are safe and effective for all patients. Clinician communication with patients has been identified as one of the most effective approaches to increase enrollment in clinical trials and healthcare research.

However, there is no formal training for trainees or clinicians who want to become trial investigators or more involved in clinical trials. There is a clear need to provide such opportunities for both practicing clinicians and trainees to build knowledge and skills around having effective conversations with patients about lupus clinical trials and provide all eligible patients with the opportunity to make decisions about participation in a clinical trial.

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Clinical Research in SLE

621 THE ASSOCIATION OF INTERFERON WITH KYNURENINE/TRYPTOPHAN PATHWAY ACTIVATION IN SYSTEMIC LUPUS ERYTHEMATOSUS

[1]Erik W Anderson*, [2]Ying Jin, [1]Andrew Shih, [1]Arnon Arazi, [2]Sara Goodwin, [3]Julien Roeser, [1]Richard A Furie, [1]Cynthia Aranow, [1]Bruce T Volpe, [1]Betty Diamond, [1]Meggan Mackay. *[1]The Feinstein Institutes for Medical Research, Manhasset, NY USA; [2]Cold Spring Harbor Laboratory, Cold Spring Harbor, NY USA; [3]Charles River Laboratories, South San Francisco, CA USA*

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Background Cognitive dysfunction (CD) is highly prevalent in systemic lupus erythematosus (SLE) with significant impact on quality of life, yet SLE-mediated mechanisms for CD remain poorly understood. Quinolinic acid (QA), a metabolite of the kynurenine (KYN)/tryptophan (TRP) pathway, is a N-methyl-

Abstract 621 Table 1 SLE and healthy control (HC) subject characteristics and KYN/TRP pathway metabolite ratios. All data is reported either as a mean (or median where indicated) ± standard deviation (or interquartile range), or as a frequency (%). All data refers to that which was collected at the time of evaluation

Subject characteristics	SLE (N = 72)	HC (N = 73)	*p*
Age	37.9 ± 9.6	36.2 ± 9.5	0.28
(mean # years ± SD, range)	(22 – 57)	(18 – 55)	
Ethnicity (Hispanic/Latino)	13 (18.1%)	13 (17.8%)	0.97
Race Black	43 (59.7%)	41 (56.2%)	0.91
White	16 (22.2%)	18 (24.7%)	
Other	13 (18.1%)	14 (19.2%)	
KYN/TRP ratio	**0.04 ± 0.03**	**0.03 ± 0.01**	**<0.01**
Median ± IQR (range)	**(0.01 - 0.23)**	**(0.01 - 0.13)**	
QA/KA ratio	**18.4 ± 14.7**	**8.9 ± 5.8**	**<0.01**
Median ± IQR (range)	**(4.0 - 121.2)**	**(2.9 - 45.9)**	
Disease duration	12.3 ± 8.5	n/a	n/a
Mean ± SD (range)	(1 – 38)		
SELENA SLEDAI score	5.4 ± 5.1	n/a	n/a
Mean ± SD (range)	(0 – 29)		
Prednisone dose	2.5 ± 10.0	n/a	n/a
(mg/day; median ± IQR, range)	(0 – 75)		
Current hydroxychloroquine use	54 (75.0%)	n/a	n/a
Current immunosuppressant use	34 (47.2%)	n/a	n/a
Anti-dsDNA positive (> 29 IU/mL)	50 (69.4%)	n/a	n/a
C3 low (< 81 mg/dL)	28 (38.9%)	n/a	n/a
C4 low (< 13 mg/dL)	24 (33.3%)	n/a	n/a

