

Supplementary Data

S1. Supplementary Material and Methods.

S1.1. Tissue miRNA Isolation, Reverse Transcription and RT-PCR.

Frozen skin samples were pulverised, and total RNA was isolated using miRNeasy mini kit (Qiagen). Quantity and quality were evaluated in Nanodrop and Agilent 2100 Bioanalyzer. In all cases only those samples with RIN > 8 were included. Ten ng of RNA were used for first-strand cDNA synthesis using Universal cDNA synthesis kit II (Exiqon). Subsequent RT-PCR was performed in triplicate using PCR ExiLENT SYBR Green (Exiqon) in a CFX384 PCR detection system (Bio-Rad).

S1.2. MiRNA Target Profiling

Sequencing reads were processed with a pipeline that used FastQC (www.bioinformatics.babraham.ac.uk/projects/fastqc) to assess read quality, and Cutadapt to trim sequencing reads, eliminating Illumina adaptor remains, and to discard those that were shorter than 30 bp. Resulting reads were aligned against a human transcriptome reference (GRCh38 assembly, release 91) and gene expression was quantified with RSEM (Li and Dewey, 2011). Raw counts were processed with an analysis pipeline that used Bioconductor package Limma (Liu *et al.*, 2015) for normalisation (using TMM method) and differential expression testing, taking into account only those genes expressed at a minimal level of 1 CPM in a number of samples equal to the number of replicates of the condition with less replicates. A blocking variable was used to define pairs of samples obtained from the same patient. Changes in gene expression were considered significant if associated to a Benjamini and Hochberg adjusted p -value < 0.05. Differentially expressed genes were further filtered by selecti.

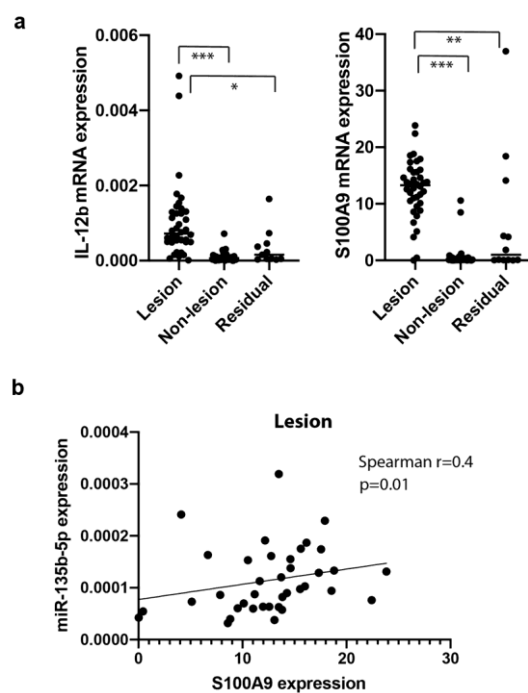


Figure S1. IL-12b and S100A9 expression in skin samples as inflammatory markers. **(a)** mRNA expression of IL-12b and S100A9 in skin samples of psoriatic patients (lesion, non-lesion and residual lesion). Data correspond to the relative levels respect to the expression of GAPDH. **(b)** Positive correlation between the levels of miR-135b-5p in and the expression of S100A9 in psoriatic skin lesions. Data were analysed using Spearman test.

