Integrated bioinformatic analysis of differentially expressed genes and signaling pathways in plaque psoriasis

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Abstract. Psoriasis is an immune-mediated cutaneous disorder with a high incidence and prevalence. Patients with psoriasis may experience irritation, pain and psychological problems. The cause and underlying molecular etiology of psoriasis remains unknown. In an attempt to achieve a more comprehensive understanding of the molecular pathogenesis of psoriasis, the gene expression profiles of 175 pairs of lesional and corresponding non-lesional skin samples were downloaded from 5 data sets in the Gene Expression Omnibus (GEO) database. Integrated differentially expressed genes (DEGs) were obtained with the use of R software. The gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment were analyzed using the DAVID online analysis tool. The protein-protein interaction (PPI) network was constructed on the STRING platform and hub genes were calculated with the use of Cytoscape software. Finally, GEO2R was used to determine the expression of the hub genes in scalp psoriasis.

Psoriasis, as characterized by a well-demarcated erythematous plaque with silver scales, is a chronic, immune-mediated disorder that mainly affects the skin and joints (1). The worldwide prevalence rates of psoriasis range from 0.9-8.5% in adults and 0-2.1% in children (2). Although this condition rarely poses a threat to life, the irritation, pain and especially the aberrant appearance make these patients susceptible to psychological problems, such as anxiety and depression (3,4). With recent advances in the understanding of psoriasis, an increasing number of therapies have emerged, however a high recurrence rate persists. Therefore, it is important to better understand the underlying molecular pathogenesis of psoriasis in order to identify more effective therapeutic approaches for the control of psoriasis development and progression.

Gene expression microarrays have been widely applied in psoriatic research and represent an important new tool for use in the identification of disease-related molecules associated with psoriasis. Recently, comprehensive analysis of microarray data from multiple centers has become a popular research area. Ainali et al investigated gene expression patterns in lesional and non-lesional psoriatic tissue samples from 2 GEO data sets to establish a molecular sub-groups within the clinical phenotype of plaque psoriasis (5). Mei and Mei screened differentially expressed genes based on 4 psoriatic data sets followed by characterization of gene functions and mutual interactions (6). Sevimoglu and Arga analyzed and integrated data from 12 studies to identify the potential candidates for disease biomarkers and therapeutic targets (7).

However, analysis of the unpaired data obtained from lesional and non-lesional samples may lead to a potential...
377 genes were identified as DEGs, with 277 of these genes gene expression from these 175 pairs of psoriatic skin samples, psoriatic lesions. Databases exhibited a similar expression profile as that in scalp psoriatic patients, was used as a means to validate whether the hub genes obtained from the aforementioned databases exhibited a similar expression profile as that in scalp psoriatic lesions.

Through integration of the bioinformatic analyses of the gene expression from these 175 pairs of psoriatic skin samples, 377 genes were identified as DEGs, with 277 of these genes being upregulated and 96 genes downregulated. We revealed that these genes covered a wide range of biological functions in epidermal development, keratinization, immune responses, metabolic pathways, cell cycle and extracellular spaces. These results provide a comprehensive understanding of the molecular pathogenesis of the disease, which may guide subsequent studies on psoriasis research.

Materials and methods

Microarray data sets and data calibration. Using the keyword ‘psoriasis’, data sets using the descriptors ‘paired biopsy from both lesional and non-lesional skin’ and ‘pre-treatment status’ were screened. The raw files of 5 enrolled microarray data sets, including GSE14905 (8), GSE30999 (9,10), GSE34248 (11), GSE41662 (11) and GSE53552 (12), from the Gene Expression Omnibus ( GEO) database. A total of 175 pairs of lesional and non-lesional skin samples from plaque psoriatic patients were selected. With use of bioinformatic methods, integrated differentially expressed genes (DEGs) were identified, followed by the Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment. Protein-protein interaction (PPI) analysis and hub gene calculation were subsequently performed. Finally, an additional GEO data set, GSE75343 (13), which contained a study of gene expression levels in scalp psoriatic patients, was used as a means to validate whether the hub genes obtained from the aforementioned databases exhibited a similar expression profile as that in scalp psoriatic lesions.

