EXTENDED REPORT

Discovery and confirmation of a protein biomarker panel with potential to predict response to biological therapy in psoriatic arthritis

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ABSTRACT

Objective Biological therapies, which include antitumour necrosis factor-α and T-cell inhibitors, are potentially effective treatments for psoriatic arthritis (PsA) but are costly and may induce a number of side effects. Response to treatment in PsA is variable and difficult to predict. Here, we sought to identify a panel of protein biomarkers that could be used to predict which patients diagnosed with PsA will respond to biologic treatment.

Methods An integrated discovery to targeted proteomics approach was used to investigate the protein profiles of good and non-responders to biological treatments in patients with PsA. Reverse-phase liquid chromatography coupled to tandem mass spectrometry was used to generate protein profiles of synovial tissue obtained at baseline from 10 patients with PsA. Targeted proteomics using multiple reaction monitoring (MRM) was used to confirm and prevalidate a potential protein biomarker panel in 18 and 7 PsA patient samples, respectively.

Results A panel of 107 proteins was selected, and targeted mass spectrometry MRM assays were successfully developed for 57 of the proteins. The 57 proteins include S100-A8, S100-A10, Ig kappa chain C fibrinogen-α and γ, haptoglobin, annexin A1 and A2, collagen alpha-2, vitronectin, and alpha-1 acid glycoprotein. The proteins were measured simultaneously and confirmed to be predictive of response to treatment with an area under the curve of 0.76. In a blinded study using a separate cohort of patients, the panel was able to predict response to treatment.

Conclusions The approach reported here and the initial data provide evidence that a multiplexed protein assay of a panel of biomarkers that predict response to treatment could be developed.

Trial registration number ISRCTN23328456.

INTRODUCTION

Psoriatic arthritis (PsA) is a systemic inflammatory arthritis (IA) associated with the skin disorder, psoriasis.[1] Studies have shown that about 30% of patients with psoriasis develop PsA at an average of 10 years after the onset of the disease.[2–5] The pathogenesis of psoriasis has been linked to the colonisation of the skin by microorganisms, which include yeast and gut flora.[6] Two patterns of major histocompatibility complex antigens have been linked with the phenotype of psoriatic disease; the classic psoriasis susceptibility gene, HLA-C*06 primarily linked with skin involvement and HLA-B*27 more closely associated with the development of arthritis.[7 8]

Key cytokines known to be involved in the pathogenesis of PsA include tumour necrosis factor alpha (TNF-α), interleukins (IL) IL-1, IL-2, IL-6, IL-8, IL-12, interferon-gamma (IFN-γ) and transforming growth factor-beta (TGF-β).[9–12] As a pro-inflammatory cytokine, TNF-α increases blood vessel formation and levels of C-reactive protein (CRP).[12 13] Hence, TNF-α is a target for therapeutic intervention and has proven very effective in randomised clinical trials for PsA and other inflammatory diseases.[14] However, the lack of efficacy in about 30% of patients, a diverse degree of response to therapy in patients as well as high treatment cost and significant adverse drug events mean there is an urgent need for improved selection of patients who are likely to respond to treatment.[15]

Liquid chromatography mass spectrometry (LC-MS) methods are increasingly been used to profile biological samples for potential protein markers for diagnostic, prognostic and therapeutic response tests. Protein quantification with mass spectrometry can be done using either label-free or isotope-labelled methods. Intensity-based label-free LC-MS methods[16] (as opposed to spectral counting-based label-free LC-MS[17]) have emerged as an attractive alternative to isotope labelling-based strategies for clinical or preclinical studies for the analysis of a large number of samples and when integration of metabolic or chemical labels might not be possible during sample preparation. Proteome coverage in label-free proteomics method is improved by employing a directed MS/MS approach incorporating reinjection of samples with peptide inclusion list to supplement the identifications acquired in data-dependent analyses.[18–20]

In recent years, the use of selected/multiple reaction monitoring (S/MRM) for proteomics studies has emerged as a powerful method for robust, sensitive and routine targeted quantification of proteins in complex biological samples.[21 22] These characteristics have led to wide adoption and development of the technique for the targeted quantification of discrete sets of proteins for studies in both model systems[23–25] and clinical samples.[26–28] Selection of the signature peptide is important in S/MRM assay design and factors considered include uniqueness of tryptic peptide to the

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corresponding protein of interest, mass and specific sequence of peptide, physicochemical properties of peptides and the sensitivity of the mass spectrometer for a given mass.[29] The recent development of methods and software has substantially decreased the time required for the development of robust and sensitive S/MRM assays as well as the analysis of data.[30–33] In this study, synovial tissue (ST) samples from patients with PsA before treatment (baseline) were subjected to intensity-based label-free LC-MS discovery proteomic study to evaluate whether the tissue contains proteins that might be associated with a therapeutic response to adalimumab. Adalimumab binds specifically to TNF-α and blocks its interaction with the p55 and p75 cell surface TNF receptors, resulting in the modulation of TNF-induced or regulated biological processes.[34]

