**T helper cells in autoimmune diseases**

- Abnormal germinal center (GC) hyper-reaction is important in antibody-mediated autoimmune diseases.
- Development of autoreactive GCs could be a result of dysregulation in APCs, B cells, and/or T helper cells.
- An imbalance in inflammatory Th17 versus regulator Treg has been associated with disease activity in autoimmune diseases.
- Increased numbers or hyperactivity of follicular T-helper (Tfh) cells has been correlated with the pathogenesis and severity of disease in several autoimmune conditions including systemic lupus erythematosus (SLE).

**Hypothesis and Questions**

1. Does deficiency of IL-21 lead to increase of Treg cells or Tfr cells in autoimmune conditions?
2. Whether IL-21 can inhibit Tfr and regulate Tfh/Tfr balance to promote GC formation?

**BXD2 Mice Develop Spontaneous Autoreactive GC and Erosive Arthritis**

- H&E staining
- anti-IgM
- anti-IgG

**IL-21 Deficiency Led to Defect of GC B Cells and Tfh Cells**

- Serum IL-21 level (Absorbance at A450)
- B6
- BXD2

Mountz et al. Scan J Immunol 2004
Hu et al. Arthritis Rheum. 2006

Question 1

Is there increase of Treg cells or Tfr cells in BXD2-Il21-/- mice?

Increased Frequency of Tfr Cells and the Ratio of Tfr/Tfh in BXD2-Il21-/- Mice

No Increase of Conventional Treg in BXD2-Il21-/- Mice

Question 2:

Whether IL-21 can inhibit Tfr and regulate Tfh/Tfr balance to promote GC formation, especially in autoimmune condition?

IL-21 Inhibited the Phenotypic Features of Tfr Cells in vitro
Determine the Inhibition Effect of Tfr Cells *in vitro*

![Image of CD4 T cells and Tfr cells](image1)

**IL-21 Counteracted the Inhibition of Tfr Cells on Th and B Cells *in vitro***

![Graph showing T cells proliferation](image2)

Determine if Tfr Cells Inhibit GC Formation *in vivo*?

![Flowchart showing FACS staining and ELISPOT](image3)

**Transfer of IL-21−/− Tfr Cells Decreased Autoantibody Production in BXD2 Mice**

![Graph showing autoantibody production](image4)

Summary and Conclusions

![Diagram showing T-reg and IL-21](image5)

**Significances:**
Manipulating Tfr/Th and IL-21 signaling: Elastic transfer of Tfr cells plus inhibition of IL-21 may be a promising approach to restore the T-dependent B-cell immune homeostasis in autoimmune conditions.

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Questions?