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## Looking within the lesion: Large scale transcriptional profiling of psoriatic plaques

Mimoso C *et al.* Psoriatic transcriptome

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**Abstract**

Psoriasis is a lifelong, chronic, recurring and highly variable skin disease. Psoriatic plaques are formed through induction of inflammation in the epidermis and deregulation of keratinocyte proliferation and differentiation. This results in red or silvery scaly patches on the surface of the epidermis. To look within the lesions and define the changes in gene expression in psoriasis, investigators compared the transcriptomes of psoriatic plaques, of uninvolved skin of patients and of skin from healthy individuals. In several large studies with many patients, the genes expressed at much higher level in psoriatic plaques included those responsible for the cell cycle, keratinocyte differentiation, and response to wounding; conversely, lipid and fatty acid metabolism enzymes were expressed at reduced levels. The nonlesional and healthy skin appeared fairly similar. The largest study included paired biopsies from 85 individual patients. The same group used transcription profiling to follow the course of treatment in a set of patients, and correlated changes in the transcriptome of blood samples of psoriatic patients. Importantly, a noninvasive technique involving tape-stripping of skin, has been shown effective in transcriptional studies of psoriasis. Current efforts are focused on deconvoluting the contributions of various cell types in psoriasis, keratinocytes, lymphocytes, fibroblasts etc. Taken as a whole, these efforts will lead to personalized medicine, *i.e.,* to specific, individualized treatments of patients with psoriasis.

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**Key words:** Cytokines; Inflammation; Metaanalysis; Microarrays; Skinomics

**Core tip**: Dermatology was among the first medical specialties to adopt bioinformatics methodology, and Psoriasis, with its high prevalence, among the first diseases. Genome-wide association studies identified close to 50 genetic predisposition loci, to date. Recently, large-scale transcriptome analysis using DNA microarrays identified the important signaling pathways and regulators of gene expression in psoriasis. These efforts, and the fundamental knowledge they provide will lead to personalized medicine, *i.e.*, to specific, individualized treatments of psoriatic patients in the near future.

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**INTRODUCTION**

According to the National Psoriasis Foundation, psoriasis affects 7.5 million Americans and 125 million people worldwide. It is a chronic autoimmune disease with a multifactorial (genetic and environmental) etiology[1]. Past research suggests that external, internal and/or environmental triggers, such as stress, systemic illnesses and environmental allergens, combined with the genetic predisposition, may result in an altered immunity and an increased risk for the development of psoriasis[2]. However, the initial trigger for psoriasis and development of psoriatic lesions remains unknown[3-5]. While the exact causes are unknown, in psoriasis the immune system sends out incorrect signals that speed up the proliferation of epidermal keratinocytes. While normal keratinocytes mature and desquamate in about a month, psoriatic skin ones reach the surface in only 3-4 d and, instead of sloughing off individually, they accumulate to form large flaking scraps of skin[2].

Psoriasis is typically a lifelong, chronic recurring condition. It can vary in severity from small localized areas to covering the entire body. The diagnosis of psoriasis is based on the appearance of skin, not on blood tests or specialized diagnostic procedures. Occasionally a skin biopsy may be needed to rule out other proliferative skin disorders. Psoriatic plaques are formed through an increase in inflammation in the epidermis, deregulation of cell cycle processes, increase in keratinocyte proliferation and epidermal differentiation changes. Together this results in the formation of raised, red or silvery scaly patches on the surface of the stratum corneum.

The genetic predisposition for psoriasis was known through family-based and population-based epidemiological studies, which suggested that genetic factors play a key role in the development of psoriasis[6-7]. Perhaps a third of psoriatic patients report a family history of psoriasis; reports on monozygotic twins find a 70% chance of a twin developing psoriasis if the other twin has psoriasis while this number is around 20% for paternal twins. More recently, genome-wide association scans have fine-mapped the nine susceptibility loci (PSORS1 – PSORS9) and located many previously unsuspected genomic markers on human chromosomes[6,8-11]. A current list of psoriasis susceptibility loci is given in Table 1. However, the known genetic factors for psoriasis do not account for all observed genetic susceptibility to psoriasis; additional genetic factors remain to be discovered[6]. Thus, the genetic contribution to psoriasis is not fully understood[3].

Of the five types of psoriasis (plaque, guttate, inverse, pustular, and erythrodermic), the most common is the plaque psoriasis. Plaque psoriasis is seen as red and white silvery hues of scaly patches appearing on the top of the epidermis. Plaques frequently occur on the extensor aspects of the knees and elbows, but can affect any area, including the scalp, genitals, palms and soles. Fingernails and toenails are often affected, which can be an independent symptom. Additionally, psoriasis can be associated with inflammation of the joints, which is known as psoriatic arthritis. Guttate psoriasis presents as numerous small, scaly, pink or red lesions over large areas of the body, the trunk, limbs and scalp. Inverse or flexural psoriasis occurs in skin folds, e.g., around the genitals, the armpits or under the breasts.Pustular psoriasis presents as raised pus-filled bumps, commonly on the hands and feet (*i.e.,* palmoplantar pustulosis), or generalized, occurring randomly widespread on any part of the body. Erythrodermic psoriasis involves the widespread inflammation and exfoliation over most of the body skin. While the shared symptoms, *i.e.,* the underlying inflammation and epidermal hyperproliferation, characterize all types of psoriasis, the distinct clinical presentations, the extensive and dispersed genetic underpinnings and inconsistent, variable clinical responses argue that psoriasis comprises a cluster of related but distinct disorders.

The superb international success in GWAS mapping the psoriasis susceptibility loci has been joined recently by equally outstanding transcriptional profiling studies from several laboratories that recruited very impressive numbers of patients and samples (Table 2). These studies provide deep and comprehensive insights into the molecular mechanisms of the pathology of psoriasis. Also an international effort, the transcriptional profiling is lead by two teams in the United States, that of Drs. G. Gudjonsson and J.T. Elder at the University of Michigan, and the team of Dr. J.G. Krueger at the Rockefeller University. The researchers compared the genes expressed in psoriatic plaques with those expressed in the nonlesional skin of patients, and both of these with the skin of healthy control subjects. Investigators also searched for diagnostic markers of psoriasis in the blood of patients. The current status and insights from these efforts is the subject of this review.