MATERIALS AND METHODS

Patient samples and study design

ST samples were obtained from 20 patients with PsA enrolled in a clinical trial investigating changes in ST associated with effective therapy (adalimumab) (see patient details in online supplementary table S1). These samples were part of a single-centre study performed at the Amsterdam Medical Centre, University of Amsterdam, approved by the Medical Ethics Committee of the institute (clinical trial number ISRCTN23328456). All

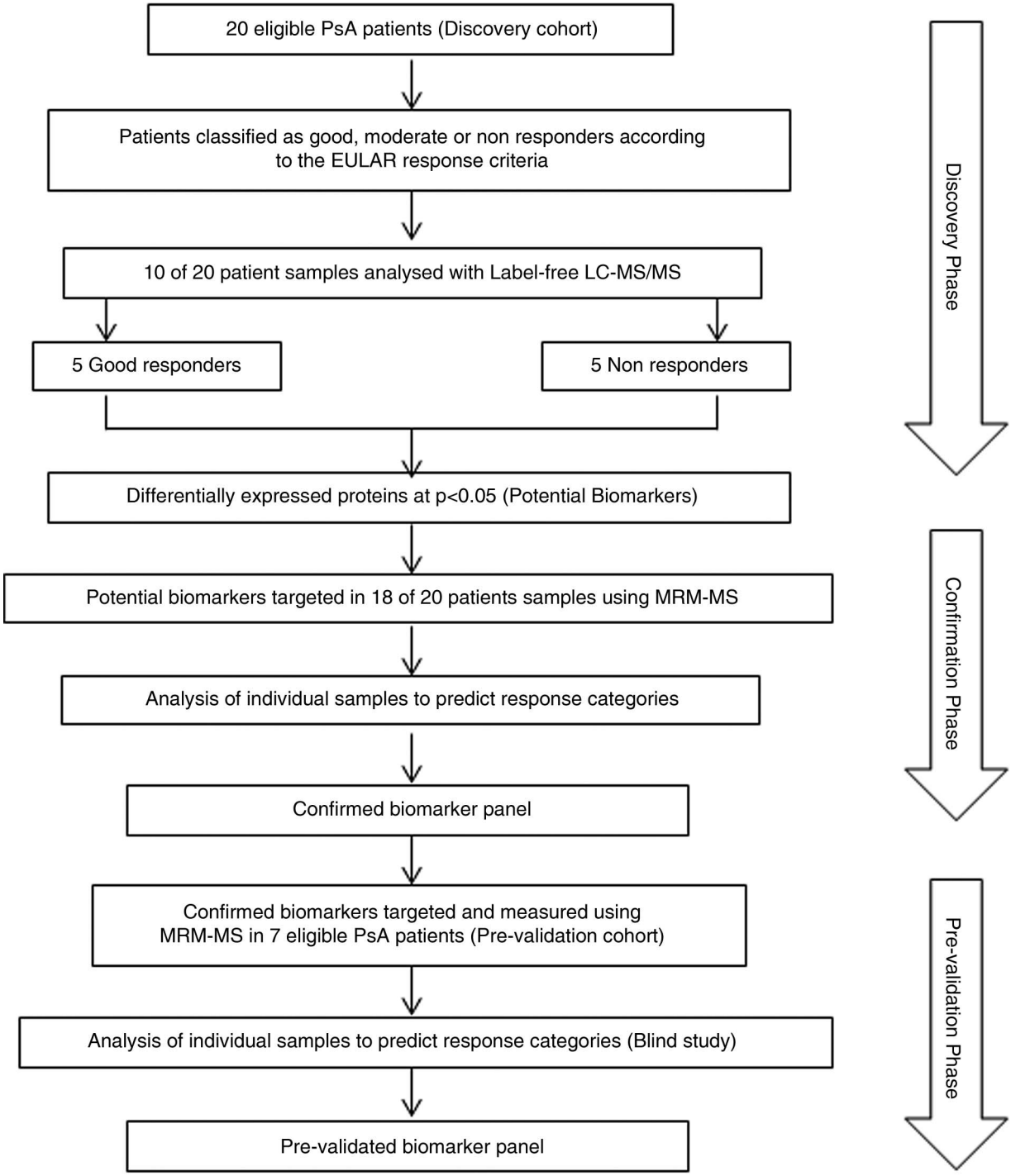

Figure 1 Overview of the study design illustrating the samples used for each phase of protein discovery to validation.

patients fulfilled the ClASsification of Psoriatic ARthritis (CASPAR) criteria for PsA.[35] Inclusion and exclusion criteria and study design have been published before.[36] In summary, patients were randomised to receive either adalimumab (40 mg subcutaneously) or placebo on day 1 and day 15, but they all went on to receive 40 mg adalimumab every other week thereafter. ST biopsies were obtained before and after 4 weeks of treatment with adalimumab or placebo and patients were followed for up to 12 weeks to determine clinical outcome. Multiple ST samples were obtained through video arthroscopy at baseline from clinically involved joints under local anaesthesia. The biopsies were snap frozen in liquid nitrogen and stored at −80°C until processing.

