

Supplemental Table 1. Differentially expressed genes in lesional versus healthy control and lesional versus non-lesional skin, ranked by Q-value, combined data from both datasets.

| Lesional Versus Healthy Control | | | | | | Lesional Versus Non-Lesional | | | | | |
|---------------------------------|------------------|------------------|---------------|------------------|------------------|------------------------------|------------------|------------------|---------------|------------------|------------------|
| Upregulated | | | Downregulated | | | Upregulated | | | Downregulated | | |
| Gene Symbol | Log2 Fold Change | Q-Value | Gene Symbol | Log2 Fold Change | Q-Value | Gene Symbol | Log2 Fold Change | Q-Value | Gene Symbol | Log2 Fold Change | Q-Value |
| CCL2 | 3.46 | 4.1 6E -13 | AHS A2 | -1.13 | 2.9 7E -09 | CCL2 | 3.31 | 1.0 6E -12 | STAR D9 | -1.10 | 1.1 9E -09 |
| CH25 H | 2.31 | 3.3 9E -11 | EBF3 | -1.00 | 3.7 5E -09 | SELE | 2.96 | 2.2 4E -11 | OSR 2 | -1.26 | 1.9 5E -06 |
| CD69 | 2.30 | 7.0 6E -11 | BOC | -1.07 | 1.8 1E -08 | CH25 H | 2.25 | 2.2 4E -11 | ABC A6 | -1.49 | 4.6 0E -06 |
| SOCS 3 | 2.27 | 7.0 6E -11 | PIK3I P1 | -1.10 | 2.4 9E -08 | SOCS 3 | 2.14 | 9.4 8E -11 | CD3 4 | -1.18 | 1.1 3E -05 |
| SELE | 2.91 | 1.6 7E -10 | TNS1 | -1.18 | 4.0 7E -08 | BYSL | 1.09 | 1.1 9E -09 | ABC A9 | -1.03 | 1.6 2E -05 |
| CEBP D | 1.02 | 1.3 9E -09 | NUA K1 | -1.26 | 4.4 0E -08 | CD69 | 1.81 | 1.2 9E -09 | ABC A8 | -1.04 | 5.1 9E -05 |
| NNM T | 2.42 | 2.9 7E -09 | VIPR 1 | -1.03 | 5.1 9E -08 | DDX2 1 | 1.79 | 2.6 2E -09 | SEPP 1 | -1.08 | 2.8 4E -04 |
| DDX2 1 | 1.78 | 2.9 7E -09 | RNPC 3 | -1.15 | 5.1 9E -08 | NOLC 1 | 1.32 | 3.0 5E -09 | RER GL | -1.14 | 3.3 8E -04 |
| BYSL | 1.09 | 2.9 7E -09 | HOX A6 | -1.57 | 5.4 2E -08 | OSM R | 1.58 | 2.4 6E -08 | LGR 5 | -1.43 | 8.6 9E -04 |
| ZNF2 59 | 1.08 | 2.9 7E -09 | CLD N5 | -1.30 | 1.0 1E -07 | RRS1 | 1.37 | 2.4 6E -08 | KRT 15 | -1.14 | 1.0 4E -03 |
| DPH3 | 1.05 | 3.3 9E -09 | SUN1 | -1.03 | 1.9 6E -07 | PAK1 IP1 | 1.24 | 3.0 7E -08 | TIM P3 | -1.05 | 1.0 8E -03 |
| MT2A | 2.30 | 4.4 8E -09 | ANK RD36 C | -1.47 | 2.4 4E -07 | MT2A | 2.01 | 3.1 0E -08 | DCL K1 | -1.19 | 1.2 2E -03 |

