Autoreactive IgG memory B cell antibodies in patients with Systemic Lupus Erythematosus arise from non-reactive and polyreactive precursors

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Zielsetzung
Persistent autoantibody production in patients with Systemic Lupus Erythematosus (SLE) suggests the existence of autoreactive humoral memory but the frequency of self-reactive memory B cells in SLE has not been determined. Therefore we wanted to characterize the reactivities of antibodies expressed by memory B cells in SLE patients.

Methodik
We isolated and single cell sorted IgG+ memory B cells (CD19+CD27+IgG+CD38-) from peripheral blood of four newly diagnosed, untreated, pediatric SLE patients. B cell transcripts were subjected to RT-PCR. Immunoglobulin heavy and light chain genes were amplified from the obtained cDNA, cloned into expression vectors and expressed in 293 HEK cells. Recombinant antibodies were harvested from the supernatants and were tested in ELISA, HEp-2 cell slides and immunoblot assay for self- and polyreactivity.

Ergebnisse
The overall frequency of polyreactive and HEp-2 self-reactive antibodies in the IgG+ memory B cell compartment in patients with SLE was similar to controls. We found 15% of IgG memory B cell antibodies highly reactive and specific for SLE-associated extractable nuclear antigens (ENA) Ro52 and La in one patient with serum autoantibody titers of the same specificity but not in the other 3 patients or healthy individuals. The germline forms of the ENA antibodies were non-self-reactive or polyreactive with low binding to Ro52 supporting the idea that somatic mutations contributed to autoantibody specificity and reactivity.

Schlussfolgerung
Heterogeneity in the frequency of memory B cells expressing SLE-associated autoantibodies suggests that this variable may be important in the outcome of therapies that ablate this compartment.