



Abstract PS5:99 Figure 1 Data showing relative C3 cleavage of Thr and FXa in the presence and absence of antibodies and inhibitors

IgG (n=2) but not anti-Thr IgG. Analysis of clinical serology records for the last 10 consecutive clinic visits of 28 anti-SP-positive patients showed a lower level of C3 (0.92 g/L) in the patients double positive for anti-FXa and anti-Thr than for anti-Thr alone (1.12 g/L) or anti-FXa alone (1.16 g/L).

Conclusions Anti-FXa and anti-Thr enhance cleavage of C3 by FXa and Thr respectively. Presence of these antibodies *in-vivo* in patients with SLE and/or APS may promote increased complement activation and disease activity. This finding may have potential translational implications for future treatment of these diseases.

PS5:100 PATOPHYSIOLOGICAL ROLE OF TYPE I AND III INTERFERONS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Systemic Lupus erythematosus (SLE) is an autoimmune disease characterised by activated autoreactive lymphocytes and autoantibodies, resulting in tissue damage in multiple organs. An important factor for the disease's mortality is the development of Lupus nephritis (LN). Type I and III interferons, which are both part of the antiviral defense, have both been associated with the disease's activity. In sera and urine of SLE patients an enhanced level of IL28/29 was described, but their distinct functional role in the course of disease need to be further investigated.

To determine the role of type I and III interferons during onset and progression of autoimmunity – with focus on the development of LN – the expression of the IFNs and their specific receptors was observed in lupus prone MRL Faspr mice. These mice develop SLE like symptoms and immunocomplex glomerulonephritis. So far we could confirm the expression of IL28 and it's receptor by tubular epithelial cells

(TEC) in the kidney of MRL Faspr mice. The overall IL28 mRNA expression increased with disease activity in renal tissue, and a positive correlation to the IFN α and IFN β expression could be observed. Further the mRNA expression of the IFN receptor mRNA in the spleen accelerated with increasing disease activity.

Furthermore MRL Faspr mice deficient of the IL28R and/or IFN α R were generated and the progression of autoimmunity and LN was monitored. In preliminary studies with MRL Faspr IL28R -/- mice, a less extenuated lymphadenopathy and less severe LN at the age of 3 month was observed, compared to their wild-type littermates. Similar observations according the Lymphadenopathy were made in MRL Faspr IFN α R -/- mice.

Our results suggest a participation of type III IFNs in the development of Lupus nephritis in MRL Faspr mice. In upcoming experiments the effect of the IL28R knockout will be compared to the effect of the IFN α R knockout and the combined IL28R-IFN α R knockout. The subsequent aim is to transfer the results obtained in the murine model to human SLE and to evaluate IL28 as disease activity marker.

PS5:101 NUCLEAR ANTIGEN-REACTIVE CD4+ T CELLS ARE EXPANDED IN ACTIVE SLE, CORRELATE WITH DISEASE ACTIVITY, INVADE TARGET ORGANS SUCH AS THE KIDNEYS, AND OUTNUMBER THEIR REGULATORY COUNTERPARTS

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