

## **Pregnant Patient Report**

- 8-8-16 (~16 weeks pregnant)
- 7-26-16 – screening panel (~14 weeks pregnant)
- 7-6-16 – screening panel (~11 weeks pregnant)
- 6-1-16 (~5.5 weeks pregnant)
- 9-15-15 (not pregnant)
- Complete HLA analysis added 1-31-14
- 12-12-13 (~10 weeks pregnant)
  - Fetal demise noted at 11 weeks
- 10-31-13 (~4 weeks pregnant)
- 2-27-13 (not pregnant)

### Clinical History

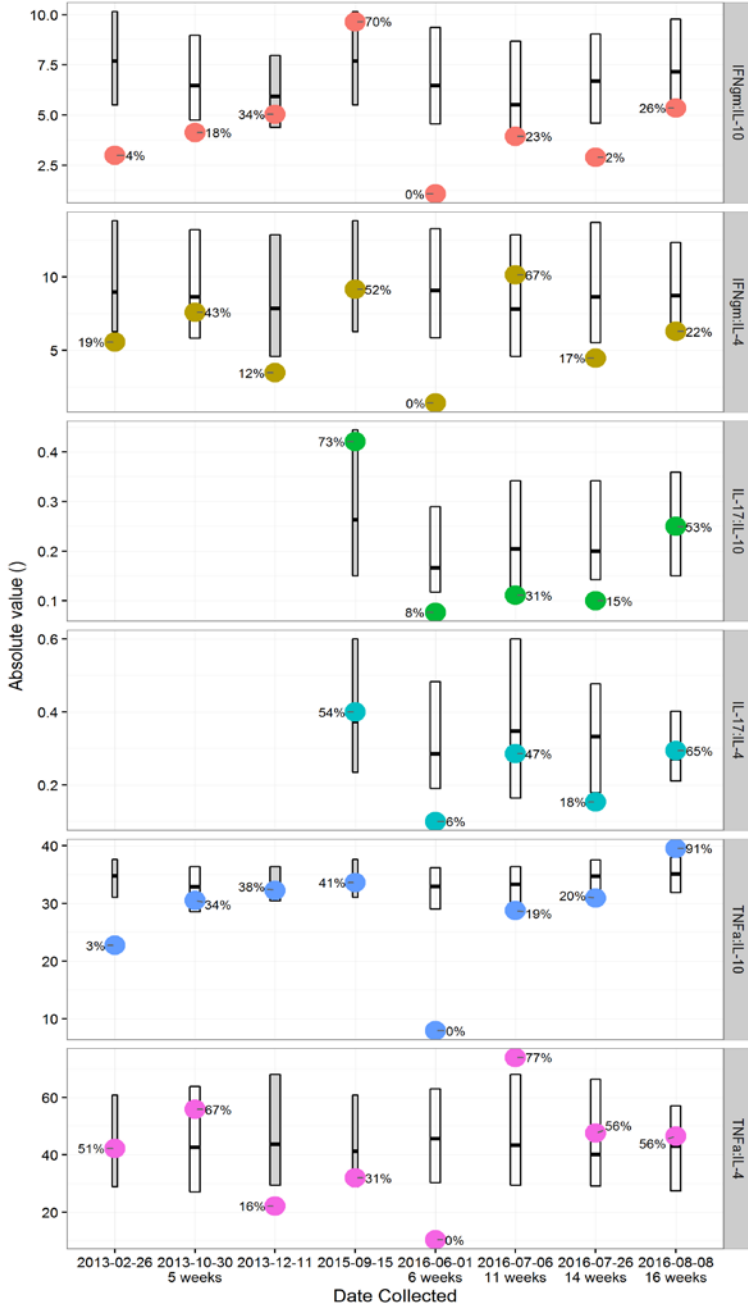
- Currently 38 years old
- History of endometriosis with laparoscopy performed in December, 2015
  - History of severe pain with menstruation
  - History of internal pain with relations
- History of low TSH
- Family history of miscarriages
- Mother and aunt with rheumatoid arthritis
- Family history of AODM

### Treatments

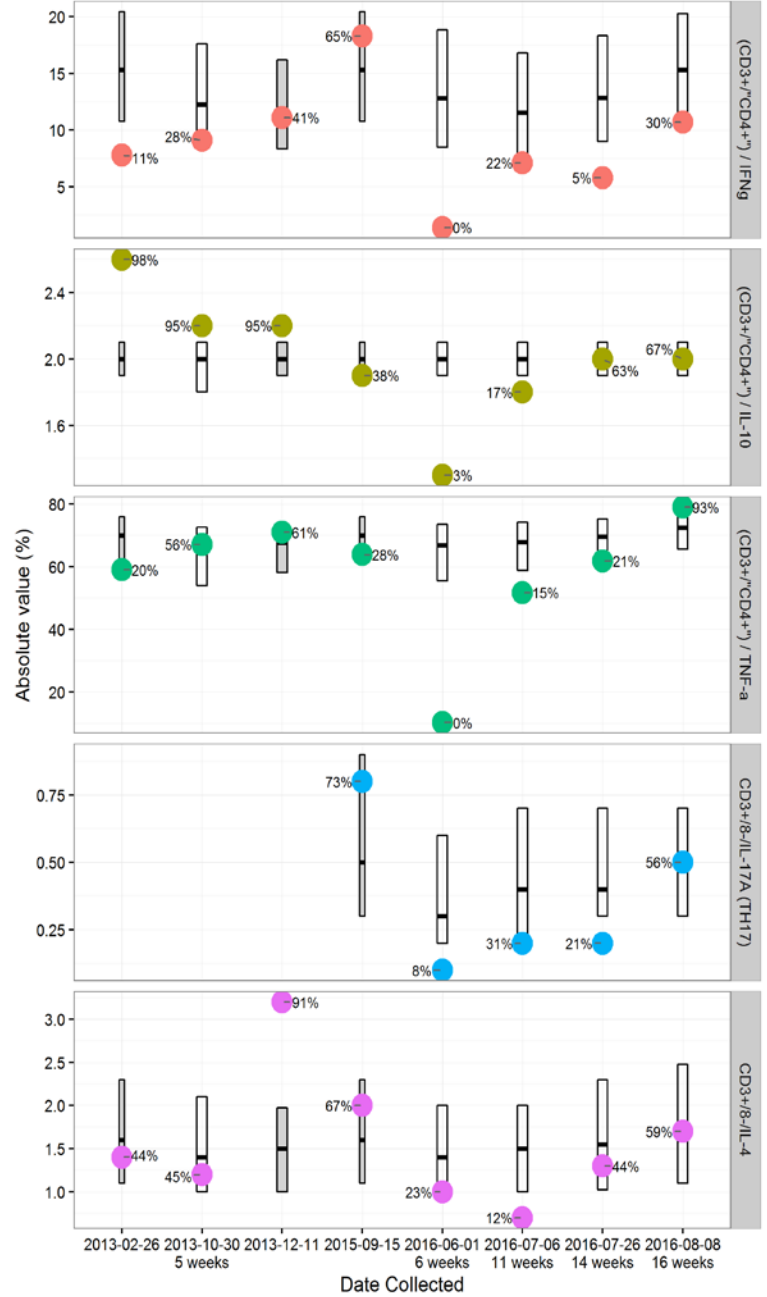
- Neupogen
  - 1 mcg/kg/day – discontinued around 7-29-16
- IVIG
  - 60 g every 4 weeks
- Prednisone
  - 10 mg BID – started tapering around 8-19-16
- Lovenox
  - 30 mg BID