The disease activity score (DAS) in 28 joints was used to classify patients' degree of response to therapy. Patients were defined as DAS28-CRP responders if their improvement in DAS28-CRP was >1.2 and their absolute DAS28-CRP was ≤3.2 at the final visit, analogous to the DAS28-ESR-based definition of EULAR good response.[37] Ten baseline samples from those enrolled in the trial were used for the discovery phase of the analysis. Candidate markers were selected based on protein analysis of variance (ANOVA) p value <0.05 for which MRM assays were developed for peptide quantification.

The candidate biomarker panel was confirmed in all available (n=18 of the 20) patient samples from the anti-TNF-α-treated patients and was used to predict response in seven patients who had baseline samples as well as follow-up data available from an initial validation cohort of 15 patients with PsA that enrolled in a clinical study investigating the effect of abatacept (a fusion protein of an immunoglobulin that inhibits the costimulation of T cells) in psoriasis and PsA (clinical trial number IM10-264). Patients enrolled had active PsA (CASPAR criteria) of more than 3 months' duration, were aged 18–80 years, with an average age of 54. PsA and cutaneous psoriasis were treated with a 6-month course of abatacept. EULAR response criteria were used. This single-centre study was blinded and placebo controlled.

Protein extraction and digestion

ST samples were homogenised by powdering in a micro dismembrator (B. Braun, Biotech International, Germany). The proteins were extracted into a urea lysis buffer (9.5M, 2% CHAPS, (3-[(3-Cholamidopropyl)dimethylammonio]-1-propanesulfonate) 0.5 g amberlite, 20 mM Tris). Insoluble particles were removed by centrifugation at 14 000 rpm (~21 000 g) for 20 min. Samples were aliquoted and stored at −80°C until protein concentration was determined using a modified Bradford assay[38] and digested in-solution with trypsin (details in online supplementary text).

LC-MS analysis and MRM

Label-free LC-MS analysis and MRM-MS assay development were undertaken as described in the online supplementary material. The mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium (http://www.proteomexchange.org) via the PRIDE partner repository[39] with the dataset identifier PXD000707.

Data analysis

The label-free LC-MS data were statistically analysed with Progenesis LC-MS software (V.2.6) that supports univariate and multivariate statistical analysis. ANOVA was used to analyse the differences between the protein expression in good and non-responders (see online supplementary text). As formal statistical analysis of the individual protein changes is inappropriate for small number of samples,[40] the MRM data were analysed with Skyline software (V.1.6) and the random forest (RF) package in R (V.2.13.1) was used to build the prediction algorithm model (see online supplementary text).

RESULTS

To determine the differential expression of proteins in good responders and non-responders, we investigated the protein profile of ST obtained at baseline from 10 patients who subsequently responded well (n=5) or did not respond well (n=5) to adalimumab using a label-free nano LC-MS/MS analysis. The MS dataset was imported into Progenesis LC-MS V.2.6 software and subjected to alignment (see online supplementary material for details). In total, 143 349 features (peptides) were detected and filtered by (i) retention time in the peptide elution portion of the gradient, (ii) 2≤charge state≤7 and (iii) number of isotopes. This resulted in about 43 000 features, of which 4092 were identified to correspond to 313 proteins. Candidate markers were selected based on protein ANOVA p value <0.05. The proteins were targeted and measured using quantitative MRM assay of the ST of 18 patients that responded well (n=10) or did not respond well (n=8) to treatment and prevalidated in an independent cohort.

The project overview is illustrated in figure 1 with the discovery phase consisting of the label-free LC-MS analysis of peptides

