167 ROLES OF SKIN-RESIDENT DENDRITIC CELLS AND T CELLS IN THE PATHOGENESIS OF CUTANEOUS LUPUS

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Background Pathogenesis of cutaneous lupus is unclear. Skin harbors at least three subsets of dendritic cells (DC): Langerhans cells (LC) that reside in the epidermis, langerin-expressing dermal DC that reside in the dermis (LangdDC), and langerin-negative dermal DC. Skin also contains T cells including skin-resident T cells called dendritic epidermal T cells (DETC). Here, we investigated the roles of skin-DC subsets and DETCs in the pathogenesis of cutaneous lupus. To allow investigations into early events leading to cutaneous lupus, we used animal models.

Methods We used MRL-Fas+/+ (MRL+/+) mice that develop lupus ~10 months of age and MRL-Faslpr/lpr (MRL-lpr) mice that develop lupus ~4 months. We applied fluorophores to the skin of these and MHCII-matched control mice to track *in vivo* migration of skin-DC to skin-draining lymph nodes. To be able to track skin-DC in steady state (without any external manipulation), we generated langerin-driven eGFP knock-in MRL+/+and MRL-lpr mice by introgressing the knock-in mutation from the stock B6 background (kindly provided by Bernard Malissen). We used *in situ* assays to identify potential sites of defect in skin-DC migration in lupus. We treated MRL mice with glycolipid GalCer that ameliorates cutaneous lupus and determined its effect on skin-DC migration, and investigated mechanisms of skin-DC migration using TCR/and CD40 L/mice. Finally, to directly test the role of skin-DCs in cutaneous lupus, we used DTR knock-in MRL mice to conditionally deplete LC and/or LangdDC.

Results Lupus-prone mice exhibit reduced LC migration but increased LangdDC trafficking to skin-draining lymph nodes. Such altered migration of these two skin-DC subsets was corrected by GalCer treatment. However, GalCer did not increase LC migration through its well-known target iNKT cells but increased DETCs that were otherwise reduced in lupus mice compared to controls. DETCs increased LC migration *in vitro*. The role of DETCs in modulating LC migration was confirmed using/mice. CD40L deficiency or antibody blockade abrogated the ability of DETCs to enhance LC migration. Finally, conditional ablation of LC worsened cutaneous lupus; this effect was abrogated when both LC and LangdDC were ablated together. LC depletion or GalCer treatment did not affect anti-DNA antibodies or lupus nephritis.

Conclusions Skin-DCs regulate the development of cutaneous lupus, but dont affect systemic disease. Different skin-DC subsets play different roles in the pathogenesis of cutaneous lupus and are differently regulated. Such specialized local regulation of autoimmunity at the tissue level has implications for developing tissue-targeted therapies without affecting systemic immunity.

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168 RELATIVE BURDEN OF PREMATURE MORTALITY IN LUPUS

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Background Disease burden is the impact of a health problem on a given area, which can be used to set healthcare and research priorities and identify high-risk populations. Disease burden can be measured using a variety of indicators such as mortality, morbidity, disability, or financial cost. Analyses of 62,843 SLE deaths from the US-CDCs database showed that SLE-mortality remains high relative to general population mortality (Yen E, *et al. Ann Int Med* 2017). However, mortality rates may not adequately measure SLE burden, because among those who died, a fifth died before reaching 40 years. Premature mortality is an important way to quantify disease burden. In constructing a measure of premature death, an arbitrary limit to life is chosen, and the years of potential life lost (YPLL) is calculated.

Methods This is a population-based observational study. Death counts were obtained from the CDC-WONDER for 28 diseases, including SLE, top 15 CDCs leading causes-of-death, and 12 other autoimmune diseases. To calculate YPLL, each decedents age at death from a specific disease was subtracted from a predetermined age of 75 years. The years of potential life lost were then added together to yield the total YPLL.

