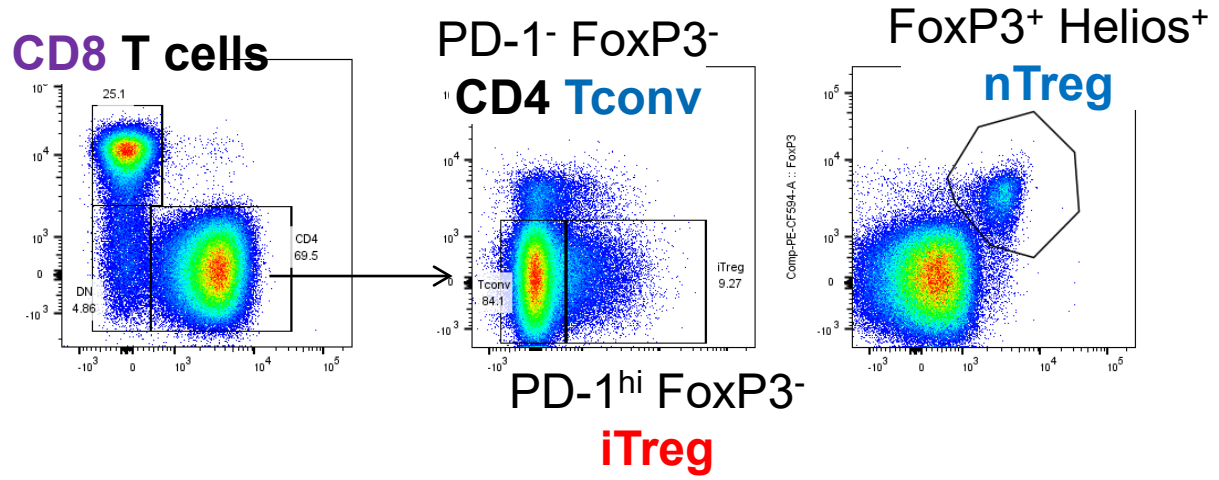


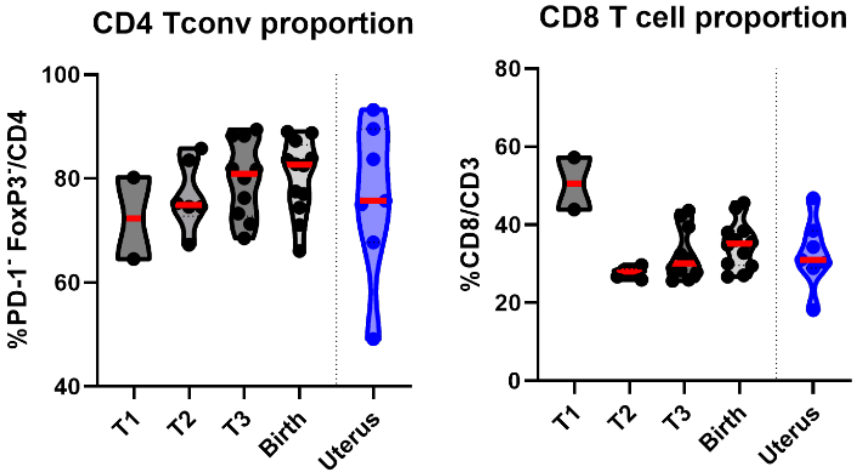


Racicot & Mor. J Clin Invest. 2017
Guerin et al. Human Reprod Update. 2009
Collier et al. Reprod Sci. 2023

Flow cytometry identifies T cell populations and functional cytokine production from maternal peripheral blood







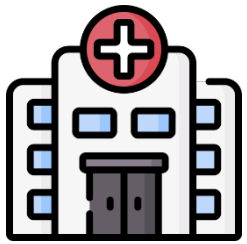
Intracellular cytokine staining: IFN-g, TNFa, IL-17a, IL-2, IL-10

Objective

Identify functional memory (CD45RO+) T cell changes in the second trimester associated with progression to PE

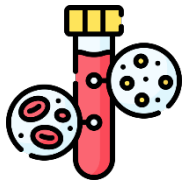
Longitudinal cohort of pregnant individuals without PE

Collection → **Flow Cytometry** → **Medical Record Review**

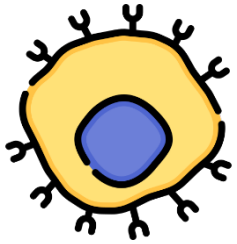


Enrolled **(n =100)**
PE **(n=6)**
Second-trimester PE samples **(n=3)**

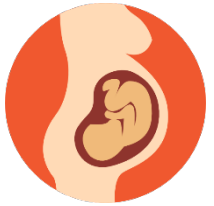
Controls **(n=13)**



Peripheral blood in pregnancy



Blood before PE onset analyzed for **proinflammatory interferon gamma (IFN-γ), tumor necrosis factor alpha (TNFα), and interleukin 17 (IL-17α) cytokine production**



