

ORIGINAL ARTICLE

Differential gene expression in peripheral blood T cells from patients with psoriasis, lichen planus, and atopic dermatitis

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Background: Psoriasis, lichen planus (LP), and atopic dermatitis (AD) are common chronic inflammatory skin diseases mediated by immune responses.

Objective: We used RNA sequencing to investigate messenger RNA expression patterns in peripheral T cells of Chinese patients with psoriasis, LP, or AD and of healthy individuals.

Methods: After peripheral T-cell proliferation, messenger RNA expression patterns were investigated by RNA sequencing, and 6 randomly selected genes were verified by real-time reverse transcriptase polymerase chain reaction.

Results: Six genes were down-regulated and 33 were up-regulated in these diseases. Gene ontology analysis revealed enrichment of genes involved in positive regulation of T-cell activation. Regulation of nuclear premessenger RNA domain containing 1B (RPRD1B) expression was enhanced in psoriasis.

Limitations: The role of hereditary factors in RPRD1B expression in T cells was not considered. Immunomodulators (thymopeptide, levamisole, BCG polysaccharide, nucleic acid injection, and transfer factor) were previously given to patients with psoriasis and LP, but not to patients with AD; the effects of these immunomodulators on gene expression is uncertain.

Conclusion: RPRD1B may be involved in T-cell activation in our Chinese psoriatic cohort, and may play a role in stimulating epidermal hyperproliferation. (J Am Acad Dermatol [10.1016/j.jaad.2013.06.030](https://doi.org/10.1016/j.jaad.2013.06.030).)

Key words: atopic dermatitis; differentially expressed genes; lichen planus; psoriasis; regulation of nuclear premessenger RNA domain containing 1B; T cells.

Psoriasis, lichen planus (LP), and atopic dermatitis (AD) are common inflammatory skin diseases mediated by immune responses and are often used to study the relationship of immune responses with specific clinical and histopathological changes. Immune abnormalities in T cells play important roles in the pathogenesis of psoriasis, LP,

and AD. It has been found that: (1) differentiation from naïve T cells to functional T cells is imbalanced in psoriasis¹⁻⁴; (2) in T cells directly differentiated from psoriatic bone-marrow CD34⁺ cells in vitro, Th1 cytokine levels are enhanced, whereas the number of Tregs decreases^{5,6}; (3) expression of the variable region of T-cell receptor is predominant in

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peripheral T cells in psoriasis⁷; (4) the number of CD3⁺ T cells and expression of CD25, CD8, and CD45RA are significantly higher in LP^{8,9}; and (5) the number of Foxp3⁺ T cells significantly increases in LP.¹⁰ CD4⁺ T cells maintain abnormal immune responses in AD by secreting Th1/Th2 cytokines.¹¹ AD manifests as a Th2-dominant model in the acute phase, which shifts to a Th1-dominant model in the chronic phase.¹²

Although all these 3 inflammatory skin diseases are mediated by T-cell immunity, psoriatic lesions are special. Psoriatic lesions are well-demarcated pink plaques with silvery scales and -sometimes include larger geographic lesions than those seen in AD and LP. The histologic appearance of psoriasis is characterized by elongation of the rete ridges and by parakeratosis with loss of the maturing granular layer, compared with liquefaction degeneration of basal cells and bandlike infiltration of lymphocyte in LP dermis. The histologic appearance of AD cannot be distinctly distinguished from other inflammation.

To understand the similarity and differences among psoriasis, LP, and AD in terms of pathogenesis, clinical manifestation, and histopathological appearance, it is necessary to study the molecular expression in 3 conditions. Therefore, we studied the messenger RNA expression profiles in peripheral blood T cells in these 3 inflammatory diseases and analyzed the differentially expressed genes (DEGs) in psoriasis.

METHODS

Specimen source

Sixty Chinese Han patients at Taiyuan City Center Hospital, and 20 volunteers (9 women and 11 men; mean age: 36.5 years) were enrolled in this study. The patients were given a diagnosis both on the basis of clinical symptoms and pathological features. The volunteers showed no systemic or autoimmune diseases. Twenty of the patients had quiescent psoriasis vulgaris with plaque lesions (9 women and 11 men; mean age: 36.5 years), and all had been treated with immunomodulators; none of them were pruritic or had a relevant family history. The Psoriasis Area and Severity Index score was 7.9 to 30.6

(average: 15.2). Twenty patients had LP (11 women and 9 men; mean age: 39.0 years) and had been treated with immunomodulators and anti-inching agents. Twenty of the patients had AD (10 women and 10 men; mean age: 21.5 years); they had been treated with anti-inching agents. No patient had been on treatment for at least 1 month before sample collection.