Results From 2000 through 2015, SLE was recorded as the cause of death in 28 411 women in the US. The ranking of SLE deaths relative to the CDCs official leading-causes-of-death in females showed that SLE is within the top 15 leading causes-of-death in reproductive age women (15–44 years) and tenth among women ages 15–24 years. YPLL for SLE was 304.2 thousand years in women ages 15–44 and 66.2 thousand years in women ages 15–24. SLE-YPLL ranked #14 in women ages 15–44, and #8 in women ages 15–24 above diabetes mellitus, HIV disease, septicemia, chronic lower respiratory disease, anemias, nephritis, and cerebrovascular disease. However, the NIH research funding for SLE is not commensurate with its relative premature mortality burden: NIH provided $97 million for SLE research in comparison to $1,084 million for diabetes mellitus and $3,780 million for HIV in 2016. Among autoimmune diseases, SLE ranked #2 in women ages 15–44 years and #1 in women ages 15–24 years.

Conclusions SLE is among the leading causes of premature mortality burden in young women, underscoring SLE as an important public health issue. This warrants further studies on SLE disease burden, which can be used to develop and prioritize public health programs, assess performance of changes in SLE management, identify high-risk populations, and set research priorities and funding.

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169 CLINICAL AND LABORATORY FEATURES OF LATE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS IN A CHINESE POPULATION

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Background Late-onset systemic lupus erythematosus (SLE) were defined as disease onset at or over the age of 50 years. Several groups have reported the differences between late-onset SLE and early-onset SLE. To further address these differences in Chinese population, we summarize the characteristics of clinical

Abstract 169 Table 1 Clinical manifestation of late- and early-onset SLE patients

Clinical manifestation	Late onset n (%)	Early onset n(%)	OR	95% CI (Lower)	95% CI (Upper)	P value
Fever	97 (48.9)	113 (57.0)	0.722	0.486	1.073	0.107
Malar rash	67 (33.8)	127 (64.1)	0.286	0.189	0.432	0.000***
Lymph Adenopathy	16 (8.08)	8 (4.04)	2.088	0.872	4.997	0.092
Raynaud's phenomenon	24 (12.1)	27 (13.6)	0.874	0.485	1.574	0.653
Arthritis	95 (47.9)	106 (53.5)	0.801	0.539	1.188	0.269
Oral Ulcer	39 (19.6)	36 (18.1)	1.104	0.667	1.825	0.700
Alopecia	23 (11.6)	56 (28.2)	0.333	0.195	0.568	0.000***
Photo sensitivity	12 (6.06)	27 (13.6)	0.409	0.201	0.832	0.011*
Dry mouth	40 (20.2)	19 (9.59)	2.385	1.327	4.288	0.003**
Dry eyes	19 (9.59)	12 (6.06)	1.645	0.776	3.487	0.190
Myalgia	12 (6.06)	10 (5.05)	1.213	0.512	2.876	0.661
Thrombosis	1 (0.50)	2 (1.01)	0.497	0.045	5.531	0.562
Dizziness	4 (2.02)	14 (7.07)	0.271	0.088	0.838	0.016*
Fatigue	55 (27.7)	41 (20.7)	1.473	0.926	2.341	0.101
Weight loss	7 (3.53)	10 (5.05)	0.689	0.257	1.848	0.457
Dyspnea	32 (16.1)	28 (14.1)	1.170	0.675	2.029	0.575
PAH	11 (5.55)	11 (5.55)	1.000	0.423	2.363	1.000
Neuropsychiatric symptoms	3 (1.51)	15 (7.57)	0.188	0.053	0.659	0.004**
Proteinuria	48 (24.2)	116 (58.5)	0.226	0.147	0.348	0.000***
Hematuria	4 (2.02)	42 (21.2)	0.077	0.027	0.218	0.000***
Edema	57 (28.7)	62 (31.3)	0.887	0.577	1.363	0.584
Serositis	48 (24.2)	37 (18.6)	1.392	0.859	2.257	0.178
Leukopenia	42 (21.2)	47 (23.7)	0.865	0.539	1.387	0.547
Thrombocytopenia	55 (27.7)	47 (23.7)	1.236	0.787	1.941	0.358