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|---------|------|------------------|------------|-------|------------------|---------|------|------------------|-------------|-------|------------------|
| S100A8 | 4.28 | 4.6 1E -09 | LDB2 | -1.15 | 2.8 4E -07 | GNL3 | 1.02 | 3.1 0E -08 | ADH 1C | -1.11 | 1.2 5E -03 |
| CLEC4A | 1.72 | 4.6 4E -09 | RERG | -1.13 | 3.8 2E -07 | CTPS1 | 1.24 | 3.5 2E -08 | ANG PTL1 | -1.37 | 1.8 5E -03 |
| NMI | 1.13 | 4.6 4E -09 | HOXA5 | -1.13 | 4.5 3E -07 | WDR3 | 1.18 | 3.7 3E -08 | SLC14A1 | -1.32 | 3.3 7E -03 |
| S100A9 | 3.25 | 6.4 2E -09 | CD86 | -2.23 | 4.7 7E -07 | PNO1 | 1.20 | 4.4 8E -08 | ADH1B | -1.14 | 3.7 1E -03 |
| MAK16 | 1.07 | 6.4 2E -09 | NKA PP1 | -1.26 | 6.3 1E -07 | NIP7 | 1.13 | 4.5 1E -08 | ACTA2 | -1.02 | 8.8 8E -03 |
| JUNB | 1.67 | 7.9 0E -09 | HECTD4 | -1.08 | 6.3 8E -07 | MYC | 1.63 | 4.5 1E -08 | AQP5 | -1.00 | 2.3 6E -02 |
| OSMR | 1.74 | 8.2 4E -09 | OSR2 | -1.46 | 6.7 3E -07 | NOP2 | 1.25 | 4.9 5E -08 | SLC12A2 | -1.07 | 3.3 8E -02 |
| LCP2 | 1.20 | 8.2 4E -09 | MAP3K4 | -1.12 | 7.9 4E -07 | JUNB | 1.40 | 4.9 5E -08 | SCGB2A2 | -1.22 | 4.8 3E -02 |
| RAN | 1.03 | 8.4 1E -09 | TET1 | -1.05 | 9.9 5E -07 | PUS7 | 1.21 | 6.2 4E -08 | | | |
| CTSL | 2.71 | 1.0 1E -08 | ZNF273 | -1.30 | 1.5 4E -06 | CLEC4A | 1.42 | 6.2 4E -08 | | | |
| MTHFD2 | 1.50 | 1.0 1E -08 | ATP1B2 | -1.07 | 1.8 6E -06 | YARS | 1.14 | 6.2 4E -08 | | | |
| HN1 | 1.10 | 1.0 1E -08 | DDX17 | -1.18 | 3.0 3E -06 | GPATCH4 | 1.06 | 6.2 4E -08 | | | |
| GARS | 1.10 | 1.0 1E -08 | SOSTDC1 | -1.20 | 3.2 2E -06 | MTHFD2 | 1.38 | 7.7 5E -08 | | | |
| PNO1 | 1.33 | 1.1 6E -08 | TG | -1.27 | 3.2 7E -06 | CDKN1A | 1.07 | 9.3 4E -08 | | | |
| GPATCH4 | 1.23 | 1.1 8E -08 | TNNI2 | -1.08 | 4.0 0E -06 | SEH1L | 1.06 | 9.7 0E -08 | | | |

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|-----------|------|------------------|-------------------|-------|------------------|--------------|------|------------------|--|--|--|--|
| KIAA 0020 | 1.04 | 1.2 1E -08 | ARH GEF2 8 | -1.22 | 4.1 6E -06 | TARS | 1.06 | 1.1 3E -07 | | | | |
| GNL3 | 1.05 | 1.2 5E -08 | SNOR A37 | -1.25 | 4.1 7E -06 | CCT2 | 1.01 | 1.1 3E -07 | | | | |
| ZFP36 | 2.07 | 1.3 8E -08 | RCA N2 | -1.03 | 4.9 9E -06 | NFIL3 | 1.13 | 1.2 9E -07 | | | | |
| PAK1 IP1 | 1.23 | 1.4 9E -08 | HBP1 | -1.04 | 5.4 2E -06 | SLC2 A3 | 1.51 | 1.4 0E -07 | | | | |
| GAS5 | 1.05 | 1.4 9E -08 | KRT1 5 | -1.68 | 6.1 5E -06 | TRIB1 | 1.18 | 1.4 0E -07 | | | | |
| LRRC 59 | 1.52 | 1.5 3E -08 | FAT3 | -1.04 | 6.3 1E -06 | ZFP36 | 1.76 | 1.4 4E -07 | | | | |
| PARP 9 | 1.20 | 1.5 3E -08 | VWF | -1.21 | 6.4 6E -06 | ETS2 | 1.28 | 1.4 4E -07 | | | | |
| PANX 1 | 1.55 | 1.6 2E -08 | LMO D1 | -1.26 | 6.7 9E -06 | EIF4A 1P2 | 1.01 | 1.8 7E -07 | | | | |
| IL1B | 2.03 | 1.9 8E -08 | CRH R1- IT1 | -1.47 | 7.7 5E -06 | MRT O4 | 1.09 | 2.0 6E -07 | | | | |
| NABP 1 | 1.89 | 3.0 6E -08 | TFCP 2L1 | -1.23 | 9.0 6E -06 | ADA MTS1 | 1.55 | 2.2 1E -07 | | | | |
| HCK | 1.35 | 3.0 6E -08 | SOX6 | -1.01 | 9.9 3E -06 | NOP1 6 | 1.03 | 2.6 1E -07 | | | | |
| RRP1 5 | 1.10 | 3.0 6E -08 | HIST 1H1E | -1.13 | 1.4 7E -05 | STEAP4 | 2.15 | 3.0 8E -07 | | | | |
| LTV1 | 1.07 | 3.6 7E -08 | TBX1 8 | -1.09 | 2.0 7E -05 | THBS 1 | 2.47 | 3.3 7E -07 | | | | |
| GPR1 83 | 1.86 | 3.6 8E -08 | FOXS 1 | -1.07 | 2.0 7E -05 | ADA MTS9 | 1.77 | 3.4 2E -07 | | | | |
| EBNA 1BP2 | 1.22 | 3.9 0E -08 | PPP6 R1 | -2.10 | 2.2 0E -05 | S100A 8 | 3.34 | 3.4 4E -07 | | | | |

