Multiple immune cells express IFNAR, but it is not known what the effect of IFN- stimulation is on each cell type and how that stimulation affects symptom presentation. We hypothesize that BIFNAR mice would be specifically protected from splenomegaly, B cell activation, and ANA production, due to IFN-s known ability to enhance the antibody response. **Methods** To examine the role of B cell responses to IFN-stimulation in mouse lupus-like disease, we studied B cell specific IFNAR-deficiency (BIFNAR) in the B6.Nba2 spontaneous lupus-like disease model, using flow cytometry, ELISA, qRT-PCR and Immunostainings. We also immunized the mice with NP-CGG or NP-Ficoll in complete Freund's adjuvant to determine the effect of IFNAR-expression by B cells during antibody responses to exogenous antigen.

Results At four months of age, BIFNAR mice displayed slightly reduced spleen sizes, although this decrease was not significant until nine months of age. Furthermore, starting at 4 months of age, BIFNAR mice displayed reduced levels of chromatin specific ANAs along with reduced populations of plasmablasts, plasma cells and activated B cells. All other measures of disease showed no difference including total IgG and IgM production, immune complex deposition and C3 complement fixation in the kidney glomeruli, and glomerular size. Somewhat surprising, antibody responses to T-dependent and T-independent immunizations were also not affected.

Conclusions IFN- stimulation on B cells contributed to splenomegaly, increased B cell activation and differentiation, and subsequent production of chromatin specific ANAs, but had no specific role in the response to exogenous antigen. Thus, IFN- remains a valid therapeutic target for SLE; especially in patients presenting with high ANAs.

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PREDICTION OF FETAL LOSS IN PREGNANT PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Abstract 250 Table 1 Patients' characteristics during pregnancy

Variables	Total n=338 (%)	Live birth n=300 (%)	Fetal loss n=38 (%)	P value
Characteristics				
Age (yr, mean±SD)	29.5±4.0	29.7±3.9	28.6±4.5	0.131
History of SLE (yr, mean±SD)	5.7±4.3	5.8±4.4	4.5±4.1	0.091
History of therapeutic abortion (frequency, mean±SD, range)	0.04±0.2 (0–2)	0.04±0.2 (0–1)	0.08±0.4 (0–2)	0.657
History of spontaneous abortion (frequency, mean±SD, range)	0.4±0.9 (0–7)	0.4±1.0 (0–7)	0.3±0.6 (0–7)	0.687
Region				
City	237 (70.1)	210 (70.0)	27 (71.1)	0.894
Rural	101 (29.9)	90 (30.0)	11 (28.9)	
Nullipara	291 (86.1)	258 (86.0)	33 (86.8)	0.888
Pre-pregnancy hypertension	10 (3.0)	6 (2.0)	4 (10.5)	0.016*
Unplanned pregnancy	45 (13.3)	32 (10.7)	13 (34.2)	0.000*
SLE clinical features				
Renal disorder	97 (28.7)	76 (25.3)	21 (55.3)	0.000*
Mucocutaneous	106 (31.4)	94 (31.3)	12 (31.6)	0.975
Hematologic disorder	66 (19.5)	53 (17.7)	13 (34.2)	0.015*
Neurologic disorder	5 (1.5)	3 (1.0)	2 (5.3)	0.181
Arthritis	70 (20.7)	63 (21.0)	7 (18.4)	0.712
Serositis	17 (5.0)	10 (3.3)	7 (18.4)	0.001*
Laboratory features during pregnancy				
24h-Urinary protein (g, mean±SD)	1.04±2.43	0.6±1.5	4.3±4.9	0.000*
Anti-dsDNA	261 (77.2)	226 (75.3)	35 (92.1)	0.020*
Anti-Ro/SSA	150 (44.4)	132 (44.0)	18 (47.4)	0.694
Anti-La/SSB	47 (13.9)	41 (13.7)	6 (15.8)	0.722
Anti-Sm	20 (5.9)	16 (5.3)	4 (10.5)	0.361
aPL	46 (13.6)	38 (12.7)	8 (21.1)	0.156
Hypocomplementania-C ₃	90 (26.6)	62 (20.7)	28 (73.7)	0.000*
Hypocomplementania-C ₄	60 (17.8)	45 (15.0)	15 (39.5)	0.000*

