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Design of a Multiplex Serum Proteome Assay to Monitor Biologic Drug Response in Rheumatoid Arthritis Patients

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

Background/Purpose: Biologic drugs have revolutionised the treatment of Rheumatoid Arthritis (RA), however these therapies are expensive and exhibit a high non-response rate (30%). Currently there are no specific biological markers which distinguish non-response early after initiating treatment. The aim of this study was to identify serum protein levels which change when disease activity score is reduced by biologic drug treatment. These proteins may give mechanistic insight into molecular events after failed therapeutic intervention.

Methods: Sera and disease activity scores (DAS28-ESR) were collected from n=25 RA patients at baseline and six months after anti-tumour necrosis factor alpha treatment. EULAR response criteria were used. Untargeted (unbiased) label free LC-MS/MS based proteomics was used initially to discover sera proteins differentially expressed at six months in responders and non-responders. Multiple reaction monitoring (MRM) assays were designed and tested on a triple quadrupole mass spectrometer.

Results: Over 500 proteins were identified in each of the pooled serum samples using the untargeted label free LC-MS/MS approach. Statistical analysis of the data revealed a list of 155 proteins that were significantly differentially expressed between good and non-responders ($p < 0.05$). 55 of these proteins were shortlisted for development of targeted MRM assays, and assays were successfully developed for 47 proteins.

Conclusion: The approach outlined here and the initial results obtained indicate the power of a combined mass spectrometry strategy for comprehensive serum proteome analysis to determine

quantitative changes, discover novel protein signatures and develop a multiplexed protein assay capable of monitoring response to biologic treatments. Such biologic drug response markers could minimise the use of expensive biologic drugs in patients who do not gain benefit and reduce adverse side effects.

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