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|--------------|------|------------------|------------|-------|------------------|--------------|------|------------------|--|--|--|--|
| MYC | 1.60 | 4.0 6E -08 | KAN K2 | -1.02 | 2.3 6E -05 | EBNA 1BP2 | 1.09 | 3.5 5E -07 | | | | |
| TRIB1 | 1.31 | 4.0 6E -08 | SYNP O2 | -1.30 | 2.5 1E -05 | TUBA 1C | 1.18 | 3.5 5E -07 | | | | |
| IFI16 | 1.35 | 4.0 8E -08 | MYL K | -1.17 | 3.2 8E -05 | LYAR | 1.07 | 4.0 2E -07 | | | | |
| RPF2 | 1.03 | 4.6 1E -08 | CKM | -1.09 | 3.8 6E -05 | SLC2 5A25 | 1.18 | 4.3 3E -07 | | | | |
| NOLC 1 | 1.18 | 4.7 0E -08 | PGM5 | -1.04 | 4.8 9E -05 | PANX 1 | 1.30 | 4.3 7E -07 | | | | |
| RND3 | 1.13 | 4.8 6E -08 | SPEN | -1.91 | 4.9 4E -05 | IL1B | 1.60 | 4.8 9E -07 | | | | |
| TARS | 1.09 | 4.8 6E -08 | PDE5 A | -1.03 | 4.9 7E -05 | LRRC 59 | 1.25 | 5.3 3E -07 | | | | |
| GNL2 | 1.04 | 4.9 1E -08 | FZD4 | -1.04 | 5.1 8E -05 | NABP 1 | 1.70 | 5.3 3E -07 | | | | |
| UTP1 4A | 1.04 | 5.4 2E -08 | RPA4 | -1.88 | 5.6 4E -05 | S100A 9 | 2.37 | 6.2 8E -07 | | | | |
| LYAR | 1.21 | 5.6 7E -08 | VPS1 8 | -2.03 | 1.0 3E -04 | NNM T | 1.62 | 6.4 7E -07 | | | | |
| SERPI NB1 | 1.31 | 7.2 1E -08 | AOC3 | -1.26 | 2.2 2E -04 | RIOK 1 | 1.03 | 6.6 3E -07 | | | | |
| PUS7 | 1.20 | 7.3 9E -08 | RERG L | -1.19 | 2.3 3E -04 | SERPI NB1 | 1.13 | 7.7 1E -07 | | | | |
| URB2 | 1.02 | 7.8 1E -08 | TIMP 3 | -1.18 | 3.1 3E -04 | TME M2 | 1.14 | 7.7 2E -07 | | | | |
| THBS 1 | 2.80 | 8.8 9E -08 | LRRC 2 | -2.27 | 3.5 0E -04 | DNAJ A1 | 1.05 | 8.4 9E -07 | | | | |
| UAP1 | 2.44 | 9.6 7E -08 | ACT A2 | -1.34 | 3.7 5E -04 | CYR6 1 | 1.74 | 9.3 8E -07 | | | | |

