SUPPLEMENT

Biomarkers in psoriasis and psoriatic arthritis

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Handling editor Tore K Kvien

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Received 27 November 2012
Revised 6 January 2013
Accepted 29 January 2013

ABSTRACT

Psoriasis is a common immune-mediated disease of the skin, which associates in 20–30% of patients with psoriatic arthritis (PsA). The immunopathogenesis of both conditions is not fully understood as it is the result of a complex interaction between genetic, environmental and immunological factors. At present there is no cure for psoriasis and there are no specific markers that can accurately predict disease progression and therapeutic response. Therefore, biomarkers for disease prognosis and response to treatment are urgently needed to help clinicians with objective indications to improve patient management and outcomes. Although many efforts have been made to identify psoriasis/PsA biomarkers none of them has yet been translated into routine clinical practice. In this review we summarise the different classes of possible biomarkers explored in psoriasis and PsA so far and discuss novel strategies for biomarker discovery.

PSORIASIS AND PSORIATIC ARTHRITIS

Psoriasis is an immune-mediated inflammatory skin disease, characterised by scaly, red and well-demarcated skin plaques, resulting from keratinocyte hyperproliferation and altered differentiation, the presence of an inflammatory cell infiltrate and neovascularisation.[1] Psoriasis affects 2–4% of the population worldwide and patients experience physical and mental symptoms as well as a decreased quality of life. Disease aetiopathogenesis is caused by the complex interaction of genetic, environmental and immunological factors,[2] all of which contribute to a wide disease spectrum.[3]

Clinical and experimental evidence points to a central role for the immune system in disease pathogenesis. In the initiation phase, activated plasmacytoid dendritic cells (pDC) contribute to the activation of dermal DC, which in turn activate skin-resident and newly recruited helper and cytotoxic T cells that dominate in disease maintenance.[1] Despite being considered a T helper (Th) type 1-mediated disease for many years, a pivotal role for Th17 cells in psoriasis has recently been revealed.[4] Th1, Th17 and also interleukin (IL)-22-producing CD4 T 'Th22' cells infiltrate psoriasis plaques, and contribute to the disease by cytokine production.[5]

In 20–30% of cases, psoriasis is associated with psoriatic arthritis (PsA),[6] a chronic arthritis causing recurrent episodes of enthesitis and dactylitis. Despite sharing some clinical aspects with rheumatoid arthritis (RA), PsA is seronegative for rheumatoid factor, has some distinctive features such as a lower number of involved joints, an asymmetric articular involvement and a generally less aggressive course.[7 8] In approximately 70% of cases, psoriasis precedes the appearance of PsA, suggesting the importance of dermatologists recognising the early signs of disease for referring the patient to further evaluation by a rheumatologist. The aetiology of PsA is complex, with alterations in immunological, inflammatory and vascular pathways in genetically susceptible individuals.[9] Many of the pathogenetic immunological mechanisms involved in psoriasis also apply to PsA, with a prominent lymphocytic infiltrate present both in psoriatic skin and PsA joints.[10] Both psoriasis and PsA are often associated with comorbidities, such as cardiovascular disease, metabolic syndrome, depression and cancer.[11] The diagnosis of psoriasis and PsA is mainly based on clinical assessment and there are no diagnostic tests or biomarkers with high sensitivity and specificity, especially at the early stages of disease.

At present there is no definitive cure, although in recent years biological therapy targeting specific inflammatory pathways has proved to be highly effective.[12]

Despite this success, long-term safety data are still being established, biological agents are expensive, and 20–30% of patients still fail to respond.

Therefore psoriasis/PsA-specific biomarkers for disease diagnosis, prognosis and treatment response would allow clinicians to practise a more effective and personalised medicine. Although many efforts have been made to identify psoriasis/PsA-specific biomarkers, none of the putative ones identified so far has resulted in a clinically relevant outcome and patient benefit.

CHARACTERISTICS OF BIOMARKERS

A biomarker is a biological characteristic that is measured and evaluated objectively as an indicator of normal biological processes, pathogenic processes or pharmacological response to therapeutic intervention.[13] They can also be used to identify disease risk factors, and could contribute to a better understanding of disease immunopathogenesis.

An 'ideal' biomarker should be specific, sensitive, reproducible, predictive and accurate. The detection assay should be robust, standardised and easy to perform.

