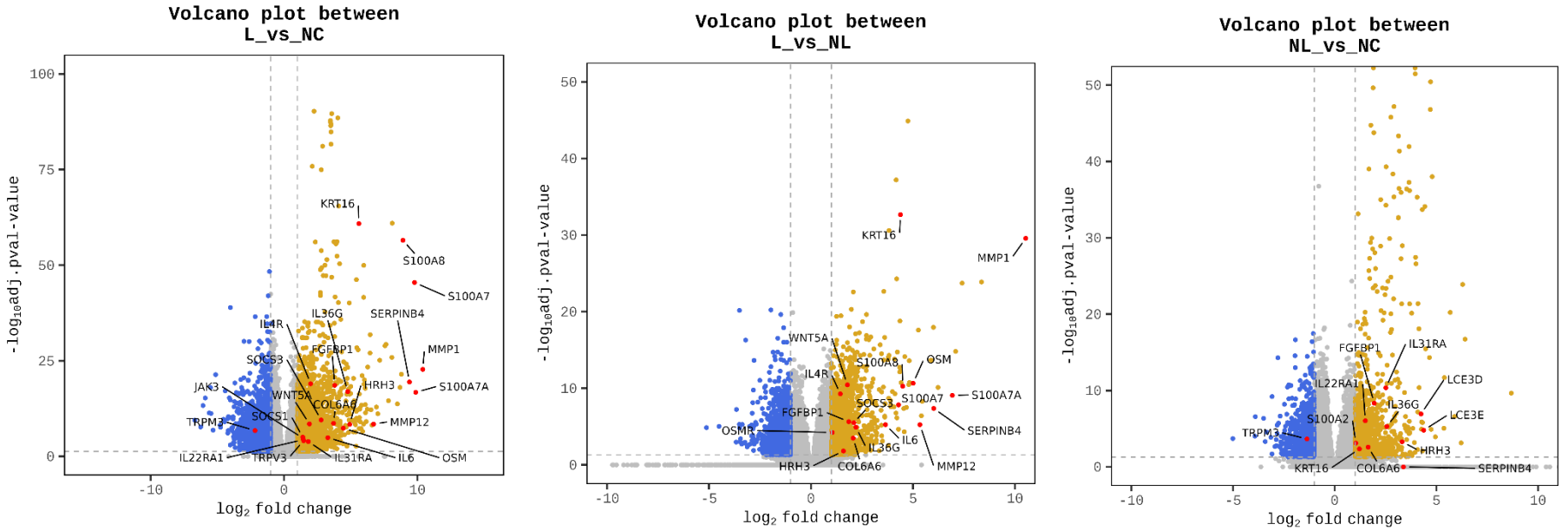
Figure S2. Enrichment of Th22/IL-22–related and keratinization-associated genes in lesional PN skin.

(a) Volcano plot showing differential expressions of canonical T-helper pathway markers between lesional (L) and normal control (NC) skin.

