Table 1.

Levels median/mean	Sudan serum	Sweden serum	P	Sudan IC	Sweden IC	P
SSA/Ro52	16/52.1	17/52.3	0.8	2.9/14.4	2.4/10.7	0.07
SSA/Ro60	2.0/47.2	3.0/48.7	0.2	1.5/14.6	1.3/12.5	0.7
SSB/La	2.0/22	2.0/22	0.6	1.1/4.2	0.8/5.5	0.02
Sm	1.0/21.7	1.0/11.4	0.0008	0.5/4.2	0.3/1.3	<0.0001
SmRNP	1.0/20.5	1.0/16	0.2	3.7/8.6	2.0/4.6	<0.0001
U1RNP	6.0/43.8	7.0/40.2	0.9	1.0/3.5	0.6/2.2	0.0005
dsDNA	14.0/124.5	28.0/198.3	0.001	32.1/50.8	12.4/25.4	<0.0001
Ribosomal P	1.0/9.3	2.0/11.7	0.0006	1.7/3.3	1.4/2.9	0.005
Histone	5.0/20.5	6.0/19.3	0.2	4.0/5.9	1.9/3.4	<0.0001
PCNA	5.0/8.4	5.0/8.9	0.6	11.1/14.2	7.0/11	<0.0001
Occurrence n(%)	serum	serum	P	IC	IC	P
SSA/Ro52	30(32.2)	105(31.7)	0.9	18(19.3)	55(16.6)	0.5
SSA/Ro60	34(36.6)	122(36.9)	0.9	27(29)	89(26.8)	0.7
SSB/La	15(16.1)	64(19.3)	0.5	9(9.7)	38(11.4)	0.3
Sm	12(12.9)	21(6.3)	0.04	6(6.4)	5(1.5)	0.008
SmRNP	15(16.1)	42(12.7)	0.4	17(18.3)	33(9.9)	0.03
U1RNP	20(21.5)	69(20.8)	0.9	22(23.7)	55(16.6)	0.1
dsDNA	31(33.3)	147(44.4)	0.055	64(68.8)	105(31.6)	<0.0001
Ribosomal P	4(4.3)	20(6)	0.5	2(2.1)	9(2.7)	0.8
Histone	10(10.7)	34(10.3)	0.9	34(36.6)	58(17.5)	<0.0001
PCNA	1(1.1)	10(3)	0.3	20(21.5)	45(13.5)	0.06

Conclusion: ANA-associated autoantibodies are more accumulated in circulating IC from Sudanese than Swedish SLE patients. The clinical significance of these findings is yet to be investigated in our upcoming analyses

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AB0128

CXCL5 DAMPENS INFLAMMATION IN THE PRE-CLINICAL MODEL OF SYSTEMIC LUPUS ERYTHEMATOSUS VIA THE ORCHESTRAL EFFECT OF REGULATING NEUTROPHIL TRAFFICKING AND SUPPRESSING HELPER T CELL-MEDIATED IMMUNE RESPONSE

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Background: Patients with systemic lupus erythematosus (SLE) suffer from severe morbidity and mortality¹⁻⁴, either from the disease itself or from side effects of immunosuppression⁵. Discovery of novel effective therapies with less toxicity is an urgent need.

Objectives: The aim of this study is to elucidate the therapeutic potential and working mechanism of cytokine CXCL5 in lupus mice.

Methods: Treatment with CXCL5, bone marrow (BM)-MSCs, standard of care (SOC) with combination of methylprednisolone and cyclophosphamide was given to 16-week-old Fas^{lpr} mice. Mice were monitored for 10 weeks. Splenic immune cell subsets were measured by flow cytometry. Circulating cytokine and immunoglobulin were detected by Luminex technology. Renal function was evaluated by urinary spot albumin creatinine ratio. In situ renal immune cell infiltration and complement 3 deposition were detected by Haematoxylin and Eosin (H&E) staining and immunohistochemistry.

