of SLE patients were reported to suffer from severe infections^{1,2}. However, due to the high cost of recruiting patients, we still do not have a holistic picture of the SLE-infection association. Administrative data which encompass all provincially funded healthcare service data shows promising opportunities to advance the knowledge and management of the SLE patients which cannot be evaluated by the conventional clinical setting with small sample size and selective samples^{3,4,5}.

Objectives: To evaluate the risk of severe infection and infection-related mortality among patients with newly diagnosed systemic lupus erythematosus.

Methods: We conducted an age- and gender- matched cohort study of all patients with incident SLE between January 1, 1997 and March 31, 2015 using administrative health data from British Columbia, Canada. Primary outcome was the first severe infection after SLE onset necessitating hospitalization or occurring during hospitalization. Secondary outcomes were total number of severe infections and infection-related mortality.

Results: We identified 5,169 SLE patients and matched them with 25,845 non-SLE individuals from the general population, yielding 955 and 1,986 first severe infections during 48,367 and 260,712 person-years follow-up, respectively. The crude incidence rate ratios for first severe infection and infection-related mortality were 2.59 (95% CI, 2.39-2.80) and 2.20 (95% CI, 1.76-2.73), respectively. The corresponding adjusted hazard ratios were 1.82 (95% CI 1.66-1.99) and 1.61 (95% CI, 1.24-2.08). SLE patients had an increased risk of a greater total number of severe infections with crude rate ratio of 3.24 (95% CI, 3.06-3.43) and adjusted rate ratio of 2.07 (95% CI, 1.82-2.36).

Conclusion: SLE is associated with increased risks of first severe infection (1.8-fold), a greater total number of severe infections (2.1-fold) and infection-related mortality (1.6-fold).

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OP0044

ANA POSITIVITY IS ASSOCIATED WITH COMPLEX IMMUNE DISTURBANCE EVEN IN INDIVIDUALS WHO DO NOT DEVELOP CLINICAL AUTOIMMUNE DISEASE

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Background: Study of pre-clinical autoimmunity can reveal immune changes that initiate or prevent clinical disease. We previously reported an At Risk cohort of ANA positive individuals referred to secondary care, of whom 16% progressed to SLE or Sjogren's syndrome during follow up[1]. Recently, we also reported that even ANA positive individuals who do not develop clinical autoimmunity, have defective pDC function and non-haematopoietic interferon-production[2].

Objectives: To describe the immunophenotype of ANA-positive progressors and non-progressors compared to healthy controls.

Methods: We conducted a prospective observational longitudinal study of At-Risk individuals in Leeds (n=150) over 3 years with annual follow up. Those who met classification criteria for autoimmune connective tissue disease (AI-CTD) during follow up were termed progressors and others; non-progressors. Among the non-progressors, those with no clinical diagnostic criteria at any time point were called absolute non-progressors (ANP).

At baseline we analysed two IFN-stimulated gene expression scores previously described[3] and flow cytometry performed for major circulating subsets. Association between progression group and biomarkers were tested using independent samples t-test.

Results: 3 year follow up data were available in 148/150 patients. Outcomes were: progressors: 30/148 (20%) [SLE=25; pSS=5] and non-progressors: 118/148 (80%). Within the non-progressors, 69/148 (47%) were ANP.

A detailed analysis of baseline biomarkers is included in Table 1. Despite not developing clinically significant disease, non-progressors had significant alterations in several biomarkers. This was also evident in the ANP sub-group.

Table 1.

