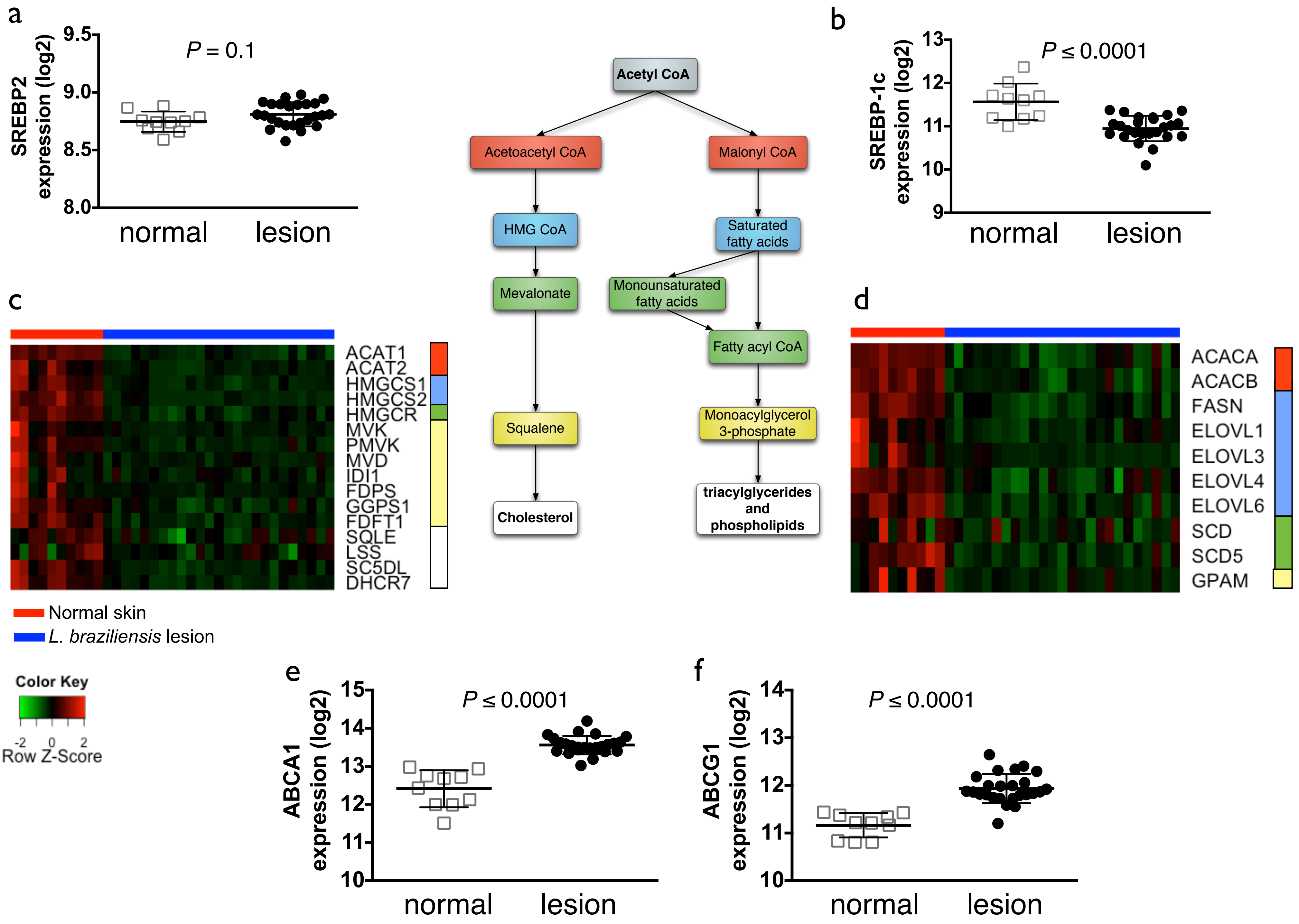
a
SREBP2 expression (log2)
9.5
9.0
8.5
8.0
P = 0.1
normal
lesion
b
SREBP-1c expression (log2)
13
12
11
10
9
P ≤ 0.0001
normal
lesion
Acetyl CoA
Acetoacetyl CoA
Malonyl CoA
HMG CoA
Saturated fatty acids
Mevalonate
Monounsaturated fatty acids
Fatty acyl CoA
Squalene
Monoacylglycerol 3-phosphate
Cholesterol
triacylglycerides and phospholipids
c
ACAT1
ACAT2
HMGCS1
HMGCS2
HMGCR
MVK
PMVK
MVD
IDI1
FDPS
GGPS1
FDFT1
SQLE
LSS
SC5DL
DHCR7
d
ACACA
ACACB
FASN
ELOVL1
ELOVL3
ELOVL4
ELOVL6
SCD
SCD5
GPAM
Normal skin
L. braziliensis lesion
Color Key
-2
0
2
Row Z-Score
e
ABCA1 expression (log2)
15
14
13
12
11
10
P ≤ 0.0001
normal
lesion
f
ABCG1 expression (log2)
14
13
12
11
10
P ≤ 0.0001
normal
lesion