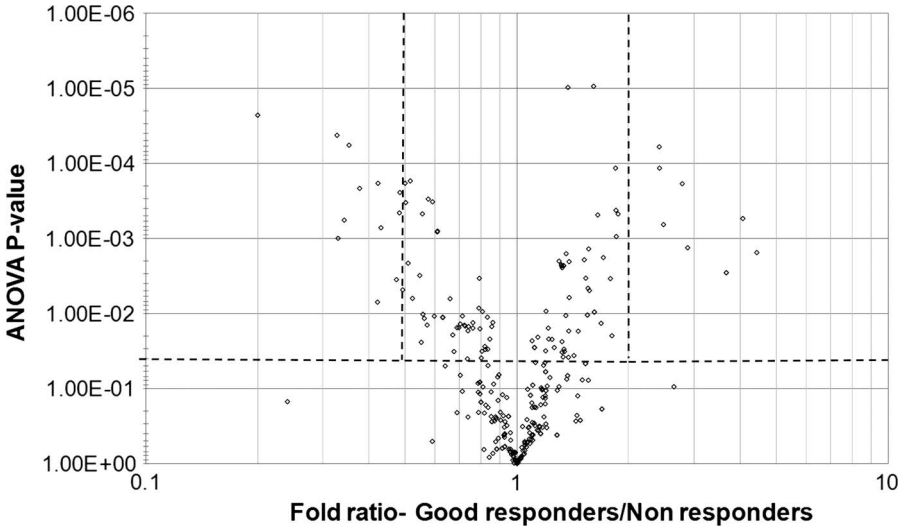

Figure 2 Volcano plot (fold change and significance) of protein expression changes. The normalised abundances (good responders/non responders) of all identified proteins were log 2 transformed and plotted against their log 10 transformed p values. Each spot represents an identified protein. Proteins significantly changing between experimental conditions at p<0.05 were considered as part of the biomarker panel and are shown above the horizontal line in the volcano plot. The threshold p=0.05 is indicated as a horizontal line, the threshold of a ratio of 1.5-fold expression change are indicated by vertical lines.

