FIG. 1

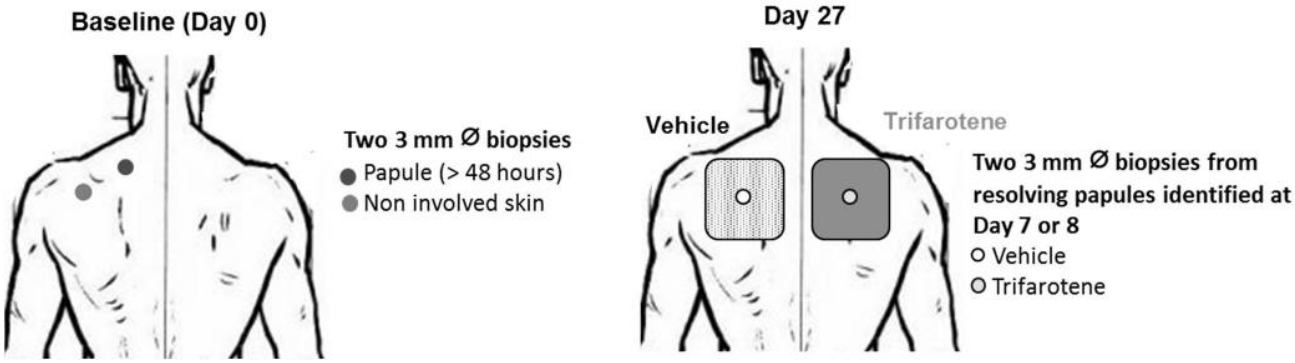

Baseline (Day 0)
Two 3 mm Ø biopsies
Papule (> 48 hours)
Non involved skin
Day 27
Vehicle
Trifarotene
Two 3 mm Ø biopsies from resolving papules identified at Day 7 or 8
Vehicle
Trifarotene