**DISCUSSION**

In a very influential study Gudjonsson *et al*[12] analyzed a large cohort of psoriatic patients and healthy controls using transcriptional profiling. Importantly, their analysis included 58 paired samples of lesional and nonlesional skin, allowing comparisons of matched samples from the same patients, and 64 control biopsies, allowing large-scale comparisons of lesional and nonlesional skin with healthy skin[11-15]. The sheer size of this study allowed the authors to identify close to a thousand differentially expressed genes in the lesional skin. The genes overrepresented in the psoriasis lesions included Serpins, β-defensin-2, S100A genes and IL-8. Suppressed genes includedβ-cellulin, IL1F7 and CCL27. The ontological categories induced in the lesions incorporated cell cycle, expected in this hyperproliferative disease, keratinocyte differentiation markers and three categories that contained cytokines, chemokines and their receptors, namely immune response, defense response and response to wounding[14]. The suppressed ontological categories incorporated lipid and fatty acid metabolism. The nonlesional and healthy skin, however, appeared rather similar, confirming the results of Yao et al. (see below)[16].

In an important follow-up a team in United Kingdom, collaborating with Dr Gudjonsson, used sophisticated bioinformatics methodologies to classify psoriatic patients and identify distinct molecular subtypes[15]. Again, the nonlesional and healthy skin appeared quite similar. Among the psoriatic plaque samples, two subtypes were identified using multidimensional scaling, one a tightly clustered group of patients at the apex of the less congruent and more dispersed subtype. The authors proposed that TGF and the ErbB pathways may be involved in distinguishing the two subtypes.

The ground-breaking large-scale transcriptional profiling of psoriatic samples was reported by the team of Dr Krueger in 2009[16]. They analyzed 33 lesional, 30 non-lesional and 21 healthy control samples. The nonlesional skin was more similar to healthy skin of other donors that to the lesional skins from the same patient. The transcriptional signatures of the plaque biopsies pointed to the infiltration of T cells and dendritic cells in the lesions. Yao *et al*[16] recognized the signatures of several cytokines implicated in psoriasis. Specifically, they compared genes differentially expressed in the lesions with the gene sets regulated by IFNα, IFNγ and by TNFαin keratinocytes. The significant overlaps substantiated the proposed roles of these cytokines in psoriasis. Several members of IFNα family, IFN-α1, IFN-α2, IFN-α6, IFN-α7, IFN-α8, IFN-α14 and IFN-α21, were overexpressed in the lesions. The results validated the TNFα-targeting and the T cell targeting therapies currently in wide use to treat psoriasis, as well as suggested IFNα as a potential target.

Interestingly, in a separate study, Dr. Krueger’s team found that a single injection of IFNγ into the dermis of nonlesional sites of psoriatics can recapitulate the transcription profile changes seen in the psoriatic plaques[17]. Apparently, IFNγ can initiate the psoriasiform immune responses by promoting influx of T cells and dendritic cells. A similar influx was seen even in the IFNγ-injected sites of healthy, non-psoriatic individuals.

The same team followed transcriptional changes in psoriatic patients treated with Etanercept[18]. Baseline transcriptional profiles were compared with those in treatment for up to 12 wk. The patients were divided into responders (11 patients) and non-responders (4 patients). Interestingly, the TNFα-regulated genes (*e.g.,* IL1β and IL8) were silenced in both groups; however the responders specifically inactivated the genes associated with the Th17 immune responses. The study highlighted the distinguishing and important role of the Th17 pathway in the pathology of psoriasis.

The largest transcriptional profiling study of psoriasis patients, to date, was reported by Suarez-Farinas in 2012[19]. The Rockefeller University team compared 85 matched pairs of lesional and nonlesional biopsies from patients. The impressively large study identified 2725 individual genes differentially expressed 2-fold or more in the plaques. Serpins and S100A proteins were among the most overexpressed genes, but also many proteases/peptidases, including Kallikrein-related peptidase-6, -13, *etc*. Conversely, β-cellulin, CCL27 and lipid and fatty acid metabolism enzymes were found suppressed in the plaques, as seen by others[12,19]. The authors confirmed the results of transcriptional profiling using extensive RT-PCR and immunohistological experiments.

In this study by Suarez-Farinas[19], the sets of regulated genes were compared with the sets identified in two previous studies[12,16]. Very high correlation was seen (scores ranging from 0.83 to 0.94) demonstrating very high concordance of the gene expression changes in psoriasis across the three large studies in two different centers. The concordance among different studies received extensive scrutiny[20-21], and it was found that, provided appropriate statistical methodologies are used, the studies are very highly concordant. The concordance allowed a metaanalysis of psoriasis transcriptomics studies[22]. The metaanalysis identified over 1000 genes that were consistently differentially expressed over 5 different studies. Moreover, this study provided a link between changes in the psoriasis transcriptome and atherosclerosis signaling, lipid and fatty acid metabolism and cardiovascular disease, thus providing a crucial link between the psoriatic skin conditions and these systemic diseases. Tian *et al*[22] in 2012, defined a “core” 20-gene set that distinguishes the psoriatic lesions. Interestingly, this core contained genes overexpressed even in psoriatic skin after successful treatment, as well as distinct genes epigenetically labeled by differential methylation in plaques.

Suarez-Farinas et al. also compared serum protein levels of 12 important secreted proteins detected as overrepresented in psoriatic plaques[19]. In large cohort of approximately 150 patients and as many controls, all 12 proteins were found at increased levels in the sera of patients. The proteins included CCL2, CCL22, CXCL5 and TNFα, which are all markers of psoriasis.

Using transient unresponsiveness to the stimulation of dendritic cells as a model of chronic inflammation, such as in psoriasis, Filkor *et al*[23] found the expression of feedback regulators of innate immunity to be suppressed, such as TNFAIP3 and TNFAIP8; these are also suppressed in the dermis of psoriatic patients.

In a study of matched lesional and nonlesional samples from 13 patients, in 2007, Reischl et al. identified 179 genes differentially expressed 2-fold or more[24]. Interestingly, 16 statistically significant genes were associated with the Wnt/β-catenin pathway, leading the authors to propose an important role for this pathway in psoriasis. Attempts to distinguish differences in the transcriptomes of plaques from different body sites, and between patients with symmetric and asymmetric plaques have not been successful[25]. In a more limited study of just 44 genes, Aubert *et al*[26] found that in psoriasis of the scalp, treatment with topical steroids restores expression of the 10 inflammation-related genes to the more basal, healthy levels. Similar results were found in a study of 5 lesional and 5 nonlesional samples, compared with similar number of blood samples[27]. Using a completely different approach, involving metaanalysis of data in public repositories, specifically the BodyMap gene expression database[28], and RNA sequencing, *Itoh* et al[29] found very similar sets of differentially expressed genes. Others have noted the overlaps between genes differentially expressed in psoriasis and regulated by cytokines in epidermal keratinocytes[30-36].