The use of biomarkers in disease areas such as infections, cardiovascular disease, immunological and genetic disorders, cancer and chronic inflammatory diseases is well established.[14] In RA, rheumatoid factor, an autoantibody against the Fc portion of IgG, and anticitrullinated protein antibodies are used in both disease diagnosis and

prognosis. Interestingly, the occurrence of anticitrullinated protein antibodies is associated with an environmental risk factor for RA, such as smoking and the presence of major susceptibility genes such as HLA-DR.[15] Moreover, patients with early RA who smoke are less likely to respond to treatment with methotrexate and tumour necrosis factor (TNF) inhibitors, thus predicting therapeutic response.[16] Periostin serum levels in asthma patients have recently been identified as a useful biomarker to predict anti-IL-13 therapy response.[17]

However, one has to take into account the distinction between actual pathogenic factors underlying the disease and biomarkers used for diagnosis, prognosis and therapy prediction. In some cases, biomarkers, such as periostin,[17] fall in disease-relevant pathways and can be highly informative on disease aetiopathogenesis. In other cases, they are not related to any causative factor, as is the case with serum C-reactive protein (CRP), a marker of unspecific inflammation that is increased in several immune-mediated inflammatory diseases (IMID).[18]

Clinically relevant biomarkers are still missing for psoriasis/PsA, and biomarkers predictive of therapy response would have an immediate application in the stratification of patients undergoing biological treatment. More than 20 systemic agents, spanning from biological agents to small molecules, are currently being tested for psoriasis/PsA.[12] In addition to the well known beneficial effect of anti-TNF therapy, good efficacy results have been obtained by targeting IL-12/23,[19] and more recently with IL-17A blockade.[20 21] Despite these encouraging results, there are still approximately 20% of patients who do not respond to treatment, probably as a result of specific genetic backgrounds or inflammatory status. Moreover, no predictive markers for patients at risk of developing serious side effects, following biological therapy, have been identified so far. Therefore, biomarkers for guiding therapy selection, disease monitoring and side effect development are required.

Overall more data are available on psoriasis biomarkers compared to PsA. Below we describe different classes of possible biomarkers classified according to their ontology and/or tissue distribution for review purposes, and discuss novel strategies for biomarker discovery.

GENETIC BIOMARKERS

Psoriasis is a complex genetic disease in which multiple genetic variants contribute to genetic susceptibility. Psoriasis susceptibility region 1 (PSORS1) within the major histocompatibility complex is the strongest susceptibility locus and HLA-Cw6 is considered to be the primary associated allele. Clinical subgroups of psoriasis are genetically heterogeneous at PSORS1 level, with early onset and guttate psoriasis being associated with PSORS1, while late onset and palmoplantar psoriasis are not.[22] As a result of the extensive single nucleotide polymorphism (SNP) genotyping in genome-wide association studies 36 susceptibility loci have been associated with psoriasis in individuals of European descendant.[23] In particular, psoriasis-associated genes have been identified in areas related to skin barrier function (eg, *LCE3B/3C*), Th17 cell activation (eg, *IL23R*), type I interferon (IFN) induction (eg, *IFHIH1*) and the nuclear factor κB pathway (eg, *NFKBIA*).[24] Most of these susceptibility genes are involved in immunological and inflammatory processes, further supporting a central role for the immune system in psoriasis pathogenesis. A strong heritability is also evident for PsA, and although many PsA susceptibility genes overlap with those identified for psoriasis (eg, *HLA-Cw6*, *IL12B*, *IL23A*, *IL23R*, *LCE* and *TNIP1*), there are some that are PsA specific. HLA gene alleles may distinguish particular patterns of PsA (*HLA-B27* with spinal involvement, *B38* and *B39* with peripheral polyarthritis) or predict disease prognosis (eg, *HLA-B22* is protective for disease progression).[25] Interestingly, the *HLA-Cw6* allele has a significantly higher frequency in psoriasis-only patients and is associated with a milder form of PsA.[22]