FIG. 2

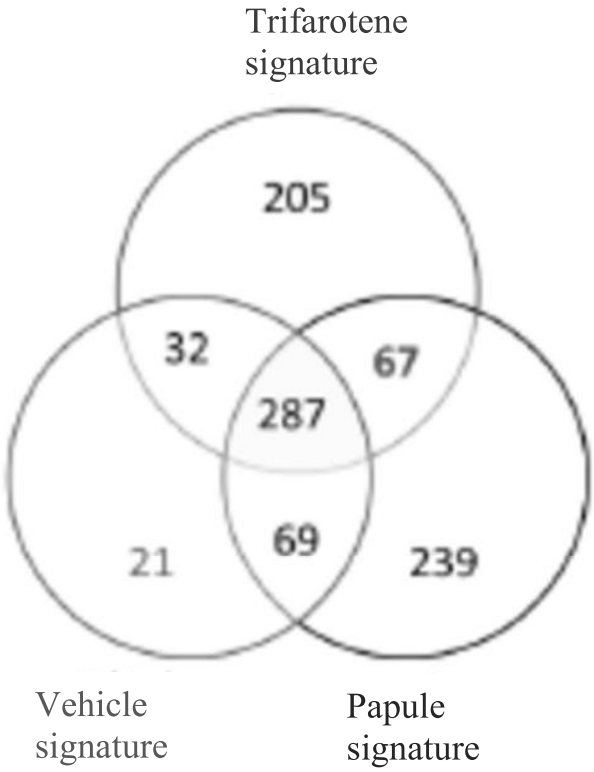
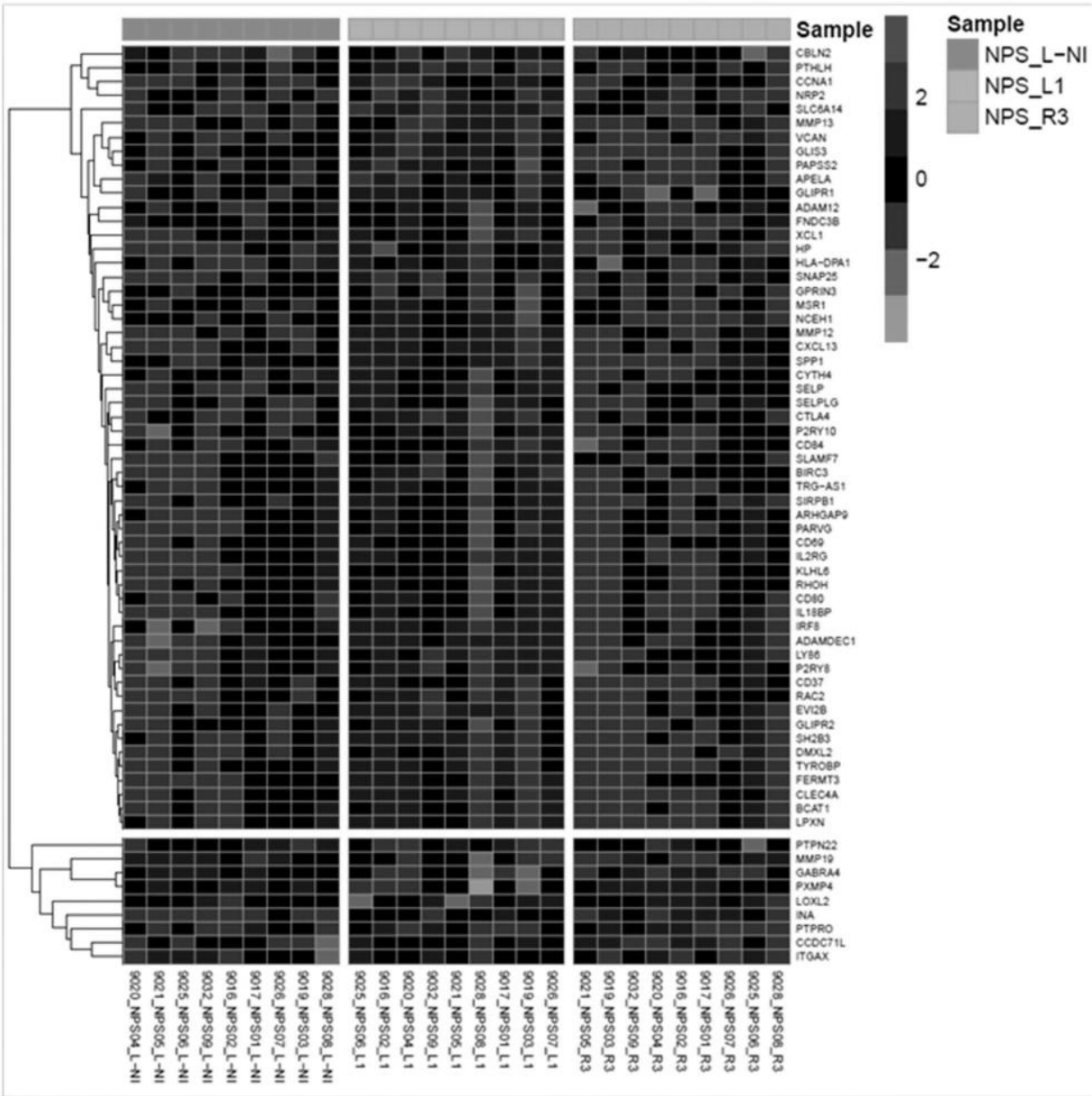

Trifarotene signature
205
32
67
287
69
21
239
Vehicle signature
Papule signature

FIG. 3


Sample
CBLN2
PTHLH
CCNA1
NRP2
SLC6A14
MMP13
VCAN
GLIS3
PAPSS2
APELA
GLIPR1
ADAM12
FNDC3B
XCL1
HP
HLA-DPA1
SNAP25
GPRIN3
MSR1
NCEH1
MMP12
CXCL13
SPP1
CYTH4
SELP
SELPLG
CTLA4
P2RY10
CD84
SLAMF7
BIRC3
TRG-AS1
SIRPB1
ARHGAP9
PARVG
CD69
IL2RG
KLHL6
RHOH
CD80
IL18BP
IRF8
ADAMDEC1
LY86
P2RY8
CD37
RAC2
EVI2B
GLIPR2
SH2B3
DMXL2
TYROBP
FERMT3
CLEC4A
BCAT1
LPXN
PTPN22
MMP19
GABRA4
PXMP4
LOXL2
INA
PTPRO
CCDC71L
ITGAX
9020_NPS04_L-NI
9021_NPS05_L-NI
9025_NPS06_L-NI
9032_NPS09_L-NI
9016_NPS02_L-NI
9017_NPS01_L-NI
9026_NPS07_L-NI
9019_NPS03_L-NI
9028_NPS08_L-NI
9025_NPS06_L1
9016_NPS02_L1
9020_NPS04_L1
9032_NPS09_L1
9021_NPS05_L1
9028_NPS08_L1
9017_NPS01_L1
9019_NPS03_L1
9026_NPS07_L1
9021_NPS05_R3
9019_NPS03_R3
9032_NPS09_R3
9020_NPS04_R3
9016_NPS02_R3
9017_NPS01_R3
9026_NPS07_R3
9025_NPS06_R3
9028_NPS08_R3
Sample
NPS_L-NI
NPS_L1
NPS_R3
2
0
-2