In a study of matched lesional and nonlesional samples from 15 patients and 6 healthy controls, the team of Bowcock *et al*[37] a collaboration of Washington U. and Baylor U., also found overexpression of serpins and S100A proteins, but also of keratins KRT6, KRT16 and KRT17, known markers of epidermal hyperproliferation[38]. These studies also addressed the transcription factors responsible for the expression of differentially expressed genes and found NF-κB and AP1 sites evident, as expected. In addition, sites for nuclear receptors, RORa1, VDR and PPAR are found in the regulated genes, as are the motifs bound by Ikaros proteins, zinc finger transcription factors characteristic for lymphoid cell lineages. A similar set of transcription factors associated with psoriasis, additionally including E2F1 was proposed in another study[39]. Using a completely different approach, involving proteomics, NF-κB, AP1, STAT1 and STAT3 proteins were identified as important in psoriasis transcriptional deregulation[40].

In an exciting and sophisticated skinomics approach, Swindell *et al*[41] were able to assign most of the differentially expressed genes in the psoriatic plaques to the different cell types that contribute to the disease[41]. Specifically, they found that the genes induced in the plaques derive mainly from the activated keratinocytes, 56%, infiltrating T-cells, 14%, and macrophages, 11%. The suppressed genes were derived from the adipose, epidermis and dermis 4%. Swindell *et al*[41] also distinguished the patients who responded to Etanercept from the non-responders by their respective transcriptional profiles. Moreover, they confirmed the induction of genes responding to several cytokines, including IFN IL-1, IL-17A and TNF-α.

Importantly, skin samples can be obtained using noninvasive and (almost) painless technique of tape-stripping. This method provides RNA samples of quality and quantity adequate for microarray analysis[42]. Using tape-stripping followed by RT-PCR, Benson *et al*[43] have detected increased levels of mRNAs for TNFα, IF and KRT16, among others, in psoriatic plaques.

**CONCLUSIONS AND FUTURE PROSPECTS**

Whereas the future is inherently unpredictable, currently several trends seem to guide the research in transcriptional changes in psoriasis. First, stratification of patients into categories (*e.g.,* etanercept responders) will allow personalized medicine approaches to be developed and used in the treatment of psoriasis. Second, the exact roles of the immune cell types, the cytokines and chemokines they produce and the signaling pathways consequently activated in the responding keratinocytes will provide scores of additional targets, which will further advance patient-specific treatments. And third, an exciting new area of research, that of the effects of the cutaneous microbiome on psoriasis initiation, progression and resolution[44-47] has the potential to revolutionize our conceptual and practical approach to this intractable and difficult problem.

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**REFERENCES**

1 **de Cid R**, Riveira-Munoz E, Zeeuwen PL, Robarge J, Liao W, Dannhauser EN, Giardina E, Stuart PE, Nair R, Helms C, Escaramís G, Ballana E, Martín-Ezquerra G, den Heijer M, Kamsteeg M, Joosten I, Eichler EE, Lázaro C, Pujol RM, Armengol L, Abecasis G, Elder JT, Novelli G, Armour JA, Kwok PY, Bowcock A, Schalkwijk J, Estivill X. Deletion of the late cornified envelope LCE3B and LCE3C genes as a susceptibility factor for psoriasis. *Nat Genet* 2009; **41**: 211-215 [PMID: 19169253 DOI: 10.1038/ng.313]

2 **Halprin KM**. Epidermal "turnover time"--a re-examination. *Br J Dermatol* 1972; **86**: 14-19 [PMID: 4551262]

3 **Duffin KC**, Chandran V, Gladman DD, Krueger GG, Elder JT, Rahman P. Genetics of psoriasis and psoriatic arthritis: update and future direction. *J Rheumatol* 2008; **35**: 1449-1453 [PMID: 18609743]

4 **Griffiths CE**, Barker JN. Pathogenesis and clinical features of psoriasis. *Lancet* 2007; **370**: 263-271 [PMID: 17658397]

5 **Bowcock AM**, Krueger JG. Getting under the skin: the immunogenetics of psoriasis. *Nat Rev Immunol* 2005; **5**: 699-711 [PMID: 16138103]

6 **Stuart PE**, Nair RP, Ellinghaus E, Ding J, Tejasvi T, Gudjonsson JE, Li Y, Weidinger S, Eberlein B, Gieger C, Wichmann HE, Kunz M, Ike R, Krueger GG, Bowcock AM, Mrowietz U, Lim HW, Voorhees JJ, Abecasis GR, Weichenthal M, Franke A, Rahman P, Gladman DD, Elder JT. Genome-wide association analysis identifies three psoriasis susceptibility loci. *Nat Genet* 2010; **42**: 1000-1004 [PMID: 20953189 DOI: 10.1038/ng.693]

7 **Sun LD**, Cheng H, Wang ZX, Zhang AP, Wang PG, Xu JH, Zhu QX, Zhou HS, Ellinghaus E, Zhang FR, Pu XM, Yang XQ, Zhang JZ, Xu AE, Wu RN, Xu LM, Peng L, Helms CA, Ren YQ, Zhang C, Zhang SM, Nair RP, Wang HY, Lin GS, Stuart PE, Fan X, Chen G, Tejasvi T, Li P, Zhu J, Li ZM, Ge HM, Weichenthal M, Ye WZ, Zhang C, Shen SK, Yang BQ, Sun YY, Li SS, Lin Y, Jiang JH, Li CT, Chen RX, Cheng J, Jiang X, Zhang P, Song WM, Tang J, Zhang HQ, Sun L, Cui J, Zhang LJ, Tang B, Huang F, Qin Q, Pei XP, Zhou AM, Shao LM, Liu JL, Zhang FY, Du WD, Franke A, Bowcock AM, Elder JT, Liu JJ, Yang S, Zhang XJ. Association analyses identify six new psoriasis susceptibility loci in the Chinese population. *Nat Genet* 2010; **42**: 1005-1009 [PMID: 20953187 DOI: 10.1038/ng.690]