A limited number of pharmacogenetic studies to predict systemic or biological therapy response in psoriasis/PsA have been conducted so far and they have used a candidate gene approach. For systemic therapies, genes involved in drug transport and metabolism were analysed: ABCC1 and ABCG2 SNP were associated with improved methotrexate response in psoriasis, while a DHFR SNP showed the same result in PsA.[22] A study by Tejasvi *et al*[26] showed that polymorphisms in *TNAFAIP3*, a gene encoding for a zinc finger protein (A20) that is a negative regulator of TNF-induced pathways, are associated with response to anti-TNF agents, with specific SNP acting as markers of beneficial response to three TNF blockers tested. A genetic association with anti-TNF response was also found in rheumatic disease patients, including those with PsA, in which the −308 G/G genotype in the promoter of the TNF gene conferred a better response to treatment than A/A or A/G genotypes.[27] Additional studies are required to confirm these findings, thus future works on genetic biomarkers should aim to analyse large cohorts and to focus mainly on genes associated with psoriais/PsA susceptibility.

BLOOD BIOMARKERS

Circulating biomarkers have been extensively investigated because of the easy accessibility to patients' peripheral blood samples. Early studies have shown that psoriasis patients have increased serum levels of unspecific inflammation markers such as CRP, haptoglobin[28] and platelet P-selectin,[29] as well as pro-inflammatory cytokines, such as TNF, IFN-γ, IL-6, IL-8, IL-12 and IL-18.[30] Suarez-Farinas *et al*[31] have recently profiled the expression of 92 proteins in the serum of a large cohort of psoriasis patients and healthy individuals. They detected increased expression of 12 proteins, mainly inflammatory cytokines, chemokines or proteins responsive to cytokines in the serum of psoriatic patients. Interestingly, each protein was associated with corresponding increases in messenger RNA (mRNA) levels in psoriatic skin lesions. High mRNA and protein levels of IL-22 are also detected and they decrease after successful therapy.[32 33] Despite the important role of Th17 cells in psoriasis, IL-17A serum levels are not consistently found to be increased in different cohorts of psoriatic patients possibly due to low levels and sensitivity issues of the detection assays.[30 31 33] Interestingly, high IL-17A and IL-1RA serum levels are associated with eruptive inflammatory rather than chronic stable disease phenotype, suggesting that serum inflammatory cytokines differ according to morphological phenotype.[34] Circulating levels of Th1, Th17 and Th22 cells are increased in psoriasis patients compared to healthy volunteers, and the frequency of Th1 and Th17 cells is decreased after anti-TNF therapy.[35] In keeping with the importance of IL23/Th17 axis in psoriasis, there is increased expression of IL23R in circulating T cells.[36]

Given the extensive cross-talk between inflammation and coagulation, it is not surprising that psoriasis patients present with abnormalities in blood coagulation and fibrinolysis (increase of Fibrinopeptide A, prothrombin fragments 1+2, Bβ and D-dimer, fibrinogen, C4 and C4; decrease in Protein C, Plasminogen and alpha 2 -antiplasmin).[28 37]

Psoriasis has also been associated with abnormalities in lipid metabolism and oxidative stress.[38] Although conflicting data are reported, it appears that high levels of lipids (total cholesterol, triglycerides, very low-density lipoprotein and low-density lipoprotein cholesterol) and lipid peroxidation, as well as decreased anti-oxidant enzyme activity, were found in psoriasis patients compared to healthy volunteers.[39] The accumulation of high levels of oxidised low-density lipoprotein both in blood and skin[40] may account for both psoriasis pathogenesis and the risk of developing atherosclerosis. Moreover, increased serum levels of 8-hydroxy guanosine evidence reactive oxygen species-induced DNA damage in psoriasis patients. Overall, an imbalanced oxidative status influences cell proliferation, apoptosis and differentiation as well as immune response.

Reich *et al*[41] have highlighted the high prevalence of undiagnosed cases of active PsA among psoriasis patients seen by dermatologists, underlining the urgent need for soluble biomarkers for early PsA diagnosis in these patients. Biomarker research in PsA, beyond the analysis of inflammatory cells and molecules, has also focussed on circulating factors of cartilage and bone metabolism. This approach, taken from RA studies, has widened because, in contrast to RA, new bone formation, alongside bone erosion, occurs in PsA.

Serum IL-6 levels are higher in PsA patients compared to psoriasis-only patients and correlate with joint counts, erythrocyte sedimentation rate, CRP and serum IL-2Rα.[42] Chandran *et al*[43] identified a combination of serum markers (increased levels of high sensitivity CRP, osteoprotegerin, matrix metalloproteinase 3 and the CPII:C2C ratio) that could distinguish PsA and psoriasis-only patients, demonstrating the efficacy of integrating multiple markers.