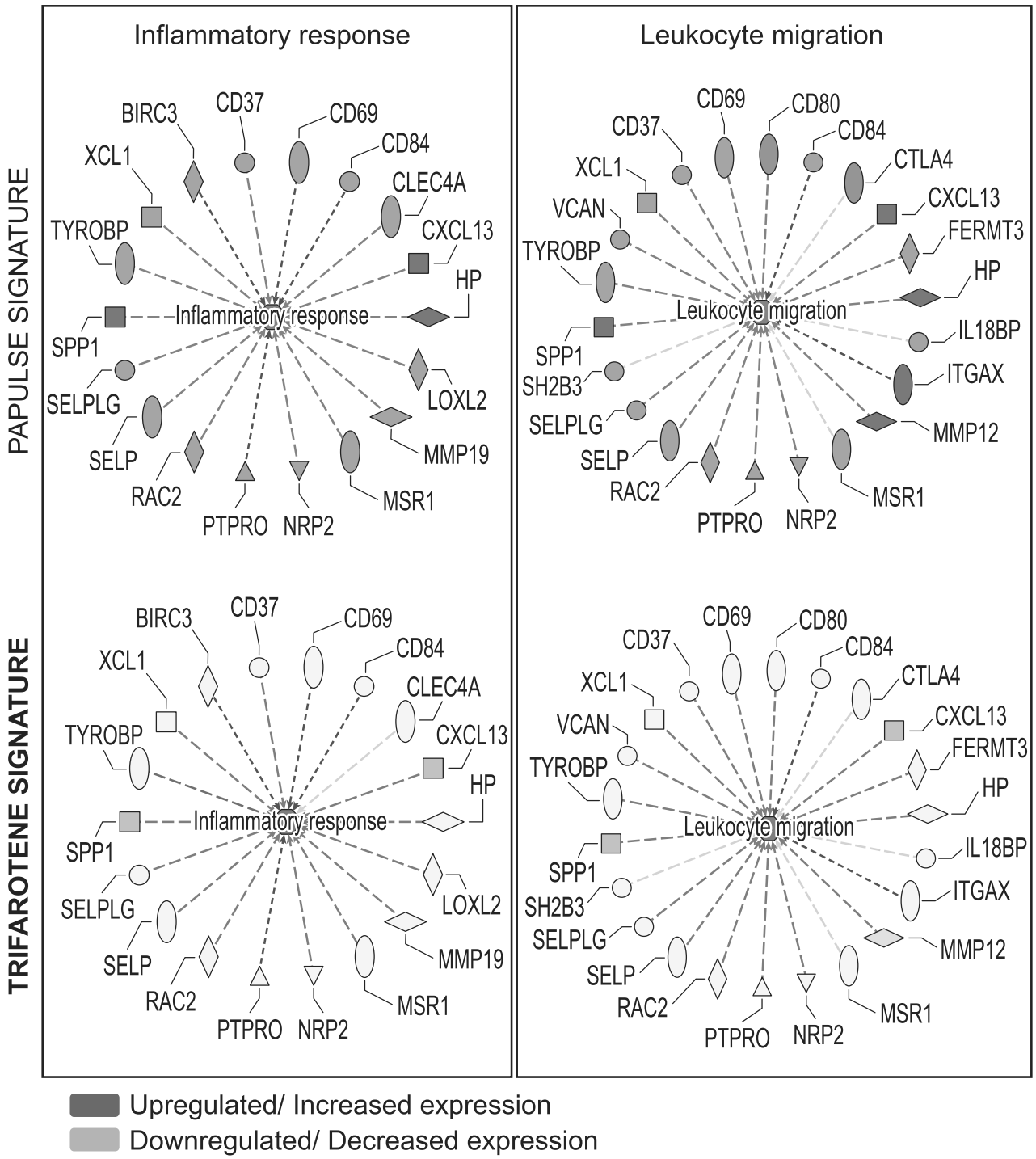

PAPULSE SIGNATURE
TRIFAROTENE SIGNATURE
Inflammatory response
Leukocyte migration
BIRC3
CD37
CD69
CD84
XCL1
CLEC4A
TYROBP
CXCL13
HP
SPP1
LOXL2
SELPLG
MMP19
SELP
RAC2
MSR1
PTPRO
NRP2
CD80
CTLA4
VCAN
FERMT3
IL18BP
SH2B3
ITGAX
MMP12
Upregulated/ Increased expression
Downregulated/ Decreased expression