8 **Tsoi LC**, Spain SL, Knight J, Ellinghaus E, Stuart PE, Capon F, Ding J, Li Y, Tejasvi T, Gudjonsson JE, Kang HM, Allen MH, McManus R, Novelli G, Samuelsson L, Schalkwijk J, Ståhle M, Burden AD, Smith CH, Cork MJ, Estivill X, Bowcock AM, Krueger GG, Weger W, Worthington J, Tazi-Ahnini R, Nestle FO, Hayday A, Hoffmann P, Winkelmann J, Wijmenga C, Langford C, Edkins S, Andrews R, Blackburn H, Strange A, Band G, Pearson RD, Vukcevic D, Spencer CC, Deloukas P, Mrowietz U, Schreiber S, Weidinger S, Koks S, Kingo K, Esko T, Metspalu A, Lim HW, Voorhees JJ, Weichenthal M, Wichmann HE, Chandran V, Rosen CF, Rahman P, Gladman DD, Griffiths CE, Reis A, Kere J, Nair RP, Franke A, Barker JN, Abecasis GR, Elder JT, Trembath RC. Identification of 15 new psoriasis susceptibility loci highlights the role of innate immunity. *Nat Genet* 2012; **44**: 1341-1348 [PMID: 23143594 DOI: 1310.1038/ng.2467]

9 **Strange A**, Capon F, Spencer CC, Knight J, Weale ME, Allen MH, Barton A, Band G, Bellenguez C, Bergboer JG, Blackwell JM, Bramon E, Bumpstead SJ, Casas JP, Cork MJ, Corvin A, Deloukas P, Dilthey A, Duncanson A, Edkins S, Estivill X, Fitzgerald O, Freeman C, Giardina E, Gray E, Hofer A, Hüffmeier U, Hunt SE, Irvine AD, Jankowski J, Kirby B, Langford C, Lascorz J, Leman J, Leslie S, Mallbris L, Markus HS, Mathew CG, McLean WH, McManus R, Mössner R, Moutsianas L, Naluai AT, Nestle FO, Novelli G, Onoufriadis A, Palmer CN, Perricone C, Pirinen M, Plomin R, Potter SC, Pujol RM, Rautanen A, Riveira-Munoz E, Ryan AW, Salmhofer W, Samuelsson L, Sawcer SJ, Schalkwijk J, Smith CH, Ståhle M, Su Z, Tazi-Ahnini R, Traupe H, Viswanathan AC, Warren RB, Weger W, Wolk K, Wood N, Worthington J, Young HS, Zeeuwen PL, Hayday A, Burden AD, Griffiths CE, Kere J, Reis A, McVean G, Evans DM, Brown MA, Barker JN, Peltonen L, Donnelly P, Trembath RC. A genome-wide association study identifies new psoriasis susceptibility loci and an interaction between HLA-C and ERAP1. *Nat Genet* 2010; **42**: 985-990 [PMID: 20953190 DOI: 10.1038/ng.694]

10 **Ellinghaus E**, Ellinghaus D, Stuart PE, Nair RP, Debrus S, Raelson JV, Belouchi M, Fournier H, Reinhard C, Ding J, Li Y, Tejasvi T, Gudjonsson J, Stoll SW, Voorhees JJ, Lambert S, Weidinger S, Eberlein B, Kunz M, Rahman P, Gladman DD, Gieger C, Wichmann HE, Karlsen TH, Mayr G, Albrecht M, Kabelitz D, Mrowietz U, Abecasis GR, Elder JT, Schreiber S, Weichenthal M, Franke A. Genome-wide association study identifies a psoriasis susceptibility locus at TRAF3IP2. *Nat Genet* 2010; **42**: 991-995 [PMID: 20953188 DOI: 10.1038/ng.689]

11 **Nair RP**, Duffin KC, Helms C, Ding J, Stuart PE, Goldgar D, Gudjonsson JE, Li Y, Tejasvi T, Feng BJ, Ruether A, Schreiber S, Weichenthal M, Gladman D, Rahman P, Schrodi SJ, Prahalad S, Guthery SL, Fischer J, Liao W, Kwok PY, Menter A, Lathrop GM, Wise CA, Begovich AB, Voorhees JJ, Elder JT, Krueger GG, Bowcock AM, Abecasis GR. Genome-wide scan reveals association of psoriasis with IL-23 and NF-kappaB pathways. *Nat Genet* 2009; **41**: 199-204 [PMID: 19169254 DOI: 10.1038/ng.311]

12 **Gudjonsson JE**, Ding J, Johnston A, Tejasvi T, Guzman AM, Nair RP, Voorhees JJ, Abecasis GR, Elder JT. Assessment of the psoriatic transcriptome in a large sample: additional regulated genes and comparisons with in vitro models. *J Invest Dermatol* 2010; **130**: 1829-1840 [PMID: 20220767 DOI: 10.1038/jid.2010.36]

13 **Ding J**, Gudjonsson JE, Liang L, Stuart PE, Li Y, Chen W, Weichenthal M, Ellinghaus E, Franke A, Cookson W, Nair RP, Elder JT, Abecasis GR. Gene expression in skin and lymphoblastoid cells: Refined statistical method reveals extensive overlap in cis-eQTL signals. *Am J Hum Genet* 2010; **87**: 779-789 [PMID: 21129726 DOI: 10.1016/j.ajhg.2010.10.024]

14 **Gudjonsson JE**, Ding J, Li X, Nair RP, Tejasvi T, Qin ZS, Ghosh D, Aphale A, Gumucio DL, Voorhees JJ, Abecasis GR, Elder JT. Global gene expression analysis reveals evidence for decreased lipid biosynthesis and increased innate immunity in uninvolved psoriatic skin. *J Invest Dermatol* 2009; **129**: 2795-2804 [PMID: 19571819 DOI: 2710.1038/jid.2009.2173]

15 **Ainali C**, Valeyev N, Perera G, Williams A, Gudjonsson JE, Ouzounis CA, Nestle FO, Tsoka S. Transcriptome classification reveals molecular subtypes in psoriasis. *BMC Genomics* 2012; **13**: 472 [PMID: 22971201 DOI: 10.1186/1471-2164-13-472]

16 **Yao Y**, Richman L, Morehouse C, de los Reyes M, Higgs BW, Boutrin A, White B, Coyle A, Krueger J, Kiener PA, Jallal B. Type I interferon: potential therapeutic target for psoriasis? *PLoS One* 2008; **3**: e2737 [PMID: 18648529 DOI: 10.1371/journal.pone.0002737]