PPI network and hub gene analyses. The STRING platform, an online tool used for the structural and functional analysis of protein interactions (15), was used to identify interactions among proteins of interest. The corresponding results were analyzed and structured with the use of the Cytoscape software 3.6.1 (https://cytoscape.org). The hub genes, which were considered to be involved in playing pivotal regulatory roles in the PPI network, were subsequently calculated based on the overlapping results obtained by MCC (Maximal Clique Centrality) and DMNC (Density of Maximum Neighborhood Component) topological analysis methods, respectively, with use of the cytoHubba app built in the software (16).

Results

Microarray data standardization and DEG identification in plaque psoriasis. With use of the quartile division method, gene expression levels of each of the 5 GEO series were standardized and the results of pre- and post-standardization are presented in Fig. 1A. After pre-processing of the data, DEGs were analyzed using paired-sample t-tests within each series using a screening criteria of P<0.05 and |log2FC|≥1 (Fig. 1B). The number of DEGs in each series, including up- and downregulated DEGs are presented in Table I. When DEGs in each series were intersected with one another, 373 genes, considered as integrated DEGs were obtained and used for subsequent analysis with 277 of these genes being upregulated and 96 downregulated (Fig. 2). The ratio of the number of upregulated genes to that of downregulated genes was close to 1:1 in each of the GEO data sets, however, in the integrated results this ratio was equal to approximately 3:1, indicating a possible commonality in the upregulated genes during psoriasis development while the downregulated genes differ in individuals.

GO term and KEGG pathway analysis of DEGs. The DAVID knowledgebase (https://david.ncifcrf.gov/), an online gene functional annotation tool, was used to analyze the function and pathway enrichment of candidate genes obtained (14). With this technique, the Fisher exact test P-value was calculated as a result of enrichment degree. The top 10 enrichment GO term or KEGG pathway annotations for both up- or downregulated DEGs obtained in our study were listed.
Table I. Information for psoriatic GEO data.

| GEO series | Platform | Sample Type | Type                | Pair no. | (Refs.)         |
|------------|----------|-------------|---------------------|---------|-----------------|
| GSE14905   | GPL570   | Paired LS and NLS | Plaque psoriasis | 28      | Yao et al (8)   |
| GSE30999   | GPL570   | Paired LS and NLS | Moderate to severe plaque psoriasis | 85      | Suárez-Fariñas et al (9) |
| GSE34248   | GPL570   | Paired LS and NLS | Mild to moderate plaque psoriasis | 14      | Bigler et al (11) |
| GSE41662   | GPL570   | Paired LS and NLS | Moderate to severe plaque psoriasis | 24      | Bigler et al (11) |
| GSE53552   | GPL570   | Paired LS and NLS | Moderate to severe plaque psoriasis | 24      | Russell et al (12) |
| GSE75343   | GPL570   | Paired scalp LS and scalp NLS | Moderate to severe plaque psoriasis with scalp involvement | 13      | Ruano et al (13) |

LS, lesional skin; NLS, non-lesional skin.

Table II. DEGs in each GEO series.

| GEO series | No. of total DEGs | No. of upregulated DEGs | No. of upregulated DEGs |
|------------|-------------------|-------------------------|-------------------------|
| GSE14905   | 1195              | 682                     | 513                     |
| GSE30999   | 1979              | 1040                    | 939                     |
| GSE34248   | 1670              | 854                     | 816                     |
| GSE41662   | 2203              | 1073                    | 1130                    |
| GSE53552   | 2220              | 1084                    | 1136                    |

DEGs, differentially expressed genes.