Cellular biomarkers such as osteoclast precursors are elevated in PsA patients, but significantly decrease after anti-TNF therapy.[44]

A recent study showed that compared with those with psoriasis and healthy controls, patients with PsA had higher circulating concentrations of Dkk-1 and M-CSF.[45]

Some of the markers altered in psoriasis patients are involved in metabolic and pro-inflammatory processes that contribute to the development of comorbidities. Serum leptin, resistin and lipocalin are increased in psoriasis patients,[46] and are potentially important for linking psoriasis to insulin resistance and cardiovascular disease. Adiponectin, a cytokine secreted by adipose tissue and that ameliorates insulin resistance, is decreased in the serum of psoriatic patients and seems to be induced following successful therapy.[47] Interestingly, an association between the serum level of different adipokines and Th17 cytokine has also been found in patients with psoriasis.[48]

Although circulating levels of several proteins, lipids, hormones and cells are altered in psoriasis patients, they have not been numerically correlated to disease status, as no precise threshold to define patient groups has far been identified, thus making them unsuitable for an objective assessment of the disease and its progression. Therefore, controlled studies on large and prospective cohorts are needed.

TISSUE BIOMARKERS

Psoriasis manifestation is very prominent in the skin, a primary tissue easily accessible for direct biomarker research.[49]

At the tissue level, most of the markers that are differentially expressed in psoriatic skin versus normal skin are related to abnormal keratinocyte differentiation and proliferation.

Psoriatic keratinocytes downregulate the expression of terminal differentiation markers such as keratin (K)1 and 10 and upregulate the expression of hyperproliferation markers such as K6 and K16, as confirmed by a recent study using a proteomic approach.[50] The upregulation of p53, Ki67, heat shock proteins (HSP60) and connexins (26 and 30) also contributes to epidermal hyperproliferation, even though a clear molecular mechanism needs to be established. Moreover, psoriatic keratinocytes show aberrant calcium metabolism[51] and resistance to apotosis.

Expression of anti-apoptotic proteins such as Bcl-X, Bax and Bak has been reported in psoriatic skin[52 53] and is correlated with response to anthralin[54] and anti-TNF therapy.[55]

Psoriatic keratinocytes also show a markedly increased production of antimicrobial peptides such as elafin, S100 family members and LL-37 and human β defensin,[56] accounting for the lack of skin infection observed in these patients.

In line with the inflammatory nature of the disease, an imbalanced cytokine milieu has been found in psoriatic lesions, with the presence of increased levels of TNF, IFN-α, IL-2, IL-6, IL-8, IL-12 and LIF-1 and reduced levels of IL-1, IL-4, IL-5 and IL-10.[38]

The pivotal role of the IL23/Th17 axis at tissue level is shown by the increased levels of IL-23, IL-23R and Th17 cytokines detected in psoriatic skin, with the latter increased in lesional versus non-lesional skin.[5]

In the case of PsA, structural, cellular and molecular changes of the joint/synovial tissue have been compared to both healthy controls and patients affected by other arthropathies, such as RA or ankylosing spondylitis.[57]

Quantitative changes in immune cell numbers, vascularity, adhesion molecule expression and activation of cellular signalling pathways have been reported in PsA.[7 58] In a recent study, immunohistochemical analysis of synovial samples showed that the CD3 T-cell number correlates with disease activity and response to both anti-IL-1R and anti-TNF treatment. A change in CD68 cell infiltration as observed in RA was not confirmed, supporting the idea that RA and PsA are distinct diseases.[59] Pro-inflammatory cytokines and promoters of angiogenesis are upregulated in PsA synovial fluid, with cytokines such as IL-1, IL-1-RA, IL-6, IL-8 and CCL3 correlating with systemic markers of inflammation (erythrocyte sedimentation rate and CRP) and decreasing following intra-articular therapy with anti-TNF.[60] In PsA, clonally expanded CD8 T cells are found independently from CD4 T cells,[7] and activated T cells in synovial fluid in PsA also contribute to osteoclastogenesisis and following bone resorption.[61]

Useful insights into disease pathogenesis have been provided by imaging,[62 63] including radiography, ultrasound and MRI, which showed capsular, entheseal and bony changes that are quite different from those observed in RA.[64 65] In particular, ultrasound and MRI can detect early inflammatory joint changes allowing for early PsA diagnosis and treatment.[66]