All the subjects were informed about the aims of the study and provided informed consent. The protocol was approved by the Medical Ethics Committee of Taiyuan City Center Hospital.

Peripheral blood T-cell proliferation

Peripheral blood mononuclear cells were isolated using density gradient centrifugation (lymphocyte separation medium, Mediatech, Herndon, VA). T cells were isolated from peripheral blood mononuclear cells by magnetic sorting (magnetic cell sorting; Miltenyi Biotec,

Cologne, Germany; CD3 magnetic beads: Invitrogen, Carlsbad, CA). The cells were resuspended in RPMI-1640 (Invitrogen) supplemented with 5 μ g/mL CD3 antibody (Becton Dickinson Labware, Franklin Lakes, NJ). Cells were seeded in a T75 cell culture flask (Corning, New York). After the refreshing of media, cells were then transferred to a T225 flask (Corning, New York). Additional fresh media were supplemented. At day 17, cells were collected and 2 to 3 $\times 10^6$ cells were labeled with FITC-CD3 antibody (Becton Dickinson Labware) to identify T-cell purity using flow cytometry (Beckman Coulter Inc, Brea, CA).

RNA isolation

Total RNA was extracted using Trizol (Invitrogen) and treated with DNase (Invitrogen). The purity was analyzed using an Agilent 2100 Bioanalyzer (Agilent Technologies, Santa Clara, CA). Messenger RNA was purified using oligo(dT) magnetic beads (Invitrogen) and used to synthesize complementary DNA (cDNA) (Takara, Dalian, China).

Tag preparation, sequencing, and gene annotation

cDNA (5 μ L) obtained from age- and gender-matched groups of 5 patients each with psoriasis, LP,

CAPSULE SUMMARY

- Differences are seen in CD8⁺ T cell, keratinocyte proliferation, and chemokine (C-X-C motif) ligand 9 expression among patients with psoriasis, lichen planus, and atopic dermatitis.
- Abnormal expression of 39 genes that affect T-cell activation was seen in these 3 diseases. Regulation of nuclear premessenger RNA domain containing 1B expression was enhanced in psoriasis.
- Regulation of nuclear premessenger RNA domain containing 1B may help differentiate among the 3 aforementioned diseases.

Abbreviations used:

AD:	atopic dermatitis
cDNA:	complementary DNA
CD30:	tumor necrosis factor receptor superfamily, member 8
CD244:	natural killer cell receptor 2B4
DEGs:	differentially expressed genes
GO:	gene ontology
IL:	interleukin
KLRC2:	killer cell lectin-like receptor subfamily C, member 2
LP:	lichen planus
PCR:	polymerase chain reaction
RGS16:	regulator of G-protein signaling 16
RPRD1B:	regulation of nuclear premessenger RNA domain containing 1B
RT:	reverse transcriptase

or AD, and from healthy subjects was digested with *Nla*III and *Mme*I to generate 21-base pair tags. These tags were sequenced by the synthesis method. The obtained genes were annotated by referring to a gene database (ftp://ftp.ncbi.nih.gov/refseq/H_sapiens/mRNA_Prot/human.rna.fna.gz).

DEGs between 2 groups of samples were identified using digital gene expression profiles.¹³ DEGs were defined as genes with false discovery rate less than or equal to 0.001 and with more than 2-fold differences between the groups compared.

Analysis of significantly enriched genes by gene ontology and pathway analysis

All the DEGs were mapped to the gene ontology (GO) database (<http://www.geneontology.org/>) and the Kyoto Encyclopedia of Genes and Genomes database. GO and pathway enrichment analysis was performed using hypergeometric tests. GO terms and pathways with *P* less than .05 were defined as enriched among the DEGs.