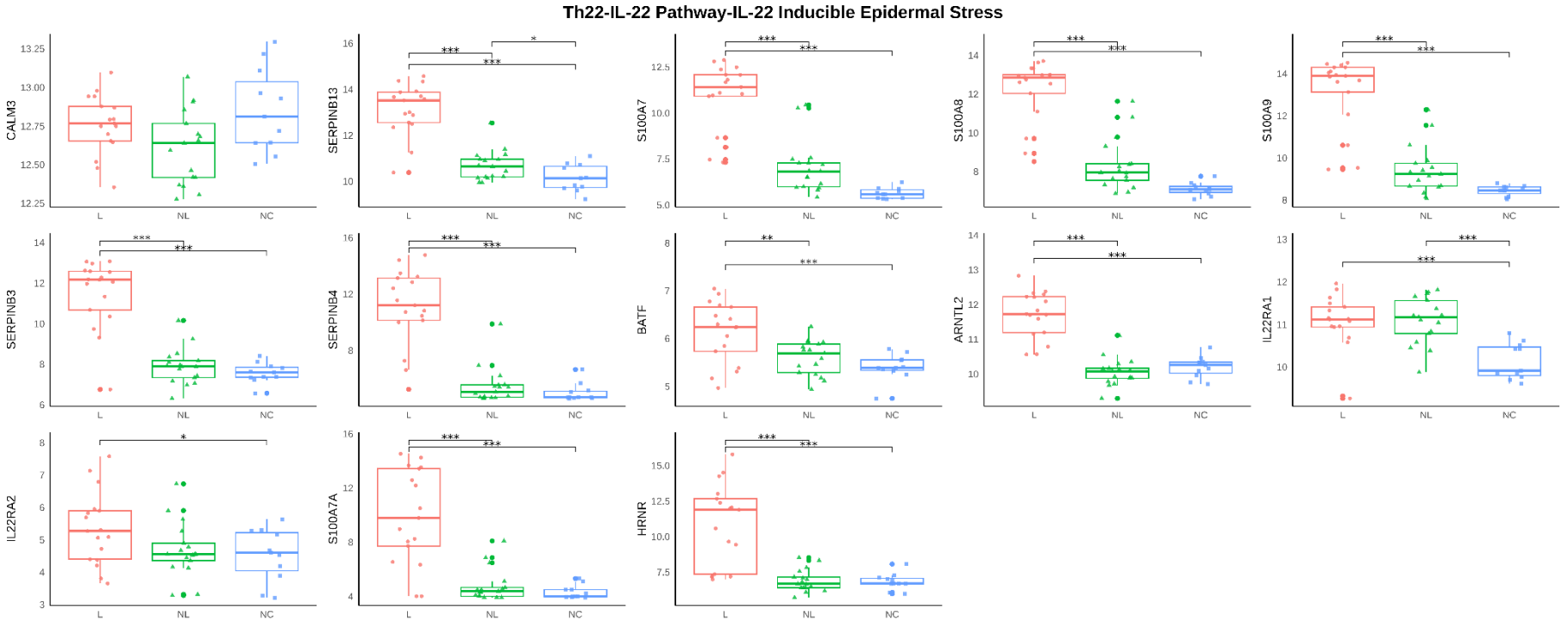
(b) Boxplots of representative DEGs from Th22-associated (*S100A7, S100A8, S100A9, SERPINB4, IL36RN, IL36B, IL36G, IL22RA1, IL22RA2*), Th1-related (*IL1B, IL2RA, IL12RB2*), Th2-related (*IL4R, IL10, IL13, IL33*), and Th17-related (*CCL20, IL23A, IL17D*) pathways. Lesional skin shows marked upregulation of Th22/IL-22–associated and downstream epidermal stress genes, while *IL17D* is downregulated.

(c) Boxplots of keratinization- and epidermal hyperplasia-associated genes (*KRT6A, KRT6C, KRT16, KRT17, LCE3D*). Lesional skin shows strong induction, with non-lesional samples displaying intermediate expression consistent with subclinical activation of epidermal repair programs.

(a)



(b)


Th22-IL-22 Pathway-IL-22 Inducible Epidermal Stress
CALM3
SERPINB13
S100A7
S100A8
S100A9
SERPINB3
SERPINB4
BATF
ARNTL2
IL22RA1
IL22RA2
S100A7A
HRNR
L
NL
NC

(c)

