Neutrophil extracellular traps (NETs) are part of the innate immune system and are pathogenic in SLE. We therefore investigated 56 lupus patients who met at least 4 SLICC criteria. Results were compared to 20 age, sex, and race matched healthy controls. We found that curli/eDNA induced more NETs in SLE PMNs compared to healthy controls. In SLE, patients who were high inducers of NETs triggered by curli/eDNA complexes were also a high inducer of NETs triggered by LPS and PMA. Interestingly, patients who were anti-dsDNA positive made more NETs in response to curli/eDNA complexes and LPS. We did not observe this in patients who were anti-dsDNA negative. Mechanistically, we found that curli/eDNA induce NETs via NADPH oxidase. Finally, we found patients who had bacteriuria had a higher amount of NET production in response to curli/eDNA complexes and PMA compared to patients with no bacteriuria. We conclude

1) that lupus PMNs are in a chronic inflammatory state. And 2) that curli/eDNA complexes can activate neutrophils and exposure to UPECs could be a mechanism to sustain autoantigens in the form of neutrophil extracellular traps.
via flow cytometry to identify immune cell subsets. Spleen cells were treated with vehicle or TLR7/8 agonist overnight prior to supernatant analysis. In a parallel experiment, mice were treated for two weeks with a topical TLR7 agonist (R848) to assess effects on immune cell populations.

Results Immune cell subsets in spleen were similar in all mice. Cell counts of ex vivo and Flt3L- cultured BM-DCs were reduced in NOER mice. Conventional DCs (cDCs) were increased in MOER mice, and NOER mice trended higher in CD19+ cells. Other immune populations remained similar. NOER mice trended lower in IL-6 response after overnight R848 stimulation.

Conclusion Preliminary results suggest membrane ERα-initiated events are required to develop certain innate immune cell subsets and for robust expansion of DCs. Membrane and nuclear functions of ERα may compensate for each other in some cases. More studies are needed to clarify the role of ERα localization in modulating immune cell development and function.

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CHARACTERIZATION OF REGULATORY RECEPTORS ON PLASMACYTOID DENDRITIC CELLS IN LUPUS

Regulatory or suppressive receptors on plasmacytoid dendritic cells (PDCs) are an attractive therapeutic target in systemic lupus erythematosus (SLE), given the role type I interferon (IFN) plays in this disease. In this study, we determine whether SLE patient PDC regulatory receptor expression and function associates with disease features in SLE. We used quantitative multicolor flow cytometry to measure regulatory receptors on PDCs from SLE patients and control subjects, including immunoglobulin like transcript 7 (ILT7), bone marrow derived antigen 2 (BDCA2), ILT3, leukocyte-associated immunoglobulin-receptor 1 (LAIR1), natural killer cell P44-related protein (NKP44), bone marrow stromal cell antigen 2 (BST2), and dendritic cell (DC) immunoreceptor (DCIR). For functional studies, cells from 9 SLE patients and 9 controls were treated with ILT7 and BDCA2 crosslinking antibodies followed by TLR9 agonists. ILT7 and BDCA2 expression on SLE patient PDCs were inversely correlated with disease activity by SLEDAI score. High IFN SLE patients had increased levels of the ILT7 ligand BST2, and at the same time reduced ILT7 expression. BDCA2 levels were 5-fold higher than ILT7 levels, and crosslinking ILT7 only weakly inhibited IFN secretion. Crosslinking BDCA2 significantly reduced IFN production in SLE patient cells, but this effect on IFN was much greater in patients with low SLEDAI scores than those with high SLEDAI scores. In conclusion, we identify associations between PDC regulatory receptor expression and clinical disease in SLE, and dominant inhibitory function of BDCA2 over ILT7 in PDC type I IFN secretion with dependency upon disease activity.

URINE COMPLEMENT ACTIVATION PRODUCTS IN LUPUS NEPHRITIS

Background Complement activation plays a critical role in the development of kidney injury during lupus nephritis (LN). Clinical trials targeting the complement pathway are now underway in LN. It is therefore important to understand the...