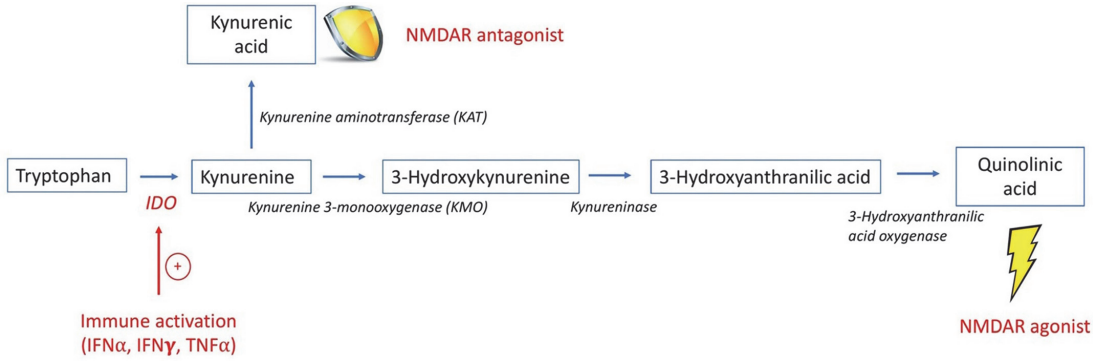
Abstract 621 Table 2 Correlations Between IFN Scores and Serum KYN/TRP Pathway Metabolite Levels in SLE Subjects According to ISG Expression Subgroup. SLE subjects were assigned to 1 of 3 subgroups: "IFN high" (Z-IFN score ≥2 SD above HC mean), "IFN low" (Z-IFN score ≥1 to <2) or "IFN similar to HC" (Z-IFN score <1). In each subgroup, correlations between both IFN scores (derived from ISG-A and the 19 type I ISG) and metabolite ratios are displayed.

ISG Expression Subgroup	IFN Score Method (z-scores)	KYN/TRP (r_s)	p	QA/KA (r_s)	p
IFN high	**ISG-A**	0.490	0.002*	0.129	0.453
(N=36)	**19 Type I ISG**	0.487	0.003*	0.216	0.205
IFN low	**ISG-A**	-0.174	0.427	-0.286	0.187
(N=23)	**19 Type I ISG**	0.269	0.215	-0.210	0.335
IFN similar to HC	**ISG-A**	0.170	0.578	-0.126	0.681
(N=13)	**19 Type I ISG**	0.242	0.426	0.000	1.000

* remained significant after Benjamini-Hochberg correction for multiple comparisons

D-aspartate receptor (NMDAR) agonist that can cause excessive glutamatergic excitotoxicity to neurons,[1] while kynurenic acid (KA) is an NMDAR antagonist with potential to protect neurons from excitotoxic damage (figure 1).[1] Type I and II interferon (IFN) contributes to SLE pathogenesis and stimulates the KYN/TRP pathway, producing an elevated QA/KA ratio, a potential neurotoxic imbalance. We determined whether peripheral blood IFN- stimulated gene (ISG) expression associates with elevated serum KYN/TRP and QA/KA ratios in SLE.

Methods We measured ISG expression (whole blood RNA sequencing) and serum metabolite ratios (High Performance Liquid Chromatography) in 72 SLE subjects and 73 healthy controls (HC). We identified ISG based on published gene sets from Arazi et al[2] ("ISG-A," N=110 ISG), Chiche et al[3] ("19 type I ISG" more responsive to type I than type II IFN), and the Interferome database.[4] We derived individual IFN scores to analyze associations with metabolite ratios and clinical parameters. These analyses were performed in SLE subgroups based on level of ISG expression ("IFN high", "IFN low" and



Abstract 621 Figure 1 The Kynurenine/Tryptophan Pathway. This is a simplified schematic of the KYN/TRP pathway, highlighting the intermediates and enzymes involved in the production of quinolinic acid (QA) and kynurenic acid (KA). The enzyme IDO is stimulated by inflammatory cytokines, such as IFN, that results in the breakdown of TRP into KYN. KYN may be further metabolized by KMO ultimately to QA, an NMDAR agonist, or by KAT to KA, an NMDAR antagonist. Since the enzyme KMO has higher affinity for KYN than KAT, metabolism proceeds preferentially towards the production of QA in the setting of inflammation.[5]
* IDO, indoleamine 2,3-dioxygenase; IFNα, interferon-alpha; IFNγ, interferon-gamma; NMDAR, N-methyl D-aspartate receptor; TNFα, tumor necrosis factor-alpha.