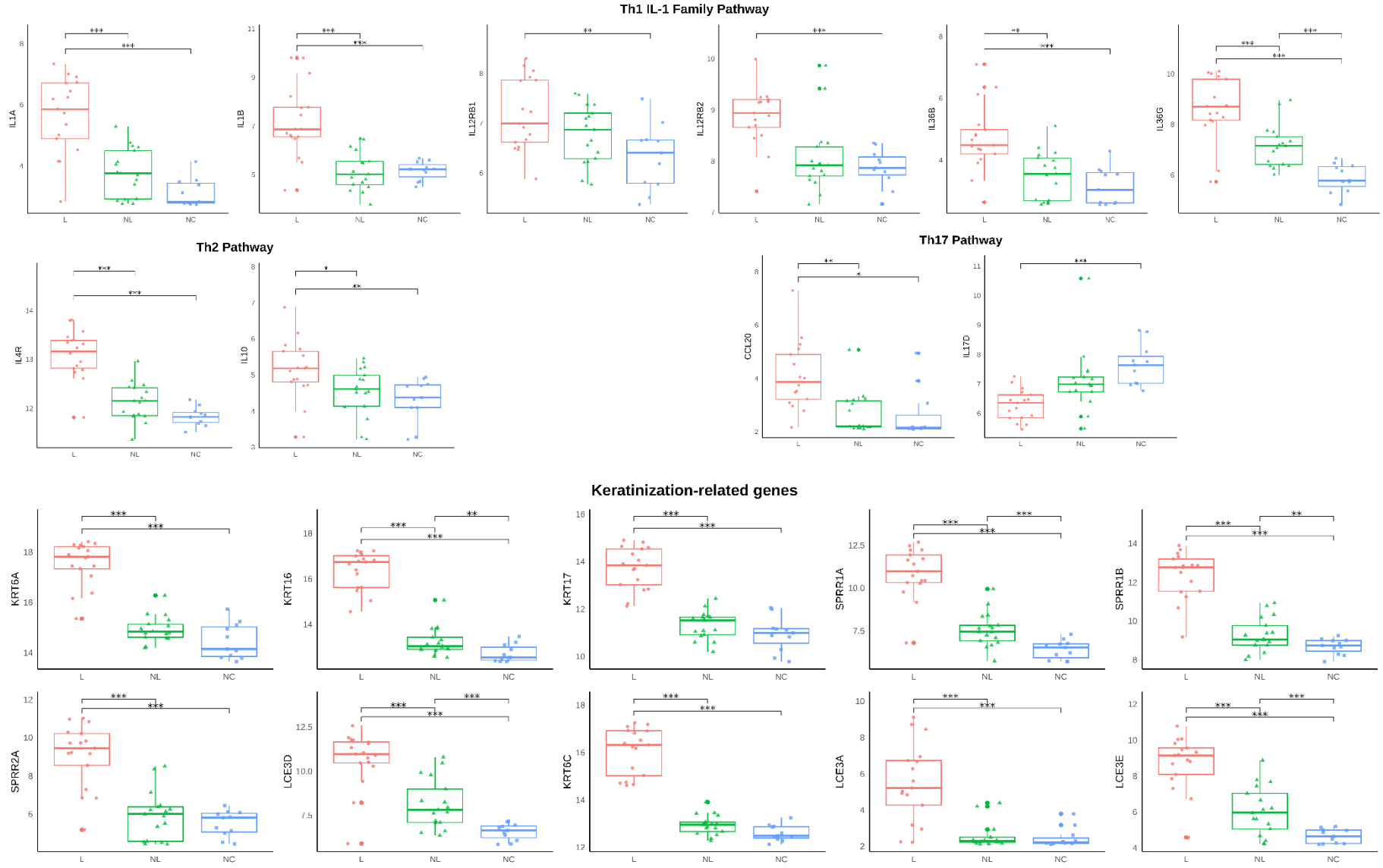

Th1 IL-1 Family Pathway
IL1A
IL1B
IL12RB1
IL12RB2
IL36B
IL36G
Th2 Pathway
IL4R
IL10
Th17 Pathway
CCL20
IL17D
Keratinization-related genes
KRT6A
KRT16
KRT17
SPRR1A
SPRR1B
SPRR2A
LCE3D
KRT6C
LCE3A
LCE3E
L
NL
NC

Figure S3. Expression profiles of key pathogenic pathways and selected genes of interest in PN.

Boxplots showing representative DEGs from major biological domains implicated in PN pathogenesis:

(a) Fibroblast activation and cytokine–JAK-STAT signaling — *WNT5A, IL6, OSM, OSMR, IL31RA, JAK3, PTPN7, PTPRE, SOCS1, SOCS3*. Lesional skin shows marked upregulation of fibroblast-remodeling and cytokine–JAK-STAT pathway components, consistent with profibrotic and chronic inflammatory signaling.