# Summary of 8-8-16 Data

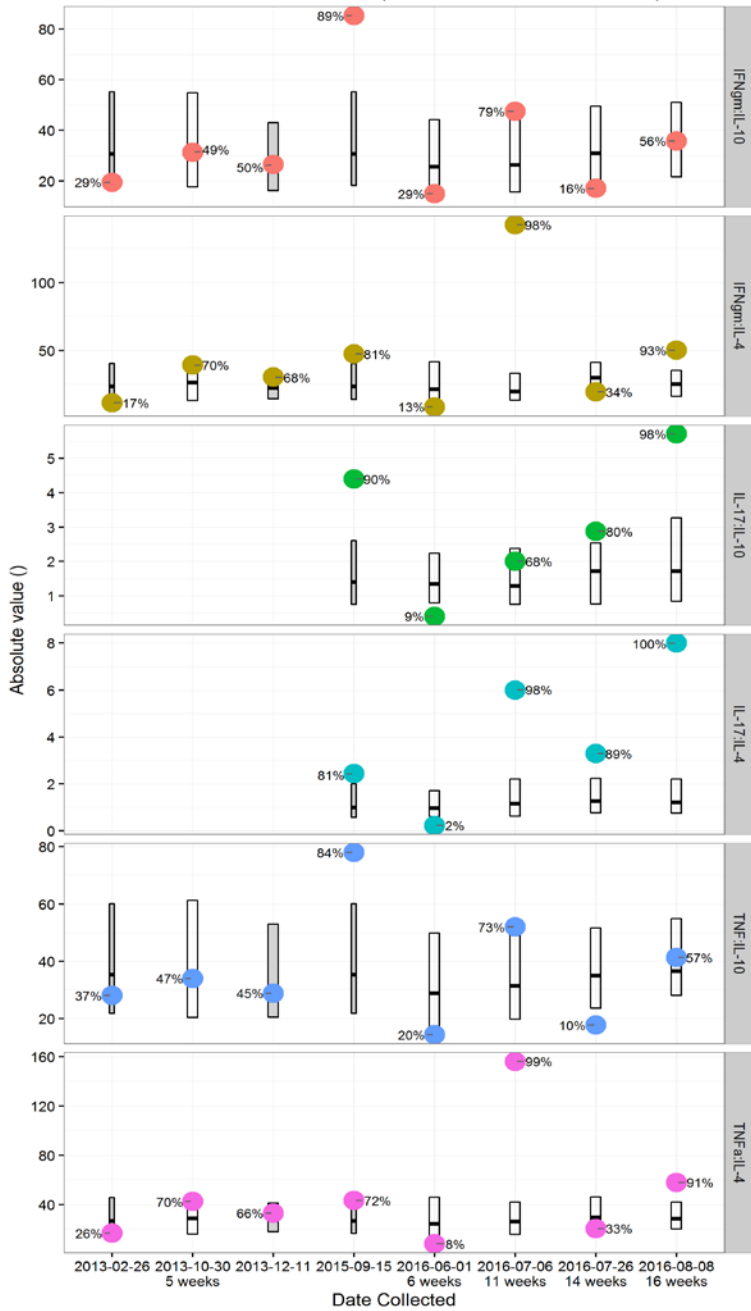
IC Ratios - CD4+ T Cells (Last collection: 2016-08-08)



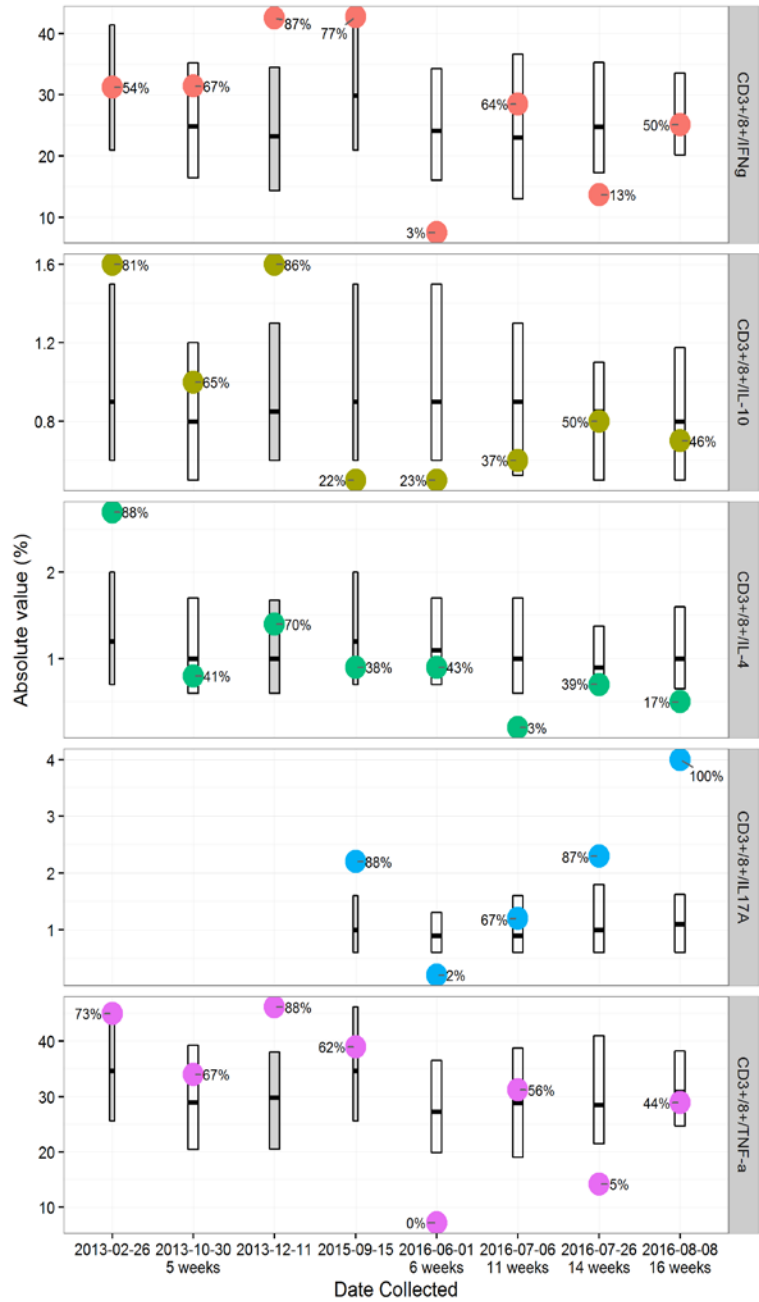
IC - CD4+ T Cells (Last collection: 2016-08-08)