Real-time polymerase chain reaction

cDNA from each group was used for real-time polymerase chain reaction (PCR) (ABI, Cheshire, UK) in 20- μ L reaction mixtures containing 2 μ L of cDNA, 10 μ L of premix EX Taq II buffer (master mix, Takara), 0.4 μ L of Rox reference dye (Takara), and 0.2 μ L of primers (BGI, Beijing, China). PCR reactions were carried out under the following reaction conditions: 30 seconds at 95°C and 40 cycles each consisting of 5 seconds at 95°C and 30 seconds at the appropriate annealing temperature (60°C for *ACTB* and regulator of G-protein signaling 16 [*RGS16*]; 58°C for natural killer cell receptor 2B4 [*CD244*] and interleukin [*IL*]-4; 57°C for regulation of nuclear premessenger RNA domain containing 1B [*RPRD1B*]; and 56°C for killer cell lectin-like receptor subfamily C, member 2 [*KLRC2*] and tumor necrosis

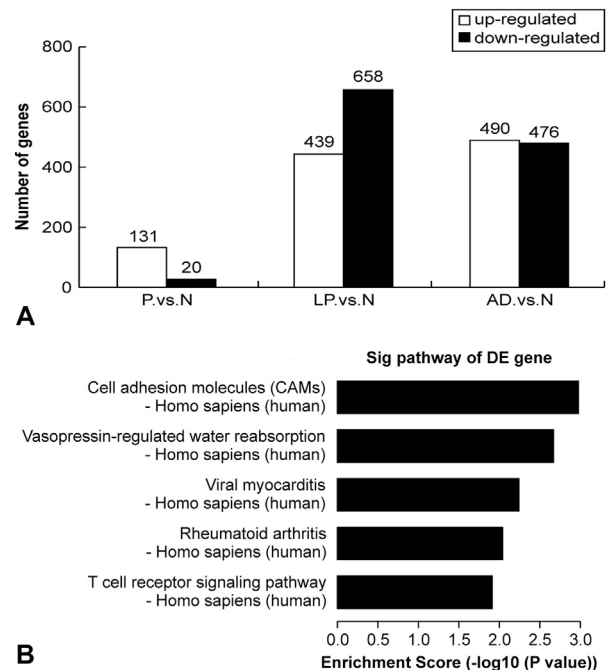


Fig 1. Number of differentially expressed genes and pathways enriched in up-regulated genes. **A**, Number of genes differentially expressed in patients with psoriasis (*P*), lichen planus (*LP*), and atopic dermatitis (*AD*), compared with those in healthy subjects (*N*). **B**, Pathway enriched in case of up-regulated genes in 3 diseases. *DE*, Differentially expressed.

factor receptor superfamily, member 8 [*CD30*]). Melting curves were obtained from 60°C to 95°C, with the temperature increasing at a rate of 0.2°C/s. PCR products were identified using 2% agarose gel electrophoresis. Differences in gene expression were analyzed using the $2^{-\Delta\Delta C_t}$ method.¹⁴

RESULTS

Profiles of DEGs in psoriasis, LP, and AD, compared with those in healthy subjects

We first analyzed gene expression in patients with the 3 inflammatory diseases and in healthy subjects. As shown in Fig 1, A, compared with healthy subjects, the up-regulated genes were 131, 439, and 490, and the down-regulated genes were 20, 658, and 476 in psoriasis, LP, and AD, respectively.

Among the 131 genes up-regulated in psoriasis, 55 were up-regulated and none were down-regulated in LP, and 48 genes were up-regulated and 3 were down-regulated in AD. Two genes were up-regulated in LP but down-regulated in AD. In all, 33 genes were up-regulated in both LP and AD (Table I).

Among the 20 genes down-regulated in psoriasis, none were up-regulated in LP and AD, whereas 10 and 12 were down-regulated in LP and AD,