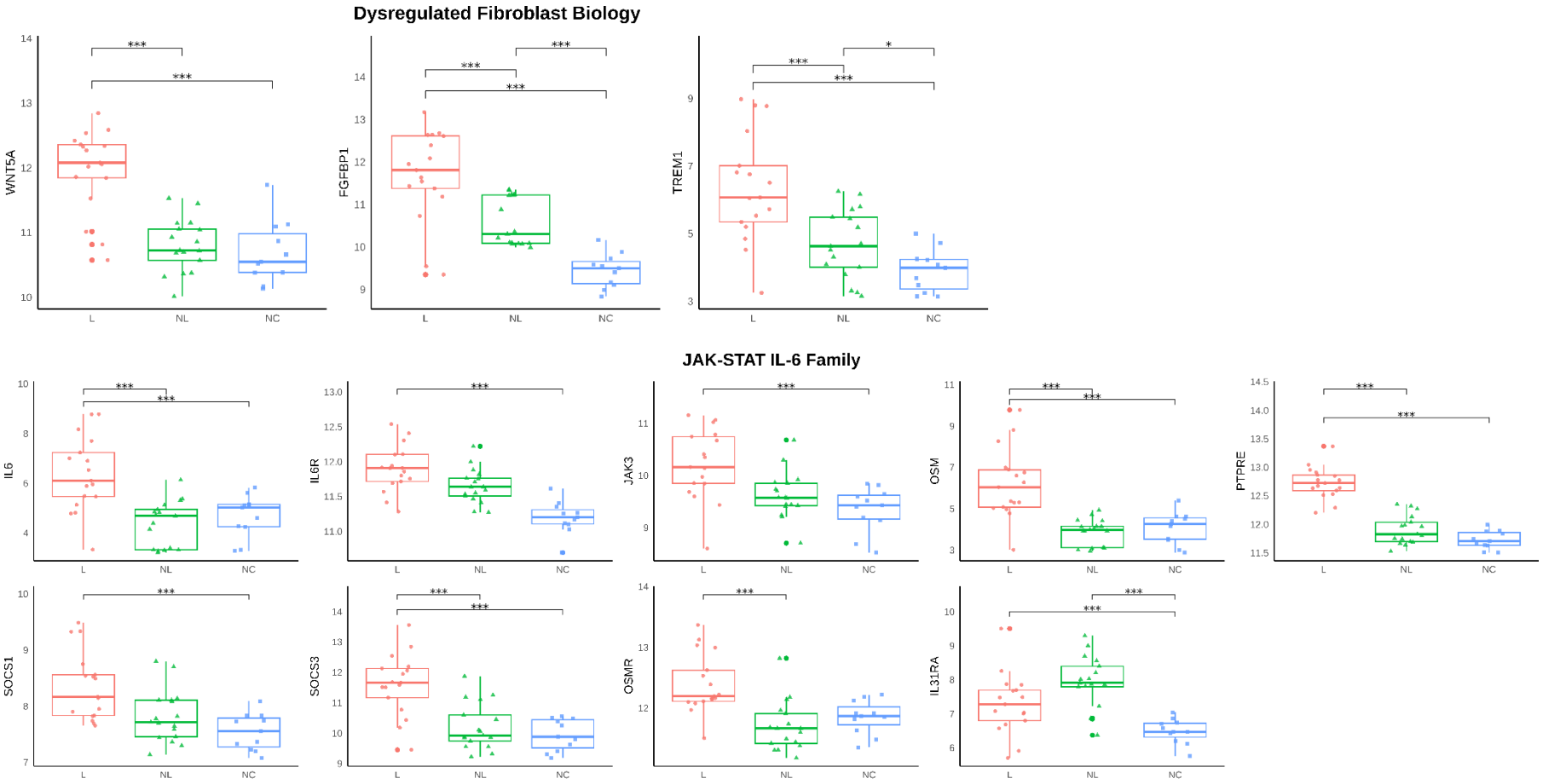
(b) Neuroimmune signaling and sensory receptor regulation—*HRH1, HRH2, HRH3, NTRK1, OPRK1, TRPM8, MRGPRX2, TRPV3*. Lesional PN skin demonstrates increased expression of neuroimmune effectors (e.g., *CHAT, TRPV3*) and reduced expression of the inhibitory receptor *OPRK1*, consistent with neuronal sensitization and heightened itch signaling.