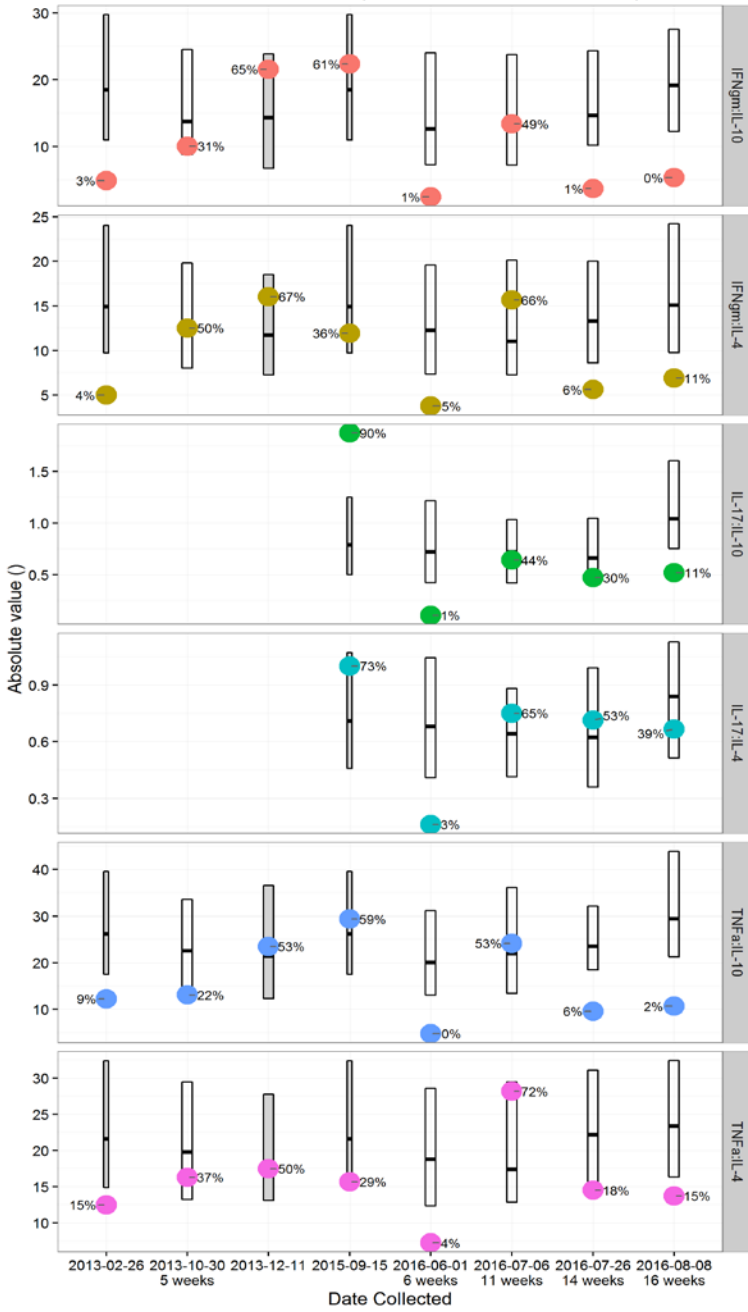
IC Ratios - CD8+ T Cells (Last collection: 2016-08-08)



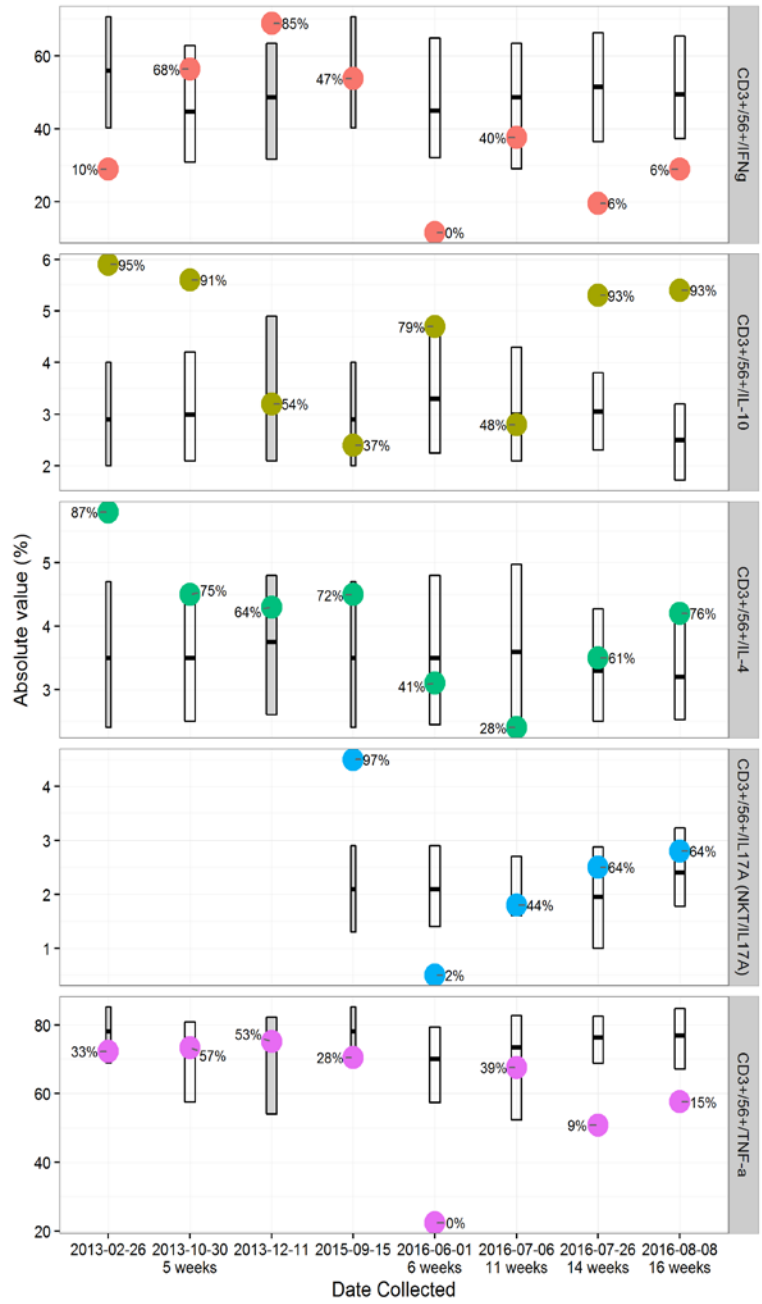
IC - CD8+ T Cells (Last collection: 2016-08-08)