17 **Johnson-Huang LM**, Suárez-Fariñas M, Pierson KC, Fuentes-Duculan J, Cueto I, Lentini T, Sullivan-Whalen M, Gilleaudeau P, Krueger JG, Haider AS, Lowes MA. A single intradermal injection of IFN-γ induces an inflammatory state in both non-lesional psoriatic and healthy skin. *J Invest Dermatol* 2012; **132**: 1177-1187 [PMID: 22277938 DOI: 1110.1038/jid.2011.1458]

18 **Zaba LC**, Suárez-Fariñas M, Fuentes-Duculan J, Nograles KE, Guttman-Yassky E, Cardinale I, Lowes MA, Krueger JG. Effective treatment of psoriasis with etanercept is linked to suppression of IL-17 signaling, not immediate response TNF genes. *J Allergy Clin Immunol* 2009; **124**: 1022-10.e1-395 [PMID: 19895991 DOI: 10.1016/j.jaci.2009.08.046]

19 **Suárez-Fariñas M**, Li K, Fuentes-Duculan J, Hayden K, Brodmerkel C, Krueger JG. Expanding the psoriasis disease profile: interrogation of the skin and serum of patients with moderate-to-severe psoriasis. *J Invest Dermatol* 2012; **132**: 2552-2564 [PMID: 22763790 DOI: 2510.1038/jid.2012.2184.]

20 **Suárez-Fariñas M**, Lowes MA, Zaba LC, Krueger JG. Evaluation of the psoriasis transcriptome across different studies by gene set enrichment analysis (GSEA). *PLoS One* 2010; **5**: e10247 [PMID: 20422035 DOI: 10.1371/journal.pone.0010247]

21 **Bigler J**, Rand HA, Kerkof K, Timour M, Russell CB. Cross-study homogeneity of psoriasis gene expression in skin across a large expression range. *PLoS One* 2013; **8**: e52242 [PMID: 23308107 DOI: 52210.51371/journal.pone.0052242.]

22 **Tian S**, Krueger JG, Li K, Jabbari A, Brodmerkel C, Lowes MA, Suárez-Fariñas M. Meta-analysis derived (MAD) transcriptome of psoriasis defines the "core" pathogenesis of disease. *PLoS One* 2012; **7**: e44274 [PMID: 22957057 DOI: 10.1371/journal.pone.0044274]

23 **Filkor K**, Hegedűs Z, Szász A, Tubak V, Kemény L, Kondorosi É, Nagy I. Genome wide transcriptome analysis of dendritic cells identifies genes with altered expression in psoriasis. *PLoS One* 2013; **8**: e73435 [PMID: 24039940 DOI: 73410.71371/journal.pone.0073435.]

24 **Reischl J**, Schwenke S, Beekman JM, Mrowietz U, Stürzebecher S, Heubach JF. Increased expression of Wnt5a in psoriatic plaques. *J Invest Dermatol* 2007; **127**: 163-169 [PMID: 16858420]

25 **Quekenborn-Trinquet V**, Fogel P, Aldana-Jammayrac O, Ancian P, Demarchez M, Rossio P, Richards HL, Kirby B, Nguyen C, Voegel JJ, Griffiths CE. Gene expression profiles in psoriasis: analysis of impact of body site location and clinical severity. *Br J Dermatol* 2005; **152**: 489-504 [PMID: 15787818]

26 **Aubert J**, Reiniche P, Fogel P, Poulin Y, Lui H, Lynde C, Shapiro J, Villemagne H, Soto P, Voegel JJ. Gene expression profiling in psoriatic scalp hair follicles: clobetasol propionate shampoo 0.05% normalizes psoriasis disease markers. *J Eur Acad Dermatol Venereol* 2010; **24**: 1304-1311 [PMID: 20337827 DOI: 1310.1111/j.1468-3083.2010.03637.x]

27 **Coda AB**, Icen M, Smith JR, Sinha AA. Global transcriptional analysis of psoriatic skin and blood confirms known disease-associated pathways and highlights novel genomic "hot spots" for differentially expressed genes. *Genomics* 2012; **100**: 18-26 [PMID: 22584065 DOI: 10.1016/j.ygeno.2012.1005.1004]

28 **Hishiki T**, Kawamoto S, Morishita S, Okubo K. BodyMap: a human and mouse gene expression database. *Nucleic Acids Res* 2000; **28**: 136-138 [PMID: 10592203]

29 **Itoh K**, Kawasaki S, Kawamoto S, Seishima M, Chiba H, Michibata H, Wakimoto K, Imai Y, Minesaki Y, Otsuji M, Okubo K. Identification of differentially expressed genes in psoriasis using expression profiling approaches. *Exp Dermatol* 2005; **14**: 667-674 [PMID: 16098126]

30 **Mee JB**, Johnson CM, Morar N, Burslem F, Groves RW. The psoriatic transcriptome closely resembles that induced by interleukin-1 in cultured keratinocytes: dominance of innate immune responses in psoriasis. *Am J Pathol* 2007; **171**: 32-42 [PMID: 17591951]

31 **Yano S,** Banno T, Walsh R, Blumenberg M. Transcriptional responses of human epidermal keratinocytes to cytokine interleukin-1. *J Cell Physiol* 2008; **214**: 1-13

32 **Yano S**, Banno T, Walsh R, Blumenberg M. Transcriptional responses of human epidermal keratinocytes to cytokine interleukin-1. *J Cell Physiol* 2008; **214**: 1-13 [PMID: 17941080]

33 **Yano S**, Strober BE, Haider SA, Blumenberg M. Transcriptional profiling analysis applied to psoriasis. *Giornale Italiano di Dermatologia e Venerologia* 2007; **142**: 519-531

34 **Gazel A**, Rosdy M, Bertino B, Tornier C, Sahuc F, Blumenberg M. A characteristic subset of psoriasis-associated genes is induced by oncostatin-M in reconstituted epidermis. *J Invest Dermatol* 2006; **126**: 2647-2657 [PMID: 16917497]

35 **Banno T**, Gazel A, Blumenberg M. Effects of tumor necrosis factor-alpha (TNF alpha) in epidermal keratinocytes revealed using global transcriptional profiling. *J Biol Chem* 2004; **279**: 32633-32642 [PMID: 15145954]