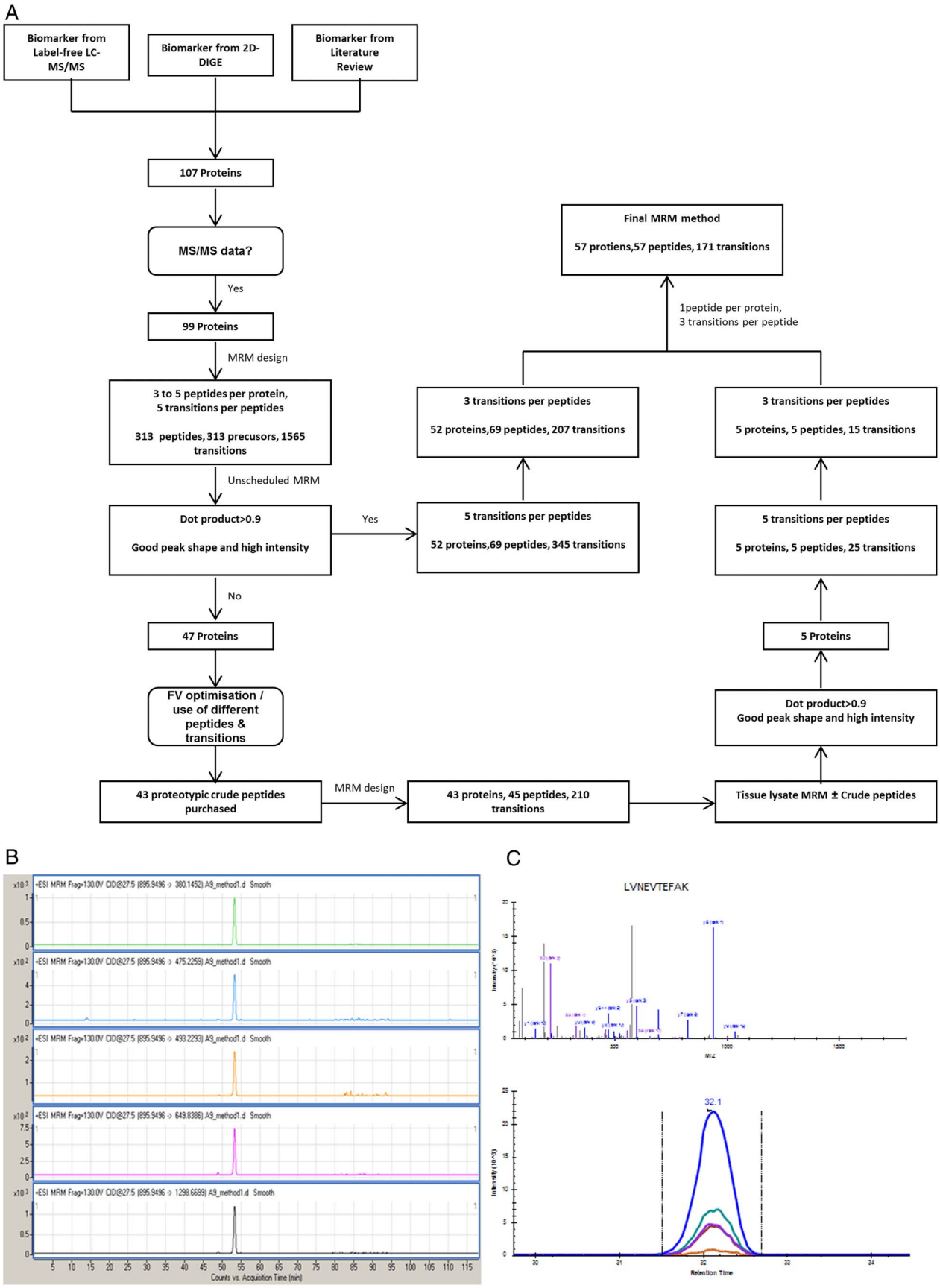

Figure 3 (A) Multiple reaction monitoring (MRM) development outline. MRM assay was developed from proteotypic peptides to each protein using synovial tissue lysate and crude peptides; the best five transitions matching the spectral library were selected and monitored for quantification. The final MRM method consisted of 57 proteins quantified by one peptide and their three most intense transitions. FV, fragmentation voltage. (B) Qualitative analysis of MRM using MassHunter software. (C) Qualitative analysis of MRM using Skyline software to manually inspect the individual transitions of the peptides for selection of the best transitions as well as the most intense peak for quantification.

and the assembly of differentially expressed proteins (proteins that were significantly upregulated or downregulated at $p<0.05$ between good and non-responders). The confirmation phase tested the biomarker panel on individual patient samples (n=18) and a prevalidation phase used a small number of patient samples (n=7) to blindly test the predictive ability of the panel.

Protein identification and biomarker panel

The different response categories studied revealed different characteristic features. Three hundred and thirteen proteins were identified from the discovery experiment; about one-eighth of which were significantly different at $p<0.05$ as shown in the volcano plot (figure 2).

Novel protein candidates on the biomarker panel include protein S100-A10, myosin light polypeptide 6, plastin-2, Ig-gamma-4-chain C, mimecan, lumican and prolifin. The final potential biomarker panel consisted of 107 proteins that were assembled from the label-free LC-MS/MS discovery experiment, previous in-house two-dimensional differential gel electrophoresis results from PsA studies, as well as the meta-analysis of the literature (details in online supplementary figure S1 and table S2). As shown in online supplementary figure S1, 30 of the proteins are novel from the discovery experiment while 77 of the proteins have previously been identified as being important in IA from the literature and previous work. Online supplementary table S2 shows all the proteins in the biomarker panel, the unique peptides used for measurement, as well their sources.

Of the 107 proteins in the panel, 99 proteins have MS/MS data available in the ST lysate spectral library (MS/MS spectrum acquired by data-dependent acquisition) built to support MRM development. Successful MRM methods were developed for 57 of these proteins (see online supplementary figures S2A, B). Figure 3A shows the MRM method development process from the candidate assembly to the final 57-protein biomarker panel. Figure 3B, C shows the peak shape and transition intensities of one of the successful MRMs developed as visually inspected from MassHunter and Skyline software, respectively. All MRM assays met a variety of assay validation criteria, which include good peak shape and intensities, highly ranked peptides/transitions, accurate retention time prediction and dot product >0.9.

Biomarker panel confirmation

The 57-protein MRM method was used to test and confirm the biomarker panel on 18 individual patient tissue samples from the same cohort of patients commenced on anti-TNF-α treatment (adalimumab). A heat map profile of good responders and non-responders is shown in figure 4A. The analysis confirmed the biomarker correlation with clinical endpoints. The ability of the biomarker panel to predict the response categories of the individual patient samples was carried out statistically using RF package in R, which confirmed the ability of the biomarker panel to predict response to adalimumab in ST of patients with PsA with a modest area under the curve (AUC) of 0.76 (figure 4B). Some of the predictive proteins include S100-A8, S100-A10, Ig kappa chain C, fibrinogen-α and γ, haptoglobin, annexin A1 and A2, collagen alpha-2, vitronectin, alpha-1 acid glycoprotein, cofilin, prolargin, 14-3-3 protein epsilon and clusterin isoform 1.