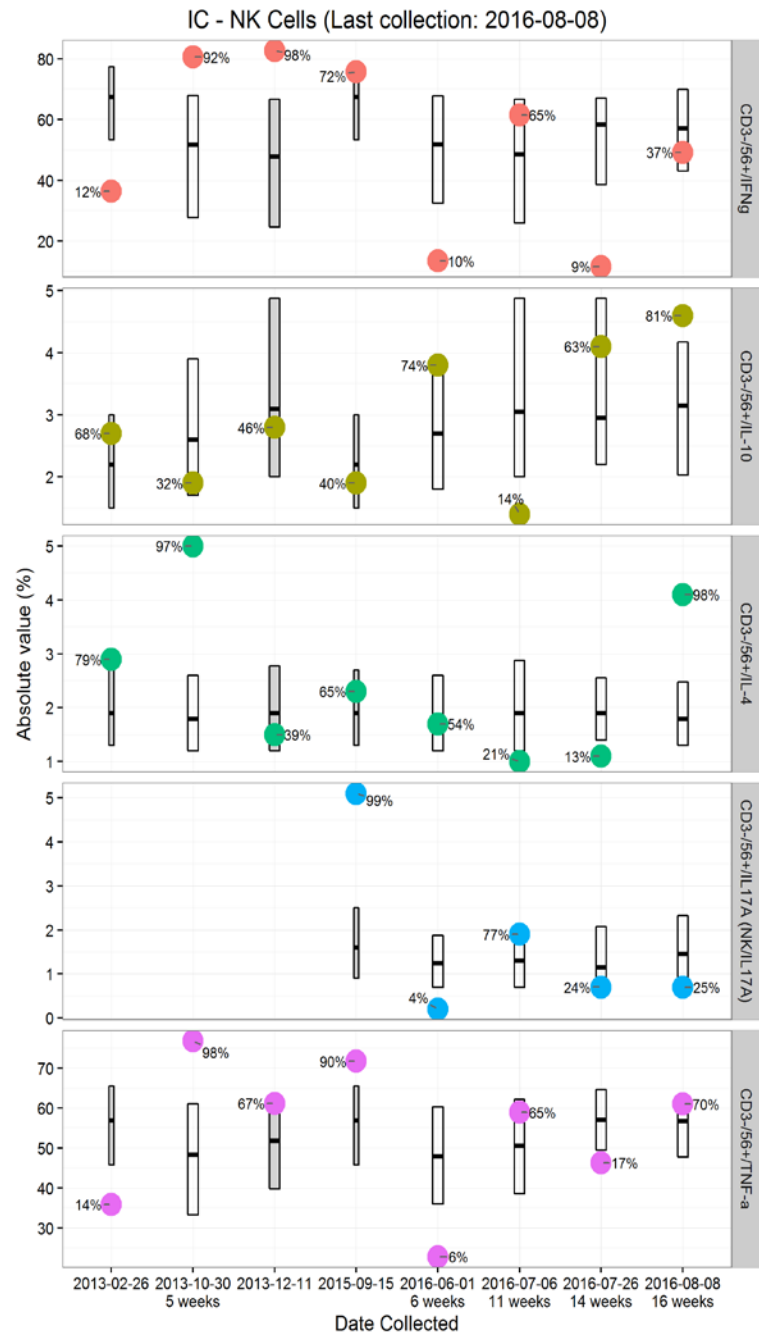
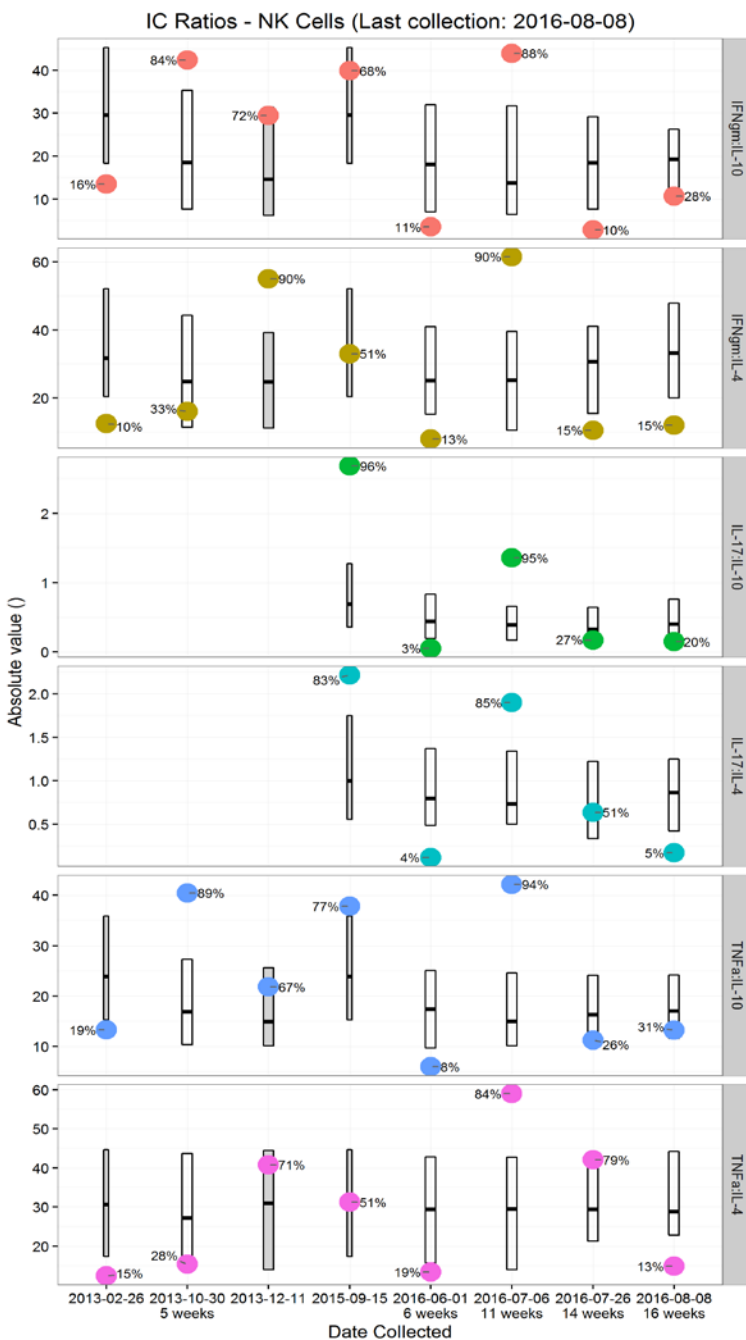