identified according to the Fisher’s exact test P-value are listed in Tables III and IV. The corresponding visual diagrams are presented in Fig. 3A and B. Within the biological process function group, upregulated DEGs were mainly enriched in GO terms of immune responses, ectoderm development, defense responses, keratinization and epidermal development while downregulated DEGs were mainly enriched in the regulation of smooth muscle contraction and muscle organ development. Notably, with the exception of enrichment of the cornified envelope, which is an extremely tough structure formed beneath the cell membrane (17) in the upregulated DEGs group, both up- and downregulated DEGs were enriched in the extracellular space within the cellular component enrichment analysis. Within the molecular function enrichment group, the upregulated DEGs were mainly enriched in chemokine activity, chemokine receptor binding and endopeptidase inhibitor activity, while downregulated DEGs were enriched in cytoskeletal protein binding processes. The KEGG pathway enrichment was performed using the same analysis tool and the results, in which only the pathways for the upregulated genes are displayed by figure, due to the limited number of enrichment pathways in the downregulated group, are presented in Table V and Fig. 4. In upregulated DEGs, signaling pathways were mainly enriched in metabolic pathways, measles, influenza A and chemokine signaling pathways, while aldosterone-regulated sodium reabsorption and PPAR signaling pathways were enriched in downregulated DEGs.

**PPI network construction and hub gene selection.** The online database STRING was used to obtain PPI information on the 373 DEGs, including the 277 upregulated and 96 downregulated genes and the PPI network, with 2 notable functional modules, was constructed with use of Cytoscape software (Fig. 5A). Hub genes were then calculated using the cytoHubba app from the network we constructed. As a result of these calculations, 17 genes with the highest scores were considered as hub genes and were automatically divided into 2 groups exactly corresponding to the modules in Fig. 5A. One group consisted of TTK, AURKA, DLGAP5, HMMR, CDC43, CENPE, SPC25, MCM10, NDC80, RRM2, CKS2 and NUF2, which are genes involved in the cell cycle, mitosis and proliferation. The second group consisted of IFI16, ISG20, IFI11, RSAD2 and IFI27, all of which belong to IFN-α-inducible genes (Fig. 5B). Notably, these 17 hub genes all belong to the upregulated genes of the DEGs we obtained, which further demonstrated the importance of these upregulated genes in the molecular pathogenesis of psoriasis.

**Hub gene expression levels in scalp psoriasis.** To investigate whether scalp psoriasis displayed a similar gene expression profile as that of skin psoriasis, 13 pairs of scalp lesional and adjacent non-lesional samples were selected from GSE75343 (Table I). With use of the online analysis tool, GEO2R, expression levels of these 17 hub genes were determined. The results revealed that statistically significant differences were obtained in the expression of IFI16, ISG20, RSAD2 and IFI27, all of which belong to IFN-α-inducible genes (Fig. 5B), but not in the other hub genes (data not shown). Further analysis revealed that 4 out of 6 IFN-α-inducible genes exhibited significant differences with regard to gene expression, while in genes involved in the cell cycle, mitosis and proliferation, only 2 of them exhibited differences in gene expression.

**Discussion**

Psoriasis, one of the most common skin ailments, afflicts millions of people worldwide. In addition to its negative
aspects on physical and mental health, the cost of psoriasis places a huge burden on both individuals and society (17). Although dozens of medications are available for relief of the symptoms of this disease, no cure for psoriasis currently exists. Therefore, it is clear that the identification of pivotal molecules that play critical roles in the pathogenesis of this disease for potential development of therapeutic targets represents an important area of investigation.

Gene expression microarrays provide a comprehensive view of genome-wide expression profiles of clinical samples and have been widely used to analyze genes which are differentially expressed in psoriasis. However, few studies exist which have integrated such high-throughput gene expression microarray data of paired lesional and non-lesional skin samples. In the present study, gene expression profiles of 175 pairs of psoriatic skin samples and the corresponding normal tissues from 5 GEO data sets were integrated and analyzed with use of bioinformatic methods. Our results demonstrated several important pathways and the pivotal genes associated with the molecular pathogenesis of psoriasis.