(c) Senescence and stress-associated genes — *CDKN1A, CXCL8, SERPINE1, PLAUR*. Upregulation indicates activation of senescence-associated secretory phenotype (SASP) programs and persistent tissue stress.

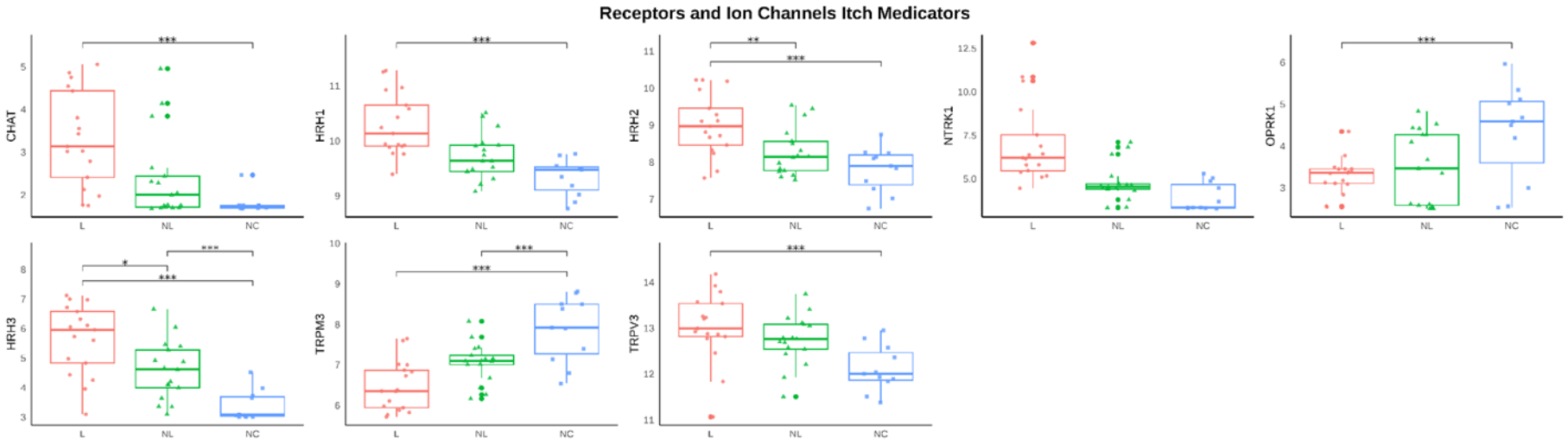
(d) Ethnicity-associated itch modulators — *S100A2* and *SLC24A5* are significantly elevated in lesional PN skin, suggesting potential ethnic-specific modulation of sensory thresholds and disease expression.