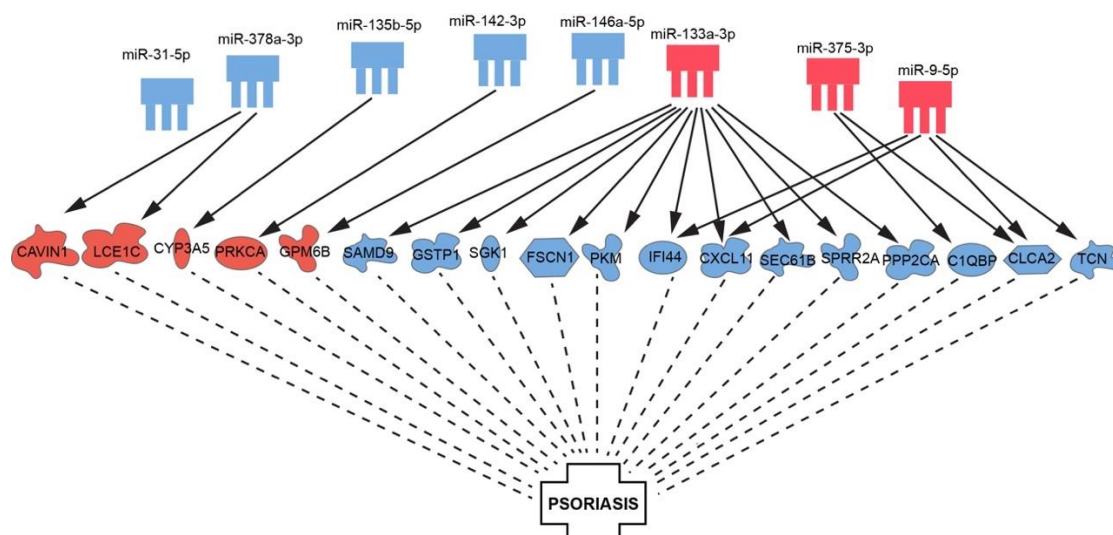


Figure S2. Interaction Network of miRNAs and target mRNAs associated with Psoriasis. Networks showing interactions between differentially expressed miRNAs and differentially expressed messenger RNA targets associated with psoriasis. Interactions were identified using IPA tool “microRNA Target Filter” of Qiagen’s Ingenuity Pathway Analysis. Interacting pairs were filtered to keep only those with anti-correlated expression. Only targets experimentally observed or predicted with high confidence were included. Up-regulated molecules are shown in blue and down-regulated ones in red.

Table S1. Differentially expressed miRNAs in lesional, non-lesional psoriatic skin and healthy skin.

miRNA ID	FC ^a	<i>p</i> -val ^a	FC ^b	<i>p</i> -val ^b	FC ^c	<i>p</i> -val ^c
hsa-mir-31	11.460	0.0001	2.219	0.1779	-5.163	0.0037
hsa-mir-9-5p	“-inf”	0.0045	“-inf”	0.0202	2.437	0.3574
hsa-mir-378a	4.163	0.0002	1.984	0.0821	2.097	0.0282
hsa-mir-378c	3.766	0.0017	1.335	0.5354	-2.820	0.0074
hsa-mir-135b	3.956	0.0039	1.771	0.0876	-2.233	0.1647
hsa-mir-33b	3.794	0.0046	4.276	0.0041	1.1268	0.8742
hsa-mir-375	-5.721	0.0060	-2.777	0.0624	2.059	0.2674
hsa-mir-4772	3.799	0.0109	2.279	0.0561	-1.666	0.4085
hsa-mir-454	2.457	0.0130	1.499	0.3140	-1.638	0.1091
hsa-mir-186	-2.652	0.0156	-2.055	0.0758	1.290	0.445
hsa-mir-365a	-2.656	0.0175	-1.997	0.0938	1.329	0.4097
hsa-mir-365b	-2.581	0.0203	-1.889	0.1153	1.366	0.3847
hsa-mir-30c-2	-2.234	0.0221	-1.225	0.3681	1.824	0.1298
hsa-mir-320b-1	-5.897	0.0226	-2.821	0.1939	2.090	0.2395
hsa-mir-18b	4.916	0.0228	3.361	0.0362	-1.462	0.7102
hsa-mir-26a-1	-2.347	0.0307	-1.547	0.2061	1.516	0.3076
hsa-mir-202	-2.789	0.0316	-2.367	0.1297	1.178	0.4687
hsa-mir-142	2.684	0.0326	1.243	0.6770	-2.158	0.0672
hsa-mir-3687	-10.245	0.0339	-2.210	0.2952	4.634	0.1849
hsa-mir-320b-2	-3.108	0.0344	-2.621	0.0273	1.185	1
hsa-mir-1307	2.497	0.0390	2.035	0.0798	-1.227	0.6602
hsa-mir-320a	-3.174	0.0438	-2.035	0.2446	1.559	0.3141
hsa-mir-1468	-3.780	0.0482	-3.130	0.0388	1.207	1
hsa-mir-615	-1.423	0.8773	3.822	0.0090	5.442	0.0052
hsa-mir-133a-2	-2.084	0.1979	2.562	0.1359	5.341	0.0064
hsa-mir-551b	1.4294	0.3447	-1.597	0.1742	-2.283	0.0223
hsa-mir-3687	1.657	0.4717	6.593	0.0030	3.979	0.0256
hsa-mir-3145	10.3349	0.2110	inf	0.0025	inf	0.0403
hsa-mir-4423	1.893	0.0992	-1.258	0.5818	-2.381	0.0273
hsa-mir-21	2.434	0.2828	5.328	0.0010	2.188	0.0306
hsa-mir-504	-2.132	0.0745	1.470	0.8375	3.135	0.0372
hsa-mir-125b	-2.341	0.0982	1.026	0.7754	2.404	0.0395
hsa-mir-374b	-1.628	0.2777	1.375	0.3396	2.239	0.0396
hsa-mir-4687	-1.135	0.9760	3.238	0.0613	3.677	0.0553
hsa-mir-934	-8.436	0.0663	-31.291	0.0020	-3.709	0.1355
hsa-mir-3615	1.268	0.2911	2.817	0.0098	2.221	0.1215
hsa-mir-122	-7.776	0.0766	-11.719	0.0163	-1.507	0.4682
hsa-mir-17	1.975	0.1671	2.085	0.0253	1.055	0.4461
hsa-mir-376a-2	1.805	0.3578	3.066	0.0257	1.698	0.2085
hsa-mir-1304	2.228	0.2281	3.522	0.0268	1.580	0.3448
hsa-mir-376a-1	2.428	0.1821	2.839	0.0297	1.168	0.4614
hsa-mir-296	-2.003	0.1878	-2.400	0.0336	-1.198	0.4471
hsa-mir-1228	1.225	0.3524	3.987	0.0337	3.254	0.2118
hsa-mir-224	1.949	0.1184	2.045	0.0349	1.049	0.6413
hsa-mir-1468	-3.780	0.0482	-3.130	0.0388	1.207	1
hsa-mir-3622a	-3.532	0.0658	-3.275	0.0395	1.078	0.8768
hsa-mir-4520a	-2.271	0.2600	-4.489	0.0447	-1.654	0.3732
hsa-mir-132	1.344	0.4658	2.125	0.0451	1.580	0.2158
hsa-mir-496	1.5690	0.6252	7.634	0.0453	4.865	0.1267
hsa-mir-1910	10.2481	0.1410	10.382	0.0487	1.013	0.6984
hsa-mir-487b	1.255	0.6141	2.073	0.0488	1.651	0.1508