Adverse pregnancy outcomes

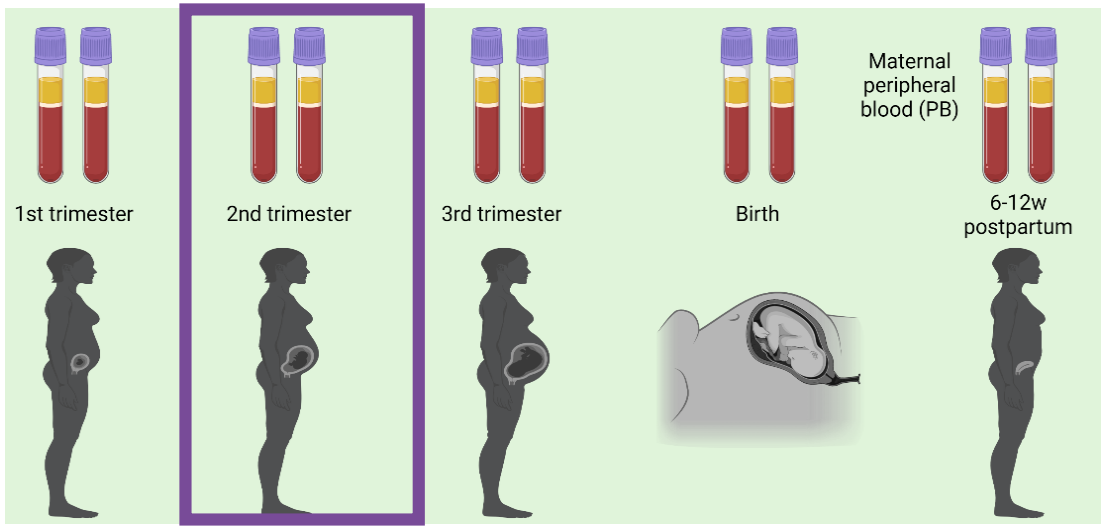
Preeclampsia

Baseline characteristics

	PE* with severe features N=3	Control N=13
Maternal age (years)	35 (34-37)	34 (32-36)
Chronic medical conditions		
Hypertension	33%	15%
Diabetes	33%	8%
Obesity	0%	62%
Autoimmune disease	33%	0%
Nulliparity	100%	39%
Gestational age at birth (week)	37 (37-38)	39 (37-39)

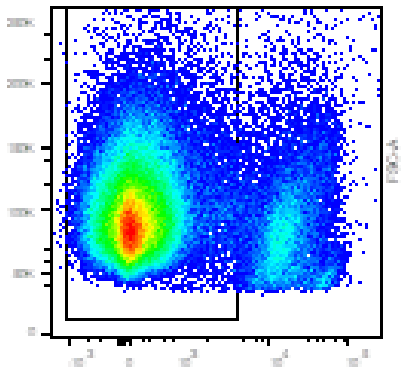
Data presented as median (interquartile range) or number (percent)

We identified memory T cell populations and quantified double positive cytokine production in 2nd trimester samples using flow cytometry