Psoriasis is an immune-mediated inflammatory cutaneous disease characterized by an overt proliferation and differentiation of keratinocytes (1). Our GO biological process enrichment results, especially with regard to upregulated genes, included immune responses, keratinization, inflammatory responses and keratinocyte differentiation, all of which are commonly accepted components of the pathogenesis and pathological changes of psoriasis. In addition, the enrichment in defense responses and responses to wound healing processes indicates two important psoriatic precipitating factors: infection (18) and trauma (Koebner phenomena) (19), both of which are associated with the activation of innate immunity involved in the initial pathogenesis of psoriasis (20). Additional reported risk factors include smoking (21), alcohol (22) and obesity (23).

In the cellular component enrichment analysis, in addition to mitosis-associated components such as chromosome...
kinetochore and the Ndc80 complex, enrichment in the extracellular matrix of both up- or downregulated genes revealed the significance of this component. The extracellular matrix (ECM) is a collection of non-cellular molecular networks that regulate diverse cellular functions, such as growth, migration and homeostasis (24,25). The ECM is composed of interstitial matrix and basement membrane, both of which are reported to be involved in the development of psoriasis. Findings from a guttate psoriasis prognosis study, indicate that psoriasis disease progression is believed to be governed by the triggering of humoral immune responses, which could produce extracellular antibodies to neutralize the streptococcal lytic enzyme and prevent disruption of the laminin layer in the basement membrane caused by the enzyme (26). Recently, neutrophil extracellular traps (NETs), which are web-like structures consisting of DNA associated with histones, antimicrobial peptides and enzymes (27,28), were reported to act as a source of autoantigens which contribute to the occurrence of several autoimmune diseases (29,30), including psoriasis. For example, Lin et al reported that mast cells and neutrophils release IL-17 through extracellular trap formation in psoriasis (31). In molecular function enrichment analysis, it was observed that in upregulated genes, several GO terms indicated endopeptidase inhibitor activity, which contains a family of serine protease inhibitors (serpins). Serpins, such as \textit{SERPINA3}, \textit{SERPINB4}, \textit{SERPINA1}, \textit{SERPINB12}, \textit{SERPINB3} and \textit{SERPINB13} in our enrichment gene list represent a broad family of protease inhibitors that utilize conformational changes to inhibit target enzymes (32); and it has been suggested that these serpins play a role in psoriatic pathogenesis. Similar to the results obtained in our analysis, Johnston et al detected upregulation of two endogenous protease inhibitors, serpins A1 and A3, both of which are present in psoriasis vulgaris and generalized pustular psoriasis. These serpins may play a counter-regulated role to control the activity of IL-36, whose activation requires N-terminal peptide cleavage by neutrophil serine protease (33).

