Protein Array Technology Identifies Rituximab-Treated Non-Responder Rheumatoid Arthritis Patients to Generate New Autoantibody Repertoires during Treatment

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SESSION INFORMATION

Date: Sunday, November 5, 2017

Session Title: B Cell Biology and Targets in Autoimmune Disease Poster

Session Type: ACR Poster Session A

Session Time: 9:00AM-11:00AM

Background/Purpose: Rituximab (RTX) has shown clinical efficacy but up to 40 % of RTX treated rheumatoid arthritis (RA) patients are poor responders (Ann-Rheum-Dis. 2005 Feb;64(2):246-52) and the commonly used RA biomarkers (RF/ACPA) are poor predictors for therapy response. In this study the autoantibody repertoire analysed on protein macorarrays from RA patients under RTX treatment was correlated to clinical DAS28 response.

Methods: Screening of RA sera was conducted on 37.830 unique human proteins on protein marcoarrays with sera taken before and 24 weeks after treatment. The autoantibody response of different immunoglobulin classes IgD, IgA, and IgG was recorded and bioinformatically evaluated. Response was determined according to DAS28 criteria. DAS 28 scores in the responder group before treatment was from 5.4 – 7.8 and in the non-responder group 5,6 – 6,8. We analyzed 26 RA patient sera (9 responder, 7 non-responder and 10 patients with blinded response classification) investigated the data of found autoantigens in silico and by hierarchical clustering.

Results: In the cohort of 26 patients 1292 different autoantigens (IgD,IgA,IgG) were detected. Using protein array we investigated clusters of autoantigen responses that disappeared or developed during RTX treatment of RA patients. RA autoantigenic patterns
before and 6 month after RTX treatment were patient-specific and no relevant autoantigenic cluster was found that was shared between patients or associated with response. However, RTX reduced the repertoire of autoantibodies after 24 weeks of treatment in the tested RA patient cohort on average by 60%. RA patients which do not respond are generating on average 63% new autoantibodies. In good responders to RTX only 5,5% (+/-3%) new autoantibodies can be detected. The IgA and IgG autoantibody
repertoire in the serum after 24 weeks of RTX treatment is reduced (IgA: 41%, IgG :31%) in good responders whereas it is increased (IgA: 1,3%, IgG: 24%) in non responders to RTX.

Conclusion: After 6 month of RTX treatment the autoantibody repertoire in all good responding RA patients is reduced and non-responders to RTX change their autoantibody repertoire directed against new but patient specific antigens. The fast rebuilding of functional B cells is only detected in non-responders to rituximab.