IC Ratios - NKT Cells (Last collection: 2016-08-08)

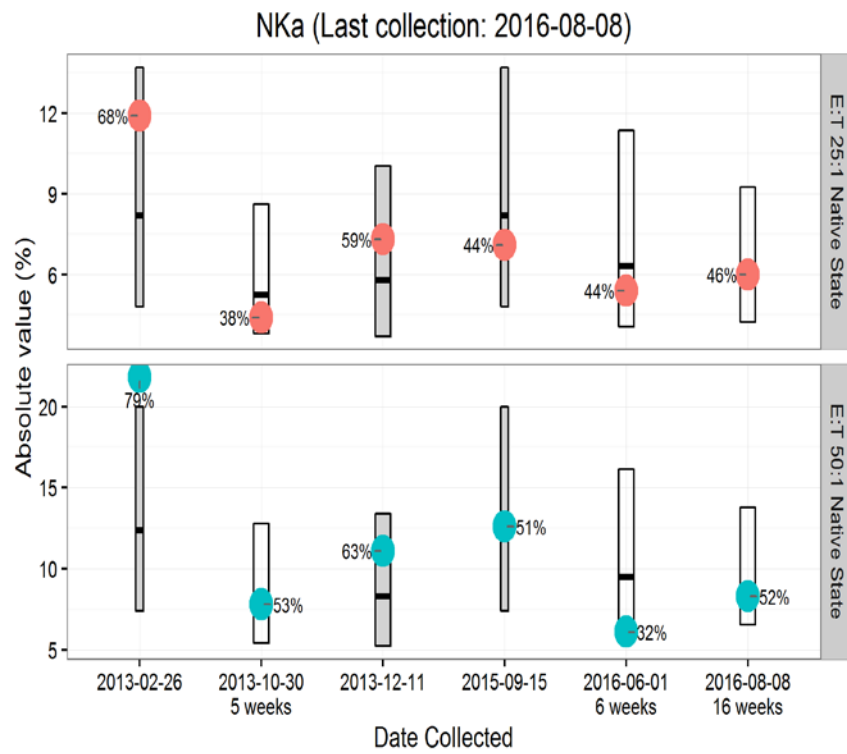


IC - NKT Cells (Last collection: 2016-08-08)



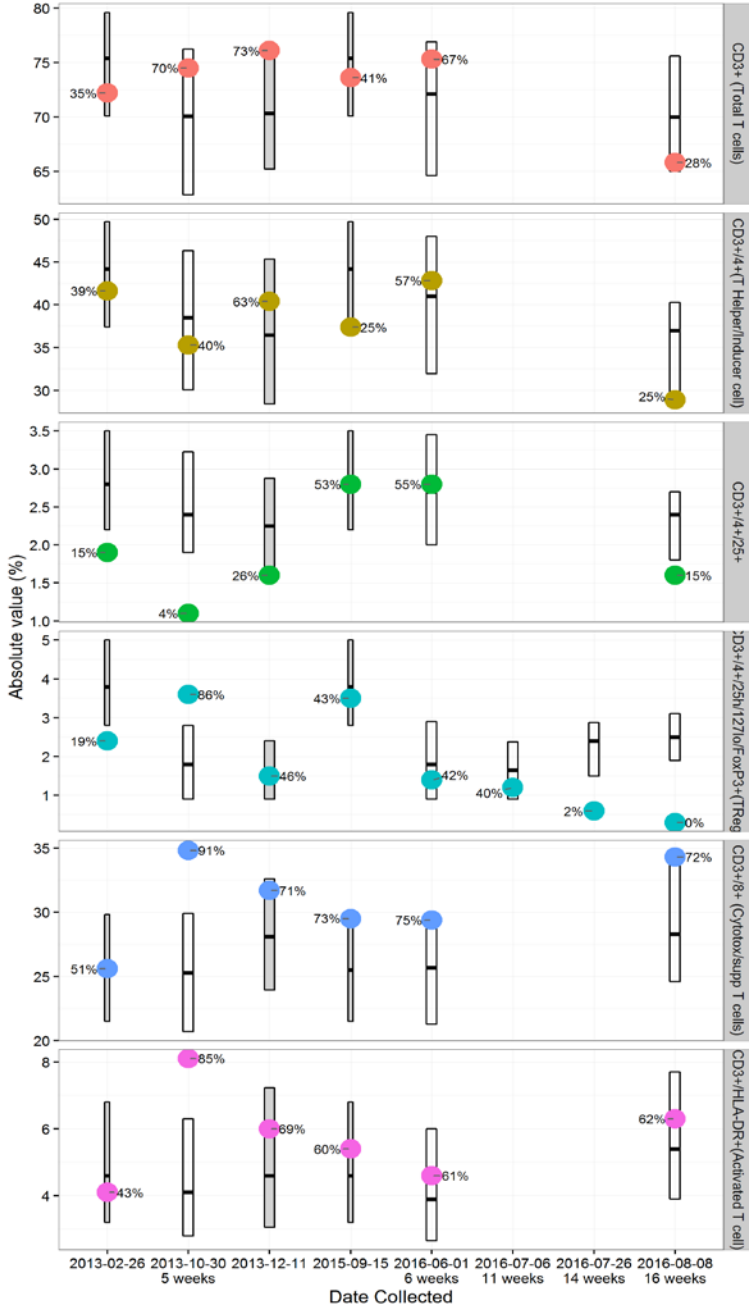


- Compared with results of testing performed on blood from 7-26-16 (~14 weeks pregnant), levels of TNF $\alpha$  positive, IFN $\gamma$  positive, and IL-17 positive cells increased for all tested cell types (CD4+ T cells, CD8+ T cells, NKT cells, NK cells) except for IL-17 positive NK cells (NK17 cells) which remained unchanged and mildly low. This included an increase in TNF $\alpha$  positive CD4+ T cells and NK cells from normal to elevated levels, and IL-17 positive CD8+ T cells (Tc17 cells) from elevated to highly elevated levels. IL-4 positive CD8+ T cells decreased, while IL-4 positive CD4+ T cells, NKT cells, and NK cells increased. These changes to levels of individual intracellular cytokine (IC) positive cells resulted in a slight Th1 shift from a Th2 bias to Th1/Th2 neutrality. Together with the Th1 shift, there was an increase in almost all CD4+ T cell, CD8+ T cell, and NKT cell IC ratios. This included an increase in your CD8+ T cell TNF $\alpha$ :IL-4 and IFN $\gamma$ :IL-4 ratios from normal to elevated levels, and your CD8+ T cell IL-17:IL-4 and IL-17:IL-10 ratios from elevated to highly elevated levels.

