provide the first evidence that EBV infection and EVs are linked to the pathogenesis of LN and confirm that EBV as a model for studying EV-mediated cell-cell. Our results support the model of exosome-mediated tubulointerstitial communication and inflammation and agree with the observation that systemic pro-inflammatory EVs target specific cell types in target organs.

S3a – Immunopathogenesis I

S3A:4 OX40/OX40L AXIS IMPAIRS FOLLICULAR AND NATURAL REGULATORY T CELL FUNCTION IN HUMAN SYSTEMIC LUPUS

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The mechanisms responsible for the Treg deficiency in SLE remain unclear. Our group recently reported that OX40L stimulation induces CD4 +T cells to express T follicular helper cells (TFH) associated molecules, and is sufficient to induce CD4 +T cells to become functional B cell helpers.

We hypothesised that OX40L/OX40 axis was implicated in Treg and regulatory follicular helper T cell (TFR) dysfunction in SLE.

Methods Flow cytometry was used for analysis of SLE patients (n=61) and healthy donors (HD) (n=16). Using recombinant sOX40L, *in vitro*-generated SLE-DCs expressing OX40L, and DCs from patients, the impact of OX40/OX40L axis on the function of cTregs (CD4 +CXCR5-CD25high Foxp3+) and TFR (CD4 +CXCR5+CD25 high Foxp3+) purified from HD was studied.

Results OX40L/OX40 axis engagement on Tregs and TFR not only specifically impaired their ability to regulate T effector cells proliferation but also their ability to suppress TFH-dependent B cell activation, and immunoglobulin secretion. Indeed, we observed that soluble and membrane-bound OX40L decreased suppressive Treg function ($p<0.05$), without inducing Treg cell death. Treg suppressive function was restored when *in vitro*-generated SLE-DCs expressing OX40L were pre-incubated with a blocking anti-OX40L mAb. Furthermore, purified tonsils TFR cells previously cultured or not with sOX40L were cultured with purified TFH and memory B cells in the presence of SEB. We observed higher immunoglobulin production and increased differentiation of B cells into CD38 +plasmablasts in co-cultures with TFR exposed to sOX40L.

APCs from active SLE patients (n=5) mediated Tregs dysfunction in an OX40L-dependent manner ($p=0.01$). We also observed an inverse correlation between OX40L expression on SLE-APCs and their ability to hamper Tregs cell suppressive function ($r=-0.85$, $p=0.0001$).

OX40L-expressing cells co-localised with FoxP3 positive cells in active SLE skin lesions, suggesting that OX40L+cells Treg contact actually operates *in vivo* within inflammatory tissues.

In vitro, engagement of OX40L/OX40 axis resulted in FoxP3 down-regulation in Tregs. FoxP3 expression in SLE Tregs negatively correlated with the proportion of circulating OX40L-expressing mDCs, suggesting that OX40L-dependent Foxp3 down-regulation also operates *in vivo*.

Conclusion These data support that OX40L/OX40 signals are implicated in T regulatory cell dysfunction in SLE. Blocking OX40L/OX40 axis appears as promising therapeutic strategy.

S3A:5 AUTOANTIBODIES AGAINST HUMAN SERUM ALBUMIN IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Objectives Autoantibody production and aberrant immune complex formation belong to the pathological hallmarks of systemic lupus erythematosus (SLE). This study aimed to determine the occurrence of autoantibodies against human serum albumin (HSA) and their potential association with antibodies against bovine serum albumin (anti-BSA) in patients with SLE.

Methods Sera of 180 well-defined SLE patients included into the Swiss SLE Cohort Study and 188 age- and sex-matched healthy controls were evaluated. Levels of anti-HSA IgG and anti-BSA IgG were quantified by ELISA. Selected samples were further characterised with regard to the occurrence of monomeric versus albumin-complexed IgG using serum fractions obtained by fast liquid chromatography (FPLC).

Results SLE patients had increased levels of antibodies against HSA ($p=0.002$) but similar levels of anti-BSA IgG as compared to matched healthy controls. Anti-HSA IgG levels correlated with the SLE Disease Activity Index (SLEDAI), which was more pronounced in patients with an additional physician's global assessment (PGA) of greater or equal 1 ($r=0.309$, $p=0.0066$). The analysis of selected samples indicates that anti-HSA IgG are partially complexed with serum albumin but also occur as monomeric autoantibodies in highly positive SLE patients. However, SLE patients were not found to have strikingly increased levels of albumin-IgG complexes compared to matched controls. Interestingly, a positive correlation between anti-HSA IgG and anti-BSA IgG was found that was stronger in SLE patients than in healthy controls ($r=0.3172$, $p<0.001$ vs $r=0.2122$, $p<0.0035$). This might be due to a partial cross-reaction as binding of anti-BSA IgG could partially be inhibited by the presence of HSA in samples with double positivity for anti-HSA and anti-BSA (median inhibition 47.9%, range 0.9%–100%).

Conclusions SLE patients were found to have an increased prevalence of anti-HSA antibodies that are associated with SLE disease activity. As anti-HSA were also found to be associated with the occurrence of anti-BSA antibodies, anti-HSA might be triggered by food-derived bovine albumin.