Systemic lupus erythematosus (SLE) is a prototypic autoimmune disease resulting in multi-organ damage and a high rate of morbidity. Onset of SLE is characterised by dysregulated activation of T and B lymphocytes and the production of autoantibodies directed against nuclear components. The auto-antibodies generated during the onset of SLE often recognise components released by neutrophils during NETosis, a type of cell death defined by the generation of neutrophil extracellular traps (NETs). The endonuclease DNase1 has been shown to be involved in the clearance of NET components. The sera of SLE patients contain inhibitors of DNase 1 and/or anti-NET antibodies that block the ability of DNase 1 to degrade NETs. Thus, whilst NETs are important for clearing infection they must be tightly regulated and degraded to prevent the onset of autoimmunity.

In this study we monitored the production of auto-antibodies in the serum of wild type and DNase 1-deficient mice from the age of 2 to 12 months, along with proteinuria levels and the development of glomerulonephritis. We show that DNase 1-deficient mice develop a SLE-like phenotype with elevated auto-antibody production and kidney damage by 12 months. This model also demonstrates the female bias in SLE as the female DNase 1-deficient mice had the highest level of kidney damage. As DNase 1 activity, B cells and aberrant NETosis are central to progression of SLE understanding their mechanisms of action are of great therapeutic interest.

**Abstracts**

**PS5:92** CLARIFICATION OF THE ROLE OF DNASE 1 ON THE ONSET OF SYSTEMIC LUPUS ERYTHEMATOSUS IN A MURINE MODEL

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Systemic lupus erythematosus (SLE) is a prototypic autoimmune disease resulting in multi-organ damage and a high rate of morbidity. Onset of SLE is characterised by dysregulated activation of T and B lymphocytes and the production of autoantibodies directed against nuclear components. The auto-antibodies generated during the onset of SLE often recognise components released by neutrophils during NETosis, a type of cell death defined by the generation of neutrophil extracellular traps (NETs). The endonuclease DNase1 has been shown to be involved in the clearance of NET components. The sera of SLE patients contain inhibitors of DNase 1 and/or anti-NET antibodies that block the ability of DNase 1 to degrade NETs. Thus, whilst NETs are important for clearing infection they must be tightly regulated and degraded to prevent the onset of autoimmunity.

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**REFERENCE**


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**PS5:94** CHARACTERISATION OF SLE B CELLS FROM PATIENTS IN REMISSION – PERSISTENT IL-10 SECRETORY DEFECT

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Background SLE is an autoimmune disorder characterised by polyclonal Bcell activation, the production of anti-double stranded (ds) DNA autoantibodies and cytokines. Molecular and clinical studies regarding SLE often address clinically active patients and not patients in remission. This study reports on immunoglobulin, anti-dsDNA-aab and IL-10 secretory capacity of cultures of CD19 +lymphocytes from SLE patients in remission in comparison to normal donors. The aim was to evaluate whether endogenous factors (BAFF, CD40, IL4), exogenous factors (CpG-ODN-motifs, SAC) or their combinations differentially influence immunoglobulin, cytokine and anti-dsDNA-aab production in not active SLE patients vs healthy controls.

Methods Blood samples were obtained from a group of 13 SLE patients attending clinics at the rheumatology unit at the Heinrich-