NETosis-derived bioproducts were further evaluated by multiplex assay and specific commercial kits, respectively. Besides, miRNomes were identified using next-generation sequencing. Clinical significance of the biomolecules analyzed was explored by correlation/association studies with immunological and CV-risk features.

Results: A significant relationship among the incidence of CVD (i.e. thrombosis or cardiac involvement) and the positivity for anti-dsDNA antibodies was recognized in the first SLE cohort. Accordingly, in the second SLE cohort, significantly impaired micro-vascular endothelial function (identified by reduction of hyperemia post-occlusion area), increased atherogenic index and pathologic increase in the CIMT were assessed in patients positive for anti-dsDNA in relation to anti-dsDNA negative patients. Around a 65% of SLE patients displayed a sustained positivity for anti-dsDNA antibodies for more than 7 years. These patients showed a distinctive and specific molecular profile compared with patients that had remained negative for anti-dsDNA, including increased inflammatory profile (IL1B, IL2, IL6, IL17, EOTAXIN, FGF, GM-CSF, IFN γ , IP10, RANTES, TNF), enhanced oxidative status (lipoperoxides), and higher NETosis (nucleosomes, elastase). Levels of those biomolecules were closely interconnected and associated to their regulatory miRNAs, which accordingly exhibited differential expression in SLE anti-dsDNA(+) vs anti-dsDNA(-) patients. Finally, the frequency for positivity of anti-dsDNA significantly correlated both with markers of endothelial dysfunction and with the presence of atheroma plaques in SLE patients, pointing at the direct involvement of anti-dsDNA-Abs in the development of these processes.

Conclusion: 1. Positivity for anti-dsDNA antibodies confers a specific molecular profile linked to an enhanced CV-risk in SLE patients. 2. Moreover, the sustained positivity for anti-dsDNA antibodies fosters the establishment of an atherothrombotic status in these autoimmune patients.

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AB0137 DIVERSITY ANALYSIS OF INTESTINAL FLORA IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a multiple systemic autoimmune disease and its pathogenesis is still not fully understanding. In recent years, there has been reports on the relationship between SLE and intestinal flora.

Objectives: To study the diversity and the intestinal flora intestinal microbes in patients with SLE and further provide new ideas for clinical treatment.

Methods: The stool samples of 28 patients with SLE and 125 normal healthy adults were collected. The 16S rRNA in the specimen was sequenced using the Roche/45 high-throughput sequencing platform, and the differences between the two groups were compared at the level of the phylum and genus.

Results: In SLE patients, as the picture show, the levels of fusobacteria, proteobacteria and TM7 were significantly higher ($P<0.05$) and the number of firmicutes was significantly decreased ($P<0.05$) than that of healthy controls at the phylum level. The percentage of bifidobacterium, collinsella, enterococcus, leuconostoc, streptococcus, bilophila were significantly higher ($P<0.05$) and the number of lachnospira, roseburia, gemmiger, devosia, desulfovibrio were significantly decreased ($P<0.05$) than that of healthy participants at the genus level.

Figure 1. the differences between patients with SLE and normal healthy adults were compared at the level of the phylum

Figure 2. the differences between patients with SLE and normal healthy adults were compared at the level of the genus

Conclusion: The diversity of intestinal flora in patients with SLE altered from that of normal population. The differences are likely to be one of the pathogenesis of lupus, which might provide theoretical foundation for the regulation of intestinal flora to treat autoimmune diseases such as lupus.

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AB0138 INCREASED CD38 EXPRESSION LEVELS ON IMMUNE CELL SUBSETS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Plasma Cells (PCs) are implicated in the pathogenesis of Systemic Lupus erythematosus (SLE) and their targeting proved a promising treatment modality. As there is a monoclonal therapeutic antibody targeting CD38 licensed for clinical use in multiple myeloma, plasma cell depletion via CD38 seems to represent a promising path in SLE treatment. While CD38 is highly expressed on plasmacells, it is present on the surface of subsets of T and B lymphocytes as well as myeloid cells.

Objectives: Here we aim to identify the differential expression of CD38 on peripheral blood leukocytes in SLE compared to healthy controls (HC) investigate the function of CD38+ T lymphocytes

Methods: We performed flow cytometry to investigate the expression of CD38 on peripheral blood mononuclear cells of SLE patients (n=36) and HCs (n=20). We additionally analyzed the expression of T lymphocytes within the urine of patients with lupus nephritis as well as the skin of SLE patients. We investigated the

inflammatory potential of CD38 positive memory T lymphocytes after stimulation and performed single-cell RNA sequencing analyses.

Results: CD38 Expression is increased on certain immune cell subsets: Plasmablasts and unswitched Memory B cells, as well as plasmacytoid dendritic cells and CD16+ non-classical monocytes. We observed a drastic increase CD38 in both memory CD4 and CD8 T lymphocytes in SLE patients. These cells were mostly effector T cells (and not regulatory T cells) and expressed other markers of T cell activation and proliferation. We found an enrichment of CD38+ memory T cells in the urine of patients with lupus nephritis. After polyclonal stimulation of T cells, CD38+ produced less inflammatory cytokines. Preliminary single-cell sequencing results indicate that CD38+ CD8+ T-lymphocytes have decreased clonal diversity and that these cells express genes associated with exhaustion and type 1 interferon response.