Figure S1: Disregulated lipid metabolism in *L. braziliensis* lesions. Log2 expression of (a) *SREBP2* and (b) *SREBP-1c*, master transcriptional regulators of cholesterol and fatty acid biosynthesis, respectively. Heatmaps showing patient-level data for known targets of *SREBP2* and *SREBP-1c* involved in (c) cholesterol and (d) fatty acid biosynthesis. (e-f) Log2 expression of *ABCA1* and *ABCG1*, major cellular exporters of cholesterol and fatty acids. Pathway schematic shows steps involved in synthesis of cholesterol (left branch) and triglycerides and free fatty acids (right branch) from acetyl-CoA. Colored bar to right of heatmaps indicates which genes are involved in the synthesis of which molecules in the pathway schematic (i.e. *ACAT1* and *ACAT2* act on acetyl CoA to produce acetoacetyl CoA, while *ACACA* and *ACACB* make malonyl CoA from acetyl CoA).

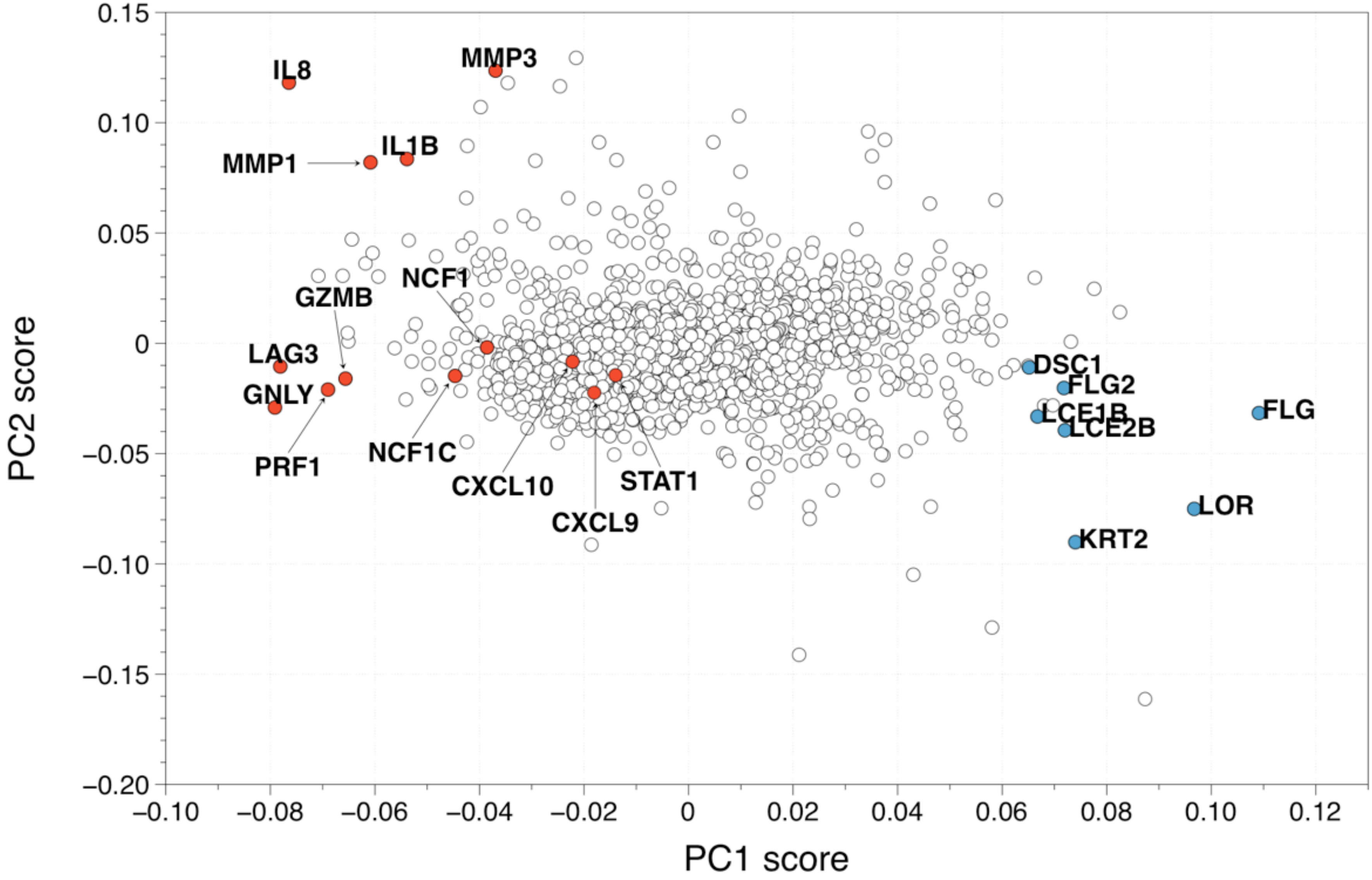

Figure S2: Scores plot from PCA of lesion biopsy samples showing PCA score (for PC1 vs. PC2) for each of the 2,028 differentially expressed genes. A selection of immune genes (red) and genes involved in maintaining skin barrier function (blue) are labeled with gene symbols and were used for correlation analysis shown in Fig. 5b. Abbreviations: PCA, principal component analysis.

Table S1: Demographic and clinical metadata from L. braziliensis patients.

Patient info.			Lesion characteristics			Response to treatment	
Identifier	**Age**	**Sex**	**Stage**	**Size (mm^2)**	**Location**	**Cure by 60 days**	**Cure 60-90 days**
early_1	24	M	early (nodular)	40	right leg	No	No
early_2	44	F	early (nodular)	36	left tight	Yes	*n.a.*
early_3	31	F	early (nodular)	56	right leg	No	No
early_4	25	F	early (nodular)	120	left leg	No	Yes
early_5	30	F	early (nodular)	25	left leg	No	No
early_6	40	M	early (nodular)	4	right leg	No	No
early_7	25	F	early (nodular)	12	left tight	No	Yes
early_8	33	M	early (nodular)	80	right leg	No	Yes
late_1	25	M	late (ulcer)	440	left leg	No	Yes
late_2	27	M	late (ulcer)	252	left leg	No	Yes
late_3	19	M	late (ulcer)	100	left leg	Yes	*n.a.*
late_4	18	M	late (ulcer)	180	left leg	Yes	*n.a.*
late_5	33	F	late (ulcer)	560	left arm	No	No
late_6	28	M	late (ulcer)	440	left leg	No	Yes
late_7	25	M	late (ulcer)	100	left leg	No	No
