A156 VACCINATION OF PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME REVEALS HYPERREACTIVE B CELL COMPARTMENT WITH A SKEWED MATURATION PATTERN

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Background Multiple immune disturbances underlying disease development and progression have been implicated in primary Sjögren's syndrome (pSS), especially defects in the B cell compartment. In this study we used vaccination as a tool to analyse defects in immune regulation in vivo in individuals with pSS, and specifically to characterise B cell development and responses.

Methods Fourteen SSA positive women with pSS and 18 gender and age matched healthy controls were vaccinated against H1N1 influenza with a priming dose and booster 3 weeks apart. Blood samples were obtained before injections and after 1 and 3 weeks. Total Ig-levels and vaccine specific responses were analysed by ELISPOT, ELISA and hemagglutination tests. Lymphocyte phenotypes were characterised by flow cytometry and clinical routine laboratory tests were performed. Serum cytokine levels and microarray-based RNA expression analysis was performed, as well as genotyping for selected markers. Clinical parameters and potential adverse reactions were monitored with a clinical questionnaire.

Results All subjects developed protective immunity to H1N1 influenza upon vaccination with a similar adverse effect profile. However, when dissecting the vaccine specific response patients developed significantly higher titers of IgG vaccine specific antibodies and significantly lower IgM titers. Interestingly, the IgG antibodies were of higher avidity, indicating that this was a specific response. In addition, hypergammaglobulinemia was induced in the patients and anti-SSA/Ro52 titers were transiently elevated.

No significant phenotypic differences were observed in the lymphocyte compartment at the start of the study, but already 1 week after the first vaccination pSS patients had significantly fewer CD19 class switched B cells and more immature B cells in circulation. This skewed pattern of B cell maturation remained throughout the study. Paradoxically, plasmablasts appeared at a significantly higher level in patients after immunisation. In accordance, significantly higher levels of several pro-inflammatory cytokines (IL-6, IL-10, IL-12p40 and TNFα), as well as the B cell promoting cytokines IL-7 and BAFF were induced upon vaccination in the patients. Microarray analysis revealed an interferon-signature in the patients.

Conclusions Patients with Sjögren's syndrome respond to vaccination with protective immunity. However, the induced IgG vaccine-specific antibodies are of significantly higher titers and of stronger avidity than in healthy controls, occuring in parallel with a skewed B cell maturation and induction of a pro-inflammatory cytokine response. This may reflect the mechanisms allowing high titers of autoantibodies to develop in pSS patients.