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Dysregulated B-cell T-cell Interactions in Immune Mediated Glomerular Diseases

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Objectives : Immune mediated glomerular diseases (IMGD) including IgA Nephropathy (IgAN), membranous nephropathy (MN), focal segmental glomerulosclerosis (FSGS) and minimal change disease (MCD) share clinical presentations. However, these IMGD result from different immune mechanisms that are poorly understood. Although the immunological mechanisms for IMGD remain relatively unknown, recently, the dysregulation of B-cells has been proposed to be a critical factor.

Methods : We studied IgAN (n=10), MN (n=10), FSGS (n=7), and MCD (n=7) patients and healthy controls (n=10). Utilizing cell sorting, the circulating T-follicular like helper (cT_{FH}) cells and naïve B-cells were collected to evaluate the cT_{FH} cell – naïve B-cell interactions. Cells were co-cultured for 6 days in the presence of a cognate antigen, and the immunoglobulins and cytokines were measured in the cell culture supernatant.

Results : Using the LEGENDplex bead-based immunoassay, we measured the concentration of IL-5, IL-13, IL-2, IL-6, IL-10, IL-17A, IL-17F, IL-4, and TNF- α secreted into the cell culture supernatant. There were significantly decreased concentrations of IL-6 and IL-4 ($P < 0.05$, one way ANOVA), and a significant increase in the IL-5 concentration ($P < 0.05$, one way ANOVA) in cells derived from IgAN patients compared to HC, MN, FSGS, and MCD patients. A significant increase was observed in the IL-10 concentration ($P < 0.05$, one way ANOVA) in cells derived from FSGS and MCD patients compared to HC and IgAN patients. Analysis of the immunoglobulins demonstrated increased secretion of IgA into the cell culture supernatants derived from IgAN patients compared to HC, MN, FSGS, and MCD patients ($P < 0.01$, one way ANOVA), and no differences in the IgG isotypes were observed.

Conclusions : Our data determined cytokine profiles generated from the cT_{FH} cell – naïve B-cell interactions have the potential to influence immunoglobulin production, which needs to be experimentally validated.