disease are to occur in the short term. We also demonstrate how the analyzed drugs act specifically on patients with strong dysregulation of gene-modules related with plasma cells.

Conclusion MyPROSLE allows to extract key information for medical practice and may be a support for more precise therapeutic decisions in the future.

1602 TRANSCRIPTOMIC PROFILES PREDICT RESPONSE TO RITUXIMAB IN SLE

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10.1136/lupus-2021-lupus21century.95

Background B cells are a common therapeutic target in SLE but responses are mixed suggesting that some aspects of disease are less B cell-dependent. Transcriptomic analyses have revealed gene-expression profiles that stratify clinical and demographic aspects of lupus. However, these have not been yet linked to response to targeted therapies. Such linkages can elucidate critical pathogenic mediators that differ between transcriptomic subsets.

Methods We developed a 96-gene Taqman assay including scores for: Interferon Score A (M1.2 and M3.4), Interferon Score B (M3.4 and M5.12), neutrophils (M4.9), plasmablasts (M4.11), myeloid (M5.7), inflammation (M4.2) and erythropoiesis (M4.4). Each was the median normalised dCT of transcripts representative of the module. This was assessed in whole blood from 123 active SLE patients starting new immunosuppresion. After exploring baseline associations, we then evaluated clinical response to a first cycle of rituximab 2x1000mg, using a BILAG-based endpoint (As reduce to B or better, ≤1 persistent B at 6 months, no new A/B)

Results Transcriptomic profiles markedly differed between patients with European Ancestry (EA, n=128) compared to African and Asian Ancestries (n=85). EA had significantly lower expression for IFN Score A (p<0.001), IFN Score B (p=0.039), and plasmablasts (p=0.001). No substantive differences were seen in neutrophil (p=0.26), erythropoiesis (p=0.26) and inflammation (p=0.85) scores. In EA, IFN

Abstract 1602 Table 1

Baseline Characteristics of NEA Clusters 1,2 and 3

Characteristic	Cluster 1 n = 9 IFN LO	Cluster 2 n = 36 GLOBAL HI	Cluster 3 n = 40 N/M LOW PL HI	p value
Female, (%)	8 (88.9)	33 (91.7)	34 (85.0)	0.66
Ancestry, n (%)				
Subcontinental Asian	3 (33.3)	11 (30.6)	13 (32.5)	
Chinese and Other Asian	0 (0.0)	7 (19.4)	4 (10.0)	0.78
African including mixed race	4 (44.4)	13 (36.1)	17 (42.5)	
Other including mixed race not otherwise specified	2 (22.2)	5 (13.9)	17 (42.5)	
Age (years), mean (95% CI)	45 (35, 54)	35 (31, 41)	37 (32,41)	
Disease duration (years), mean (95% CI)	17 (6, 16)	14 (11,17)	12 (8,15)	
BILAG A or B score, n (%)				
Mucocutaneous	1 (11.1)	12 (33.3)	18 (45.0)	0.39
Musculoskeletal	2 (22.2)	16 (44.5)	15 (45.5)	0.70
Renal	4 (44.4)	15 (41.7)	18 (48.6)	0.9
BILAG numerical score, mean (95% CI)	16.5 (12.6, 20.3)	19.5 (16.2, 22.8)	19.4 (15.9, 22.9)	
SLEDA-2K, mean (95% CI)	5.8 (1.0, 10.7)	10.6 (8.6, 12.6)	9.9 (7.4,12.3)	
SLICC damage index, mean (95% CI)	1.13 (0, 2.3)	0.8 (0.2, 1.4)	1.03 (0.5, 1.5)	
Full blood count, mean (95% CI)				
Hb	116.1 (98.0, 134.3)	110.23 (103.1, 117.3)	120.3 (112.4, 128.4)	
Neutrophils	9.6 (5.0,14.2)	6.0 (4.7, 7.2)	4.0 (2.7, 5.5)	
Lymphocytes	1.83 (1.0, 2.6)	0.79 (0.61, 1.0)	1.61 (1.1, 2.1)	
Total IgG (g/L), mean (95% CI)	7.5 (6.1, 8.9)	17.2 (14.8, 20.0)*	16.9 (14.2, 19.6)**	* **0.038** ** 0.084
Low C3 or C4, n (%) *no missing data	3 (33.3)	21 (61.8)	24 (50.0)	0.29
Concurrent Immunosuppressant, n (%)				
Any agent (MMF, CsA, Tac, MMF, AZA)	2 (22.2)	15 (38.5)	22 (55.0)	0.16
Mycophenolate mofetil	1 (11.1)	13 (36.1)	18 (45.0)	0.16
Azathioprine	0 (0.0)	3 (8.3)	2 (5.0)	0.60
Anti-malarial, m (%)	5 (55.6)	18 (50.0)	21 (47.7)	0.95
Oral prednisolone dose (mg), mean (95% CI)	19.9 (13.0, 26.6)	11.7 (8.3, 15)*	11.3 (8.9,13.7)**	* **0.033** ****0.021**
RTX response analysis n = 45				
BILAG response (6 months), n/N (%)	1/7 (14.3)	16/19 (84.2)	8/19 (42.1)	**0.002**

Score B was highly correlated with neutrophil (R=0.554, p<0.001), myeloid (R=0.725, p<0.001), plasmablast (R=0.323, p<0.001), inflammation (R=0.599, p<0.001) and erythropoiesis (R=0.0.376, p<0.001) scores. In NEA, IFN Score B correlated with myeloid (R=0.724, p<0.001) and inflammation (R=0.463, p<0.001) but only weakly with erythropoiesis (R=0.316, p=0.003) and no correlation with neutrophils (R=0.192, p=0.078) or plasmablasts (R=0.023, p=0.832).