FIG. 4

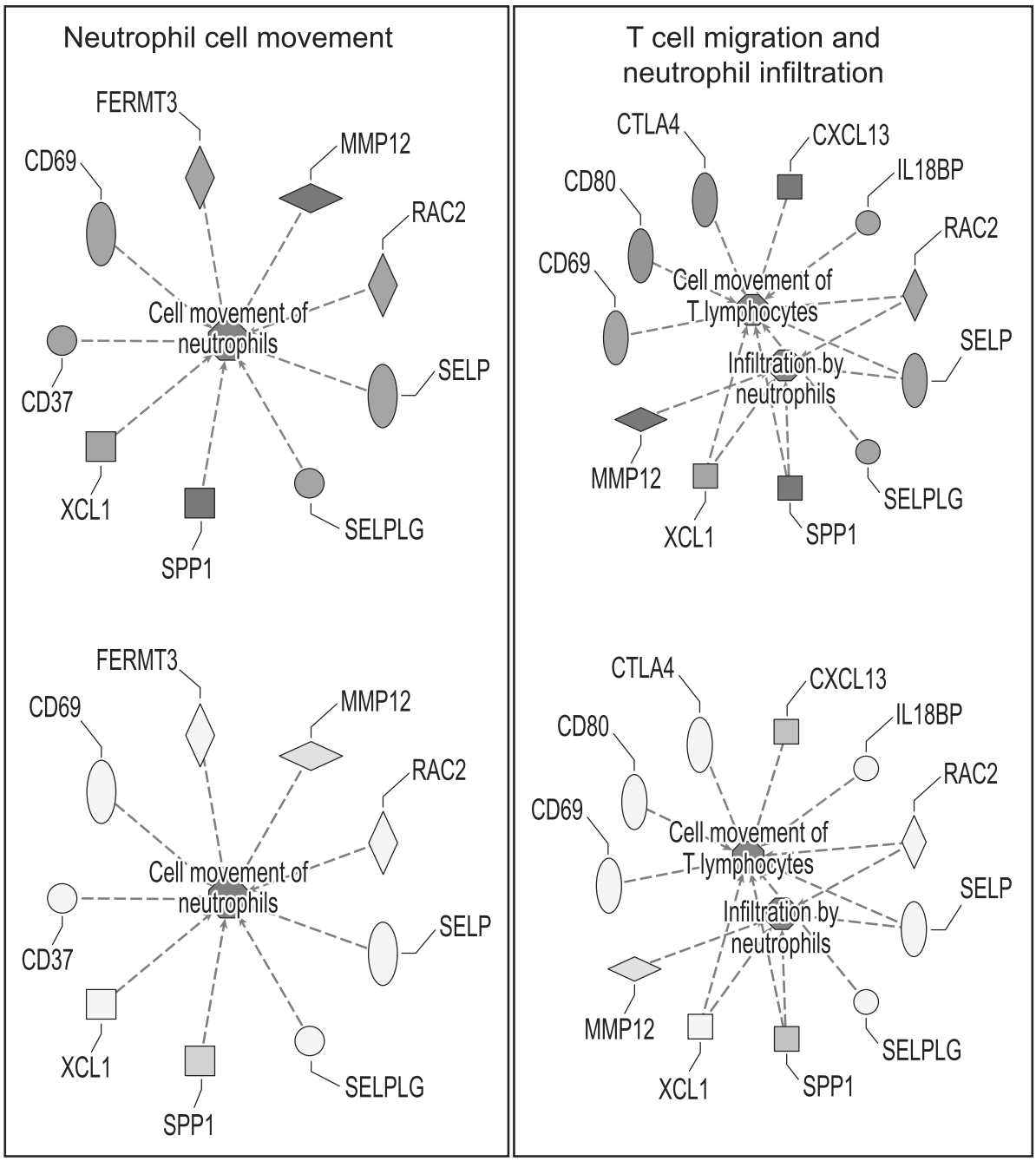

Neutrophil cell movement
FERMT3
MMP12
CD69
RAC2
Cell movement of neutrophils
CD37
SELP
XCL1
SELPLG
SPP1
T cell migration and neutrophil infiltration
CTLA4
CXCL13
CD80
IL18BP
RAC2
CD69
Cell movement of T lymphocytes
SELP
Infiltration by neutrophils
MMP12
SELPLG
XCL1
SPP1
FERMT3
MMP12
CD69
RAC2
Cell movement of neutrophils
CD37
SELP
XCL1
SELPLG
SPP1
CTLA4
CXCL13
CD80
IL18BP
RAC2
CD69
Cell movement of T lymphocytes
SELP
Infiltration by neutrophils
MMP12
SELPLG
XCL1
SPP1

FIG. 4(Cont.)

FIG. 5(A)