TRANSCRIPTIONAL BIOMARKERS

A growing number of microarray studies performed over the past 12 years has contributed to generate a list of differentially expressed genes in lesional versus non-lesional psoriatic skin, or 'psoriasis transcriptome', with the larger and most recent study identifying almost 3000 known genes as being altered in lesional skin.[67] Among the biological processes found to be significantly perturbed in psoriasis in these studies are epidermal differentiation, immune responses and hypermetabolic processes. Early studies found that psoriasis skin overexpresses types I and II IFN and TNF-inducible genes with a genomic signature indicating high infiltration of T cells and DC.[68–70] Gene expression changes occur early during psoriasis pathogenesis with non-lesional skin

showing a 'pre-psoriatic' signature characterised by decreased lipid biosynthesis and increased innate immunity compared to normal skin.[71] A recent study by Suarez-Farinas *et al*[31] has discovered and confirmed by immunohistochemistry staining previously unidentified genes as differentially expressed in lesional skin such as renin, thus providing a link to functional pathways associated with metabolic diseases and to cardiovascular risk pathways. Moreover, a meta-analytic approach is increasingly being used to combine results from individual studies, thus expanding and refining the psoriasis transcriptome.[67 72] Moreover, by combining the use of laser capture microdissection with microarray analysis of the epidermal and dermal skin compartment, Mitsui *et al*[73] have identified locally expressed psoriasis-relevant genes, for example, CCL19 and its receptor CCR7 in psoriatic dermis.

More limited data are available on expression profiles of PsA patients, whose peripheral blood mononuclear cells have reduced expression of genes suppressing immune responses (SIGIRR, STAT3, SHP1, IKBKB, IL-11RA and TCF7) compared to controls and RA patients, indicating an immune imbalance in favour of a pro-inflammatory status. Of note, the expression of nucleoporin 62 kDa could only correctly classify all controls and 94.7% of the PsA patients.[74] The translational relevance of microarray studies is evident when considering the correlation between expression patterns and response to treatment. At the skin level, a rapid reduction of inflammatory-related genes (eg, IL-6, IL-8 and IL-1 family members) follows anti-TNF therapy preceding a decreased infiltration of immune cells[75] and being concomitant with clinical improvement.[76] Even if some gene-expression changes (eg, downregulation of innate IL-1α and IL-8 sepsis cascade cytokines) are shared between anti-TNF responders and non-responders, it is only the former that inactivate the Th17 pathway.[77]

Microarray study limitations have recently been overcome by whole-transcriptome sequencing using RNA sequencing, allowing a comprehensive study of the transcriptome to an unprecedented level of sensitivity and accuracy.[78] RNA sequencing of lesional and non-lesional psoriatic skin further supported the synergistic role of IL-17 and TNF in psoriasis and revealed previously unrecognised genes.[79]

Analysis of microRNA (miRNA), short non-coding RNA that regulate gene expression at the post-transcriptional level, showed that miR-203, a skin-specific miRNA,[80] and miR-21, an inhibitor of T-cell proliferation and apotosis,[81] are both increased in psoriatic skin; while miR-146a and miR125b, both involved in the TNF pathway, are up and downregulated, respectively.[80] miRNA can also be detected in the serum, with miR1266 shown to be upregulated in psoriasis patients compared to healthy controls.[82] It could be envisaged that serum miRNA signatures might become co-diagnostics and/or prognostic biomarkers while skin miRNA might turn into therapeutic targets, the latter option supported by the easy accessibility of skin for local delivery.[83]

Gene expression can also be influenced by epigenetic alterations of DNA, and Roberson *et al*[84] have investigated global CpG methylation in psoriasis for the first time, showing that more than 1000 CpG methylation sites differ between normal and psoriatic skin, with methylation levels reverting to normal levels after anti-TNF treatment. Prediction of therapy response using gene expression is therefore feasible and offers the opportunity to move forward a cost-effective healthcare.

BIOMARKER VALIDATION

Despite a number of potential biomarkers for psoriasis and PsA present in the literature, none of them has achieved regulatory approval and thus clinical application. A key element in translating biomarkers into clinical practice, besides the robustness of its scientific rationale, is the validation process.