Abstract 621 Table 3 Correlations Between IFN Scores and Serum KYN/TRP Pathway Metabolite Levels in SLE Subjects According to ISG and Monocyte-Associated Gene Expression Subgroups. In addition to the ISG expression subgroups previously described in Table 2, SLE subjects were further designated as either "Monocyte High" (monocyte-associated gene expression > HC mean) or "Monocyte Low" (monocyte-associated gene expression ≤ HC mean). In each subgroup, correlations between both IFN scores (derived from ISG-A and the 19 type I ISG) and metabolite ratios are displayed.

ISG Expression Subgroup	Monocyte- Associated Gene Expression Subgroup	IFN Score Method (z-scores)	KYN/TRP (r_s)	p	QA/KA (r_s)	p
	Monocyte High	**ISG-A**	0.504	0.014*	0.429	0.041*
IFN high	(N=23)	**19 Type I ISG**	0.532	0.009*	0.419	0.046*
(N=36)	**Monocyte Low**	**ISG-A**	0.440	0.133	-0.132	0.668
	(N=13)	**19 Type I ISG**	0.330	0.271	0.044	0.887
	Monocyte High	**ISG-A**	-0.289	0.260	-0.326	0.202
IFN low	(N=17)	**19 Type I ISG**	0.336	0.188	-0.252	0.328
(N=23)	**Monocyte Low**	**ISG-A**	0.547	0.261	0.137	0.796
	(N=6)	**19 Type I ISG**	0.429	0.396	0.073	0.890
	Monocyte High	**ISG-A**	-0.071	0.867	-0.199	0.637
IFN similar to HC	(N=8)	**19 Type I ISG**	0.048	0.911	-0.024	0.955
(N=13)	**Monocyte Low**	**ISG-A**	0.785	0.116	0.110	0.861
	(N=5)	**19 Type I ISG**	0.500	0.391	0.100	0.873

* remained significant after Benjamini-Hochberg correction for multiple comparisons

"IFN similar to HC") and, using CIBERSORTx, according to the level of monocyte-associated gene expression.

Results Serum KYN/TRP and QA/KA ratios were higher in SLE versus HC ($p<0.01$) (table 1). SLE subjects were racially diverse, reflective of disease demographics, with a wide range of disease activity (SLEDAI scores ranging 0-29) and medication use. There were no demographic differences between SLE and HC. Nine hundred thirty-three genes were differentially expressed ≥2-fold in SLE versus HC, with 762 genes overexpressed and 171 underexpressed ($p<0.05$). Seventy of the top 100 most highly variant genes were ISG. Of the 762 overexpressed genes in SLE subjects, 144 positively correlated with KYN/TRP ratios ($p<0.05$) and 71 (49%) of these were ISG. Similarly, 81 of the 762 overexpressed genes positively correlated with QA/KA ratios in SLE subjects ($p<0.05$), and 38 (47%) of these were ISG. In 36 "IFN high" SLE subjects, IFN scores correlated with KYN/TRP ratios ($p<0.01$), but not with QA/KA ratios (table 2). Of these 36 "IFN high" SLE subjects, 23 had high monocyte-associated gene expression and in this subgroup, the IFN scores correlated with both KYN/TRP and QA/KA ratios ($p<0.05$) (table 3).

Conclusions SLE subjects demonstrate increased KYN/TRP pathway metabolite ratios, and high ISG expression correlated with elevated KYN/TRP ratios, suggesting IFN-mediated KYN/TRP pathway activation. High ISG expression also correlated with QA/KA ratios in SLE subjects with high monocyte-associated gene expression, suggesting that KYN/TRP pathway activation may be particularly important in monocytes. These results need validation, which may aid in determining which subset of patients may benefit from therapeutics directed at the IFN or KYN/TRP pathways to ameliorate a potentially neurotoxic QA/KA imbalance.