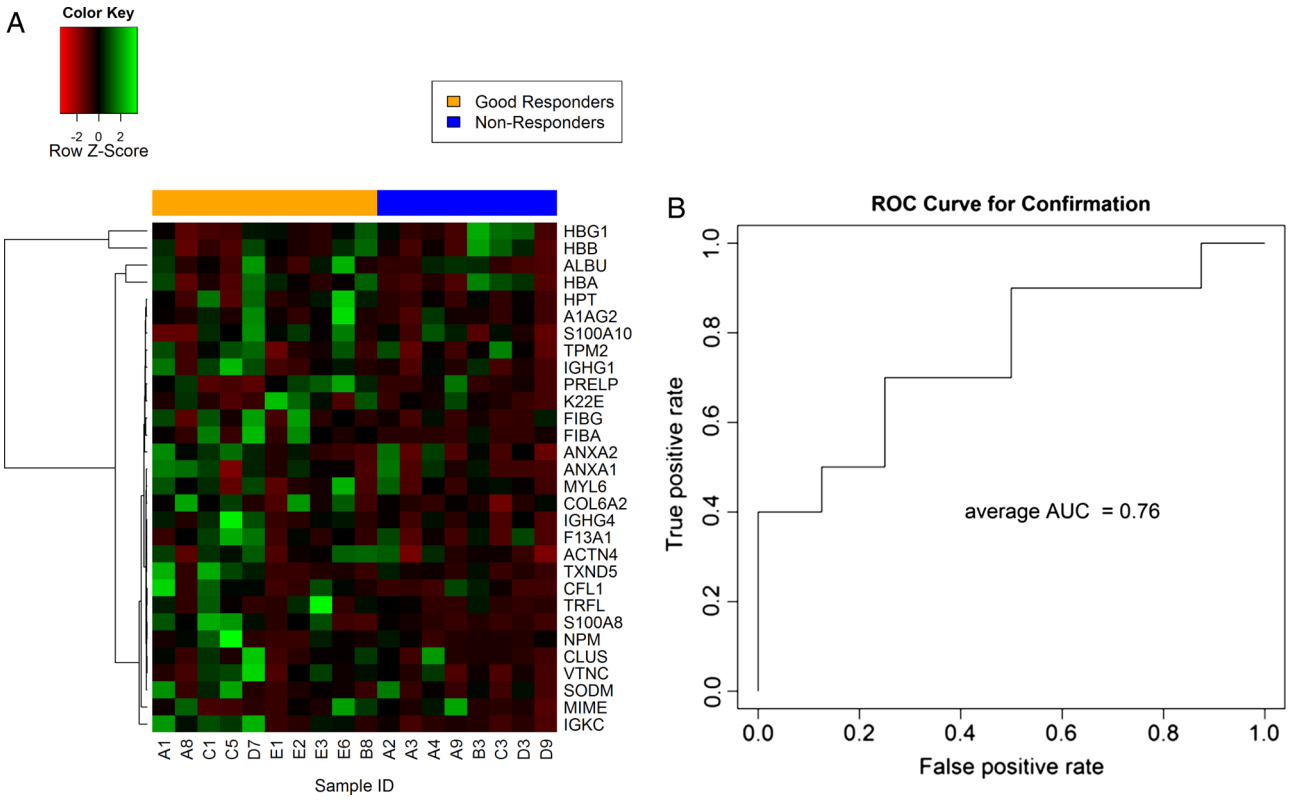

Figure 4 (A) Heat map profile of good responders and non-responders. Differentially expressed proteins are represented in the form of a heat map derived from the statistical Z score for each protein as measured in 18 individual patients by the multiple reaction monitoring assay developed. Rows represent the proteins and columns represent the individual patient samples. Upregulated and downregulated proteins are indicated in different shades, where the intensity of the shade is determined by the distance (in SD) from the mean for each peptide. (B) Area under the curve (AUC) of a relative operating characteristic (ROC) curve from Random forest statistical analysis of the biomarker panel. The ROC shows an AUC of 0.76 for the predictive proteins.

Table 1 Importance rank order of the 30 most important proteins from the prediction model

Proteins	UniProt accession numbers	Peptides measured	Random forest rank
S100-A8	P05109	LLETECPQYIR	1
Ig-kappa chain C	P01834	VYACEVTHQGLSSPVTK	2
Prolargin	P51888	NQLEEVPSALPR	3
Collagen α-2	P12110	LFAVAPNQNLK	4
Cofilin	P23528	YALYDATYETK	5
Haptoglobin	P00738	VGYVSGWGR	6
Annexin A2	P07355	DALNIETAIK	7
Fibrinogen-α	P02671	NSLFEYQK	8
Keratin	P35908	IEISELNR	9
Coagulation factorX111A	P00488	GTYIPVPIVSELQSGK	10
Alpha-1-acid glycoprotein	P19652	WFYIASAFR	11
Lactotransferrin	P02788	FQLFGSPSGQK	12
Serum albumin	P02768	LVNEVTEFAK	13
Alpha actinin	O43707	DLLLDPAWEK	14
Thioredoxin	Q8NBS9	GYPTLLWFR	15
Ig-gamma-4-chain C	P01861	GFYPSDIAVEWESNGQPENNYK	16
Tropomyosin	P07951	IQLVEEELDR	17
Haemoglobin-γ	P69891	LLVVYPWTQR	18
Haemoglobin-α	P69905	FLASVSTVLTSK	19
Vitronectin	P04004	FEDGVLDPDYPR	20
Nucleophosmin	P06748	MSVQPTVSLGGFEITPPVVLR	21
Fibrinogen-γ	P02679	VELEDWNGR	22
Ig-gamma-1-chain C	P01857	FNWYVDGVEVHNAK	23
Myosin	P60660	ALGQNPTNAEVLK	24
Mimecan	P20774	DFADIPNLR	25
Haemoglobin-β	P68871	EFTPPVQAAYQK	26
Annexin A1	P04083	NALLSLAK	27
Clusterin isoform 1	P10909	VTTVASHTSDSDVPSGVTEVVVK	28
Superoxide dismutase(Mn)	P04179	GDVTAQIALQPALK	29
S100-A10	P60903	EFPGFLENQK	30

As 100 RFs were used, the rank of the importance score for each protein over each forest was calculated, where a rank of 1 means the protein had the most predictive value. The highly ranked most predictive proteins are shown in table 1, with S100A8 being the most predictive/important protein.