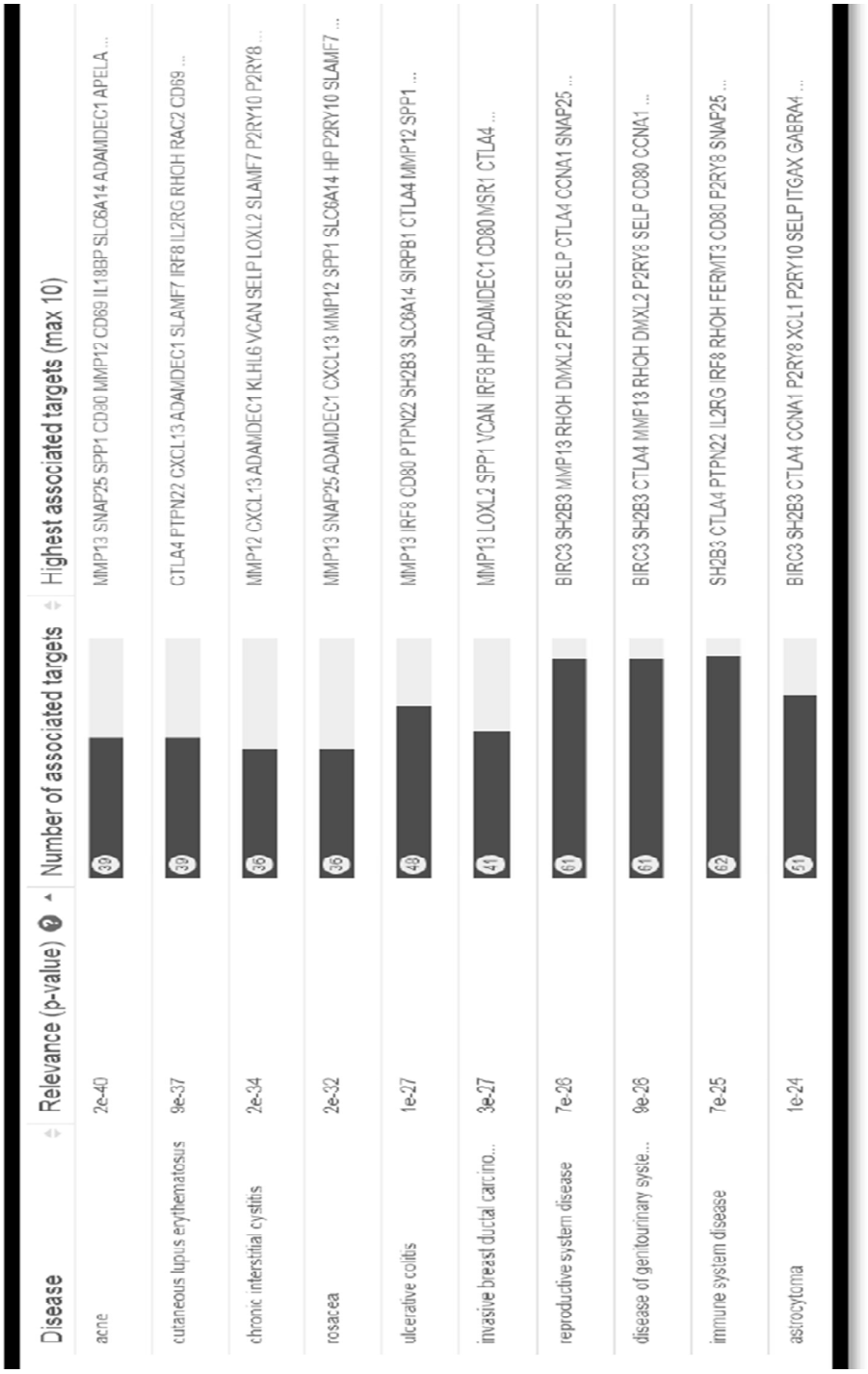

Disease
Relevance (p-value)
Number of associated targets
Highest associated targets (max 10)
acne
2e-40
39
MMP13 SNAP25 SPP1 CD80 MMP12 CD69 IL18BP SLC6A14 ADAMDEC1 APELA ...
cutaneous lupus erythematosus
9e-37
39
CTLA4 PTPN22 CXCL13 ADAMDEC1 SLAMF7 IRF8 IL2RG RHOH RAC2 CD69 ...
chronic interstitial cystitis
2e-34
36
MMP12 CXCL13 ADAMDEC1 KLHL6 VCAN SELP LOXL2 SLAMF7 P2RY10 P2RY8 ...
rosacea
2e-32
36
MMP13 SNAP25 ADAMDEC1 CXCL13 MMP12 SPP1 SLC6A14 HP P2RY10 SLAMF7 ...
ulcerative colitis
1e-27
49
MMP13 IRF8 CD80 PTPN22 SH2B3 SLC6A14 SIRPB1 CTLA4 MMP12 SPP1 ...
invasive breast ductal carcino...
3e-27
41
MMP13 LOXL2 SPP1 VCAN IRF8 HP ADAMDEC1 CD80 MSR1 CTLA4 ...
reproductive system disease
7e-26
61
BIRC3 SH2B3 MMP13 RHOH DMXL2 P2RY8 SELP CTLA4 CCNA1 SNAP25 ...
disease of genitourinary syste...
9e-26
61
BIRC3 SH2B3 CTLA4 MMP13 RHOH DMXL2 P2RY8 SELP CD80 CCNA1 ...
immune system disease
7e-25
62
SH2B3 CTLA4 PTPN22 IL2RG IRF8 RHOH FERMT3 CD80 P2RY8 SNAP25 ...
astrocytoma
1e-24
51
BIRC3 SH2B3 CTLA4 CCNA1 P2RY8 XCL1 P2RY10 SELP ITGAX GABRA4 ...

FIG. 5(B)



Pathway	Relevance (p-value)	Number of targets	Targets in pathway
Extracellular matrix organization	0.00024	6	ADAM12, MMP19, SFP1, MMP12, VCAN, MMP...
Interaction With Cumulus Cells And The Zona P...	0.0027	1	ADAM12
Signal regulatory protein family interactions	0.0056	2	TYROBP, SIRPB1
Defective PAPSS2 causes SEMD-PA	0.0069	1	PAPSS2
Variant SLC6A14 may confer susceptibility towa...	0.0069	1	SLC6A14
Crosslinking of collagen fibrils	0.0071	1	LOXL2
Chemokine receptors bind chemokines	0.0074	2	XCL1, CXCL13
Assembly of collagen fibrils and other multimeric...	0.0089	2	MMP13, LOXL2
CTLA4 inhibitory signaling	0.0095	2	CD80, CTLA4
Collagen degradation	0.010	3	MMP19, MMP12, MMP13