Effects of type 1 interferon deficiency on B-cells in lupus-prone mice

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Introduction

- Systemic Lupus Erythematosus (SLE) is a debilitating autoimmune disease that affects over 5 million people worldwide
- Lupus occurs more frequently in females than in males (8:1)
- Disease determining factors include genetics, environmental factors and sex hormones
- Symptoms of SLE in patients vary and can have multiple effects including anemia, hair loss and glomerulonephritis
- Deficiency in IFNAR ameliorates disease (Jorgensen et al, 2007) and elevating endogenous type I interferons, accelerates disease development (Jorgensen et al, 2006).

Hypothesis

Specific deletion of IFNAR in B cells will decrease autoantibody production, immune complex formation and deposition

Materials and Methods

- Cre recombinase is a reliable method used in IFNAR gene knockout that recognizes and splices specific DNA sequences (LoxP sites)
- Genotyping by ear clipping: Digestion, DNA extraction, PCR, Gel-electrophoresis
- Flow Cytometry was used for the identification of cell subsets/subpopulations
- Enzyme-linked immunosorbent assay (ELISA) was used to measure total IgG, IgM, and anti-chromatin IgG concentrations.
- Immunofluorescence staining of kidney samples with IgG-TxRd (1:500) and C3-FITC (1:500)
- Project sample size of B6.Nba2 mice:
  - IFNAR +/+: n=6
  - IFNAR flx/flx: n=9

Results

IFNAR flx/flx mice exhibit lower spleen weight and splenocyte count than IFNAR +/+ and flx/+ mice

IFNAR flx/flx mice show similar deposition of IgG than IFNAR +/+ and flx/+ mice

Conclusions

B-cell specific IFNAR deficiency in B6.Nba2 lupus-prone mice results in:
- Significantly lower spleen weight
- Significantly lower splenocyte count
- Significantly lower anti-chromatin IgG levels
- But, no difference in immune complex deposition and C3 fixation.

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References