Results: CXCL5 demonstrated consistent and potent immunosuppressive capacity in suppressing SLE with reduced autoantibody secretion, lymphoproliferation and preserved kidney function. With further exploration, we proved that CXCL5 reduced the proliferation of helper T cells (T_H1 and T_H2) in the *in vitro* functional assay. When we administrated CXCL5 to lupus mice, it promoted the proliferation of regulatory T cells and reduced the proliferation of T_H17 cells, macrophages and neutrophils. Multiple proinflammatory cytokines including IL-2, IL-6, IL-12, IL-17A, KC/CXCL1, MIP-1 β /CCL4 and TNF- α were also reduced. When combined with SOC, CXCL5 boosted its therapeutic effect and reduced the relevant indices of disease activity. When we correlated the effect of four different treatment groups (CXCL5, BM-MSCs, SOC, and CXCL5 plus SOC) on mice survival and target cell changes, we found that T_H17 cells were the key effector cells involved in the pathogenesis of SLE.

Conclusion: These findings demonstrated that CXCL5 dampens inflammation in the pre-clinical model of systemic lupus erythematosus via the orchestral effect of regulating neutrophil trafficking and suppressing helper T cell-mediated immune response. Administrating exogenous CXCL5 might be an attractive option to treat patients with lupus.

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AB0129

PCSK9 IS ASSOCIATED WITH DISEASE ACTIVITY AND IMPLICATED IN IMMUNE ACTIVATION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: LDL-levels are increased by Proprotein convertase subtilisin kexin 9 (PCSK9) which targets the LDL-receptor (LDLR). We reported that PCSK9 has immune modulatory properties in addition to LDL-lowering and ameliorates dendritic cell (DC) activation by oxidized LDL (OxLDL)¹, which is abundant in atherosclerotic plaques. OxLDL is also raised and associated with cardiovascular disease (CVD) in SLE.¹⁻³

Objectives: We here investigate the role of PCSK9 in SLE both in a clinical context and in experimental *ex vivo* studies. The objective is to investigate if PCSK9 and its inhibition could be of relevance in SLE in addition to LDL-level related properties

Methods: PCSK9-levels were determined by ELISA among SLE patients (n=109) and age- and sex-matched population-based controls (n=91). Common carotid intima-media thickness (IMT) and plaque occurrence were determined by B-mode ultrasound. Plaques were graded by echogenicity. Human peripheral blood monocytes from SLE patients or controls were differentiated into DCs. Effects of PCSK9 and its inhibition by silencing were studied.

Results: PCSK9-levels were non-significantly higher among SLE-patients as compared to controls but associated significantly with SLE disease activity, as determined by SLAM (0.020) or SLEDAI (0.0178). There was no association between PCSK9-levels and atherosclerosis as determined by IMT, prevalence of plaques or echolucent (potentially vulnerable) plaques. PCSK9 levels were significantly associated with CVD among SLE-patients but not after adjustment for age.

OxLDL induced PCSK9 in DCs and DC-maturation with increased expression of CD86 and HLA-DR. The effects were significantly stronger in DC from SLE patients than from controls. Silencing of PCSK9 abolished OxLDL-induced DC-maturation.

Conclusion: PCSK9 is associated with disease activity in SLE. One underlying cause could be OxLDL, promoting DC-activation which depends on PCSK9. OxLDL induces PCSK9, an effect which is higher among SLE-patients. PCSK9 could play an unexpected immunological role in SLE and inhibition of PCSK9 could potentially play a role in disease amelioration, pending on clinical studies.

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AB0130

SERUM ATHEROGENICITY IN WOMEN WITH UNTREATED SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is associated with an unexplained increase cardiovascular risk. The nature of the factors that contribute to progression of atherosclerosis were identified using the method for determining the atherogenicity of blood serum in cell culture in cell culture (in vitro). The term "atherogenicity" is meant as the ability of the serum and/or its components to induce intracellular accumulation of cholesterol in cultured cells.

Objectives: To compare atherogenicity of blood serum in women with untreated SLE and healthy women.

Methods: Thirty seven women (median age 30[21;39] years) with active SLE (median disease duration 45[3;102] months; SLADAI 17 [8;34]) were enrolled in the study. Lupus nephritis are defined in 15 (41%), Antiphospholipid syndrome (APS) – in 8 (22%) of 37 SLE patients (pts). The control group consisted of 30 women, median age 31[25;39] years.