Candidate proteins were also analysed with Protein ANalysis THrough Evolutionary Relationships (PANTHER) gene list analysis software (http://www.pantherdb.org), and their cellular components, molecular function, biological process, protein class and associated pathways were revealed with the aid of gene ontology (GO). Online supplementary table S3 summarises the distribution of the proteins into different categories.

Initial validation: biomarker prediction of clinical endpoints

The combined biomarker panel was evaluated for its potential to predict clinical response using targeted proteomic analysis of the baseline samples of patients commenced on T-cell inhibitor (abatacept). This was a blinded study, and the patient's response categories were accurately predicted as shown in table 2.

DISCUSSION

In this study, we show that there are differences in the baseline profile of proteins in the ST of patients with PsA that may be useful to differentiate between patients that will subsequently respond or will not respond to biological therapy.

Identification of potential protein biomarkers has been approached via both an unbiased high throughput and selective protein analyses of baseline tissue samples. This study uncovered new protein candidates indicative of response to anti-TNF-α in PsA, warranting further investigation for diagnostic utility or as potential targets. Analysing the data with GO revealed some of the differential proteins are involved in the following pathways: hypoxia response, cytoskeletal regulation, angiogenesis, apoptosis signalling and inflammation-mediated cytokine pathways.

Many of the proteins on the candidate biomarker panel have been found previously to play significant roles in inflammation, and these proteins include vimentin, fibrinogen, type 11 collagen, serum amyloid A, haptoglobin, 14-3-3 protein and the S100 family proteins (A8, A9, A11 and A12).[41–43] S100A8, which was ranked highest in the biomarker predictor panel (table 1), plays a prominent role in the regulation of inflammatory processes and immune responses. S100A8 and S100A9 proteins have been reported by Cesaro *et al*[44] as being part of a group of damage-associated molecular pattern molecules that trigger inflammatory responses, and the high concentration of S100A8/S100A9 in IA has been found to correlate with disease activity. It has been suggested that S100A8 and S100A9 proteins could be therapeutic targets looking at the fact that S100A8 exhibits anti-inflammatory functions when oxidised.[44] Although S100A10 protein belongs to the S100 family proteins, it was not found to be strongly linked to response prediction in this

Table 2 Blinded patient response category prediction (St. Vincents' University Hospital (SVUH) abatacept study)

Patient	Joint	DAS pretreatment	DAS post-treatment	Δ DAS	Response category (blinded prediction)	Response category in clinic at 6 months
1	Knee	4.58	1.38	3.2	GR	GR
2	Knee	4.91	4.36	0.55	NR	NR
3	Knee	3.48	2.08	1.4	GR	GR
4	Knee	5.4	4.47	0.93	GR	MR
5	Knee	6.35	7.42	−1.07	NR	NR
6	Knee	5.52	3.18	2.34	GR	GR
7	Knee	3.82	3.32	0.5	NR	NR

The DAS score pretreatment and post-treatment for seven patients who had their follow-on data available. All patients were in active disease with a DAS range of 3.48–6.35. From the seven patient samples available for this study, the prediction algorithm model of the 57-biomarker panel correctly predicted the response categories of six patients with a wrong prediction for patient 4 highlighted. DAS, disease activity score; GR, good responder; MR, moderate responder; NR, non-responder.

study as much as the S100A8 protein. This may be due in parts to the fact that S100A10 protein has lost its calcium binding property by losing its two carboxyl terminal lysines hence not strongly implicated in inflammatory processes as opposed to S100A8. S100A10 preferentially binds to annexin A2 in heterotetrameric form. However, S100A10 has been found to play some role in macrophage recruitment in response to inflammatory stimuli.[45 46]

From the heat map profile of good responder and non-responders (figure 4A), approximately 50% of the good responders have high expression of immunoglobulins (IGKC, IGHG4 and IGHG1) and other immune response proteins. Previous work using same samples and published earlier[36] has analysed different cluster of differentiation (CD) cells and has found a correlation between clinical improvement and decrease in CD22-positive B cells of patients. In line with our findings, this may suggest that patients with higher expression of immunoglobulins tend to be good responders.