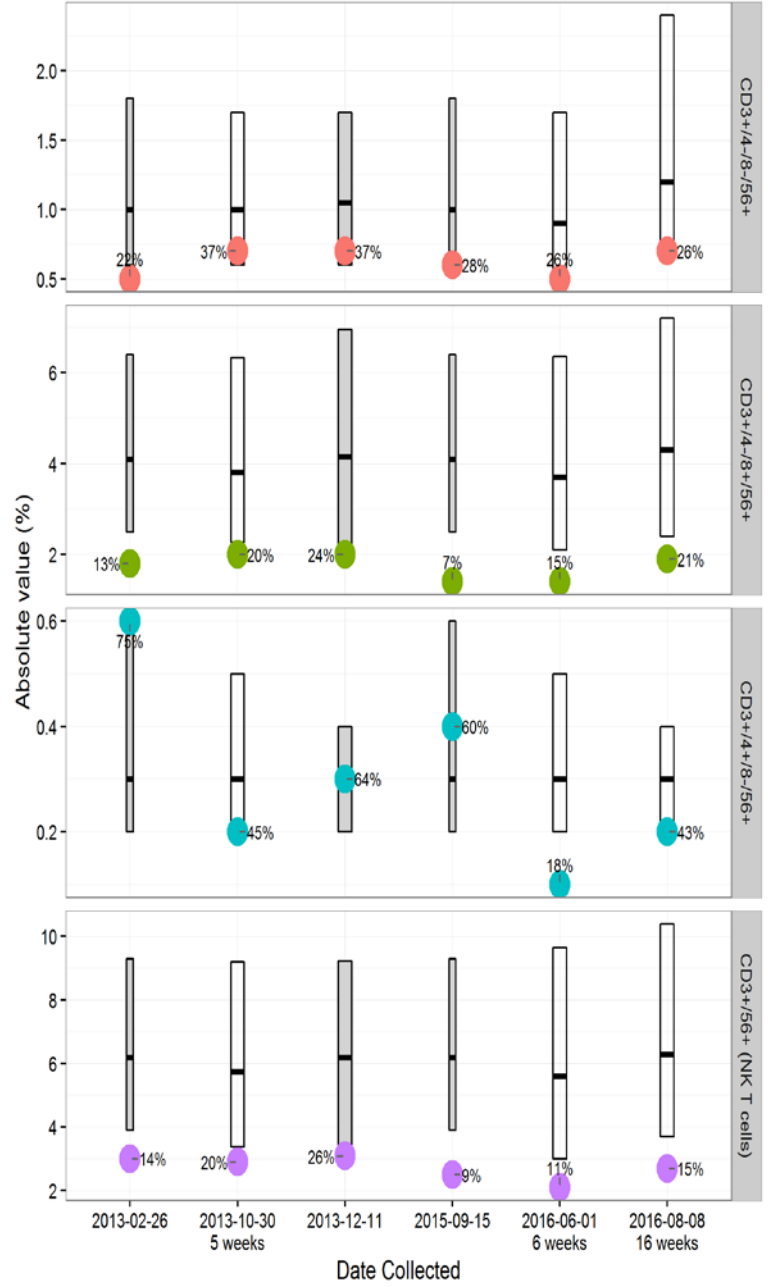


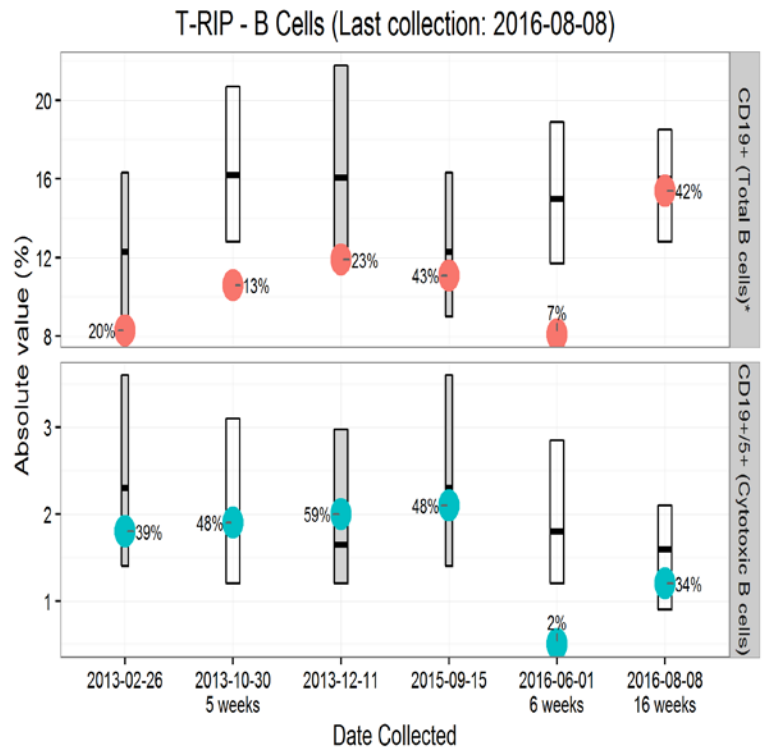
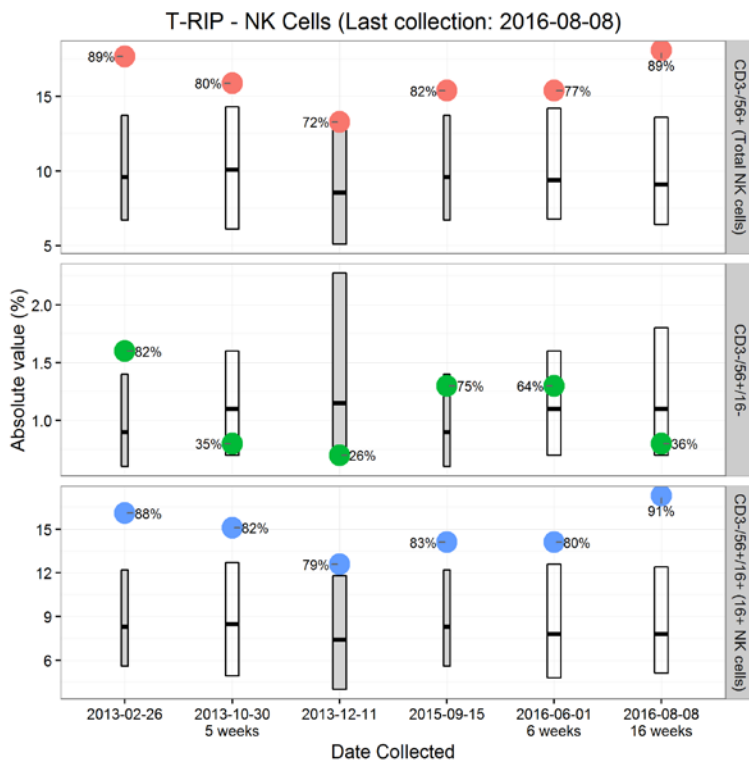
- Compared with results of testing performed on blood from 6-1-16 (~5.5 weeks pregnant), your NK cell cytotoxic activity (NKa) increased slightly but remained within normal ranges.

