A152 STEADY STATE GENERATION OF MUCOSAL IGA+ PLASMABLASTS IS NOT ABROGATED BY B CELL DEPLETION THERAPY WITH RITUXIMAB

Henrik Mei,[1,2] Daniela Frölich,[2] Claudia Giesecke,[1,2] Christoph Loddenkemper,[3] Karin Reiter,[1,2] Stefanie Schmidt,[1,2] Eugen Feist,[2] Capucine Daridon,[1,2] Hans-Peter Tony,[4] Andreas Radbruch,[1] Thomas Dörner[1,2] *[1]German Rheumatism Research Center Berlin (DRFZ), Berlin, Germany; [2]Charité University Medicine Berlin, CC12, Dept. Medicine/ Rheumatology and Clinical Immunology, Berlin, Germany; [3]Institute of Pathology, Technische Universität München, Munich, Germany; [4]University of Würzburg, Dept. Medicine/Rheumatology, Würzburg, Germany*

10.1136/ard.2010.149005.19

B cell depletion therapy with rituximab (anti-CD20) has been established for treating RA. While rituximab efficiently removes circulating B cells, its effects on tissue-based B cells, especially on those in gut-associated lymphoid tissues, remained unclear and are discussed as potential reasons for individual unresponsiveness. Here we studied the ffect of rituximab treatment on circulating and tissue-resident IgA plasmablasts as correlates of mucosal B cell activation in patients with RA.

Patients with rheumatoid arthritis were given 2x1g rituximab and peripheral blood was analyzed for circulating B cells and plasmablasts by flow cytometry before and at 2-9 months after rituximab infusion. Some patients were also analyzed additionally analyzed during a second treatment course. Cell proliferation was analyzed using Ki-67 expression and plasmablast migration was assessed towards CXCL12 and CCL28 using an in vitro transwell system.

Peripheral blood CD20+ naïve and memory B cell numbers were reduced to >0.02% of their intial numbers before therapy, while plasmablasts/plasma cells were persistently detectable in the blood at ~26-119%. These circulating plasmablasts/plasma cells expressed a mucosal phenoytpe, i.e. IgA, beta7 integrin and CCR10 before and throughout the B cell depletion phase. Recently activated plasmablasts were revelead by high epxression of HLA-DR, in vitro migration towards CXCL12 and CCL28 and Ki-67 expression. Consistently, IgA+ plasmablasts and plasma cells were also identified in lamina propria biopsies of rituxuimab treated patients. Numbers of circulating plasmablasts did not significantly correlate with DAS28 values. Notably, antibody produced by peripheral blood IgA+ plasmablasts generated during B cell depletion frequently bound to bacterial antigens.

Our results suggest the persistent generation of mucosal plasmablasts during B cell depletion with rituximab, pointing towards the resistance of some functional B cells, residing in the mucosa and permitting the differentiation of IgA+ plasmablasts. Our data suggest that rituximab has a limited capacity to target mucosal B cells and antibody production.