36 **Banno T**, Adachi M, Mukkamala L, Blumenberg M. Unique keratinocyte-specific effects of interferon-gamma that protect skin from viruses, identified using transcriptional profiling. *Antivir Ther* 2003; **8**: 541-554 [PMID: 14760888]

37 **Bowcock AM**, Shannon W, Du F, Duncan J, Cao K, Aftergut K, Catier J, Fernandez-Vina MA, Menter A. Insights into psoriasis and other inflammatory diseases from large-scale gene expression studies. *Hum Mol Genet* 2001; **10**: 1793-1805 [PMID: 11532989]

38 **Zhou X**, Krueger JG, Kao MC, Lee E, Du F, Menter A, Wong WH, Bowcock AM. Novel mechanisms of T-cell and dendritic cell activation revealed by profiling of psoriasis on the 63,100-element oligonucleotide array. *Physiol Genomics* 2003; **13**: 69-78 [PMID: 12644634]

39 **Lu X**, Du J, Liang J, Zhu X, Yang Y, Xu J. Transcriptional regulatory network for psoriasis. *J Dermatol* 2013; **40**: 48-53 [PMID: 23078099 DOI: 10.1111/1346-8138.12000]

40 **Piruzian E**, Bruskin S, Ishkin A, Abdeev R, Moshkovskii S, Melnik S, Nikolsky Y, Nikolskaya T. Integrated network analysis of transcriptomic and proteomic data in psoriasis. *BMC Syst Biol* 2010; **4**: 41 [PMID: 20377895 DOI: 10.1186/1752-0509-4-41]

41 **Swindell WR**, Johnston A, Voorhees JJ, Elder JT, Gudjonsson JE. Dissecting the psoriasis transcriptome: inflammatory- and cytokine-driven gene expression in lesions from 163 patients. *BMC Genomics* 2013; **14**: 527 [PMID: 23915137 DOI: 10.1186/1471-2164-14-527]

42 **Wong R**, Tran V, Morhenn V, Hung SP, Andersen B, Ito E, Wesley Hatfield G, Benson NR. Use of RT-PCR and DNA microarrays to characterize RNA recovered by non-invasive tape harvesting of normal and inflamed skin. *J Invest Dermatol* 2004; **123**: 159-167 [PMID: 15191556]

43 **Benson NR**, Papenfuss J, Wong R, Motaal A, Tran V, Panko J, Krueger GG. An analysis of select pathogenic messages in lesional and non-lesional psoriatic skin using non-invasive tape harvesting. *J Invest Dermatol* 2006; **126**: 2234-2241 [PMID: 16741508]

44 **Blaser MJ**. Harnessing the power of the human microbiome. *Proc Natl Acad Sci U S A* 2010; **107**: 6125-6126 [PMID: 20360554 DOI: 10.1073/pnas.1002112107]

45 **Gao Z**, Tseng CH, Strober BE, Pei Z, Blaser MJ. Substantial alterations of the cutaneous bacterial biota in psoriatic lesions. *PLoS One* 2008; **3**: e2719 [PMID: 18648509 DOI: 10.1371/journal.pone.0002719]

46 **Paulino LC**, Tseng CH, Blaser MJ. Analysis of Malassezia microbiota in healthy superficial human skin and in psoriatic lesions by multiplex real-time PCR. *FEMS Yeast Res* 2008; **8**: 460-471 [PMID: 18294199 DOI: 10.1111/j.1567-1364.2008.00359.x]

47 **Paulino LC**, Tseng CH, Strober BE, Blaser MJ. Molecular analysis of fungal microbiota in samples from healthy human skin and psoriatic lesions. *J Clin Microbiol* 2006; **44**: 2933-2941 [PMID: 16891514]

48 **Liu Y**, Helms C, Liao W, Zaba LC, Duan S, Gardner J, Wise C, Miner A, Malloy MJ, Pullinger CR, Kane JP, Saccone S, Worthington J, Bruce I, Kwok PY, Menter A, Krueger J, Barton A, Saccone NL, Bowcock AM. A genome-wide association study of psoriasis and psoriatic arthritis identifies new disease loci. *PLoS Genet* 2008; **4**: e1000041 [PMID: 18369459 DOI: 10.1371/journal.pgen.1000041]

49 **Julià A**, Tortosa R, Hernanz JM, Cañete JD, Fonseca E, Ferrándiz C, Unamuno P, Puig L, Fernández-Sueiro JL, Sanmartí R, Rodríguez J, Gratacós J, Dauden E, Sánchez-Carazo JL, López-Estebaranz JL, Moreno-Ramírez D, Queiró R, Montilla C, Torre-Alonso JC, Pérez-Venegas JJ, Vanaclocha F, Herrera E, Muñoz-Fernández S, González C, Roig D, Erra A, Acosta I, Fernández-Nebro A, Zarco P, Alonso A, López-Lasanta M, García-Montero A, Gelpí JL, Absher D, Marsal S. Risk variants for psoriasis vulgaris in a large case-control collection and association with clinical subphenotypes. *Hum Mol Genet* 2012; **21**: 4549-4557 [PMID: 22814393]

50 **Zervou MI**, Goulielmos GN, Castro-Giner F, Boumpas DT, Tosca AD, Krueger-Krasagakis S. A CD40 and an NCOA5 gene polymorphism confer susceptibility to psoriasis in a Southern European population: a case-control study. *Hum Immunol* 2011; **72**: 761-765 [PMID: 21645569 DOI: 710.1016/j.humimm.2011.1005.1014]

51 **Hiruma A**, Ikeda S, Terui T, Ozawa M, Hashimoto T, Yasumoto S, Nakayama J, Kubota Y, Iijima M, Sueki H, Matsumoto Y, Kato M, Akasaka E, Ikoma N, Mabuchi T, Tamiya S, Matsuyama T, Ozawa A, Inoko H, Oka A. A novel splicing variant of CADM2 as a protective transcript of psoriasis. *Biochem Biophys Res Commun* 2011; **412**: 626-632 [PMID: 21864505 DOI: 610.1016/j.bbrc.2011.1008.1013]

52 **Bowes J,** Orozco G, Flynn E, Ho P, Brier R, Marzo-Ortega H, Coates L, McManus R, Ryan AW, Kane D, Korendowych E, McHugh N, FitzGerald O, Packham J, Morgan AW, Bruce IN, Barton A. Confirmation of tnip1 and il23a as susceptibility loci for psoriatic arthritis. *Ann Rheum Dis* 2011; **70**: 1641-1644 [PMID: 21623003 DOI: 10.1136/ard.2011.150102]