T-RIP - T Cells (Last collection: 2016-08-08)



T-RIP - NKT Cells (Last collection: 2016-08-08)





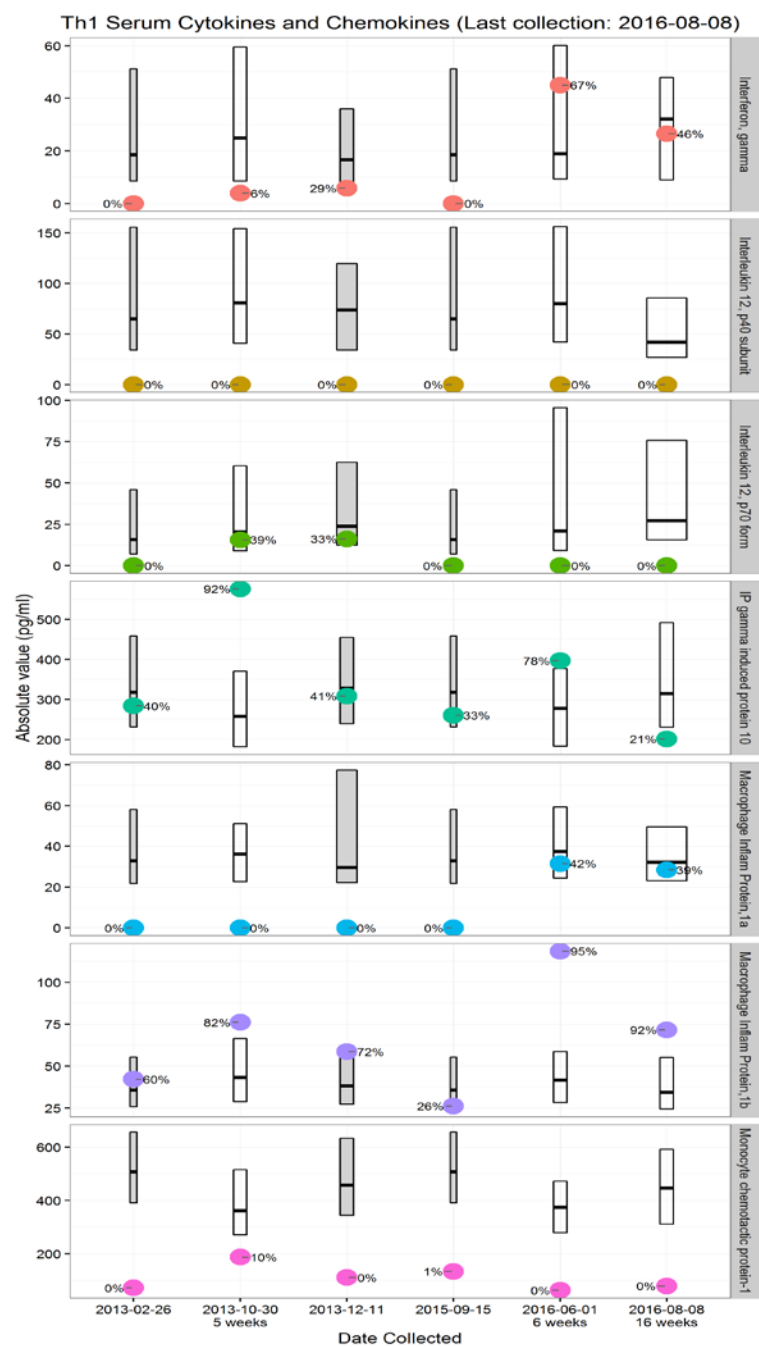
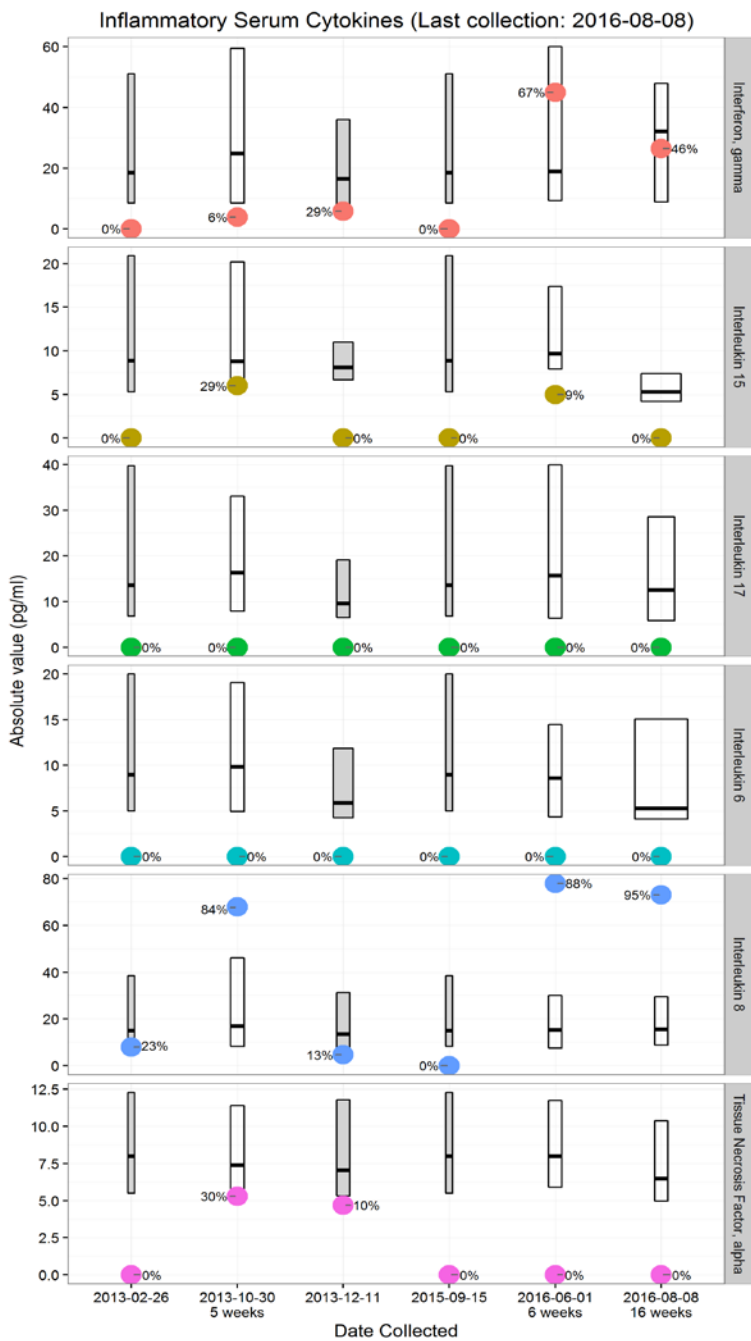
- T-RIP