| Term                                                                 | Count | Rich factor (%) | P-value     | Functional group |
|----------------------------------------------------------------------|-------|----------------|-------------|------------------|
| GO:0006955 immune response                                           | 39    | 16.04938272    | 4.38742E-13 | BP               |
| GO:0007398 ectoderm development                                      | 17    | 6.995884774    | 2.50742E-08 | BP               |
| GO:0006952 defense response                                          | 29    | 11.93415638    | 4.97398E-08 | BP               |
| GO:0031424 keratinization                                            | 9     | 3.703703704    | 1.40384E-04 | BP               |
| GO:0008544 epidermis development                                     | 15    | 6.172839506    | 3.81508E-07 | BP               |
| GO:0009611 response to wounding                                      | 25    | 10.28806584    | 5.4487E-07  | BP               |
| GO:0006954 inflammatory response                                     | 18    | 7.407407407    | 4.12036E-06 | BP               |
| GO:0030855 epithelial cell differentiation                            | 12    | 4.938271605    | 4.1551E-06  | BP               |
| GO:0030216 keratinocyte differentiation                               | 9     | 3.703703704    | 4.20155E-06 | BP               |
| GO:0009913 epidermal cell differentiation                             | 9     | 3.703703704    | 8.13933E-06 | BP               |
| GO:0006935 chemotaxis                                               | 12    | 4.938271605    | 1.83209E-05 | BP               |
| GO:0001533 cornified envelope                                        | 6     | 2.469135802    | 1.19845E-05 | CC               |
| GO:0005576 extracellular region                                      | 49    | 20.16460905    | 0.000143627 | CC               |
| GO:0005615 extracellular space                                       | 23    | 9.465020576    | 0.000294727 | CC               |
| GO:0031262 Ndc80 complex                                             | 3     | 1.234567901    | 0.001187266 | CC               |
| GO:0044421 extracellular region part                                 | 25    | 10.28806584    | 0.004874319 | CC               |
| GO:0005792 microsome                                                | 10    | 4.11526337     | 0.00688315  | CC               |
| GO:0042598 vesicular fraction                                       | 10    | 4.11526337     | 0.008255849 | CC               |
| GO:0001772 immunological synapse                                     | 1     | 1.234567901    | 0.000416898 | CC               |
| GO:0000777 condensed chromosome kinetochore                          | 5     | 2.057613169    | 0.009278963 | CC               |
| GO:0000793 condensed chromosome                                      | 7     | 2.880658436    | 0.010321628 | CC               |
| GO:0008009 chemokine activity                                       | 7     | 2.880658436    | 3.62741E-05 | MF               |
| GO:0004867 serine-type endopeptidase inhibitor activity              | 9     | 3.703703704    | 3.72441E-05 | MF               |
| GO:0042379 chemokine receptor binding                                | 7     | 2.880658436    | 5.23427E-05 | MF               |
| GO:0004866 endopeptidase inhibitor activity                          | 10    | 4.11526337     | 0.000171511 | MF               |
| GO:0030414 peptidase inhibitor activity                              | 10    | 4.11526337     | 0.00025684 | MF               |
| GO:0004252 serine-type endopeptidase activity                        | 9     | 3.703703704    | 0.001273205 | MF               |
| GO:0008236 serine-type peptidase activity                            | 9     | 3.703703704    | 0.003155874 | MF               |
| GO:0017171 serine hydrolase activity                                 | 9     | 3.703703704    | 0.003376462 | MF               |
| GO:0005125 cytokine activity                                         | 9     | 3.703703704    | 0.005452577 | MF               |
| GO:0004175 endopeptidase activity                                    | 13    | 5.349794239    | 0.005566809 | MF               |

GO, gene ontology; BP, biological process; CC, cellular component; MF, molecular function.
Such a negative regulatory effect, although unlikely to balance the protease expression revealed in the study by Lin et al. (31), may provide for new insights into the development of psoriasis therapy.
Table V. KEGG analysis of deGs associated with psoriasis.

