injury, and reduced renal deposition of immune-complexes compared to untreated mice. Regarding Th cell subsets, the proportion of Th1 and Th2 cells decreased and regulatory T cells (Tregs) increased in splenocytes from secretome treated mice. In addition, expression of mature dendritic cells and plasma cells in splenocytes, as well as M1 macrophages in the peritoneum decreased following secretome treatment. Secretome treatment resulted in a decrease of serum cytokines of interferon-γ, interleukin (IL)-17A, and anti-dsDNA, whereas IL-10 level was increased. No toxic effect of secretome was shown in mice. Treatment of CD4+ T cells isolated from SLE patients with secretome induced an increase of Tregs.

Conclusions Our results suggest secretome could be a promising therapeutic agent for SLE.

LO-043 SINGLE-CELL RNA SEQUENCING REVEALS THE DYNAMICS OF CIRCULATING IMMUNE CELLS IN SLE PATIENTS TREATED WITH BELIMUMAB

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Background Systemic lupus erythematosus (SLE) has been well known to be associated with B cell hyperactivation with over-expression of B cell-activating factor of the TNF family

Abstract LO-043 Figure 1 Dynamics of circulating immune cells in SLE patients after anti-BAFF treatment. (A) UMAP visualization of 26 cell types. (B) UMAP visualization of T cells. (C) UMAP visualization of B cells. (D) Bar graph comparing the frequency of B cell subtypes at different timepoints. (E) Bar graph comparing the frequency of T cell subtypes at different timepoints. (F) IFN-γ related genes compared by CD4+ T cell subtypes.
Belimumab (anti-BAFF therapy) was approved as the first targeted biological drug for SLE. We investigated dynamic feature of immune cells over the Belimumab treatment using longitudinal single-cell transcriptome data.

**Methods**
We conducted single-cell RNA sequencing (scRNA-seq) along with T cell receptor (TCR) and B cell receptor (BCR) repertoire from serial longitudinal PBMC samples (0, 2 weeks, 1, 3, 6 and 12 months after Belimumab) from four Korean patients with SLE.

**Results**
We profiled more than 130,000 PBMC from the four patients at six distinct time points during Belimumab treatment. The mean SELENA-SLEDAI score from the patients decreased from 12.5 at baseline to 3.5 at 12 months. We observed the dynamic changes of several B cell components during Belimumab treatment; decrease of naïve B cells at one month followed by progressive decline in plasmablasts at six months (figure 1). However, although ‘age-associated B’ cell population was clearly identified at the single-cell level in SLE patients, its proportion did not change much over the course of treatment. Intriguingly, there was a notable upregulation of cytotoxic-associated genes (LTB, FCGR3A, KLRC4) in effector memory CD8 T cells (Tem) followed by a significant increase in the frequency of Tem. Peripheral T helper cells (Tph) exhibit higher IFN-G related gene expression compared to other T cell subtypes, which is drastically reduced shortly after Belimumab treatment.

**Conclusions**
We identified dynamic changes of immune cell components along with transcriptomic signatures during Belimumab treatment, suggesting that therapeutic effects of Belimumab occurs through its effect on T cell lineage as well as its effect on B cell lineage.

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**Plenary session 4: practical treatment issues**

**LO-023 REMISSION OF LUPUS NEPHRITIS: THE TRAJECTORY OF HISTOLOGIC RESPONSE IN SUCCESSFULLY TREATED PATIENTS**

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**Background**
Lupus nephritis (LN) is characterized by glomerular and tubulointerstitial (TI) inflammation that presumably must resolve with treatment to achieve remission. Here we sought to document the trajectory of histologic resolution using protocol kidney biopsies during LN treatment.

**Methods**
A cohort (n=110) of proliferative LN patients was prospectively followed during treatment with standard (glucocorticoids plus MMF or cyclophosphamide) therapy. Patients underwent a diagnostic kidney biopsy (Bx1), a biopsy within the first treatment year (Bx2, 9.7 months), and a biopsy after ≥3 years of total immunosuppression (Bx3, 42.6 months). At each biopsy NIH activity and chronicity indices (AI, CI) were calculated.

**Results**
Patients were followed for a median of 109 months. Treatment was successful. At last follow-up only 2 patients had ESKD and only 5 developed new CKD (eGFR <60 ml/min/1.73m²). AI decline was biphasic, rapidly falling immediately after starting treatment and then slowing (figure 1). At Bx2 the percent of biopsies positive for cellular crescents (CC), fibrinoid necrosis (FN), and neutrophil infiltration (NEU) fell precipitously, while endocapillary hypercellularity (EH) and hyaline deposits (HD) declined gradually. At Bx3 fewer than 5% of biopsies had residual CC, FN, NEU, or interstitial inflammation, but 25% still had EH and HD (figure 1). Over 90% of diagnostic biopsies had IgG and complement components C3 and Clq. At Bx3 only 30–40% of biopsies continued to show IF for complement, but IgG persisted in 66% of biopsies. Chronicity increased in most patients after Bx1. The rate of increase of glomerulosclerosis, tubular atrophy, and interstitial fibrosis was greatest from Bx1 to Bx2 and slowed between Bx2 and Bx3 (figure 1).

**Conclusions**
The most inflammatory LN lesions respond rapidly to conventional immunosuppression, but EH and HD are more resistant. Complement deposition resolves quickly, but IgG can persist in glomeruli for years. Despite rapid improvement in inflammation, chronic damage accumulates early.