^a Lesional skin vs non-lesional skin, ^b Lesional skin vs healthy, ^c Non-lesional skin vs healthy. *p* values correspond to Bonferroni *p* adjusted. FC, fold change.

Table S2. microRNAs selected from Next Generation Sequencing data.

ID	Fold Change ^{a,b,c}	<i>p</i> -val
hsa-mir-31-5p	11,4607802 ^a	0,000108979
hsa-mir-378a	4,16345336 ^a	0,000259515
hsa-mir-135b-5p	3,956695567 ^a	0,003991344
hsa-mir-9-5p	"-inf" ^a	0,004577766
hsa-mir-375	-5,721231656 ^a	0,006054568
hsa-mir-33b	4,27637697 ^c	0,004110427
hsa-mir-3145	inf ^c	0,00258317
hsa-mir-133a-3p	5,341909193 ^b	0,006448522
hsa-mir-3687	6,593690863 ^c	0,003087092
hsa-mir-615	5,442890822 ^b	0,005291634
hsa-mir-934	-31,29178488 ^c	0,002017792
hsa-mir-142-3p	2,68 ^a	0,032614484

^a fold change lesional/non-lesional skin, ^b fold change non-lesional/healthy skin, ^c fold change lesional/healthy skin.

Table 3. Demographic and clinical characteristics.

	Total <i>n</i> = 44
Age (years), mean±SD	49.9±15.1
	<45 <i>n</i> = 16
	45-65 <i>n</i> = 20
	>65 <i>n</i> = 8
Sex (fem/male)	20/24
Smoking	14 (31.8)
Hypertension	12 (27.2)
Diabetes	7 (15.9)
Dyslipidaemia	7 (15.9)
Psoriatic arthritis	11 (25)
Treatment (Biol/C-Syst)	33/11

Data correspond to “*n*” (%). Abbreviations. Biol: biological treatment, C-Syst: conventional systemic treatments.

Table S4. PASI after 3 months of treatment with biological therapy in those patients with a second biopsy ($n = 15$).

PASI	anti-IL-17	anti-IL-12/IL-23	anti-TNF-a	Total
50	0	2	0	2
75	0	0	1	1
90	2	5	0	7
100	1	1	3	5

Number of patients per group.

Table S5. Univariate logistic regression to compare different levels of improvement and a set of relevant clinical variables.

	OR (95% CI)	<i>p</i> Value
Age	0.95 (0.91-1.99)	0.04
Smoking	2.2 (0.50-9.89)	0.29
BMI	0.98 (0.93-1.03)	0.49
Treatment		
* anti-IL12/IL23	0.29 (0.05-1.44)	0.131
anti-TNFa	0.53 (0.07-3.6)	0.521
DM	2.92 (0.51-16.1)	0.22
NL miRNA-146a	1.70 (0.94-3.06)	0.076
L miRNA-135b	3.49 (1.18-10.25)	0.023

*reference value anti-IL17 treatment. Only miRNAs with $p < 0.1$ are shown.