Table I. List of differentially expressed genes

ID	P vs N	LP vs N	AD vs N	Gene symbol	Genbank link
3822	Down-regulated	Down-regulated	Down-regulated	KLRC2	http://www.ncbi.nlm.nih.gov/gene/?term=3822
51316	Down-regulated	Down-regulated	Down-regulated	PLAC8	http://www.ncbi.nlm.nih.gov/gene/?term=51316
5159	Down-regulated	Down-regulated	Down-regulated	PDGFRB	http://www.ncbi.nlm.nih.gov/gene/?term=5159
51744	Down-regulated	Down-regulated	Down-regulated	CD244	http://www.ncbi.nlm.nih.gov/gene/?term=51744
83888	Down-regulated	Down-regulated	Down-regulated	FGFBP2	http://www.ncbi.nlm.nih.gov/gene/?term=83888
463	Up-regulated	Up-regulated	Down-regulated	ZFH3	http://www.ncbi.nlm.nih.gov/gene/?term=463
79833	Up-regulated	Up-regulated	Down-regulated	GEMIN6	http://www.ncbi.nlm.nih.gov/gene/?term=79833
5996	Up-regulated	Up-regulated	Up-regulated	RGS1	http://www.ncbi.nlm.nih.gov/gene/?term=5996
6004	Up-regulated	Up-regulated	Up-regulated	RGS16	http://www.ncbi.nlm.nih.gov/gene/?term=6004
10221	Up-regulated	Up-regulated	Up-regulated	TRIB1	http://www.ncbi.nlm.nih.gov/gene/?term=10221
64764	Up-regulated	Up-regulated	Up-regulated	CREB3L2	http://www.ncbi.nlm.nih.gov/gene/?term=64764
10857	Up-regulated	Up-regulated	Up-regulated	PGRMC1	http://www.ncbi.nlm.nih.gov/gene/?term=10857
11123	Up-regulated	Up-regulated	Up-regulated	RCAN3	http://www.ncbi.nlm.nih.gov/gene/?term=11123
3596	Up-regulated	Up-regulated	Up-regulated	IL-13	http://www.ncbi.nlm.nih.gov/gene/?term=3596
4753	Up-regulated	Up-regulated	Up-regulated	NELL2	http://www.ncbi.nlm.nih.gov/gene/?term=4753
112464	Up-regulated	Up-regulated	Up-regulated	PRKCDBP	http://www.ncbi.nlm.nih.gov/gene/?term=112464
50616	Up-regulated	Up-regulated	Up-regulated	IL22	http://www.ncbi.nlm.nih.gov/gene/?term=50616
160418	Up-regulated	Up-regulated	Up-regulated	TMTC3	http://www.ncbi.nlm.nih.gov/gene/?term=160418
51626	Up-regulated	Up-regulated	Up-regulated	DYNC2L1	http://www.ncbi.nlm.nih.gov/gene/?term=51626
27018	Up-regulated	Up-regulated	Up-regulated	NGFRAP1	http://www.ncbi.nlm.nih.gov/gene/?term=27018
5169	Up-regulated	Up-regulated	Up-regulated	ENPP3	http://www.ncbi.nlm.nih.gov/gene/?term=5169
2706	Up-regulated	Up-regulated	Up-regulated	GJB2	http://www.ncbi.nlm.nih.gov/gene/?term=2706
54674	Up-regulated	Up-regulated	Up-regulated	LRRN3	http://www.ncbi.nlm.nih.gov/gene/?term=54674
3383	Up-regulated	Up-regulated	Up-regulated	ICAM1	http://www.ncbi.nlm.nih.gov/gene/?term=3383
55223	Up-regulated	Up-regulated	Up-regulated	TRIM62	http://www.ncbi.nlm.nih.gov/gene/?term=55223
3565	Up-regulated	Up-regulated	Up-regulated	IL4	http://www.ncbi.nlm.nih.gov/gene/?term=3565
3576	Up-regulated	Up-regulated	Up-regulated	IL8	http://www.ncbi.nlm.nih.gov/gene/?term=3576
55676	Up-regulated	Up-regulated	Up-regulated	SLC30A6	http://www.ncbi.nlm.nih.gov/gene/?term=55676
58490	Up-regulated	Up-regulated	Up-regulated	RPRD1B	http://www.ncbi.nlm.nih.gov/gene/?term=58490
653365	Up-regulated	Up-regulated	Up-regulated	ASAH2C	http://www.ncbi.nlm.nih.gov/gene/?term=653365
80854	Up-regulated	Up-regulated	Up-regulated	SETD7	http://www.ncbi.nlm.nih.gov/gene/?term=80854
8496	Up-regulated	Up-regulated	Up-regulated	PPFIBP1	http://www.ncbi.nlm.nih.gov/gene/?term=8496
85019	Up-regulated	Up-regulated	Up-regulated	TMEM241	http://www.ncbi.nlm.nih.gov/gene/?term=85019
8600	Up-regulated	Up-regulated	Up-regulated	CD254	http://www.ncbi.nlm.nih.gov/gene/?term=8600
920	Up-regulated	Up-regulated	Up-regulated	CD4	http://www.ncbi.nlm.nih.gov/gene/?term=920
940	Up-regulated	Up-regulated	Up-regulated	CD28	http://www.ncbi.nlm.nih.gov/gene/?term=940
943	Up-regulated	Up-regulated	Up-regulated	CD30	http://www.ncbi.nlm.nih.gov/gene/?term=943
9455	Up-regulated	Up-regulated	Up-regulated	HOMER2	http://www.ncbi.nlm.nih.gov/gene/?term=9455
9531	Up-regulated	Up-regulated	Up-regulated	BAG3	http://www.ncbi.nlm.nih.gov/gene/?term=9531