53 **Knight J**, Spain SL, Capon F, Hayday A, Nestle FO, Clop A, Barker JN, Weale ME, Trembath RC. Conditional analysis identifies three novel major histocompatibility complex loci associated with psoriasis. *Hum Mol Genet* 2012; **21**: 5185-5192 [PMID: 22914738 DOI: 5110.1093/hmg/dds5344]

54 **Hyder LA**, Gonzalez J, Harden JL, Johnson-Huang LM, Zaba LC, Pierson KC, Eungdamrong NJ, Lentini T, Gulati N, Fuentes-Duculan J, Suárez-Fariñas M, Lowes MA. TREM-1 as a potential therapeutic target in psoriasis. *J Invest Dermatol* 2013; **133**: 1742-1751 [PMID: 23407402 DOI: 1710.1038/jid.2013.1768]

55 **Xu N**, Meisgen F, Butler LM, Han G, Wang XJ, Söderberg-Nauclér C, Ståhle M, Pivarcsi A, Sonkoly E. MicroRNA-31 is overexpressed in psoriasis and modulates inflammatory cytokine and chemokine production in keratinocytes via targeting serine/threonine kinase 40. *J Immunol* 2013; **190**: 678-688 [PMID: 23233723 DOI: 610.4049/jimmunol.1202695]

56 **Krueger JG**, Fretzin S, Suárez-Fariñas M, Haslett PA, Phipps KM, Cameron GS, McColm J, Katcherian A, Cueto I, White T, Banerjee S, Hoffman RW. IL-17A is essential for cell activation and inflammatory gene circuits in subjects with psoriasis. *J Allergy Clin Immunol* 2012; **130**: 145-54.e9 [PMID: 22677045 DOI: 110.1016/j.jaci.2012.1004.1024]

57 **De Benedetto A**, Rafaels NM, McGirt LY, Ivanov AI, Georas SN, Cheadle C, Berger AE, Zhang K, Vidyasagar S, Yoshida T, Boguniewicz M, Hata T, Schneider LC, Hanifin JM, Gallo RL, Novak N, Weidinger S, Beaty TH, Leung DY, Barnes KC, Beck LA. Tight junction defects in patients with atopic dermatitis. *J Allergy Clin Immunol* 2011; **127**: 773-86.e1-7 [PMID: 21163515 DOI: 710.1016/j.jaci.2010.1010.1018]

58 **Suárez-Fariñas M**, Shah KR, Haider AS, Krueger JG, Lowes MA. Personalized medicine in psoriasis: developing a genomic classifier to predict histological response to Alefacept. *BMC Dermatol* 2010; **10**: 1 [PMID: 20152045 DOI: 10.1186/1471-5945-10-1]

59 **de Jongh GJ**, Zeeuwen PL, Kucharekova M, Pfundt R, van der Valk PG, Blokx W, Dogan A, Hiemstra PS, van de Kerkhof PC, Schalkwijk J. High expression levels of keratinocyte antimicrobial proteins in psoriasis compared with atopic dermatitis. *J Invest Dermatol* 2005; **125**: 1163-1173 [PMID: 16354186 DOI: 10.1111/j.0022-202X.2005.23935.x]

60 **Jabbari A**, Suárez-Fariñas M, Dewell S, Krueger JG. Transcriptional profiling of psoriasis using RNA-seq reveals previously unidentified differentially expressed genes. *J Invest Dermatol* 2012; **132**: 246-249 [PMID: 21850022 DOI: 210.1038/jid.2011.1267]

61 **Mitsui H**, Suárez-Fariñas M, Belkin DA, Levenkova N, Fuentes-Duculan J, Coats I, Fujita H, Krueger JG. Combined use of laser capture microdissection and cDNA microarray analysis identifies locally expressed disease-related genes in focal regions of psoriasis vulgaris skin lesions. *J Invest Dermatol* 2012; **132**: 1615-1626 [PMID: 22402443 DOI: 1610.1038/jid.2012.1633]

62 **Johnson-Huang LM**, Pensabene CA, Shah KR, Pierson KC, Kikuchi T, Lentini T, Gilleaudeau P, Sullivan-Whalen M, Cueto I, Khatcherian A, Hyder LA, Suárez-Fariñas M, Krueger JG, Lowes MA. Post-therapeutic relapse of psoriasis after CD11a blockade is associated with T cells and inflammatory myeloid DCs. *PLoS One* 2012; **7**: e30308 [PMID: 22348003 DOI: 30310.31371/journal.pone.0030308]

63 **Kulski JK**, Kenworthy W, Bellgard M, Taplin R, Okamoto K, Oka A, Mabuchi T, Ozawa A, Tamiya G, Inoko H. Gene expression profiling of Japanese psoriatic skin reveals an increased activity in molecular stress and immune response signals. *J Mol Med* (Berl) 2005; **83**: 964-975 [PMID: 16283139]