| Regulation   | ID      | Term                                | Count | Rich factor (%) | P-value     | Genes                                                                 |
|--------------|---------|-------------------------------------|-------|-----------------|-------------|------------------------------------------------------------------------|
| Upregulated  | hsa05164| Influenza A                         | 11    | 4.280155642     | 0.00022787 | IRF7, OAS3, CXCL8, IL1B, RSAD2, OAS1, OAS2, MX1, STAT1, TMRPS54, CXCL10 |
| Upregulated  | hsa05162| Measles                             | 9     | 3.501945525     | 0.00073285 | CCNE1, PRKCQ, IRF7, OAS3, IL1B, OAS1, OAS2, MX1, STAT1                |
| Upregulated  | hsa04062| Chemokine signaling pathway         | 10    | 3.891050584     | 0.00162187 | CXCL1, CCL22, CCL20, CXCL13, CXCL9, CXCL8, CXCR2, STAT1, CCL18, CXCL10 |
| Upregulated  | hsa05160| Hepatitis C                         | 7     | 2.723735409     | 0.01355117 | IFIT1, IRF7, OAS3, CXCL8, OAS1, OAS2, STAT1                           |
| Upregulated  | hsa05168| Herpes simplex infection            | 8     | 3.112840467     | 0.01820027 | CDK1, IFIT1, IRF7, OAS3, IL1B, OAS1, OAS2, STAT1                      |
| Upregulated  | hsa00240| Pyrimidine metabolism               | 6     | 2.33463035      | 0.01847329 | TYMP, NSC3A, RRM2, UPP1, PNP, CMPK2                                  |
| Upregulated  | hsa04620| Toll-like receptor signaling pathway | 6     | 2.33463035      | 0.01989591 | IRF7, CXCL9, CXCL8, IL1B, STAT1, CXCL10                              |
| Upregulated  | hsa05146| Amoebiasis                           | 6     | 2.33463035      | 0.01989591 | ARG1, CXCL8, IL1B, SERPINB4, SERPINB13, SERPINB3                    |
| Upregulated  | hsa01100| Metabolic pathways                  | 27    | 10.50583658     | 0.03117996 | XDH, GDA, KYNU, HSD1B2, NT5C3A, GALN6, CYP2C18, UPP1, AASS, PNP, CMPK2, ARG1, CYT5, ST1, CXCL8, OAS1, OAS2, STAT1 |
| Upregulated  | hsa04110| Cell cycle                           | 6     | 2.33463035      | 0.0359891  | CCNB1, CCNE1, CDK1, CDC45, TTK, CDC20                                |
| Upregulated  | hsa04060| Cytokine-cytokine receptor interaction | 8    | 3.112840467     | 0.05301106 | CXCL20, CXCL13, CXCL9, CXCL8, IL1B, CXCR2, IL7R, CXCL10              |
| Upregulated  | hsa04623| Cytosolic DNA-sensing pathway        | 4     | 1.55642023     | 0.06819191 | IRF7, IL1B, AIM2, CXCL10                                            |
| Upregulated  | hsa04668| TNF signaling pathway                | 5     | 1.945525292     | 0.07110534 | CXCL1, NOD2, CCL20, IL1B, CXCL10                                    |
| Upregulated  | hsa04115| p53 signaling pathway               | 4     | 1.55642023     | 0.07600871 | CCNB1, CCNE1, CDK1, RRM2                                            |
| Upregulated  | hsa04622| RIG-I-like receptor signaling pathway| 4     | 1.55642023     | 0.08420339 | ISG15, IRF7, CXCL8, CXCL10                                          |
| Downregulated| hsa04960| Aldosterone-regulated sodium reabsorption | 3   | 3.488372093      | 0.01441983 | HSD11B1, NR3C2, ATP1A2                                             |
| Downregulated| hsa03320| PPAR signaling pathway              | 3     | 3.488372093      | 0.03821865 | ACOX2, LPL, ACADL                                                  |

KEGG, Kyoto Encyclopedia of Genes and Genomes; DEGs, differentially expressed genes.
The results from our KEGG pathway analysis revealed that a high enrichment in metabolic and viral infection pathways was present in upregulated genes. There were 26 genes enriched in metabolic pathways, including XDH, GDA, KYNU, HSD17B2, NT5C3A, GALNT6, CYP2C18, UPP1, AASS, PNP, CMPK2, ARG1, TYMP, HPSE, ALOX12B, FUT2, SPTLC2, DHRS9, HYAL4, ST6GALNAC1, SLE, RRM2, AKR1B10, LIPG, GK, SMPD3, and PLA2G4D. Among these genes, ALOX12B, one of the lipoxygenases, is reported to play an important role in the regulation of epithelial proliferation, differentiation, wound healing and inflammatory skin diseases (34). PLA2G4D, a member of phospholipase A2, was revealed to have a strong gene expression in the upper spinous layer of psoriatic epidermis, while in normal skin the expression of PLA2G4D was not detected (35). The expression or functions of the other genes in our list have received little attention with regard to their roles in cutaneous disorders. Therefore, these genes may provide important new research targets for the understanding and treatment of psoriasis. Most of the genes enriched in viral infection KEGG pathways are IFN-α-inducible genes which belong to one group of the hub genes in the PPI network.