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| TNFA IP6 | 3.78 | 1.1 0E -07 | TPM2 | -1.07 | 4.4 2E -04 | PNP | 1.62 | 9.8 3E -07 | | | | |
| CCR1 | 1.60 | 1.3 3E -07 | KCN K5 | -1.12 | 5.3 4E -04 | CXCL 1 | 1.32 | 9.8 8E -07 | | | | |
| WDR 3 | 1.08 | 1.4 0E -07 | MYO C | -1.20 | 7.9 8E -04 | CTSL | 2.02 | 1.0 1E -06 | | | | |
| SLC3 9A14 | 2.41 | 1.4 2E -07 | ACTB L2 | -1.10 | 8.6 1E -04 | MPZL 2 | 1.05 | 1.0 7E -06 | | | | |
| DNAJ A1 | 1.21 | 1.4 2E -07 | DES | -1.50 | 1.2 0E -03 | SLC3 9A14 | 1.54 | 1.3 1E -06 | | | | |
| CYTI P | 1.42 | 1.7 3E -07 | ATP1 B1 | -1.11 | 1.3 4E -03 | IL4R | 1.08 | 1.4 9E -06 | | | | |
| DDX1 0 | 1.11 | 1.7 3E -07 | MYL 9 | -1.12 | 1.4 3E -03 | HSPH 1 | 1.30 | 1.5 4E -06 | | | | |
| HSPA 4 | 1.03 | 1.9 7E -07 | EPB4 2 | -1.05 | 1.4 9E -03 | GPR1 83 | 1.41 | 1.7 9E -06 | | | | |
| HSP9 0AA1 | 1.01 | 2.0 3E -07 | RHPN 2 | -1.13 | 1.8 6E -03 | IL6 | 2.52 | 1.8 6E -06 | | | | |
| YARS | 1.07 | 2.1 0E -07 | FRZB | -1.13 | 2.1 1E -03 | IFI16 | 1.02 | 1.9 5E -06 | | | | |
| STEA P4 | 2.29 | 2.1 7E -07 | ACT G2 | -1.14 | 2.3 1E -03 | IRF1 | 1.08 | 2.1 1E -06 | | | | |
| ETS2 | 1.28 | 2.2 2E -07 | CCD C66 | -1.03 | 2.9 1E -03 | CD18 0 | 1.03 | 2.6 8E -06 | | | | |
| SLC2 A3 | 1.50 | 2.4 4E -07 | AQP5 | -1.24 | 4.1 5E -03 | LDLR | 1.41 | 2.9 7E -06 | | | | |
| CXCR 2 | 1.27 | 2.4 7E -07 | GPA M | -1.16 | 5.7 4E -03 | WAR S | 1.46 | 3.8 1E -06 | | | | |
| CYR6 1 | 1.94 | 2.6 1E -07 | FABP 7 | -1.48 | 7.8 4E -03 | FCGR 2A | 1.67 | 3.8 1E -06 | | | | |

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| MAR S | 1.12 | 2.6 2E -07 | SCGB 1D1 | -1.11 | 7.9 9E -03 | UAP1 | 1.97 | 4.0 1E -06 | | | | |
| DNAJ C2 | 1.09 | 2.7 0E -07 | MUC L1 | -1.60 | 9.8 0E -03 | SLC1 A3 | 1.19 | 4.0 6E -06 | | | | |
| IRF1 | 1.25 | 3.0 5E -07 | SLC1 4A1 | -1.12 | 1.0 6E -02 | SOD2 | 1.73 | 4.3 3E -06 | | | | |
| MMP 19 | 1.03 | 3.0 5E -07 | SCGB 1D2 | -1.54 | 1.1 3E -02 | CCR1 | 1.17 | 4.8 8E -06 | | | | |
| RRS1 | 1.16 | 3.4 5E -07 | SLC1 2A2 | -1.08 | 1.1 8E -02 | DUSP 6 | 1.14 | 5.2 5E -06 | | | | |
| CXCL 1 | 1.45 | 3.8 4E -07 | ACT A1 | -1.10 | 1.3 7E -02 | ADA MTS4 | 2.11 | 5.8 8E -06 | | | | |
| HAS2 | 1.61 | 3.9 4E -07 | SERH L2 | -1.07 | 1.7 8E -02 | SRM | 1.14 | 6.0 8E -06 | | | | |
| HSPH 1 | 1.37 | 4.3 7E -07 | SCGB 2A2 | -1.26 | 2.9 6E -02 | PTGS 2 | 1.26 | 8.9 9E -06 | | | | |
| SRGN | 2.42 | 4.4 1E -07 | PIP | -1.67 | 3.2 7E -02 | TNFR SF12 A | 1.18 | 9.2 6E -06 | | | | |
| LCP1 | 1.54 | 4.4 6E -07 | | | | EGR1 | 1.58 | 1.0 1E -05 | | | | |
| SLC2 5A25 | 1.25 | 5.0 8E -07 | | | | CCL8 | 1.10 | 1.0 2E -05 | | | | |
| TUBA 1C | 1.14 | 5.7 9E -07 | | | | SRGN | 1.90 | 1.0 2E -05 | | | | |
| FCGR 2A | 1.95 | 5.8 6E -07 | | | | PLSC R1 | 1.16 | 1.0 7E -05 | | | | |
| ADA MTS1 | 1.52 | 5.9 3E -07 | | | | THBD | 1.17 | 1.0 7E -05 | | | | |
| PI3 | 1.69 | 6.1 1E -07 | | | | SLC5 A6 | 1.17 | 1.1 1E -05 | | | | |