NOTE: * = P<0.05

Abstract 250 Table 2 Multivariable analysis of fetal loss

Variables	Risk Factors Included Individually OR(95% CI)	Risk Factors Included Simultaneously OR(95% CI)	Risk Factors Selected Using Stepwise Regression OR(95% CI)
Unplanned pregnancy	4.33 (1.71–11.00) **	3.01 (0.90–10.02)	2.84 (1.12–7.22) *
Pre-pregnancy hypertension	6.45 (1.60–26.06) **	5.24 (0.74–37.38)	-
Hypocomplementania-C ₃	11.43 (5.15–25.33) **	7.09 (2.60–19.36) **	5.46 (2.30–12.97) **
Hypocomplementania-C ₄	3.80 (1.81–7.98) **	0.56 (0.19–1.60)	-
Renal disorder	3.58 (1.76–7.28) **	0.33 (0.09–1.15)	-
Hematologic disorder	2.19 (1.02–4.69) *	0.90 (0.32–2.53)	-
Anti-dsDNA	3.62 (1.07–12.17) *	2.58 (0.65–10.24)	-
24h-Urinary protein			
urinary protein<0.3 g/24 hour	1	1	1
0.3≤urinary protein<1.0 g/24 hour	3.34 (1.05–10.68) *	3.23 (0.90–11.65)	2.10 (0.63–6.95)
urinary protein≥1.0 g/24 hour	14.85 (6.25–35.31) **	16.20 (3.90–67.29) **	5.89 (2.30–15.06) **

NOTE: *p<0.05; **p<0.01; Multivariable models adjusted for age at conception (continuous), history of SLE (continuous), history of therapeutic abortion (continuous), history of spontaneous abortion (continuous), region (city vs rural), nullipara (nullipara vs multipara)

Abstract 250 Table 3 Adjusted odds ratio and B coefficient from cohort with multivariable logistic regression model and corresponding risk score

Variables	Ajusted OR	B	Score
Unplanned pregnancy			
Planned pregnancy	1		0
Unplanned pregnancy	2.84	1.04	1
Hypocomplementemia-C₃			
Non-Hypocomplementemia-C ₃	1		0
Hypocomplementemia-C ₃	5.46	1.70	2
24h-Urinary protein			
Urinary protein<0.3 g/24 hour	1		0
0.3≤Urinary protein<1.0 g/24 hour	2.10	0.74	1
Urinary protein≥1.0 g/24 hour	5.89	1.77	2

Abstract 250 Table 4 The risk classification for fetal loss according to the risk score system

Risk	N	%	Fetal loss(N)	Fetal loss(%)
Low risk (0–3)	295	87.3%	15	5.1%
High risk (>3)	43	12.7%	23	53.5%
Total	338	100%	38	11.2%

p<0.01

Background Systemic lupus erythematosus (SLE) is a multi-system autoimmune disease, and it primarily affects women of childbearing age. While numerous studies have identified risk factors for fetal loss in pregnant women with SLE, results varied among studies. It is essential and helpful if the clinician is able to predict the risk of fetal loss in pregnant patients with SLE in the early stages of gestation, which can allow special monitoring and treatment as early as possible. However, a few studies have proposed such a predictive model or risk score.

Abstract 250 Figure 1 Diagonal segments are produced by ties

We therefore sought to develop a predictive model for fetal loss in women with SLE.

Methods A retrospective observational study of 338 pregnancies with SLE at a tertiary medical center was performed from September 2011 to May 2017, and relevant medical records were reviewed. Multiple gestations and artificial abortions were excluded for personal reasons. A stepwise regression to identify the predictors related to the fetal loss and coefficient B of each variable was used to develop a predictive model and make a corresponding risk classification. The Hosmer-

Abstract 250 Figure 2 Score – morbidity of fetal loss

Lemeshow test, Omnibus test and area under the receiveroperating characteristic (ROC) curve (AUC) were used to assess the goodness-of-fit and discrimination of the predictive model. A 10-fold cross validation was used to assess the model for over-fitting.

Results Unplanned pregnancies (OR 2.84, 95% CI=1.12–7.22), C3 hypocomplementemia (OR 5.46, 95% CI=2.30–12.97), and 24 hr-urinary protein level (0.3 protein <1.0 g/24 hour: OR 2.10, 95%CI=0.63–6.95; protein 1.0 g/24 hour: OR 5.89, 95%CI=2.30–15.06) were selected by the stepwise regression. The Hosmer-Lemeshow test resulted in $p=0.325$; the Omnibus test resulted in $p<0.001$ and the AUC was 0.829 (95% CI=0.744–0.91) in the regression model. The corresponding risk score classification was divided into low risk (0–3) and high risk groups (>3), with a sensitivity of 60.5%, a specificity of 93.3%, positive likelihood ratio of 9.03 and negative likelihood ratio of 0.42.

Conclusions A predictive model for fetal loss in women with SLE was developed using the timing of conception, C3 complement and 24 hr-urinary protein level. This model may help clinicians in identifying women with high risk pregnancies, thereby carrying out monitoring or/and interventions for improving fetal outcomes.