The PPI network was constructed by Cytoscape software and hub genes were then determined. With this analysis, 17 genes were identified and divided into 2 groups according to protein-protein interactions. One group of these were IFN-α-inducible genes, which were also enriched in KEGG viral infection pathways, and included IFI16, IFI27, IFIT1, RSAD2 and ISG20. A role for IFN-α in psoriasis development has been gradually revealed. For example, Garcia-Romo et al demonstrated that in the initial phase of disease development, cutaneous accumulated plasmacytoid pre-dendritic cells become activated and produce IFN-α, which then drives the stimulation of autoimmune T cells in pre-psoriatic skin (30). Such a mechanism provides an explanation for the role of innate immunity in connecting environmental triggers, such as viral or bacterial infection and wound healing with disease-associated autoimmune T cells. This also clarifies the reason for an absence of IFN-α in our analysis, since the samples we selected were all from chronic plaque psoriasis patients. The expression of IFN-α-inducible genes in our study was also observed in scalp psoriatic samples, demonstrating an important role for IFN-α in the pathogenesis of psoriasis within different skin areas. The other group of genes including, CSK2, CDC45, MCM10, SPC25, NDC80, NUF2, AURKA, CENPE, RRM2, DLGP5, HMMR and TTK, were associated with the regulation of the cell cycle, mitosis and proliferation (36,37). Notably, there are two kinases in this group of hub genes:
Aurora kinase A, essential for chromosome segregation (38) and TTK, whose expression is at high levels in tissues which contain large numbers of proliferating cells (39). While the relationship between these kinases and psoriasis development is yet unclear, there exists a potentially important role that they may play in the pathogenesis of psoriasis. In contrast to the results in the IFN-α-inducible gene group, the expression of most hub genes associated with the cell cycle and proliferation in scalp psoriatic samples (except for MCM10 and SPC25), revealed no significant differences from that of paired control samples. Within the scalp area a large proportion of follicles are in anagen, which may contribute to a set of highly expressed genes associated with the cell cycle and proliferation. This can be contrasted with that of skin samples from other areas where most hair follicles are in catagen or telophase. Histologically, in the initial stages of this disease scalp psoriasis mainly affects the interfollicular epidermis with perifollicular inflammation (13), while later stages include destruction of hair follicles with perifollicular fibrosis and hair loss (40). Based on these findings, it was hypothesized that the expression of these cell cycle-related genes, which are assumed to be at high expression levels in psoriatic samples, is relatively reduced in...
sculptural scalp psoriatic samples where hair follicle destruction occurs as compared to normal scalp tissues, as reflected in our results.

Although a similar bioinformatical study on psoriasis has been performed (7), in our present study, we limited our data sets to paired lesional and non-lesional psoriatic skin samples and performed DEG analysis with use of paired-sample t-tests in each data set. An overlap method was subsequently employed to combine these DEG results as a means to obtain an overall set of DEGs corresponding with that of each data set. With use of these strict screening methods, we consider that our results have a relatively high degree of specificity for detecting pivotal disease-associated molecules, however the resultant low sensitivity would be considered as a limitation of this study. In our future research, if ethical approval is obtained, RT-qPCR validation of these identified target genes in clinical samples will be conducted. In conclusion, through a comprehensive bioinformatic re-analysis of these original GEO data, an overall view regarding the molecular pathogenesis of psoriasis and the potential for identification of therapeutic targets for this disease was provided.

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Availability of data and materials

All data generated or analyzed in the present study are included in this published article.

Authors’ contributions

YJZ collected the online microarray data and the corresponding clinical information and drafted the manuscript. YJZ and YZS performed the bioinformatic and statistical analysis. XHG and RQQ contributed to the study design and performed the proofreading and revision of the manuscript. All authors read and approved the manuscript and agree to be accountable for all aspects of the research in ensuring that the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

All authors declare that they have no competing interests.

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