AD, Atopic dermatitis; ID, identity; LP, lichen planus; N, healthy individuals; P, psoriasis.

respectively. Among these, 6 genes were down-regulated in both LP and AD (Table I).

GO enrichment analysis of significant biological processes

Down-regulated and up-regulated genes were analyzed further. The up-regulated genes were significantly enriched for 17 gene terms ($P < .05$), including T-cell costimulation, and positive regulation of T-cell activation (Table II). Because there were only 3 down-regulated genes mapped to the GO database, we were interested in the enriched terms involved in all 3 genes. The gene terms

significantly enriched in the 3 down-regulated genes included signal transduction and cell communication ($P < .05$) (Table II). Most of the enriched terms were related to immune responses and signaling, both of which are involved in inflammation.

Pathway enrichment analysis

When we analyzed the DEGs for pathway enrichment (Fig 1, B), we found that the pathway significantly enriched among the down-regulated genes was natural killer cell-mediated cytotoxicity, involving CD244//KLRC2. The pathways enriched in up-regulated genes were viral myocarditis or T-cell receptor signaling. The

Table II. Significantly enriched gene ontology

GOID*	Term†	Fold enrichment‡	P value§	Enrichment score	Genes¶
0002831#	Regulation of response to biotic stimulus	27.082670	.000177	3.752213	TRIB1//CD4//CD28
0045086#	Positive regulation of interleukin-2 biosynthetic process	98.608696	.000180	3.745377	CD4//CD28
0045058#	T-cell selection	53.413043	.000629	3.201096	CD28//CD4
0038032#	Termination of G-protein-coupled receptor signaling pathway	32.869565	.001666	2.778365	RGS1//RGS16
0002697#	Regulation of immune effector process	10.338008	.002906	2.536671	ICAM1//CD28//CD4
0042108#	Positive regulation of cytokine biosynthetic process	22.489703	.003527	2.452556	CD4//CD28
0032270#	Positive regulation of cellular protein metabolic process	5.710080	.004747	2.323607	LRRN3//CD28//TRIB1//CD4
0031295#	T-cell costimulation	17.092174	.006030	2.219721	CD4//CD28
0002285#	Lymphocyte activation involved in immune response	16.434783	.006506	2.186660	ICAM1//CD28
0019722#	Calcium-mediated signaling	16.434783	.006506	2.186660	CD4//RCAN3
0051247#	Positive regulation of protein metabolic process	5.027110	.007429	2.129074	LRRN3//CD28//TRIB1//CD4
0042110#	T-cell activation	6.222879	.011839	1.926689	ICAM1//CD4//CD28
0007166#	Cell surface receptor signaling pathway	2.367337	.013416	1.872392	CD4//RGS1//HOMER2//RGS16// ICAM1//TRIB1//NGFRAP1//CD28
0008624#	Induction of apoptosis by extracellular signals	10.682609	.014869	1.827733	NGFRAP1//CD28
0046641#	Positive regulation of alpha-beta T-cell proliferation	53.413043	.018569	1.731210	CD28
0009987#	Cellular process	1.170279	.026796	1.571924	ZFHX3//GEMIN6//ICAM1//LRRN3// CREB3L2//BAG3// NGFRAP1//CD4//NELL2//PPFIBP1// RGS1//SETD7//TRIB1// ASAH2C//ENPP3//CD28// HOMER2//RCAN3//GJB2// RGS16//DYNC2LI1//SLC30A6// RPRD1B
0050870#	Positive regulation of T-cell activation	7.585284	.028230	1.549282	CD4//CD28
0007165**	Signal transduction	3.757838	.018834	1.725058	PDGFRB//KLRC2//CD244
0007154**	Cell communication	3.283296	.028240	1.549132	KLRC2//PDGFRB//CD244
0051716**	Cellular response to stimulus	3.100968	.033521	1.474677	KLRC2//PDGFRB//CD244

GOID, Gene ontology identity.