OR: odds ratio

Abstract 169 Table 2 Laboratory results of late- and early-onset SLE patients

Lab Test	Late onset SLE		Early onset SLE		P Value
	Median	IQR	Median	IQR	
WBC (x10^9L)	5.01	(3.33–7.385)	5.565	(3.505–8.485)	0.056
Hemoglobin (gL)	108	(92 - 122)	102	(87 - 118)	0.06
CH50	43.7	(23.95–55.66)	34.4	(19.2–46.94)	<0.001***
C3 (gL)	0.7	(0.49–0.94)	0.59	(0.42–0.79)	<0.001***
C4 (gL)	0.12	(0.07–0.2)	0.1	(0.06–0.17)	0.04*
IgG (gL)	14.9	(11.93–20.33)	13.35	(9.42–18.63)	0.003**
IgA (gL)	3.37	(2.46–4.45)	2.3	(1.77–2.92)	<0.001***
IgM (gL)	0.88	(0.52–1.45)	1.03	(0.625–1.44)	0.372
IgG4 (gL)	0.44	(0.185–0.92)	0.28	(0.14–0.67)	0.091
RF	11.5	(10.1–22.2)	10.7	(10.05–13.4)	0.39
Urine PCR (mg/g)	618	(90.3–1562)	934.2	(173.9–2703)	0.076
ANA titer	640	(320–1280)	640	(320–1280)	0.324
Anti dsDNA antibody (IU/L)	26.01	(10.6–91.81)	29.37	(12–60.17)	0.861

WBC: White blood cell; ESR: Erythrocyte sedimentation rate; C3: complement 3; C4: complement 4; RF: rheumatoid factor; PCR: Protein/creatinine ratio; ANA: anti-nuclear antibody

Abstract 169 Table 3 Anti-Extractable Nuclear Antigen (ENA) antibody profile of late- and early- onset SLE patients

Anti-ENA Profile	Late onset n (%)	Early onset n(%)	OR	95% CI (Lower)	95% CI (Upper)	P value	
Anti-Sm	18 (11.3)	14 (8.04)	0.302	1.469	0.705	3.062	
Anti-U1RNP	44 (27.8)	29 (16.6)	0.014	1.930	1.137	3.276	*
Anti-SSA Ro60	63 (41.1)	32 (18.3)	0.000	3.106	1.883	5.125	***
Anti-SSA Ro52	22 (14.0)	28 (16.0)	0.598	0.850	0.464	1.557	
Anti-SSB La	20 (12.6)	4 (2.29)	0.000	6.159	2.057	18.444	***
Anti-PM Scl	1 (0.66)	1 (0.57)	0.916	1.161	0.072	18.724	
Anti-Scl70	2 (1.26)	1 (0.57)	0.506	2.218	0.199	24.699	

OR: odds ratio

features, laboratory results of late-onset systemic lupus erythematosus in a tertiary rheumatology center in China.

Methods We retrospectively analyzed 198 patients with late-onset SLE admitted to RenJi Hospital, Shanghai Jiaotong University School of medicine from Jan, 2013-Jan, 2018. A control group of randomly selected 198 SLE patients with disease onset earlier than the age of 50 admitted to the same hospital at the same time period was recruited. Clinical and laboratory data were collected through chart review.

Results Between January 2018 and August 2018, 198 SLE patients fulfilled definition for late-onset SLE. The predominance of women among late-onset SLE (4.7 : 1) was decreased as compared with that observed in early-onset SLE (18.8 : 1). The following clinical manifestations were less common in late-onset SLE when compared to that observed in early-onset group: malar rash (33.8% vs 64.1%, p=0.000), alopecia (11.6% vs 28.2%, p<0.001), photosensitivity (6.06% vs 13.6%, p=0.011), nephropathy (proteinuria: 24.2% vs 58.5%; hematuria 2.02% vs 21.2%, p<0.001), neuropsychiatric symptoms (1.51% vs 7.57%., p=0.004), while a higher incidence of xerostomia existed in late-onset SLE (9.59% vs 20.2% p=0.003) (table 1). Complement levels (C3, C4, CH50) were significantly higher in late-onset group when compared to those in early-onset group. Immunoglobulin G and A levels were higher in late-onset group than those in early-onset group (table 2). A non-significant decrease of urine protein creatinine ratio was observed in the late-onset group. A significantly increased incidence of positive anti-U1RNP, anti-SSA Ro60, and anti-SSB La was observed among the late-onset SLE patients (table 3).