GO analysis of the differentially expressed proteins (see online supplementary table S3) shows the association of heat shock proteins with vascular endothelial growth factor signalling pathway and angiogenesis; these proteins have been previously reported to be linked to clinical endpoint in joint diseases as well as the involvement of haptoglobin and S100 proteins in immune processes.[47]

The major drug-binding proteins in serum, human serum albumin and alpha-1-acid glycoprotein are among the most important predictive biomarkers of response in this study and can be supported with previous work by Veering *et al*,[48] who suggested that the concentration of human serum albumin could either reduce or decrease the binding of drugs. Our results suggest that the level of some of the markers may be responsible for the neutralisation effect of anti-TNF-α in PsA.

The predictive value of the biomarker panel was confirmed in 18 individual samples with an overall AUC of 0.76. An initial validation dataset obtained from the abatacept cohort also confirms the ability of this panel to predict patients' response categories blindly. However, the only moderate responder in the cohort was not accurately predicted due to the fact that the model was not designed nor capable of predicting the moderate response category of patients. From table 2, the data suggest that the treating physician would have used an alternative treatment in three patients who turned out to be non-responders. Further validation would need to be performed on a separate cohort for the predictive accuracy of this panel.

This panel may help to identify patients that will likely benefit from treatment including TNF-α inhibition and T-cell modulation, help monitor treatment and support the design of personalised treatment for patients. To date, the findings have not been confirmed in more readily available biological fluids (serum or synovial fluid). This clearly would be the ultimate goal of this work as synovial biopsies are more invasive.

It has been reported that single biomarkers often lack specificity to produce confident diagnosis and hence measuring multiple markers may be more specific.[49] The use of MRM protein assays has been predicted to likely increase the number of validated medically important protein biomarkers for a range of diseases.[50 51] Recently, in rheumatology, proteomics have been directed towards biomarker discovery and search for key elements in the pathogenesis of rheumatic disease.[50] The value of proteomics in biomarker discovery in rheumatology has been reviewed elsewhere.[2 3 52 53]

The work reported here has a number of limitations. It is clear that to date the panel of 57 proteins for which an MRM assay has been developed was tested on a very small number of independent patient samples (n=7). Further work is required to validate the accuracy of the biomarker panel to predict patient response categories. However, the quality of the samples used, the fact that biopsies were taken from six or more sites of the joint during each procedure to minimise sampling error as well as the multiplexed nature of the measurements made give us the potential to at least in part accommodate the almost unavoidable issue of limited sample numbers.

In addition, the existing panel of 57 proteins represents just some of the candidates on an initial panel of 107 potential biomarkers. Hence, strategies to get the other potential biomarkers measurable should be put in place. Furthermore, the relative quantification used might not be sufficient and an absolute quantification of peptides or proteins might require individual isotopically labelled reference peptides or proteins to be spiked into the samples. The use of isotopically labelled peptides might be able to correct for incomplete or unspecific digestion of proteins.[21]

In summary, we have described a new biomarker panel that can be measured at baseline to predict PsA patients' response to biologics (adalimumab and abatacept). We propose that the use of the panel as opposed to individual biomarkers may provide more insight into the diverse degree of response to biological therapy. Further studies to validate the findings are underway in an independent and larger cohort. The identified groups of proteins are promising biomarker candidates to distinguish at an early stage between effective and ineffective treatment of PsA with biologics. It is anticipated that this tissue-based assay would be further developed, refined, tested and adapted for the development of a similar but serum-based assay that could be useful for disease monitoring or as potential therapeutic targets.

This study provides a significant proof of principle that label-free LC-MS can provide putative biomarkers of therapeutic response and putative biomarkers from multiple sources can be integrated into an MRM assay for large-scale verification studies.

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Contributors OF and SRP conceived and designed the study. OSA performed the experiments and drafted the article. OF, SRP, OSA, BH, EC and CR participated in the analysis and interpretation of the data. Other authors provided samples and guidance. All authors revised the article for intellectual content and approved the final version of this article.

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Competing interests None.

Patient consent Obtained.

Ethics approval ST samples used for the discovery experiment were obtained as part of a randomised, double-blind, placebo-controlled, single-centre study performed at the Amsterdam Medical Centre (AMC), Amsterdam, the Netherlands. The study protocol was approved by the Medical Ethics Committee of the institute with the informed consent of all patients. The clinical trial number is ISRCTN23328456. ST for the initial validation study was approved by the Institutional Review Board/Independent Ethics Committee (IRB/IEC) and St. Vincents' University Hospital (SVUH) ethics committee. The clinical trial number is IM10-264.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium (http://www.proteomexchange.org) via the PRIDE partner repository with identifier PXD000707. The details: Project name: Discovery and Confirmation of a Protein Biomarker Panel with Potential to Predict Response to Biologic Therapy in Psoriatic Arthritis Project accession: PXD000707 Reviewer account: Username: reviewer14202@ebi.ac.uk; Password: IK6qS30P. To access the data please visit: http://tinyurl.com/ouscby2No.

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