Conclusion: Increased CD38 expression on various lymphocyte subsets provides an additional rationale for investigating CD38-directed therapies in SLE. Targeting CD38 could not only deplete plasma cells but also has the potential to target interferon alpha producing plasmacytoid dendritic cells and modulate inflammatory T cell functions.

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AB0139 T FOLLICULAR HELPER CELLS MAY BE INVOLVED IN THE LUPUS DEVELOPMENT IN HIGH FAT DIET-INDUCED OBESITY MICE

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Background: System lupus erythematosus (SLE) is an autoimmune disease that is associated with skin rash and multiple organs lesion. It is known that obesity is a major factor contributing to the onset and progression of autoimmune diseases including SLE. Our previous study showed that circulating T follicular helper (Tfh) cells played an important role in autoantibody production in SLE patients. A recent study showed that Tfh cells promote B cell production of IgA antibodies, which help shape the composition of the gut microbiota and may modulate obesity.

Objectives: By establishing an obesity-associated lupus mouse model, we investigated the pathophysiologic link of obesity, SLE and Tfh cells using MRL/lpr lupus prone mice.

Methods: Twenty MRL/lpr mice (10 male and 10 female) were randomized equally fed with a regular diet (RD) or high fat diet (HFD, 60% calories comprised of fat). Their body weights were recorded weekly as an indicator of obesity achievement. SLE progression was monitored weekly by development of skin lesion and urine protein levels assessed by Bradford assay. Blood was collected for IgG, anti-dsDNA and anti-nuclear antibody (ANA) detection. At the endpoint of week 14, spleen was measured and weighted. Spleen, kidney, and dorsum of neck skin were collected and embedded for H&E, PAS, Masson's staining, and immune complex staining to detect active histopathological lupus lesions and be quantified as histological skin score and kidney index. Tfh cells in spleen was identified by immunohistochemistry (IHC) staining glomerulus of kidney.

Results: Obesity was achieved with a significant difference of mouse body weight between the RD and HFD groups by week 3 and continued until week 14 ($p < 0.05$ to $p < 0.01$). Evidence of SLE development, such as skin rash on the dorsal neck and back in HFD group showed up as earlier as week 6 and occurred in 55.6% of the HFD group vs 11.1% of the RD group ($p < 0.05$), with a higher histological score of skin in HFD group ($p < 0.05$). Proteinuria was increased from 11 to 14 week in male HFD group with an elevated kidney index and immune-complex deposits in their glomerulus of kidney. There was an increase trend of anti-dsDNA and IgG titer in HFD group, but no difference of ANA was observed between these two groups. Splenomegaly was observed in the HFD mice ($p < 0.05$). The Tfh cells in the spleen of HFD group were higher than RD group.

Conclusion: Our results show accelerated and greater severity of lupus development in MRL/lpr mice with HFD compared to mice on RD, indicating HFD-induced obesity exacerbates lupus development in mice. Tfh cells may be involved in the relation of SLE and obesity. This model could be used to

investigate the mechanism underlying the link between obesity and SLE development. Interventions to reduce body weight or target Tfh cells may improve both lupus symptoms and outcomes in genetically predisposed SLE patients.

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AB0140 BAFF NEUTRALIZATION HAS JANUS-FACED EFFECT ON ATHEROSCLEROSIS ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Cardiovascular diseases (CVD) are the leading cause of death in systemic lupus erythematosus (SLE). B cells play a key role in the pathogenesis of lupus and anti-BAFF therapy has been approved in SLE. Since mature B cells also promote atherosclerosis, BAFF neutralization is expected to have an atheroprotective effect in SLE.

Objectives: The aim of our study was to test this hypothesis using a new mouse model with a mix susceptibility to lupus and atherosclerosis that received or not an anti-BAFF treatment, and in a cohort of SLE patients in whom we monitored carotid plaques, the B cell compartment and BAFF levels.

Methods: The effect of BAFF on atherosclerosis associated with lupus was investigated in the atherosclerosis- and lupus-prone *Apoe*^{-/-}D227K mouse model and in a cohort of SLE patients. Mice were treated with a blocking anti-BAFF monoclonal antibody (Ab), while fed with a standard chow diet. Carotid plaque and carotid intima media thickness were assessed by ultrasound at baseline and during follow-up in SLE patients asymptomatic for CVD.

Results: Anti-BAFF Ab in *Apoe*^{-/-}D227K mice *ii*/ induced a B cell depletion, *iii*/ efficiently treated lupus, *iii*/ improved atherosclerosis lesions in mice that had low plasma cholesterol levels but worsened the lesions in mice with high cholesterol levels. In that case, the atheroprotective effect of the BAFF-BAFFR signaling inhibition on B cells was counterbalanced by the proatherogenic effect of the BAFF-TACI signaling inhibition on macrophages. In SLE patients, BAFF blood levels were associated with subclinical atherosclerosis. Anti-BAFF Ab treatment had a differential effect on the intima media thickness progression in SLE patients depending on the body mass index

Conclusion: Depending on the balance between metabolic- and B cell-induced proatherogenic conditions, anti-BAFF could be respectively detrimental or beneficial on atherosclerosis development in SLE

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AB0141 MYCOPHENOLATE MOFETIL, INHIBITOR OF INOSINE-5'-MONOPHOSPHATE DEHYDROGENASE, REGULATES DIFFERENTIATION, MATURATION AND FUNCTION OF HUMAN DENDRITIC CELL SUBSETS

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Background: Systemic lupus erythematosus (SLE) is a heterogeneous disease in which excessive inflammation, autoantibodies, and complement