INTERFERONS (IFN) have been shown to play an integral role in driving immune dysregulation in SLE (1) and their levels, as measured by IFN-induced gene (IG) expression in whole peripheral blood, are associated with markers of disease activity such as antibody-stranded DNA antibodies, clinical SLEDAI-2K, and reduced serum complement levels in cross-sectional studies (2). However, the observation that IG expression remains relatively stable over time in longitudinal studies has raised speculation that the levels of IG expression in whole peripheral blood may not accurately reflect those in the adaptive immune cell subsets such as T helper and B cells that are thought to play an important role in flare (3). In this study, we used a novel mass cytometry approach to investigate IG expression in individual immune cell populations to determine if there is an individual immune cell basis to assess the correlation between IFN-induced protein (IP) expression and expansion/activation of various immune populations during and after flares.

**RESULTS**

**IP expression correlates with E2 expression profile in most cell subsets**

- **Figure 1.** Cytometry bars chart showing correlation between IFN induction and IP expression in whole blood and in 7 major immune cell subsets. All IP expression was measured by mass cytometry.

**Assessment of peripheral blood immune profile in 26 immune populations**

- **Figure 2.** UMAP of the individual cell types showing their differential abundance and coexpression. A: 26 immune cell populations were obtained in healthy controls and SLE patients. Only the gene expression of those immune cell populations were plotted on the 2D plane (A). B: UMAP of the individual cell types showing their differential abundance and coexpression. A: 26 immune cell populations were obtained in healthy controls and SLE patients. Only the gene expression of those immune cell populations were plotted on the 2D plane (A).

**Significant IP expression variability between and within immunologic populations**

- **Figure 3.** UMAP of different immune cells showing their differential abundance and coexpression. A: 26 immune cell populations were obtained in healthy controls and SLE patients. Only the gene expression of those immune cell populations were plotted on the 2D plane (A). B: UMAP of the individual cell types showing their differential abundance and coexpression. A: 26 immune cell populations were obtained in healthy controls and SLE patients. Only the gene expression of those immune cell populations were plotted on the 2D plane (A).

**IP expression at baseline predicts disease activity at 1 year follow up**

- **Figure 4.** Heatmap showing the division of patients into 5 IFN light; Intermediate, or low based on the median IP score in each cell type. Patients were considered to be IFN light if at least 75% of their cell subset had IP expression below the median. IFN light had less than 50% of IFN light expressing cells.

**IP expression at baseline predicts disease activity at 1 year follow up**

- **Figure 5.** Heatmap showing the division of patients into 5 IFN light; Intermediate, or low based on the median IP score in each cell type. Patients were considered to be IFN light if at least 75% of their cell subset had IP expression below the median. IFN light had less than 50% of IFN light expressing cells.

**IP expression at baseline predicts disease activity at 1 year follow up**

- **Figure 6.** Heatmap showing the division of patients into 5 IFN light; Intermediate, or low based on the median IP score in each cell type. Patients were considered to be IFN light if at least 75% of their cell subset had IP expression below the median. IFN light had less than 50% of IFN light expressing cells.

**CONCLUSION**

- **IP score reflects IG expression found in whole blood**
- **IP follow a similar pattern of expression in most cell subsets**
- **Flaring patients have higher IP in most cell subsets than quiescent patients**
- **Many of the changes in activation and trafficking molecules and are more disease status confirmed by IFN incubation assays**
- **IP expression can be used to predict subsequent flare, particularly in the pre-ABC and ABC populations**

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**REFERENCES**

5. Schroeder Arthritis Institute, Krembil Research Institute, University of Toronto Lupus Clinic, Division of Rheumatology, and Princess Margaret Cancer Centre, University Health Network, Toronto, Canada.