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TYPE II BUT NOT TYPE I INTERFERON SIGNIFIES CLINICAL RESPONSE TO USTEKINUMAB IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Treatment with ustekinumab (UST), an anti-IL-12/23, p40-neutralizing monoclonal antibody, improved global and organ-specific measures of disease activity in a randomized, placebo (PBO)-controlled trial of patients with active SLE (NCT02349061).¹ Type I interferon (IFN-I) and type II IFN (IFN-gamma) are elevated in a subset of SLE patients. Although targeting IFN-I (anifrolumab) has demonstrated inconsistent efficacy and a preliminary study with anti-IFN-gamma mAb (AMG811) failed to establish benefit,^{2 3} we sought to determine if UST affects either pathway and if those effects correlated with a positive SRI-4 response at wk24.

Methods A phase-2, PBO-controlled study enrolled 102 adults with seropositive SLE (SLICC criteria) and active disease (baseline SLEDAI score 6 and 1 BILAG A and/or 2 BILAG B scores) despite standard-of-care therapy.¹ Gene expression analysis using a 21 gene IFN-I gene signature (IGS)⁴ or IFN-gamma signature⁵ was performed by microarray analysis using whole blood PAXgene RNA samples. Serum IFN-gamma and IFN- levels were assessed using MSD (IFN-gamma) and Quantiferix (IFN-).

Results Serum IFN-gamma and IFN- and the IGS were elevated at baseline in SLE compared to healthy controls ($p<0.0001$). IGS was increased in approximately 67% of the

SLE patients at baseline. No decrease was observed with IFN-protein or IGS levels after treatment with either UST or PBO. Whereas the proportion of patients achieving an SRI-4 response at wk24 was numerically greater in the IGS low patients (81.8% UST vs. 54.5% PBO) versus IGS high (48.6% UST vs. 20% PBO), the magnitude of the treatment effect (UST vs. PBO) was similar in both subsets (IGS low effect size=27.3% vs. IGS high effect size=28.6%). Despite similar baseline levels, UST-treated patients achieving an SRI-4 response at wk24 exhibited a significant decrease in IFN-gamma protein versus non-responders ($p<0.05$) at 4 and 8 wks and IFN-gamma gene signature at 4 wks ($p<0.0001$) and 24 wks ($p<0.05$) post-dosing.

Conclusions In this SLE trial population which had significant upregulation of IFN-I at baseline, clinical response to UST was not associated with IFN-I reduction. In contrast, a significant decrease in IFN-gamma protein and gene signature was associated with UST response. These findings suggest that a broad population of SLE patients may respond to UST regardless of baseline IFN-I status. Moreover, UST may have affected TH1 responses in SLE since IFN-gamma levels decreased following treatment.

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REFERENCES

1. VanVollenhoven RF. *Lancet* 2018;**392**:1330.
2. Furie R. *Arthritis Rheumatol* 2017;**69**:376.
3. Boedigheimer MJ. *Lupus Sci Med* 2017;**4**:e000226.
4. Yao Y. *Human Genomics Proteomics* 2009. doi:10.4061/2009/374312
5. Welcher AA. *Arthritis & Rheumatol* 2015;**67**:2713.

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PAP SCREENING RATES IN SYSTEMIC LUPUS ERYTHEMATOSUS WOMEN AT AN ACADEMIC CENTER COMPARED TO NON-SLE WOMEN WITH RACIAL COMPARISONS

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Background Compared with the general population, women with systemic lupus erythematosus (SLE) tend to have higher rates of cervical neoplasia and pre-malignant lesions and in particular, SLE women treated with immunosuppressant therapies such as methotrexate, azathioprine and mycophenolate mofetil may be at even higher risk when compared to SLE women treated with antimalarials alone. Previous studies have suggested suboptimal cervical cancer screening among SLE patients and racial disparity studies have also shown that black SLE patients endure delayed SLE diagnosis and higher morbidity and mortality from SLE related disease compared to non-black SLE patients.

Methods This was a cross-sectional study using electronic health records to identify women aged 21–65 years old with ICD code of SLE M32.9, positive ANA and who have prescription for hydroxychloroquine on their medication list. We compared this to controls (women 21–65 years of age with a ICD code of asthma ICD J45*, negative ANA and excluded patients with SLE diagnosis). For both groups we excluded patients who underwent hysterectomy with removal of the cervix. We used statistical calculator to ‘N-1’ Chi-squared test

Results Much higher proportion of SLE women are overdue for pap smears compared to non SLE women (60.09% vs