Biomarker	Healthy Controls	Non-progressors	Difference from healthy controls	Absolute non-progressors	Difference from healthy controls	Progressors	Difference from healthy controls
	Mean (95% CI)	Mean (95% CI)	p	Mean (95% CI)	p	Mean (95% CI)	p
IFN score A	-6.27 (-6.88, -5.65)	-5.22 (-5.64, -4.80)	0.016	-5.11 (-5.91, -4.32)	0.120	-4.14 (-5.11, -3.18)	0.001
IFN score B	-5.43 (-6.00, -4.85)	-5.30 (-5.62, -4.98)	0.193	-4.96 (-5.45, -4.47)	0.949	-4.27 (-4.90, -3.65)	0.136
% Mono-cytes	14.80 (10.50, 19.11)	15.46 (12.96, 17.97)	0.187	14.94 (11.42, 18.47)	0.738	10.36 (7.42, 13.30)	0.227
% CD4	62.90 (57.75, 68.05)	64.89 (60.86, 68.92)	0.001	68.72 (62.97, 74.47)	0.267	60.93 (53.64, 68.21)	0.001
T cells	32.18 (27.47, 36.90)	28.60 (25.12, 32.09)	0.135	25.02 (20.28, 29.77)	0.044	31.51 (25.63, 37.40)	0.875
% Naive	65.59 (56.56, 74.61)	73.74 (70.02, 77.46)	0.001	76.86 (72.21, 81.51)	0.128	68.86 (60.62, 75.84)	0.173
% Memory	29.56 (20.42, 38.72)	19.72 (15.84, 23.61)	<0.000	23.13 (16.65, 29.61)	0.054	25.57 (17.18, 33.96)	0.163
% B cells	1.12 (0.81, 1.43)	0.91 (0.58, 1.24)	0.964	1.01 (0.44, 1.58)	0.457	0.81 (0.53, 1.10)	0.112
% NK cells	13.65 (9.65, 17.65)	12.30 (8.90, 15.71)	0.480	12.35 (6.65, 18.05)	0.781	11.90 (8.65, 15.14)	0.195

Conclusion: Clinically benign ANA positivity is a complex immune state with many features seen in active SLE, including pDC exhaustion, keratinocyte interferon production and strong skin interferon score, increased blood interferon score, and disturbance of B cell subsets. These findings suggest that other factors are necessary for clinical disease, or that regulatory mechanisms stabilise autoimmunity. Further work in this cohort will address these questions.

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OP0045

NLRP12 INVOLVES IN THE LUPUS WITH POSITIVE INTERFERON SIGNATURE

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Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease with diverse etiological factors. It was recognized that interferon (IFN) signature involved in the progress of SLE. NLRP12 (NOD-like receptor family (NLR) pyrin domain containing 12) is a pyrin containing NLR protein that we had linked its new biological function to the cross-regulation of Toll like receptor (TLRs) and Rig-I like receptor (RIG-I) pathways. NLRP12 acts as an innate immune check-point in regulating type I IFNs expression during TLRs and RIG-I activation. The importance of NLRP12 in lupus disease activity remained to be elucidated.

Objectives: To clarify the role of NLRP12 in regulating the interferon signature.

Methods: Peripheral blood mononuclear cells (PBMCs) were collected from SLE patients and healthy donors for analysis of NLRP12 and IFN- α gene expression by RT-QPCR. PBMCs were applied for Chromatin immunoprecipitation (ChIP) assay and electrical mobility shift assay (EMSA) to determine the putative transcription factor that regulates NLRP12 expression. An involvement of epigenetic regulation of NLRP12 expression in SLE patients was also analyzed. Bone marrow derived dendritic cells (BMDCs) were collected from wild type mouse and Nlrp12 knocked-out mice. Another CD14+ monocytes were isolated from 10 cases of lupus patients and 8 cases of healthy control, following by stimulating different type of nucleic acids, and IFN- α and IL-6 were measured with ELISA assay. CD14+ monocytes in lupus patients were also pre-treated with IFNAR2 antibody for further nucleic acid stimulation. Two mice models were applied for evaluation the role of Nlrp12: intraperitoneal injection of TMPD (2,6,10,14-tetramethylpentadecane, or pristane) in C57BL/6 mice and Fas^{lpr} mice. Both models were conducted with and without Nlrp12 knockout.