AUTOANTIBODIES ASSOCIATED WITH RNA ARE MORE ENRICHED THAN ANTI-DS DNA ANTIBODIES IN CIRCULATING IMMUNE COMPLEXES IN SLE

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Background and objective We have earlier shown that polyethylene glycol (PEG)-precipitated circulating immune complexes (CIC) from systemic lupus erythematosus (SLE) patients induce cytokines in vitro, and that levels of both CIC and CIC-induced cytokines are dependent on (1) SLE disease activity and (2) the occurrence of anti-SSA but not anti-dsDNA autoantibodies. These findings implicated anti-SSA in immune complex formation, but the formal proof that anti-SSA participates in the formation of SLE CIC to a greater degree than did other antinuclear antibody-associated autoantibodies was lacking. The aim of this study was to investigate to what extent different autoantibodies accumulate in SLE immune complexes, and whether such accumulation is dependent on SLE disease activity.

Methods Circulating immune complexes were isolated from SLE sera by both PEG precipitation (n=19) and C1q binding (n=8). Autoantibody specificities were determined with a semiquantitative lineblot assay quantified by densitometry. To compare the relative levels of autoantibodies they were normalised against total IgG measured by ELISA in sera and CIC in parallel. Samples were investigated both in a cross-sectional design (n=19), as well as in a paired design with samples obtained during active and inactive SLE (n=10).

Results All autoantibodies were enriched in CIC compared to in serum. The group of antibodies against RNA-associated antigens showed higher median enrichment than anti-dsDNA (anti-RNP/Sm p=0.0228, anti-Sm p=0.0392, anti-SSA/Ro60 p=0.0539, anti-SSA/Ro52 p=0.0122, anti-SSB/La p=0.0342).
Similarly, the other DNA-associated antigens (antihistones and antinucleosomes) were also less enriched as compared with the RNA-associated specificities. These findings were corroborated by analysis of autoantibody content in C1q-bound CIC. There was no difference in degree of accumulation of the investigated autoantibodies in CIC during active and inactive SLE.

**Conclusion** Our findings demonstrate a difference in enrichment between autoantibodies against RNA- and DNA-associated autoantigens in isolated SLE CIC, suggesting that the RNA-associated autoantibodies are more prone to form complexes in the circulation in SLE, in contrast to antibodies against DNA-associated autoantigens including dsDNA. These findings have implications on by what mechanisms different autoantibodies accumulate in target organs in SLE.