If the test is to be used in clinical practice, it must be reliable, with an acceptably low rate of false positive and/or false negative results. To evaluate the performance of a test in detecting a disease or characteristic in a given population, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) are the parameters to be calculated.[85] Sensitivity (or true positive rate) is the probability that a test will indicate 'disease' among diseased individuals; and specificity (or true negative rate) is the probability that a test will indicate 'no disease' among individuals without disease. While sensitivity and specificity are intrinsic characteristic of the test, PPV and NPV are influenced by disease prevalence, as PPV is the proportion of positive test results that are true positives (such as correct diagnoses), while NPV is the proportion of individuals with a negative test result who are correctly diagnosed. The accuracy of a test or biomarker can be assessed by a receiver-operating characteristic plot that is a graphic display of the trade-offs of the true positive rate and false positive rate (1–specificity), generating an area under the curve that can range from 0.5 (random chance, or no predictive ability) to 1 (perfect discrimination/accuracy). In general, a biomarker for clinical use needs good sensitivity and good specificity (values ≥0.9),[86] explaining why only a small fraction of potential biomarkers translate into clinical use. Most candidate biomarkers, not only those specific to psoriasis, are in the so-called 'translation from basic science to human studies phase', often encountering typical hurdles related to translational research.[87] In figure 1 we show the complex pipeline of biomarkers in psoriasis and PsA from discovery to validation and clinical adoption.

NEW APPROACHES FOR BIOMARKER DISCOVERY

Biomarkers are not necessarily to be found in one measure, but could be the result of a panel of markers, or molecular signatures, accounting for the complexity of human pathophysiology. Accordingly, biomarker research should be driven by tools that allow the simultaneous and unbiased analysis of multiple cellular types and molecular pathways. In this sense few promising technologies and analysis strategies have emerged in recent years, and here we briefly describe multiparameter cellular analysis and systems biology as representative examples.

Over the past few decades, flow cytometry (FC) has become a powerful technique for multiparameter cell analysis, thanks to its ability to interrogate simultaneously multiple biological signatures at a single cell level. This has been particularly useful to unravel the complexity of the human immune system, and could be functional to investigate the number and function of multiple immune cells in psoriasis at both the peripheral and local level. As mentioned earlier, attempts to evaluate the immune cells in psoriasis peripheral blood mononuclear cells have been made in small patient cohorts.[35] However, a comprehensive and multidimensional immunophenotyping and monitoring study on a large patient cohort is still missing. We believe that for such a study FC should be highly standardised and this could be achieved, at least in part, with the use of preformatted lyophilised FC reagents in combination with computational analysis, enabling the rapid screening of patients in multicentre trials.

FC limitations have been exceeded by the newly emerged cytometry by time-of-flight, in which fluorochromes are replaced by stable metal isotopes allowing the investigation of 30–100