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| MT1J P | 1.07 | 6.2 8E -07 | | | | TNFA IP6 | 2.86 | 1.5 4E -05 | | | |
| FGFB P1 | 1.79 | 6.5 4E -07 | | | | HAS2 | 1.34 | 1.6 7E -05 | | | |
| ADA MTS9 | 1.72 | 6.9 2E -07 | | | | FOSL 1 | 1.16 | 1.6 8E -05 | | | |
| SPRR 2A | 2.95 | 7.3 2E -07 | | | | SPRE D1 | 1.23 | 2.0 0E -05 | | | |
| SLA | 1.16 | 7.8 9E -07 | | | | HBEG F | 1.12 | 2.1 9E -05 | | | |
| SAMS N1 | 1.05 | 8.2 6E -07 | | | | ODC1 | 1.22 | 2.2 8E -05 | | | |
| PLAU R | 1.25 | 8.7 0E -07 | | | | ATP1 3A3 | 1.01 | 3.3 8E -05 | | | |
| LCE2 A | 1.33 | 8.7 3E -07 | | | | DSG3 | 1.16 | 4.1 8E -05 | | | |
| IL4R | 1.22 | 8.8 6E -07 | | | | NR4A 3 | 1.20 | 4.3 1E -05 | | | |
| CTPS 1 | 1.04 | 9.0 3E -07 | | | | TREM 1 | 1.37 | 4.3 3E -05 | | | |
| S100A 12 | 2.03 | 9.1 8E -07 | | | | SLC7 A5 | 1.29 | 4.3 6E -05 | | | |
| IL36G | 1.19 | 9.1 8E -07 | | | | FPR2 | 1.40 | 4.3 7E -05 | | | |
| NOP2 | 1.04 | 9.7 2E -07 | | | | SECT M1 | 1.26 | 4.5 6E -05 | | | |
| NCF2 | 1.66 | 1.0 6E -06 | | | | PI3 | 1.21 | 4.7 6E -05 | | | |
| LCE1 C | 1.84 | 1.0 7E -06 | | | | CXCL 2 | 1.11 | 5.0 0E -05 | | | |

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| CRISP LD2 | 1.30 | 1.0 7E -06 | | | | S100A 12 | 1.50 | 6.4 3E -05 | | | |
| GNA1 5 | 1.10 | 1.0 7E -06 | | | | SERPI NE1 | 1.01 | 6.8 4E -05 | | | |
| TIMP 1 | 2.07 | 1.0 9E -06 | | | | ACSL 4 | 1.06 | 1.0 2E -04 | | | |
| SPRR 2D | 2.90 | 1.1 4E -06 | | | | HAS3 | 1.13 | 1.3 9E -04 | | | |
| STEA P1 | 1.36 | 1.1 4E -06 | | | | DOK5 | 1.39 | 1.5 5E -04 | | | |
| SPRR 2E | 2.67 | 1.3 0E -06 | | | | AQP3 | 1.07 | 1.6 2E -04 | | | |
| SRM | 1.27 | 1.3 5E -06 | | | | OSM | 1.19 | 1.8 6E -04 | | | |
| GALN T6 | 1.15 | 1.3 9E -06 | | | | NCF2 | 1.10 | 1.8 6E -04 | | | |
| IL1R1 | 1.01 | 1.4 8E -06 | | | | CSRN P1 | 1.10 | 2.0 4E -04 | | | |
| CD18 0 | 1.09 | 1.5 4E -06 | | | | SELL | 1.34 | 2.0 7E -04 | | | |
| CCL8 | 1.26 | 1.6 1E -06 | | | | PTX3 | 2.84 | 2.1 8E -04 | | | |
| RAC2 | 1.24 | 1.6 2E -06 | | | | MMP 1 | 1.01 | 2.1 9E -04 | | | |
| GLIP R1 | 1.07 | 1.7 0E -06 | | | | KRT1 6 | 1.82 | 2.4 4E -04 | | | |
| CSF3 R | 1.43 | 1.7 6E -06 | | | | SERPI NE2 | 1.69 | 2.4 7E -04 | | | |
| KRTD AP | 1.23 | 2.0 5E -06 | | | | HIF1 A | 1.06 | 3.5 1E -04 | | | |

