Introduction

- Neonates mount adult like protective immune responses to vaccines only after multiple immunizations.
- Impaired follicular helper T cell (TFH) and germinal center (GC) B cell development likely responsible for weak vaccine responses in neonates.
- The underlying mechanisms in ablated TFH and GC B cell response are not known.

Results

1. High TFR : TFH Ratio Persists Through Out the Immune Response in Neonatal Mice

   A. Adult Gated on CD4+CXCR5+PD-1hi and TFR cells among Foxp3+CD4+ cells are plotted. The ratio of TFR to TFH cells (TFR : TFH) are plotted.

2. Co-administration of IL-6 with PPS14-TT Vaccine Suppresses TFR Cell Generation and Antibody Responses in Neonatal Mouse

   A. Adult Gated on CD4+CXCR5+PD-1hi and TFR cells among Foxp3+CD4+ cells are plotted.

3. IL-6 Signaling Is Impaired in Neonatal TFH Cells

   A. Media vs IL-21 and IL-6 vs IL-21 stimulation.

   B. IL-21 stimulation ratio of pSTAT3+Foxp3+ and pSTAT3+Foxp3- among TFH cells.

4. Inhibitory IL-2 signaling is promoted by IL-6 in neonatal vaccine

   A. IL-2R expression in CD4+ T cells.

   B. IL-2R expression in Foxp3+T cells.

   C. IL-2R expression in Foxp3+Fox3+ cells.

5. TLR9 and detoxified TLR4 ligand improve anti-bacterial Th1 response

   A. IgG1, IgG2c, IgM, IgA in adult and neonatal mice.

   B. Serum anti-PPS14 IgG and IgA titers were determined in ELISA 6 weeks after immunization.

   C. CD4+ and TFR cells among Foxp3+CD4+ cells are plotted.

6. Mechanism of TLR ligand-based adjuvant in neonatal immune system

   A. IL-2R expression in CD4+ T cells.

   B. IL-2R expression in Foxp3+T cells.

   C. IL-2R expression in Foxp3+Fox3+ cells.

   D. IL-2R expression in Foxp3+Fox3+Fox3+ cells.

Summary and Conclusion

- IL-6 improves TFH generation by suppressing IL-2R in adult mice. In contrast to our surprise, IL-6 is detrimental for TFH generation in neonatal mice because IL-6 stimulates IL-2R expression on TFH cells, thereby rendering them susceptible to IL-2 mediated suppression. Our adjuvant study further highlight this mechanism because CpG and LPS both reduced IL-6R and IL-2R expression on TFH cells.