Conclusions Our study confirmed that in a Chinese population, late-onset SLE patients were different from early-onset SLE patients in terms of clinical manifestations and laboratory results.

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170 COMPARING THE PERFORMANCE OF TWO INTERFERON-GAMMA RELEASE ASSAYS IN AUTOIMMUNE SKIN DISEASE PATIENTS: A PROSPECTIVE STUDY

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Background Autoimmune skin disease patients are standardly screened for tuberculosis via interferon-gamma release assays (IGRAs) prior to starting new immunosuppressive drugs or enrolling in clinical trials. Two commercial IGRAs, T-SPOT.TB and QuantiFERON-Tb Gold (QFT-G), are reported as either determinate (positive or negative) or indeterminate. Both tests utilize similar immunoenzymatic reactions for interferon-gamma detection, but differ in its quantification. Though the QFT-G is more widely used, studies have demonstrated that the T-SPOT.TB has lower rates of indeterminate results in immunosuppressed patients, and thus may prevent a delay in the initiation of necessary therapies or enrollment in clinical trials. The newest generation of QFT-G, the QuantiFERON-TB Gold Plus (QFT-Plus), has not been compared to the T-SPOT.TB in this patient population. We aim to investigate the performance of both the T-SPOT.TB and QFT-Plus, as indeterminate results represent a major barrier to receiving appropriate treatment in autoimmune skin disease patients.

Methods This ongoing prospective study included 48 patients seen at the Hospital of the University of Pennsylvania. Venous blood samples were collected from patients and underwent tuberculosis screening with QFT-Plus and T-SPOT.TB IGRAs. The proportions of indeterminate and determinate (positive and/or negative) results among the two tests were compared.

Results In the study population of 48 patients, 29% had a primary diagnosis of cutaneous lupus (n=14). There were 2 indeterminate results with the QFT-Plus and no indeterminate results with T-SPOT.TB. There was also one positive result that was seen with both the QFT-Plus and T-SPOT.TB. All patients with a primary diagnosis of cutaneous lupus had negative results for both QFT-Plus and T-SPOT.TB. Using a one-tailed Fischer test, there was no statistical significance when comparing QFT-Plus and T-SPOT.TB in autoimmune skin disease patients (p=0.25).

Conclusions In this prospective study, the T-SPOT.TB had fewer indeterminate results compared to the QFT-Plus. Though this finding was not statistically significant, it is clinically important as indeterminate results preclude autoimmune skin disease patients from receiving necessary treatment. Compared to previous studies on the older generation of the QFT-G test, the QFT-Plus showed improvement in reducing the amount of indeterminate results. Despite this, we suggest using the T-SPOT.TB in tuberculosis screening for autoimmune skin disease patients who have an indeterminant QFT-G or QFT-Plus, as this test did not display any indeterminate results. The results of this study are limited by the small sample size.

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171 CONCORDANCE OF DORIS REMISSION CRITERIA WITH THE TREATING PHYSICIANS (DORIS-)INDEPENDENT REMISSION JUDGMENT IN A SLE-COHORT AT A TERTIARY CENTER

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Background The definition of an accurate target for a treat to target (T2T) approach in SLE has been challenging over the past years. Recently four definitions of remission were presented by the international DORIS task force. Aim of this study was to evaluate the frequency of remission in our outpatient SLE cohort and to assess feasibility and concordance of the remission definitions with the treating physicians opinion regarding the patients state.

Methods In this monocentric cross-sectional study patients with SLE according to the 1997 American College of Rheumatology (ACR) criteria were enrolled and assessed between September 2016 and December 2017. DORIS remission definitions were applied and demographic and laboratory data as