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|--------------|------|------------------|--|--|--|--------------|------|------------------|--|--|--|
| SPIN K5 | 1.22 | 2.0 5E -06 | | | | IVL | 1.25 | 3.6 6E -04 | | | |
| FPR3 | 1.61 | 2.2 1E -06 | | | | FGFB P1 | 1.09 | 3.8 1E -04 | | | |
| TME M2 | 1.12 | 2.2 5E -06 | | | | B4GA LT5 | 1.05 | 4.9 1E -04 | | | |
| LCE2 B | 1.82 | 2.4 0E -06 | | | | KRT6 A | 2.14 | 6.2 8E -04 | | | |
| PLSC R1 | 1.30 | 2.5 4E -06 | | | | GZM B | 1.04 | 7.0 6E -04 | | | |
| PNP | 1.53 | 2.5 6E -06 | | | | PLAU | 1.14 | 8.5 4E -04 | | | |
| SAM HD1 | 1.04 | 2.6 5E -06 | | | | SLC7 A11 | 1.00 | 9.1 6E -04 | | | |
| FLG2 | 1.20 | 2.6 7E -06 | | | | AQP9 | 1.20 | 1.1 4E -03 | | | |
| ASPR V1 | 2.04 | 2.8 7E -06 | | | | ATF3 | 1.22 | 1.1 4E -03 | | | |
| NR4A 3 | 1.51 | 2.9 3E -06 | | | | SPRR 2A | 1.38 | 1.1 4E -03 | | | |
| IL6 | 2.51 | 3.1 2E -06 | | | | CCL1 9 | 1.12 | 1.2 9E -03 | | | |
| AQP3 | 1.34 | 3.3 6E -06 | | | | S100A 2 | 1.09 | 1.5 6E -03 | | | |
| SERPI NB4 | 2.52 | 3.4 3E -06 | | | | FOSB | 1.95 | 1.7 9E -03 | | | |
| BIRC 3 | 1.16 | 3.9 0E -06 | | | | S100A 7 | 1.49 | 3.3 3E -03 | | | |
| S100A 7 | 2.68 | 4.0 6E -06 | | | | SERPI NB4 | 1.44 | 4.0 3E -03 | | | |

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| C1QB | 1.32 | 1.4 1E -02 | | | | | | | | | |
| ATP1 2A | 1.32 | 4.0 7E -02 | | | | | | | | | |
| IGJ | 1.06 | 4.1 6E -02 | | | | | | | | | |

Supplementary Table 2. Top 10 upregulated ToppGene pathways in CSU lesional skin versus healthy control skin.

| Pathway | Q-Value | Genes Upregulated | Perc enta ge* (%) |
|--------------------------------|--------------|---|----------------------------|
| 1. Keratinization | 4.62E -56 | <i>KRT6C, KRTAP5-8, LCE1C, LCE1B, LCE1E, LCE1A, LCE2D, LCE2C, LCE3B, LCE3A, LCE2A, LCE3E, KRTAP4-7, LCE5A, KRTAP4-9, KRT26, CDSN, KRTAP12-2, KRTAP12-1, KRT80, PI3, KLK5, KRT23, CSTA, KLK13, KRTAP5-5, KRTAP10-11, KRTAP10-4, KRTAP10-7, KRTAP10-12, LCE2B, KRTAP5-2, KRTAP5-7, KRTAP5-11, DSC1, KRTAP1-5, KRTAP3-2, KRTAP3-1, KRTAP9-8, KRTAP9-3, KRTAP17-1, KRTAP19-1, KRTAP19-5, KRTAP20-2, KRTAP5-4, KRTAP5-10, FLG, LCE6A, KRTAP9-6, SPRR1A, SPRR1B, SPRR2A, SPRR2B, SPRR2D, SPRR2E, SPRR2F, SPRR2G, KRTAP4-4, LCE3D, SPINK5, TGM1, KLK8, LCE4A, KRTAP4-8, KRTAP2-2, KRTAP9-1, KRTAP9-4, KRTAP4-1, KRTAP4-5, KRTAP4-2, KRTAP4-3, KRTAP3-3, KRTAP2-4, KRTAP9-7, IVL, RPTN, KRTAP26-1, KRT1, KRT2, KRT6A, KRT10, KRT16, KRT33A, KRT33B, KRT34, KRT83, KRT86, LORICRIN, KRTAP1-1, KRTAP1-3, KRTAP4-6, KRTAP9-9, KRTAP2-1</i> | 43.5 |
| 2. Neutrophil degranulation | 1.69E -23 | <i>SERPINA3, ACP3, ADAM8, MMP9, MNDA, ALOX5, ANPEP, ARG1, CREG1, GGH, C3AR1, C5AR1, PNP, FCGR2C, CD14, CD33, CD53, CD68, ADGRE5, CTSC, SERPINA1, GCA, PLAU, PLAUR, GMFG, PRG2, CTSS, CYBB, PRSS2, PRSS3, CD55, PTAFR, CMTM6, PTPRC, PTX3, PYGL, CRISPLD2, DSC1, SIGLEC14, SERPINB1, PSMD14, PGM2, STOM, LILRB2, DOK3, FABP5, S100A7, S100A8, S100A9, S100A11, S100A12, TUBB4B, FCER1G, FCGR2A, FCGR3B, FCN1, SERPINB3, SELL, FPR1, FPR2, CCT2, SLC2A3, CD93,</i> | 19.1 |