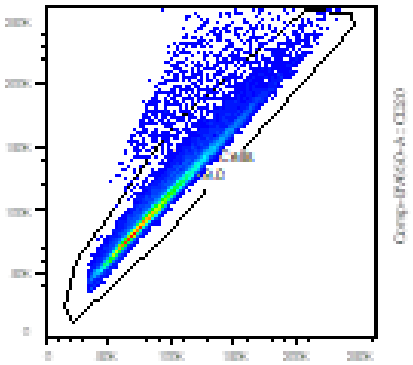


CD45RO+ memory

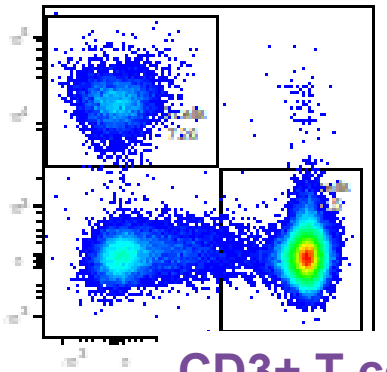
Live cells



Singlets

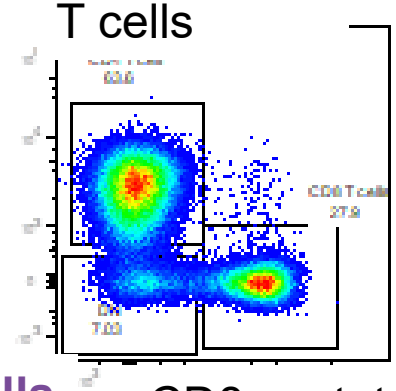


CD20+ B cells

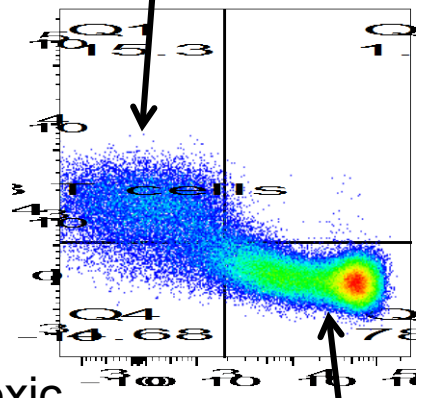


CD3+ T cells

CD4+ helper T cells

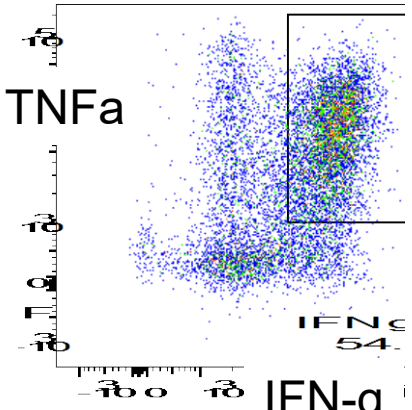


CD8+ cytotoxic T cells



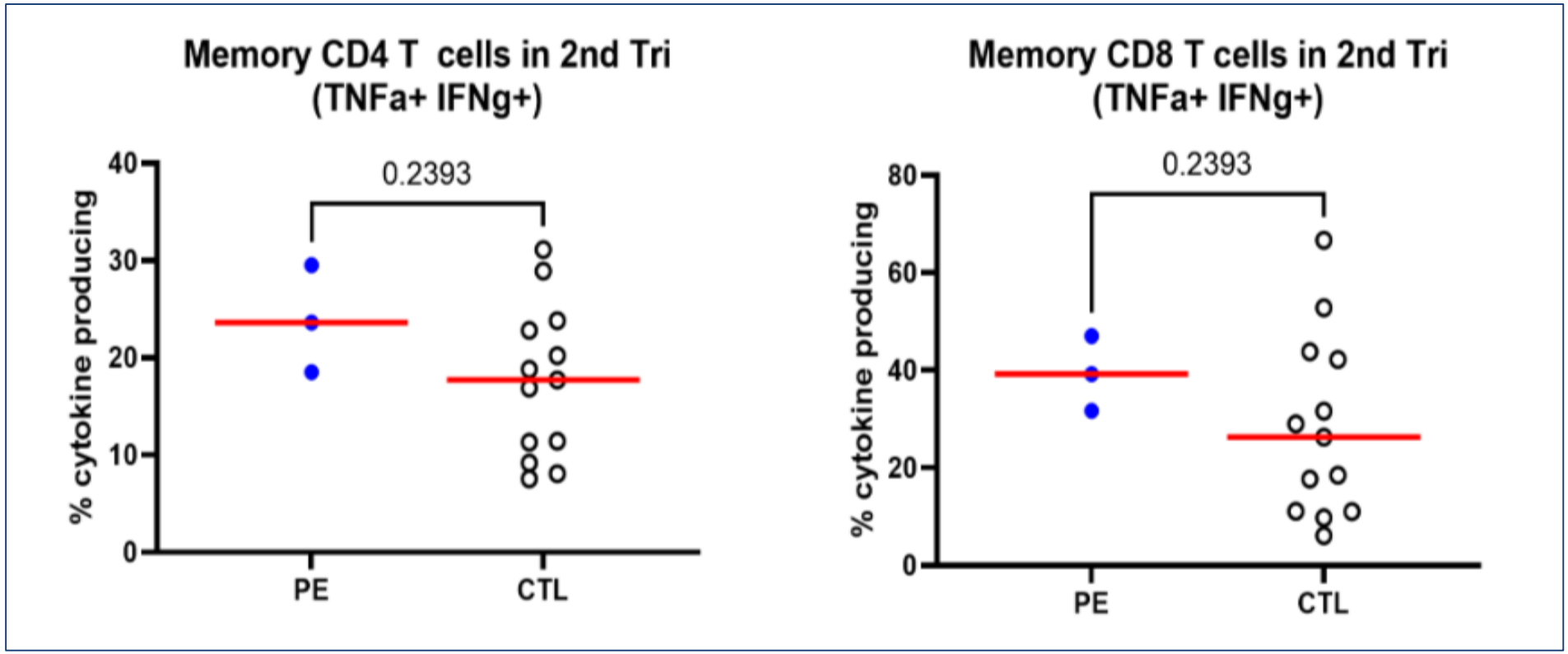
CD45RA+ Naive

TNFa



IFN-g

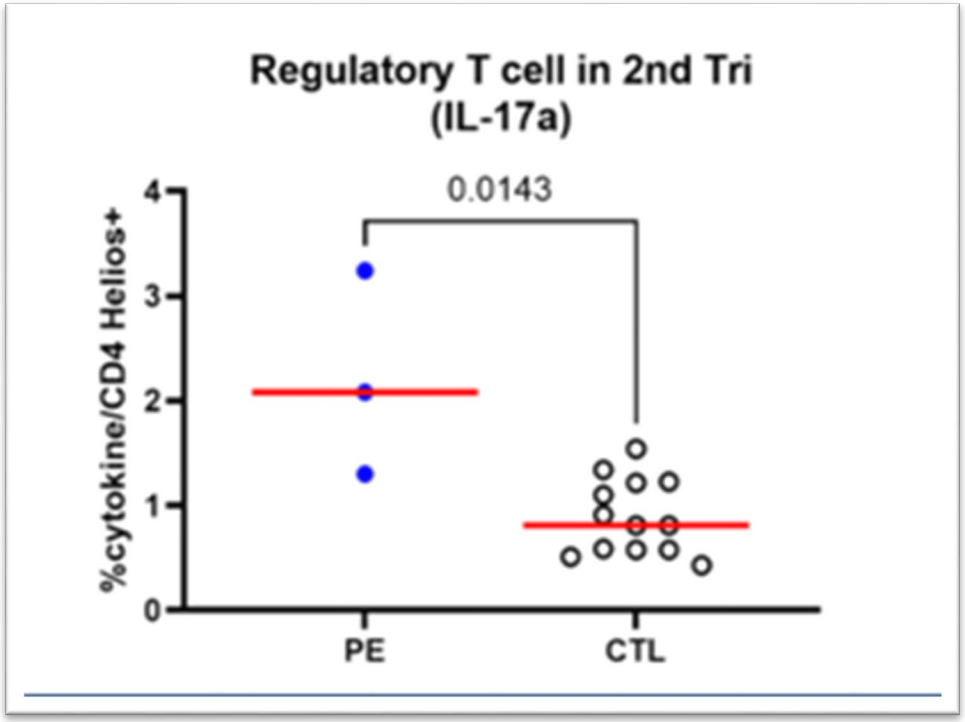
Memory T cells in the 2nd trimester had a higher proinflammatory cytokine profile in PE compared to controls



Regulatory T cells in preeclampsia had significantly higher production of pro-inflammatory IL-17 prior to PE onset

Association of PE with IL-17α Treg production

IL-17 producing CD4 Tregs			
	PE N=3	Control N=13	P-value
IL-17 CD4 Tregs	2.1 (1.3, 3.2)	0.8 (0.58, 1.2)	0.01



Conclusions

- Higher pro-inflammatory IFN-γ and TNFα CD8 and CD4 memory T cells from participants who developed PE
- Results were not statistically significant

Strengths & Limitations

- Ability to examine immune profile preceding clinical disease
- Potential to correlate T cell cytokine assays with serum cytokine levels
- Low sample size

Future Directions

- Evaluate effect of TNFα inhibitor therapies (currently approved for chronic inflammatory diseases) in pregnant individuals at risk for PE
- Probe existing large cohorts to evaluate cytokine production prior to PE

Acknowledgements

- PI and mentor: Ai-ris Collier
- OBGYN Research Team: Michele Hacker, Anna Modest
- Labor and Delivery providers, Medical staff in OB clinic
- Fellow CRCs: Tina Yi Jin Hsieh, Emily Stonestreet, Nadiha Noor Chelsea, Rafaela Germano Toledo
- Barouch Immunology Team

Thank you for your time!

Any Questions?

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Additional Baseline characteristics

	PE with severe features N=3	Control N=13
Race		
Asian	0 (0%)	1 (7.7%)
Black	1 (33.3%)	1 (7.7%)
White	2 (66.7%)	9 (69.2%)
Multiple/Other	0 (0%)	2 (15.4%)
Hispanic	0 (0%)	2 (15.4%)