late_8	45	F	late (ulcer)	100	right arm	Yes	*n.a.*
late_9	21	M	late (ulcer)	48	right arm	No	Yes
late_10	26	F	late (ulcer)	48	left leg	No	Yes
late_11	37	M	late (ulcer)	550	left leg	No	Yes
late_12	19	M	late (ulcer)	960	right leg	No	Yes
late_13	19	F	late (ulcer)	192	right leg	No	Yes
late_14	25	M	late (ulcer)	380	right leg	Yes	*n.a.*
late_15	30	M	late (ulcer)	250	abdome	No	No
late_16	33	F	late (ulcer)	100	right leg	Yes	*n.a.*
late_17	40	M	late (ulcer)	400	right leg	Yes	*n.a.*

Table S2: Normalized, batch corrected Log2 expression and average Log2 FC for 20,942 genes across all 35 skin samples (10 normal, 8 early lesions, 17 late lesions) represented by one or more probesets from the Illumina HT-12v4 beadarray. Abbreviations: FC, fold-change. Data can be viewed and downloaded at: http://dx.doi.org/10.6084/m9.figshare.1099772

Table S3: Log2 expression and average Log2 FC for 2,028 genes across all 35 skin samples (10 normal, 8 early lesions, 17 late lesions) differentially expressed with a FC ≥ 2 and FDR ≤ 1%. Abbreviations: FC, fold-change; FDR, false discovery rate. Data can be viewed and downloaded at: http://dx.doi.org/10.6084/m9.figshare.1099765

Table S4: Pathway enrichment analysis. Excel spreadsheet showing pathways and their enrichment score from Fig. 2b found by GSEA to be enriched 16 fold (FDR ≤ 1%) in *L. braziliensis* lesions, relative to normal skin. Functionally related pathways manually grouped together for simplified representation in Fig. 2b are shown as a separate tab in the spreadsheet. Abbreviations: GSEA, gene set enrichment analysis; FDR, false discovery rate. Data can be viewed and downloaded at: http://dx.doi.org/10.6084/m9.figshare.1099764

Table S5: Comparison of transcriptional responses in *L. braziliensis* lesions with published psoriasis meta-analysis. Log2 FC in gene expression between skin lesion and normal control skin for 17,070 genes in common between the *L. braziliensis* data and published psoriasis 'MAD3' data. Rank order is shown for both *Leishmania* and psoriasis data in which genes were ranked from most highly upregulated in lesion (rank = 1) to most downregulated in lesion (rank = 17,070). Abbreviations: FC, fold change. Data can be viewed and downloaded at: http://dx.doi.org/10.6084/m9.figshare.1099767