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| | | <i>SLC11A1, SLPI, CALML5, HPSE, FGL2, ADGRE3, GLIPR1, LILRB3, RAB31, ARHGAP9, NFAM1, CXCL1, MMP25, TLR2, TNFAIP6, MCEMP1, HLA-C, ABCA13, TYROBP, HSPA8, HSP90AA1, RETN, CXCR1, CXCR2, FLG2, ITGAM, ITGAX, ITGB2, KRT1, LAIR1, LYZ</i> | |
| 3. Formation of the cornified envelope | 1.69E -23 | <i>LCE1C, LCE1B, LCE1E, LCE1A, LCE2D, LCE2C, LCE3B, LCE3A, LCE2A, LCE3E, LCE5A, CDSN, PI3, KLK5, CSTA, KLK13, LCE2B, DSC1, FLG, LCE6A, SPRR1A, SPRR1B, SPRR2A, SPRR2B, SPRR2D, SPRR2E, SPRR2F, SPRR2G, LCE3D, SPINK5, TGM1, KLK8, LCE4A, IVL, RPTN, LORICRIN</i> | 50.7 |
| 4. Innate Immune System | 4.50E -17 | <i>SERPINA3, ACP3, ADAM8, CCR2, MMP9, MNDA, ALOX5, ANPEP, BIRC3, ARG1, ATP6V1B2, NCF2, NCF4, CREG1, CFB, GGH, POLR3D, IER3, NFKBIB, C1QB, C3AR1, C5AR1, PNP, CASP4, FCGR2C, CD14, CD33, TREM1, CD53, CD68, ADGRE5, CDKN1A, CTSC, NLRC4, SERPINA1, PI3, PLA2G2A, GCA, PLAU, PLAUR, APBB1IP, MAP3K8, POLR1C, GMFG, PPP2CA, PRG2, MAPK13, MAP2K3, CTSI, CTSV, CTSS, CYBB, LGMN, PRSS2, PRSS3, CD55, PTAFR, DEFA3, CMTM6, DEFB4A, PTPRC, CLEC4A, PTX3, PYGL, CRISPLD2, DSC1, HBEGF, DUSP1, DUSP2, DUSP5, DUSP6, SIGLEC14, ARPC1B, ACTR3, SERPINB1, SPRED1, PSMD14, PGM2, STOM, EREG, LILRB2, NCF1, DOK3, CD209, FABP5, S100A7, S100A8, S100A9, S100A11, S100A12, TUBB4B, FCER1G, FCGR2A, FCGR3A, FCGR3B, FCN1, SERPINB3, FGF7, SELL, FOS, FPR1, FPR2, CCT2, SLC2A3, POLR3G, CD93, S100A7A, SLC11A1, SLPI, CD300E, DEFB103B, CALML5, HPSE, FGL2, NOD2, RNASE7, ADGRE3, GLIPR1, LILRB3, RAB31, ARHGAP9, NFAM1, CXCL1, MMP25, TLR2, TLR4, TNFAIP3, TNFAIP6, HCK, MCEMP1, HLA-C, ABCA13, TYROBP, HSPA8, HSP90AA1, LAT2, IFI16, RETN, IL1B, CXCR1, CXCR2, IRF1, PANX1, FLG2, ITGAM, ITGAX, ITGB2, ITGB3, MAPKAPK3, KRT1, LAIR1, LCP2, CD180, LYN, LYZ</i> | 11.8 |
| 5. Developmental Biology | 1.60E -14 | <i>H2AC6, KRT6C, MMP9, MSN, KRTAP5-8, NOTCH1, CACNB4, RPS6KA4, DOK2, LCE1C, LCE1B, LCE1E, LCE1A, LCE2D, LCE2C, LCE3B, LCE3A, LCE2A, LCE3E, KRTAP4-7, LCE5A, KRTAP4-9, KRT26, CDSN, CEBPD, KRTAP12-2, KRTAP12-1, KRT80, PI3, CLTB, KLK5, APBB1IP, COL4A4, KRT23, PPP2CA, CSTA, KLK13, KRTAP5-5, KRTAP10-11, KRTAP10-4, KRTAP10-7, KRTAP10-12, LCE2B, PTPRC,</i> | 12.0 |