*Identity of gene ontology term used in project.

†Name of gene ontology term.

‡GOID fold enrichment value.

§Significance testing value of GOID; result obtained from top gene ontology of bioconductor.

||GOID enrichment score value, which equals $-\log_{10}(P \text{ value})$.

¶Differentially expressed genes associated with GOID.

#Terms enriched for up-regulated genes.

**Terms enriched for down-regulated genes.

T-cell receptor signaling-enriched pathway was particularly promising in the context of our study.

Verification with real-time reverse transcriptase-PCR

We verified the above expression patterns by performing real-time reverse transcriptase (RT)-

PCR for some randomly selected genes. As shown in Figs 2 and 3, A and B, *CD30*, *IL-4*, and *RGS16* expression was up-regulated in psoriasis, LP, and AD, consistent with RNA sequencing. Furthermore, *CD244* and *KLRC2* expression was down-regulated in psoriasis, consistent with the results of RNA sequencing. However, *CD244* and *KLRC2*

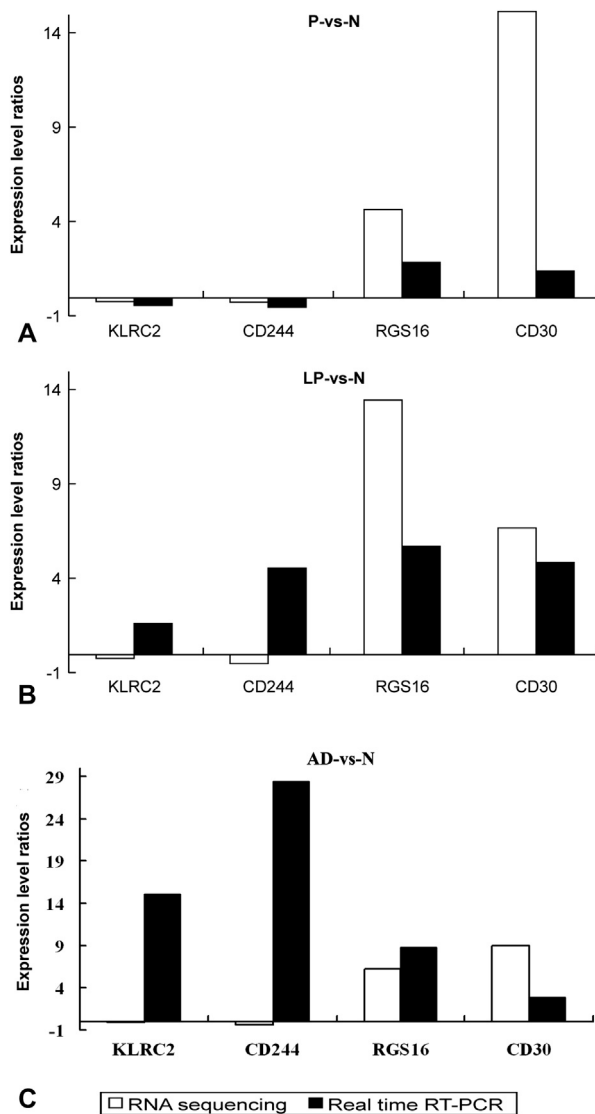


Fig 2. Expression levels of tumor necrosis factor receptor superfamily, member 8 (*CD30*), regulator of G-protein signaling 16 (*RGS16*), natural killer cell receptor 2B4 (*CD244*), and killer cell lectin-like receptor subfamily C, member 2 (*KLRC2*) in patients with psoriasis (*P*), lichen planus (*LP*), or atopic dermatitis (*AD*) compared with those in healthy subjects (*N*) by real-time reverse transcriptase (*RT*) polymerase chain reaction (*PCR*) and RNA sequencing. **A**, *P* vs *N*; **B**, *LP* vs *N*; **C**, *AD* vs *N*.

expression in *LP* was up-regulated by 4.675535- and 1.724436-fold, respectively, which was inconsistent with the results of RNA sequencing. Moreover, *CD244* and *KLRC2* expression in *AD* was higher than in healthy subjects.