Since in NEA these weaker correlations presented a more heterogeneous transcriptomic picture, we further analysed this group using hierarchical clustering of individual transcript expression. This revealed 3 clusters; cluster 1 (low IFN, low plasmablast); cluster 2 (globally high); and cluster 3 (low neutrophil and myeloid, high plasmablast). In the rituximab study these clusters differed in clinical response, which was not explained by other clinical features. Cluster 1 were older with higher glucocorticoid dose and low rituximab response rate. Clusters 2 and 3 were similar in clinical features but rituximab response was significantly higher for cluster 2 (table 1). IFN Score B was the strongest predictor of rituximab response (OR=3.021/unit (95% CI 1.4, 6.6, p=0.006).

Conclusions NEA SLE patients have more heterogeneous transcriptomic profiles, which predict clinical response to B cell targeted therapy independent of clinical features.

Acknowledgments Rituximab treatment data were provided as part of the MRC funded MASTERPLANS consortium.

1700 – B cells and autoantibodies

1701 CURLI AMYLOID/DNA COMPLEXES FROM BACTERIAL BIOFILMS BREAK TOLERANCE IN MURINE LUPUS USING T CELL-INDEPENDENT AND T CELL-DEPENDENT MODALITIES

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10.1136/lupus-2021-lupus21century.96

Background Epidemiological studies suggest that bacterial infections promote SLE disease in predisposed individuals, but the underlying mechanisms remain unknown. We have found that a subset of SLE patients has asymptomatic bacteriuria associated with markers of inflammation and flares, suggesting that chronic exposures to microbial products may trigger flares in lupus. Our labs have shown that the bacterial amyloid curli, expressed in multicellular communities (*biofilms)* by many bacteria including *E. coli*, plays a major role in triggering lupus autoimmunity during infection. Curli amyloid/DNA complexes strongly activate dendritic cells and macrophages. When given systemically, curli/DNA complexes and infections with curli-expressing *E. coli* trigger production of anti-dsDNA and anti-chromatin autoantibodies in lupus prone mice and in wild type mice. This stimulation is diminished in TLR2 or TLR9 deficient mice, suggesting a TLR-mediated activation of innate immunity. *We have now focused on the effects of curli/DNA complexes on B cells.*

Methods Young wild type C57BL/6 mice, lupus prone Sle1,2,3 mice, 3H9 mice and CD40L-/- mice were injected with curli/DNA complexes from biofilms or infected with amyloid for short and long-term studies. Splenic B cells were stained by flow cytometry *ex vivo*. For *in vitro* experiments, B cells were sorted by positive selection with CD45R (B220), supplemented with anti-CD43Ab-Biotin. B cell purity (>98%), proliferation, activation markers and signaling molecules were measured by Flow cytometry, Western Blot and qRT-PCR. Autoantibodies were measured by ELISA.

Results *In vitro,* curli/DNA complexes could induce class switch to IgG, in the absence of T cell help, in wildtype B cells, and even more in Sle1,2,3 and 3H9 B cells, which recognize DNA, suggesting an antigen-specific activation of B cells by curli/DNA. Curli/DNA induced non-canonical NFκB activation and transcription of *aicda*, the master regulator of class switch recombination. *In vivo*, exposure to curli/DNA broke tolerance to DNA in 3H9 mice. Moreover, it induced autoantibodies in CD40L-/- mice, though at lower levels than in WT mice.

Conclusions The induction of non-canonical NFκB activation, *aicda*, and class switch recombination, in the absence of T cells help *in vitro*, suggests that the fibrillar structure of curli/DNA complexes can cross-link BCRs, some recognizing DNA, and can also trigger a second pathway which substitutes T cell help to induce isotype switching. The lower levels of autoantibodies elicited by curli/DNA in mice deficient of T cell help suggests that curli/DNA complexes break tolerance to DNA with T cell-independent and T cell-dependent modalities.

Acknowledgments This work was supported by the NIH, NIAID grant R21-AI119947 and the Lupus Research Institute, now Lupus Research Alliance, Innovative Grant (SG); NIH NIAMS grant R01-AR061569, R56-AR072115, Lupus Research Alliance, TIL (RC); NIH, NIAID R21-AI125429, R21-AI132996, R21-AR072115 (CT).

1702 COMPARISON OF THE B CELL RESPONSE TO SELF- VERSUS FOREIGN- ANTIGEN IN MICE REVEALED BY SINGLE CELL TRANSCRIPTOMICS

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10.1136/lupus-2021-lupus21century.97

Background In an autoimmune environment, rogue self-reactive B cells escape tolerance, differentiate to a variety of self-antigens (epitope spreading) and are selected into germinal centers (GC) in a T cell dependent manner. We investigated this question using a mixed bone marrow chimera model that combines transgenic B cells from lupus-like mice (564 Igi) with those from wild type (WT) B6 mice. In this model, WT B cells, specific for self-antigens distinct from those targeted by the Tg B cells, expand and dominate in GC.

Methods Autoimmune and WT chimeric mice were prepared using the tamoxifen-inducible *Aicda*-CreERT2-EYFP mice to track WT cells. WT chimeras were immunized with NP-CGG. At peak GC stage, EYFP+ splenic B cells from both cohorts, were sorted and processed for gene expression using RNAseq.