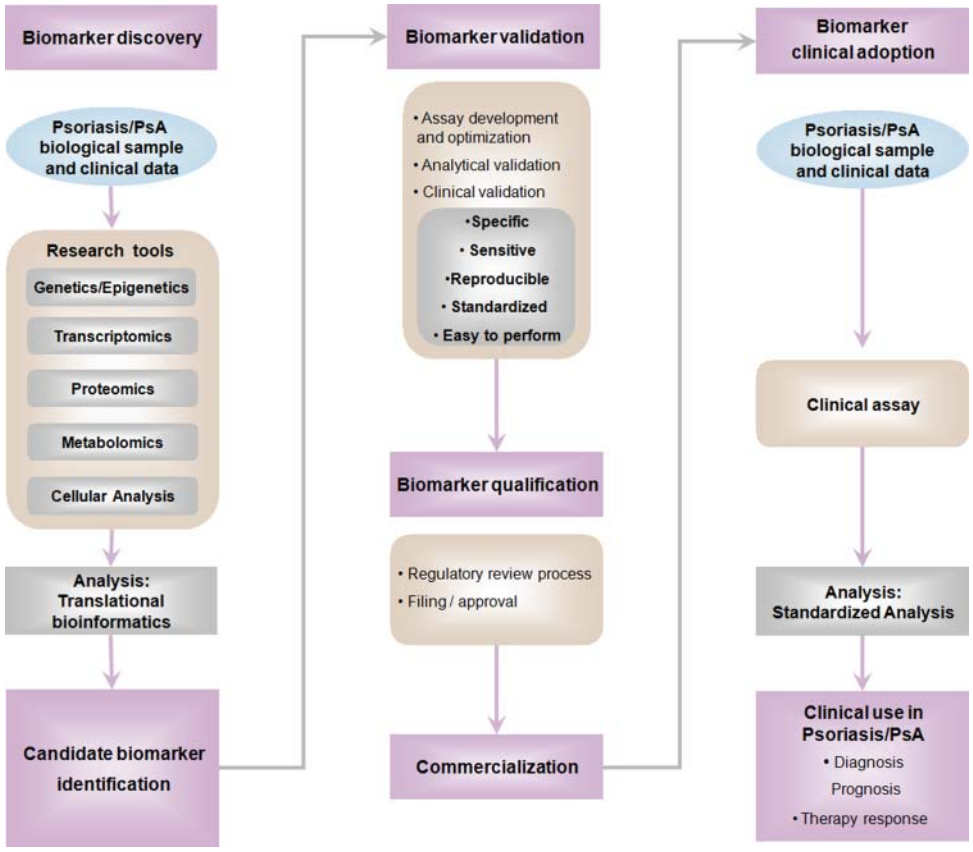

Figure 1 Biomarker discovery pipeline in psoriasis and psoriatic arthritis (PsA). A three-step process, from discovery to validation and clinical adoption is required before a newly identified biomarker can be routinely used for disease diagnosis, prognosis and therapy response.

markers.[88 89] As this novel technology lacks the speed and high-throughput characteristics of FC, it is possible to envision a complementary role in biomarker discovery. Mass cytometry could be used as a first step to perform high multidimensional screening identifying a smaller set of indicative markers, which can then be developed into standardised clinical tests to run on the faster and widely available FC platform.

The large amount of data ('omics') generated by next-generation technologies need advanced computational approaches to be deciphered, analysed and mined, calling for translational bioinformatics. Bioinformatics is used not only to deconvolute large datasets, but also to integrate different types of data (such as genetic variation, gene expression, proteomics and clinical data) and effectively to compare the molecular profiling of different diseases to improve disease classification.[90] This integrative approach is especially useful in complex diseases such as psoriasis, in which the multiple levels of biological hierarchies can be modelled as networks using systems biology.[91] We have employed a systems biology approach to model and quantify immune cell interactions that contribute, by cytokine signalling, to human skin inflammation.[92] The relationship between genetic variants and small alterations to cytokine production profiles can modify feedback loop interactions between immune cells and lead to pathological inflammatory levels. We have also recently presented a novel pipeline for patient stratification through an integrated analysis of the psoriasis transcriptome generated using publically available data.[93] By employing a computational methodology based on decision tree predictors, psoriatic samples were clustered on the basis of gene expression patterns, revealing a gene expression signature that discriminated between two molecular disease subtypes. Pathways particularly enriched in one of the two subgroups included transforming growth factor β and ErbB, thus suggesting that patients in this group may be more responsive to therapies directed against these targets.[93]

CONCLUSIONS

We have presented different classes of possible biomarkers identified in psoriasis and PsA to date. Although some genetic, blood, tissue and transcriptional markers are associated with the disease stage, progression and/or or response to therapy, many of these associations are not unique for psoriasis/PsA, but are also shared with other IMID. Moreover, they do not meet all the requirements needed to fit the definition of a biomarker.

In addition, it is becoming clear that molecular signatures rather than single markers are likely to be clinically relevant. New technologies and analysis strategies are now available to translational scientists and bioinformaticians to perform a comprehensive and unbiased biomarker discovery in psoriasis and other IMID.

Acknowledgements The authors would like to apologise to all the authors whose work could not be discussed and cited because of space limitations. We thank F.O.N. laboratory members for their contribution over the years to the work cited in this review.

Funding The research was funded/supported by the National Institute for Health Research (NIHR) Biomedical Research Centre based at Guy's and St Thomas' NHS Foundation Trust and King's College London. Authors also acknowledge support by the EuFP7 programme MAARS (Microbes in Allergy and Autoimmunity Related to the Skin).

The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

Competing interests None.

Provenance and peer review Commissioned; externally peer reviewed.

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Ann Rheum Dis 2013 72: ii104-ii110
doi: 10.1136/annrheumdis-2012-203037