A16 ANTI-CITRULLINATED PROTEIN ANTIBODIES HAVE A LOW AVIDITY COMPARED TO ANTIBODIES AGAINST RECALL- ANTIGENS

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Anti-citrullinated protein antibodies (ACPA) are specific for rheumatoid arthritis (RA), their presence is predictive for development to RA and have been implicated in disease-pathogenesis in animal studies. Despite the important implications for diagnoses and etiology, the natural development and biology of the ACPA response is poorly studied. Here the authors determined the avidity and avidity maturation of the ACPA response and compared this to the avidity of antibodies against recall-antigens.

Our data show that the avidity of ACPA against several citrullinated antigens is considerably lower as compared to the avidity of antibodies against recall antigens such as tetanus toxoid or diphtheria toxoid. Intriguingly, despite high titers and extensive isotype switching, no avidity maturation in the ACPA response was observed during longitudinal follow-up.

Our data indicate that the natural evolution of ACPA differs from the development of antibodies against prototype T cell dependent recall antigens. Moreover, these data point to an independency of avidity maturation and isotype-switching where full-isotype switching is taking place in the face of restricted and/or hampered avidity maturation.

As avidity maturation of ACPA differs from avidity maturation of antibodies to recall antigens, our data are of relevance to the design of anti-B cell therapeutics. Intervention in the signalling of BAFF via the different BAFF-receptors may have different results in ACPA producing B cells as compared to 'conventional' B cells.