Comparison of gene expression in psoriasis, *LP*, and *AD*

Psoriasis is characterized by specific changes in clinical and histopathological aspects; therefore, we

further analyzed the 33 DEGs among psoriasis, *LP*, and *AD*, and found that *RPRD1B* (ID 58490) expression was up-regulated in all patients with psoriasis, *LP*, or *AD* and its expression level in psoriasis was significantly higher than in *LP* and *AD* (Fig 3, *C* and *D*).

Real-time RT-PCR results showed that the *RPRD1B* expression levels in psoriasis, *LP*, and *AD* were 2.670689-, 2.14938-, and 2.358243-fold of that in healthy subjects, respectively. Moreover, *RPRD1B* expression in psoriasis was 1.242539- and 1.132491-fold that in *LP* and *AD*, respectively.

DISCUSSION

Psoriasis is a T cell-mediated chronic inflammatory skin disease similar to *LP* and *AD* in pathogenesis. Immunomodulators were used for the treatment of psoriasis and *LP*, but frequently produce a rebound phenomenon after cessation. Expression of allograft inflammatory factor-1 increases in both psoriasis and *LP*.¹⁵ In addition, the proportion of Foxp3⁺ T cells is similar in *LP* and psoriasis (25% vs 29%).¹⁶ Moreover, moderate to strongly positive CD10 expression is seen in the lesions of plaque psoriasis (16/16), *LP* (18/20), and *AD* (4/5).¹⁷ Therapeutic studies have shown that peptide analogs of the T-cell receptor have a significant therapeutic effect on psoriasis, *LP*, and *AD*, and that Toll-like receptor plays important roles in the onset of psoriasis, *LP*, and *AD*.^{18,19} Clinical studies have shown that production and secretion of IL-2, IL-4, and interferon- γ have good therapeutic effects on psoriasis, *LP*, and *AD*,²⁰ suggesting that cytokines and T cells play important roles in the pathogenesis of all 3 diseases.

Current dermatologic studies have focused on finding pathogenic differences among the 3 diseases to explain the mechanisms that result in their specific clinical and pathological characteristics. Interferon- κ is not expressed in normal-appearing skin but is highly expressed in *LP*, and only slightly enhanced in psoriasis and *AD*.²¹ The number of CD8⁺ T cells in the epidermis of psoriasis is higher than *LP* and *AD*, whereas the number of CD45RO⁺ T cells is the highest in *LP*. Compared with *LP* and *AD*, psoriasis has accelerated keratinocyte proliferation and significantly decreased keratin expression.²² Moreover, corneodesmosin is highly expressed in the stratum corneum and multiple layers of the stratum spinosum in psoriatic lesions, whereas in *LP* and chronic *AD*, it is only expressed in the stratum corneum and upper granular layer but not in the stratum spinosum.²³ Other studies have shown that chemokine (C-X-C motif) ligand 9 expression in *LP* is significantly different from psoriasis and *AD*.²⁴