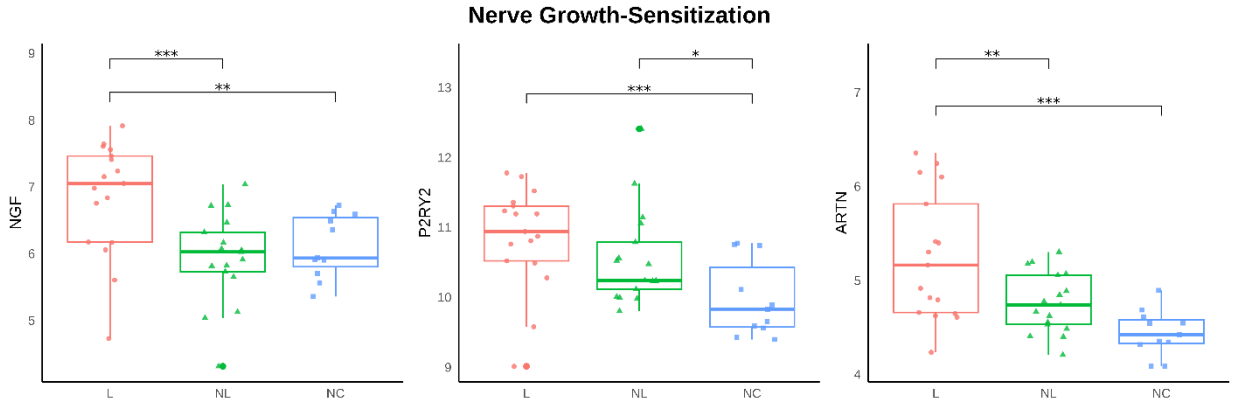
(e) Antimicrobial/alarmin response and wound healing — *IL20, DEFB103A, DEFB103B, MMP1, MMP3*. Increased expression reflects enhanced epidermal defense, inflammatory amplification, and matrix-remodeling activity.

(a)

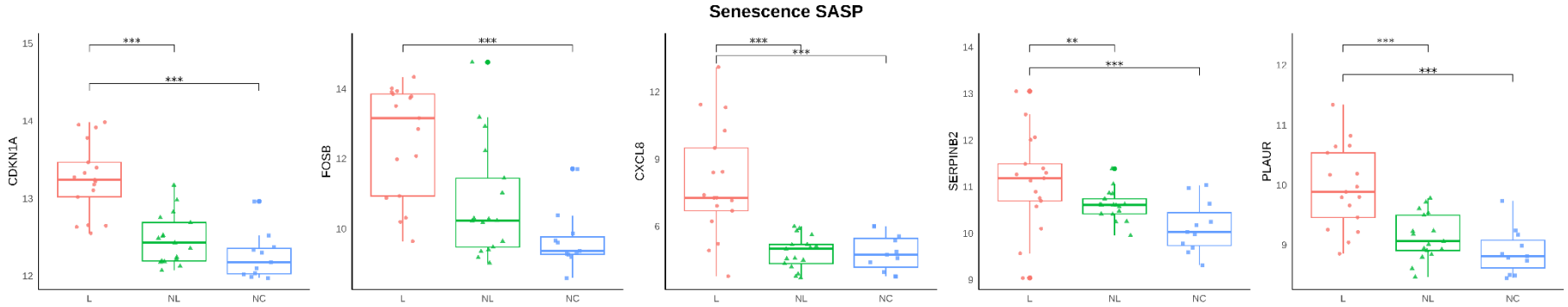

Dysregulated Fibroblast Biology
WNT5A
FGFBP1
TREM1
JAK-STAT IL-6 Family
IL6
IL6R
JAK3
OSM
PTPRE
SOCS1
SOCS3
OSMR
IL31RA
L
NL
NC
***
*

(b)