Atherogenicity of blood serum was determined in the culture of murine macrophages. Peritoneal macrophages were isolated from the ascitic fluid of the line mice according to the generally accepted method J. Goldstein et al (1979y). Serum atherogenicity was determined by the accumulation of intracellular cholesterol induced by 10% of the blood serum of the patients, and expressed as a percentage of the content of cholesterol in the control cells.

Results: Elevated atherogenicity of blood serum was detected more frequently in SLE pts (24/72 (65%) vs healthy controls (5/30 (17%), $p < 0.01$). The blood serum of SLE pts caused a 3-7-fold accumulation of intracellular cholesterol, which significantly differed from healthy women ($203 \pm 136\%$ vs $127 \pm 42\%$, $p < 0.001$). The ability to stimulate the accumulation of cholesterol esters in murine macrophages was not associated with age, duration of the disease, lipid spectrum and was the highest in pts with nephritis ($305 \pm 141\%$ vs $180 \pm 52\%$, $p < 0.05$) and APS ($253 \pm 130\%$ vs $119 \pm 75\%$, $p < 0.05$).

Conclusion: Serums of women with untreated SLE may stimulate the accumulation of cholesterol in mouse macrophages unlike of healthy women.

The highest atherogenicity was found in blood serum of SLE pts with nephritis and APS.

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AB0131

RESPIRATORY TRACT POLY(I:C) STIMULATION ACCELERATES SALIVARY GLAND IMMUNE DYSFUNCTION IN SPONTANEOUS SJÖGREN'S SYNDROME ANIMAL MODEL

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Background: Sjogren's syndrome is one of the most common autoimmune diseases, with a prevalence of 0.33% to 0.77% in Chinese people, characterized by focal infiltration of lymphocytes in glands and the production of multiple autoantibodies. Studies have shown that virus infection may play a crucial role in the occurrence and development of this disease.

Objectives: It has been shown that airway stimulation with poly(I:C) can mimic respiratory tract viral infection to some extent. Thus, this study was aimed to investigate the dynamic immune responses in salivary gland after respiratory tract poly(I:C) stimulation in NOD mice.

Methods: The 5-week-old NOD mice were given respiratory tract poly(I:C) stimulation to mimic the respiratory virus infection once every other day for a total of 5 times (the total dose is 100µg), and the control group were given the same dose of sterile PBS. After 8 weeks, the mice were sacrificed to obtain and analyze the salivary gland tissues.

Results: We found that the salivary gland flow rate was decreased and the blood glucose was influenced by the Viroid stimulation during the early stage in poly(I:C) stimulated group compared with that in PBS group. Accordingly, the pathological injury of salivary gland tissues in poly(I:C) stimulated group was more serious, including decreased volumes of the salivary glands, increased number of pathological focus score and the increased area of lymphocyte infiltration. Furthermore, we found that the expression of IL-33 in salivary glands of

poly(I:C) stimulated NOD mice was increased, especially the expression of IL-33 in the acini and ducts. Moreover, the expression of IFN-I and IFN-II is up-regulated in salivary glands.

Figure1: Functional change of the NOD mice in different groups.

A. The dynamic change of the salivary gland flow rate; B. The dynamic change of the blood glucose

Figure2: Pathological changes of salivary glands in mice after different treatments.

A. The pathological changes of different groups; B. The quantitative analysis of the volume of salivary glands in different groups; C. The quantitative analysis of the numbers of pathological lesions of salivary glands in different groups; D. The quantitative analysis of the areas of pathological lesions of salivary glands in different groups.

Figure3: The differential expression of IL-33 in the salivary glands.

A. The expression of IL-33 in different sites of salivary glands; B. The quantitative analysis of the expression of IL-33 in the acini cells site; C. The quantitative analysis of the expression of IL-33 in the ductal cells site; D. The quantitative analysis of the expression of IL-33 in the lymphocytic aggregation site.

Conclusion: The results of this study suggest that respiratory tract poly(I:C) stimulation accelerates salivary gland immune dysfunction in spontaneous sjogren's syndrome NOD mice, which mechanisms need to be further investigated.

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