- Compared with results of testing performed on blood from 7-26-16 (~14 weeks pregnant), your total white blood cells decreased from 34.2 to 19.0 although your Treg cells decreased from low to lower levels, indicative of further recruitment of these cells to the decidua from the peripheral blood.
- Compared with results of testing performed on blood from 6-1-16 (~5.5 weeks pregnant), your total and CD16+ NK cells increased slightly and remained elevated, while your CD8+ and HLA-DR+ T cells increased from normal to mildly elevated levels.

- CBC

- Elevated WBCs = 19.0
- Elevated RDW (18.7)
- Elevated absolute neutrophils (17955)
- Low MCHC (30.6)
- Low absolute monocytes (114)
- Morphological review:
  - Leukocytosis
  - Slight toxic granulation
  - Neutrophilia
  - Slight Burr cells
  - Moderate anisocytosis
  - Slight polychromasia





- Compared with results of testing performed on blood from 6-1-16 (~5.5 weeks pregnant), serum levels of several cytokines and chemokines decreased, including IFN $\gamma$ , IP-10, MIP-1 $\alpha$ , MIP-1 $\beta$ , IL-1R $\alpha$ , IL-5, IL-13, and GRO. This included a decrease in IFN $\gamma$  and IP-10 from borderline elevated to normal levels, although MIP-1 $\beta$ , IL-1R $\alpha$ , and IL-13 remained elevated.

- ANA/APA/ATA
  - 8-8-16
    - Positive for anti-TPO (23.0)
    - Positive for THAB (33.0)
    - Low C4 complement activity (13)
    - Indeterminate levels of:
      - Anticardiolipin IgM (12)
      - Antiphosphatidylglycerol IgM (19)
    - Negative for TSH receptor antibody (<6.00)
    - Normal C3 complement activity (126)
    - Negative for ANAs
    - Total 25 Hydroxy Vit D sufficiency (42.9)
      - 25 Hydroxy Vit D2 = <5.0
      - 25 Hydroxy Vit D3 = 42.9
  - 8-3-16
    - Moderate positive for anticardiolipin IgM (27)
    - Indeterminate levels of:
      - Anticardiolipin IgG (19)
      - Antiphosphatidylethanolamine IgM (16)
      - Antiphosphatidylserine IgM (16)
      - Antiphosphatidylglycerol IgM (18)
  - On 6-1-16 you had indeterminate levels of anticardiolipin IgG (10) and antiphosphatidic acid IgM (17) antiphospholipid antibodies (APAs) were positive for anti-TPO (33.0) and anti-thyroglobulin (85.0) antibodies. Levels of anti-TPO (23.0) and anti-thyroglobulin (33.0) antibodies decreased but remained positive. You are now negative for anticardiolipin IgG and antiphosphatidic acid IgM APAs although you now have indeterminate levels of anticardiolipin IgM and antiphosphatidylglycerol IgM (19) APAs.
- Summary
  - There was an overall increase in activation of your immune system at the cellular level, evidenced by an increase in levels of almost all TNF $\alpha$  positive, IFN $\gamma$  positive, and IL-17 positive cells for all tested cell types (including an increase in TNF $\alpha$  positive CD4+ T cells and NK cells from normal to elevated levels, and Tc17 cells from elevated to highly elevated levels); a slight Th1 shift from a Th2 bias to Th1/Th2 neutrality together with an increase in almost all CD4+ T cell, CD8+ T cell, and NKT cell IC ratios (including an increase in your CD8+ T cell TNF $\alpha$ :IL-4 and IFN $\gamma$ :IL-4 ratios from normal to elevated levels, and your CD8+ T cell IL-17:IL-4 and IL-17:IL-10 ratios from elevated to highly elevated levels); an increase in NKa (remained within normal ranges); and an increase in levels of total and CD16+ NK cells (remained elevated) and CD8+ and HLA-DR+ T cells (from normal to mildly elevated levels).
    - Despite the overall increase in activation of your immune system at the cellular level, your Treg cells from low to lower levels, indicative of further recruitment of these regulatory cells to the decidua from the peripheral blood.
  - There was an overall decrease in levels of systemic inflammation, evidenced by a decrease in serum levels of IFN $\gamma$ , IP-10, MIP-1 $\alpha$ , MIP-1 $\beta$ , IL-1R $\alpha$ , IL-5, IL-13, and GRO (including a decrease in IFN $\gamma$  and IP-10 from borderline elevated to normal levels, although MIP-1 $\beta$ , IL-1R $\alpha$ , and IL-13 remained elevated).
    - Levels of anti-TPO and anti-thyroglobulin antibodies also decreased although they remained positive, indicative of continued autoimmune thyroiditis. You also have indeterminate levels of anticardiolipin IgM and antiphosphatidylglycerol IgM APAs.

- Conclusions
  - Your 8-8-16 data indicate an overall decrease in levels of systemic inflammation as a trailing effect of the overall decrease in activation of your immune system at the cellular level seen with your 7-26-16 testing. However, despite continued recruitment of Treg cells to the decidua, your 8-8-16 data also show an overall increase in activation of your immune system at the cellular level. This included an increase in Tc17 cells to highly elevated levels. Our data indicate an association of elevated levels of Tc17 cells early in the first trimester with an increased risk for miscarriage. Although there is currently no evidence of an association of elevated levels of these cells later in pregnancy with an increased risk for the development of pregnancy complications, continued monitoring of your immune system function is warranted.