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**Table 1 Psoriasis susceptibility loci identified using genome-wide association studies**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Psoriasis** | **Chromosome** | **Gene** | **Locus** | **Author** |
| 1 | 1p31.3 | *IL-23R* |  | Nair *et al*[11] |
| 1 | 1p31.3 | *IL-23R* |  | Liu *et al*[48] |
| 1 | 1p31.3 | *IL-23R* | rs9988642 | Tsoi *et al*[8] |
| 2 | 1p36 | *RUNX3* | rs7536201 | Tsoi *et al*[8] |
| 3 | 1p36.11 | *IL28RA* | rs7552167 | Tsoi *et al*[8] |
| 4 | 1p36.23 | *SLC45A1, TNFRSF9* | rs11121129 | Tsoi *et al*[8] |
| 5 | 1q21 | *PSORS4* |  | Julià*et al*[49] |
| 6 | 1q21 | *LCE3D* | rs6701216 | Liu *et al*[48] |
| 7 | 1q21.3 | *LCE3B* | rs4112788 | de Cid *et al*[1] |
| 8 | 20q12-q13.12 | *NCOA5* | rs2903908 | Zervou *et al*[50] |
| 9 | 20q12-q13.2 | *CD40* | rs4810485 | Zervou *et al*[50] |
| 10 | 20q13.13 | *RNF114* | rs1056198 | Tsoi *et al*[8] |
| 11 | 22q11.21 | *UBE2L3* | rs4821124 | Tsoi *et al*[8] |
| 12 | 2p15 | *B3GNT2* | rs10865331 | Tsoi *et al*[8] |
| 13 | 2p16.1 | *FLJ16341, REL* | rs62149416 | Tsoi *et al*[8] |
| 14 | 2q14.2 | *IL1RN* |  | Julià*et al*[49] |
| 15 | 2q24.2 | *KCNH7, IFIH1* | rs17716942 | Tsoi *et al*[8] |
| 16 | 3p12.1 | *CADM2* |  | Hiruma *et al*[51] |
| 17 | 4q27 |  |  | Liu *et al*[48] |
| 18 | 5q15 | *ERAP1* | rs27432 | Tsoi *et al*[8] |
| 19 | 5q31 | *IL-13, IL-4* | rs1295685 | Tsoi *et al*[8] |
| 20 | 5q31.1-q33.1 | *IL-12B* | rs12188300 | Tsoi *et al*[8] |
| 21 | 5q32-q33.1 | *TNIP1* | rs17728338 | Bowes *et al*[52] |
| 22 | 6p21.3 | *HLA-C* |  | Knight *et al*[53] |
| 23 | 6p25.3 | *EXOC2, IRF4* | rs9504361 | Tsoi *et al*[8] |
| 24 | 6q21 | *TRAF3IP2* | rs33980500 | Ellinghaus *et al*[10] |
| 25 | 6q23 | *TNFAIP3* | rs582757 | Tsoi *et al*[8] |
| 26 | 6q25.3 | *TAGAP* | rs2451258 | Tsoi *et al*[8] |
| 27 | 7p14.1 | *ELMO1* | rs2700987 | Tsoi *et al*[8] |
| 28 | 9p12 | *DDX58* | rs11795343 | Tsoi *et al*[8] |
| 29 | 9q31 | *KLF4* | rs10979182 | Tsoi *et al*[8] |
| 30 | 9q34 | *TSC1* | rs1076160 | Bowes *et al*[52] |
| 31 | 10q22.3 | *ZMIZ1* | rs1250546 | Tsoi *et al*[8] |
| 32 | 11q11-q13 | *RPS6KA4, PRDX5* | rs645078 | Tsoi *et al*[8] |
| 33 | 11q22.3 | *ZC3H12C* | rs4561177 | Tsoi *et al*[8] |
| 34 | 11q23.3 | *ETS1* | rs3802826 | Tsoi *et al*[8] |
| 35 | 12q13.3 | *STAT2, IL23A* | rs2066819 | Tsoi *et al*[8] |
| 36 | 13q12 | *LHFP* |  | Liu *et al*[48] |
| 37 | 13q14.11 | *COG6* | rs7993214 | Liu *et al*[48] |
| 38 | 14q13 | *NFKBIA* | rs8016947 | Tsoi *et al*[8] |
| 39 | 15q21 |  | rs3803369 | Liu *et al*[48] |
| 40 | 16p11.2 | *PRSS53, FBXL19* | rs12445568 | Tsoi *et al*[8] |
| 41 | 16p13.13 | *PRM3, SOCS1* | rs367569 | Tsoi *et al*[8] |
| 42 | 17q11.2-q12 | *NOS2* | rs28998802 | Tsoi *et al*[8] |
| 43 | 17q21.31 | *PTRF, STAT3, STAT5A/B* | rs963986 | Tsoi *et al*[8] |
| 44 | 17q25 | *CARD14* | rs11652075 | Tsoi *et al*[8] |
| 45 | 18q21.2 | *POL1, STARD6, MBD2* | rs545979 | Tsoi *et al*[8] |
| 46 | 18q22.1 | *SERPINB8* |  | Julià*et al*[49] |
| 47 | 19p13.2 | *TYK2* | rs34536443 | Tsoi *et al*[8] |
| 48 | 19p13.2 | *ILF3,CARM1* | rs892085 | Tsoi *et al*[8] |

Note that many of the loci were identified in multiple studies (*e.g.,* shaded).

**Table 2 Transcriptional profiling studies targeting psoriasis in the GEO database**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Comparison Studies** | **Microarrays** | **Platform** | **Samples** | **Ref.** |
| [GSE34248](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE34248) | 14+14 | HG-U133\_Plus\_2 | Lesional + NonLes | [21] |
| [GSE41662](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE41662) | 24+24 | HG-U133\_Plus\_2 | Lesional + NonLes | [21] |
| [GSE41663](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE41663) | 15+15 (+51 treated) | HG-U133\_Plus\_2 | Lesional + NonLes | [21] |
| [GSE30999](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE30999) | 85+85 | HG-U133\_Plus\_2 | Lesional + NonLes | [19] |
| [GSE11903](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE11903) | 15+15 (+59 treated) | HG-U133A\_2 | Lesional + NonLes | [18] |
| [GSE6710](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE6710) | 13+13 | HG-U133A | Lesional + NonLes | [24] |
| [GSE14905](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE14905) | 21+33+30 | HG-U133\_Plus\_2 | Healthy + Les + NonLes | [16] |
| [GSE13355](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE13355) | 64+58+58 | HG-U133\_Plus\_2 | Healthy + Les + NonLes | [12] |
| [GSE32407](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE32407) | 20+20 (+20 IFNg treated) | HG-U133A\_2 | Healthy + NonLes | [17] |
|  |  |  |  |  |
| Related studies |  |  |  |  |
| [GSE42305](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE42305) |  |  | Monocytes | [54] |
| [GSE41905](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE41905) |  |  | Kcytes transfected wt Antimir31 | [55] |
| [GSE31652](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE31652) |  |  | All lesional, treated placebo | [56] |
| [GSE26952](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE26952) |  |  | Nonlesional only Psor AD | [57] |
| [GSE18948](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE18948) |  |  | PBMCs | [58] |
| [GSE11307](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE11307) |  |  | PCR study | 1 |
| [GSE6601](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE6601) |  |  | Psor *vs* AD | [59] |
| [GSE41745](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE41745) | 3+3 |  | RNA Sequencing | [60] |
| [GSE26866](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE26866) | 11+11 (different regions) | HG-U133A\_2 | Single *vs* double amplification | [61] |
| [GSE30768](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE30768) | 2+4 (+ 8 flare and relapse) | HG-U133A\_2 | Small number of samples | [62] |
| [GSE2737](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE2737) | 3+4+4 | HG\_U95Av2 | Small array | [63] |

1Shin J and Detmar M, unpublished.