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Clinical Research

622 CHILDHOOD-ONSET SLE OUTCOMES IN THE CARRA LUPUS REGISTRY

[1]Mary Beth Son, [2]Andrea Knight, [3]Laura Schanberg, [4]Emily von Scheven, [5]Shahla Amin, [6]Aimee Hersh. *[1]Division of Immunology, Boston Children's Hospital, Boston MA; [2]Division of Pediatric Rheumatology, Hospital for Sick Children, Toronto CA; [3]Duke Clinical Research Institute, Durham NC; [4]Division of Pediatric Rheumatology, UCSF Benioff Children's Hospital, San Francisco CA; [5]Biostatistics of Childhood Arthritis and Rheumatology Research Alliance; [6]Division of Pediatric Rheumatology, University of Utah, Salt Lake City UT*

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Objective This study aims to describe the demographic features, cumulative clinical manifestations, and treatments in a large childhood-onset (cSLE) cohort in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry. This study also assesses lupus low disease activity state (LLDAS) and examines predictors of the first attainment of LLDAS.

Methods We performed a retrospective cohort study of patients with cSLE enrolled in the CARRA Registry between March 2017 to December 2021. Inclusion criteria included: 1) diagnosis of cSLE at <18 years based on Systemic Lupus Erythematosus International Collaborating Clinics (SLICC) criteria; 2) enrollment within two years of cSLE diagnosis or at the time of a flare of lupus nephritis (LN); and 3) enrollment prior to 21 years of age. Sociodemographic and clinical data were summarized using descriptive statistics. A chi-squared test was used to assess the association between LLDAS and the categorical variables. We used logistic regression to assess enrollment predictors of LLDAS attainment at 6, 12 and 18 months of follow-up

Results The CARRA Registry includes 779 patients with cSLE (table 1). In this ethnically and racially diverse cohort, the median SLEDAI at enrollment was 4 (IQR 2-10) and median time from enrollment to end of follow up was 22 (IQR 11 to 33) months. At enrollment, 18% of patients had a SLICC damage index score greater than zero (table 2). At the end of the follow-up period, almost 50% of patients developed lupus nephritis. 5.7% and 12.4% had neurological manifestations per ACR and SLICC criteria, respectively. 94.6% were prescribed hydroxychloroquine and participants received a variety of immunosuppressive therapies. The percentage of visits where LLDAS was achieved is shown in figure 1. In multivariate analysis, statistically significant predictors of LLDAS attainment included time from diagnosis and 6, 12 and 18 months of follow-up and baseline hydroxychloroquine use.

Abstract 622 Table 1 Baseline Demographic Characteristics

Characteristic	N=779
Female gender, n (%)	674 (86.5)
Age at diagnosis, mean (SD), years	13.3 (2.9)
Age at enrollment, mean (SD), years	14.3 (2.9)
Race, n (%)	
White	192 (24.7)
Black	235 (30.2)
Hispanic	180 (23.1)
American Indian/Alaskan native	10 (1.3)
Asian	117 (15.0)
Middle Eastern/North African	11 (1.4)
Native Hawaiian/Pacific Islander	5 (0.6)
Other	13 (1.7)
Prefer not to answer/Missing	16 (2.1)
Insurance, n (%)	
Private	348 (44.7)
Public insurance	331 (42.5)
Uninsured	22 (2.8)
Other	75 (9.6)
Income, n (%)	
<25,000	103 (13.2)
25,000-49,999	123 (15.8)
50,000-74,999	75 (9.6)
75,000-99,999	64 (8.2)
100,00-150,000	70 (9.0)
≥ 150,000	72 (9.2)
Prefer not to answer/Unknown	159 (20.4)