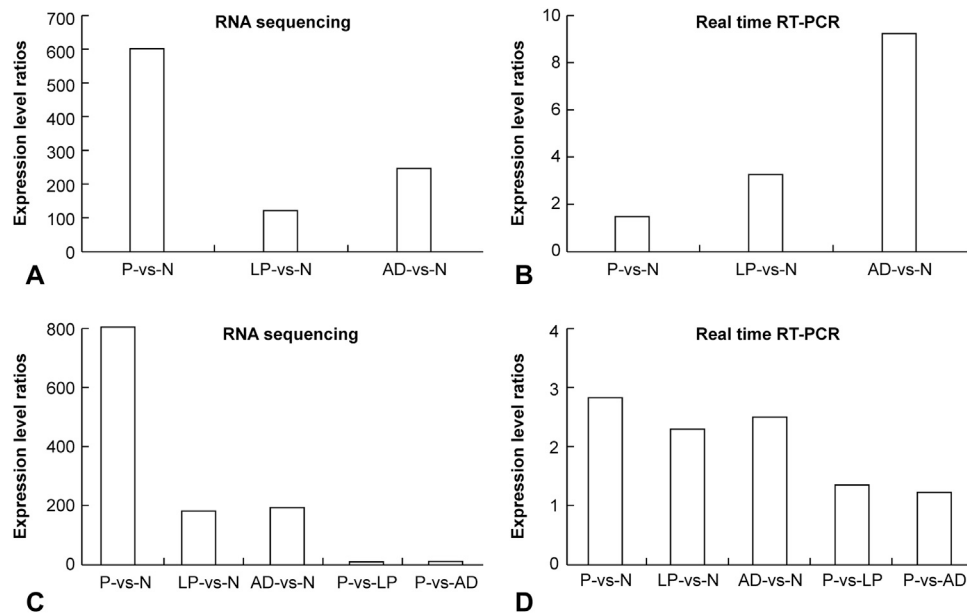


Fig 3. Messenger RNA expression levels of interleukin (*IL*)-4 and regulation of nuclear pre-messenger RNA domain containing 1B (*RPRD1B*). RNA sequencing results for *IL-4* (A) and *RPRD1B* (C). Real-time reverse transcriptase (RT)-polymerase chain reaction (PCR) results for *IL-4* (B) and *RPRD1B* (D). AD, Atopic dermatitis; LP, lichen planus; N, healthy individuals; P, psoriasis.

Studies on the differences in peripheral blood T-cell activity in psoriasis compared with LP and AD in the Chinese population are rare.

In this study, we screened the DEGs in psoriasis, LP, and AD, and further analyzed those specific to psoriasis. We found that *RPRD1B* expression is higher in peripheral blood T cells in psoriasis, LP, and AD than in healthy subjects and that *RPRD1B* expression is higher in psoriasis than LP and AD. *RPRD1B* binds to RNA polymerase II during transcription to reduce the level of phosphorylated RNA polymerase II at CTD-S5 and CTD-S7 of its promoter.²⁵ *RPRD1B* plays a crucial role in the transcription of many genes. *RPRD1B* was found to accelerate cyclin D1 expression by binding to the promoter of the corresponding gene.²⁶ It is involved in the onset of the 3 inflammatory diseases studied here by regulating the transcription of many genes, including *IL-4*, *RGS16*, and *CD30*, and enhanced *RPRD1B* expression is one of the reasons for abnormal *IL-4*, *RGS16*, and *CD30* expression in these diseases. *RPRD1B* expression is higher in psoriasis than in LP and AD, at least in Chinese individuals, and plays an important role in the occurrence of psoriasis-specific clinical and pathological manifestations, but the exact mechanism still requires further investigation. It is sometimes difficult to differentially diagnose these conditions based only on the features of the lesions. Therefore, further studies on *RPRD1B* may also be

helpful for diagnosing diseases wherein the lesions are not specific and where the patients cannot endure histologic testing.

Considering the similarities among the 3 diseases, the common DEGs between patients with any of the 3 diseases and healthy subjects were also studied. GO terms and pathways were enriched for 39 genes related to T-cell responses. In particular, the up-regulated genes were enriched for genes involved in positive regulation of T-cell activation; this finding showed that T-cell activation increases in all 3 diseases, which is in agreement with the results of previous studies and emphasizes the critical role of T cells in the pathogenesis of aforementioned diseases.

Our results showed that *IL-4* expression is augmented in patients with quiescent psoriasis, LP, and AD, which is consistent with previous findings,^{12,27-30} and supports the theory that the balance between Th1- and Th2-type cytokines shifts during the course of psoriasis and AD. Enhanced *RGS16* expression in T cells at the early G1 phase may contribute to the process through to the late G1 phase,³¹ increasing the proliferative activity of T cells and may be indirectly involved in the pathogenesis and development of these diseases.

Our RNA sequencing results showed decreased *KLRC2* expression in psoriasis, LP, and AD. However, this was not confirmed by real-time RT-PCR, suggesting that changes in *KLRC2* expression possibly resulted from T-cell activation and local cytokines

responses and did not significantly affect the onset or development of these 3 diseases. However, we could not exclude that the discordance in *KLRC2* expression as determined by real-time RT-PCR and RNA sequencing is a result of variations in the specimens collected.

CONCLUSION

RPRD1B expression is higher in psoriasis than LP and AD, at least in the Chinese population, which may play an important role in the occurrence of psoriasis-specific clinical and pathological manifestations; however, the exact mechanism requires further investigation. Further study of *RPRD1B* may also be helpful for the differential diagnosis of these diseases, when lesions are not specific and biopsy is not possible.

The up-regulated genes were enriched for the positive regulation of T-cell activation, and emphasizes the critical role of T cells in the pathogenesis of the aforementioned diseases.

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