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

Disclosure of Interests: None declared

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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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