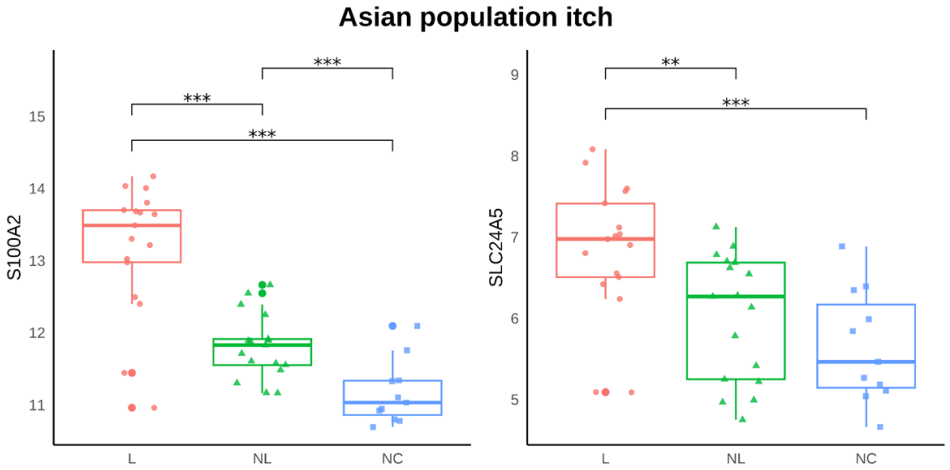

Receptors and Ion Channels Itch Medicators
CHAT
HRH1
HRH2
NTRK1
OPRK1
HRH3
TRPM3
TRPV3
L
NL
NC


Nerve Growth-Sensitization
NGF
P2RY2
ARTN
L
NL
NC

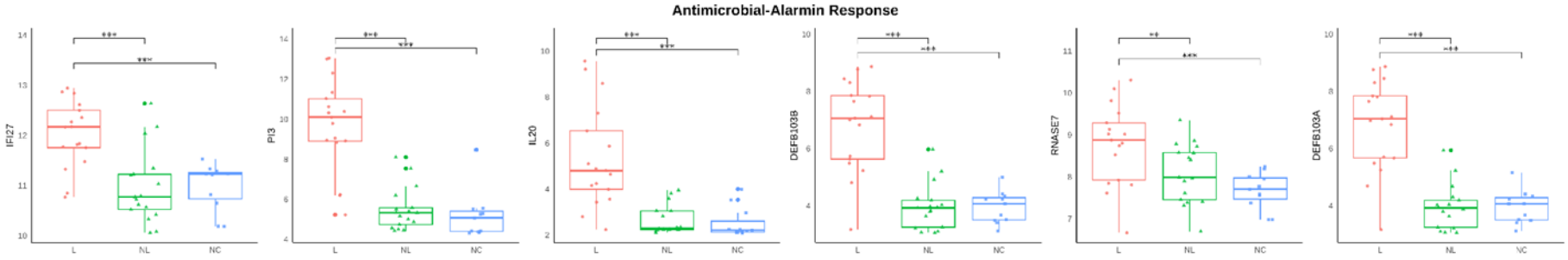
(c)

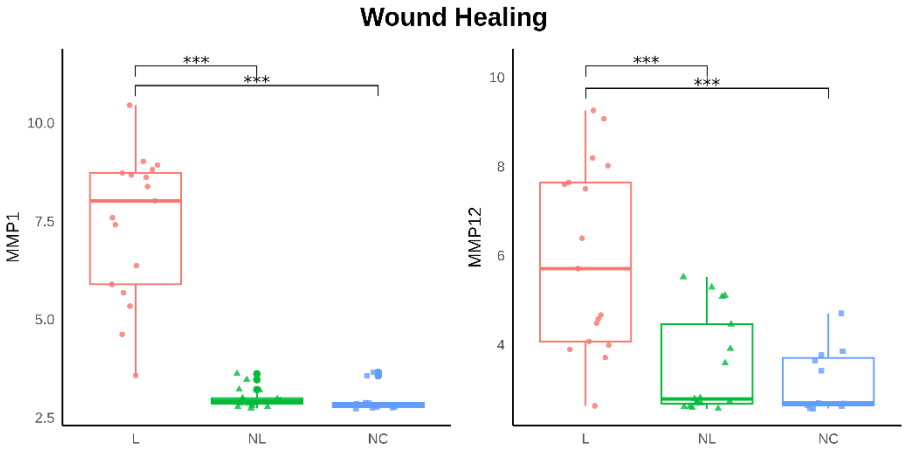

Senescence SASP
CDKN1A
FOSB
CXCL8
SERPINB2
PLAUR
L
NL
NC

(d)


Asian population itch
S100A2
SLC24A5
L
NL
NC

(e)


Antimicrobial-Alarmin Response
IFI27
PI3
IL20
DEFB103B
RNASE7
DEFB103A
L
NL
NC


Wound Healing
MMP1
MMP12
L
NL
NC