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| | | <i>MAFB, KRTAP5-2, KRTAP5-7, KRTAP5-11, RAC2, DSC1, HBEGF, DUSP1, DUSP2, DUSP5, DUSP6, ARPC1B, ACTR3, EGR2, KRTAP1-5, KRTAP3-2, KRTAP3-1, KRTAP9-8, KRTAP9-3, KRTAP17-1, SPRED1, KRTAP19-1, PSMD14, EREG, KRTAP19-5, KRTAP20-2, COL6A5, KRTAP5-4, KRTAP5-10, FGF7, FLG, MED8, LCE6A, DOK5, KRTAP9-6, SPRR1A, SPRR1B, SPRR2A, SPRR2B, SPRR2D, SPRR2E, SPRR2F, SPRR2G, STAT3, KRTAP4-4, LCE3D, SPINK5, TGM1, KLK8, TNF, TYROBP, LCE4A, KRTAP4-8, KRTAP2-2, HSPA8, KRTAP9-1, HSP90AA1, KRTAP9-4, KRTAP4-1, KRTAP4-5, KRTAP4-2, KRTAP4-3, KRTAP3-3, KRTAP2-4, KRTAP9-7, ITGB3, IVL, RPTN, KRTAP26-1, KRT1, KRT2, KRT6A, KRT10, KRT16, KRT33A, KRT33B, KRT34, KRT83, KRT86, LORICRIN, KRTAP1-1, KRTAP1-3, KRTAP4-6, KRTAP9-9, KRTAP2-1, LYN</i> | |
| 6. Cytokine Signaling in Immune system | 1.82E -14 | <i>SEH1L, MCL1, CCR2, MMP1, MMP9, ALOX5, ANXA1, BIRC3, CCL3L3, MT2A, MX2, MYC, TNFSF14, IL18RAP, GBP5, SOCS3, NUP98, TNFRSF11B, OSM, IL1RL1, OSMR, CDKN1A, CEBPD, PIM1, CCR1, CCR5, APBB1IP, MAP3K8, SAMHD1, PPP2CA, CSF1R, CSF3, CSF3R, IL20, EIF4A3, PTAFR, IL22RA1, PTGS2, HBEGF, DUSP1, DUSP2, DUSP5, DUSP6, TRIM10, EGR1, EIF4A1, SPRED1, PSMD14, EREG, TNFRSF12A, FCGR1B, IFITM3, IFI30, CCL2, CCL3, FGF7, CCL4, CCL19, BATF, FOS, FPR1, IFITM2, IL36B, IL37, GBP1, STAT3, NOD2, CXCL1, CXCL2, TIMP1, TNF, IL36G, HCKHCK, IL34, HIF1A, HLA-C, HLA-DQA2, HLA-DQB1, HLA-DQB2, HMOX1, HSPA8, VCAM1, HSP90AA1, ICAM1, IFNAR2, IL1B, IL1R1, IL4R, IL6, IL7R, IL10, IL18, IRF1, IRF4, ISG20, ITGAM, ITGAX, ITGB2, ITGB3, JUNB, KPNA2, LTB, LYN</i> | 13.5 |
| 7. Interleukin-10 signaling | 8.42E -14 | <i>CCR2, CCL3L3, CCR1, CCR5, CSF3, PTAFR, PTGS2, CCL2, CCL3, CCL4, CCL19, FPR1, STAT3, CXCL1, CXCL2, TIMP1, TNF, ICAM1, IL1B, IL1R1, IL6, IL10, IL18</i> | 46.9 |
| 8. Interleukin-4 and 13 signaling | 1.03E -13 | <i>MCL1, MMP1, MMP9, ALOX5, ANXA1, MYC, SOCS3, OSM, CDKN1A, CEBPD, PIM1, PTGS2, CCL2, BATF, FOS, STAT3, TIMP1, TNF, HIF1A, HMOX1, HSPA8, VCAM1, HSP90AA1, ICAM1, IL1B, IL4R, IL6, IL10, IL18, IRF4, ITGAM, ITGAX, ITGB2, JUNB</i> | 29.8 |
| 9. Staphylococcus | 2.85E -11 | <i>CFB, C1QB, C3AR1, C5AR1, FCGR2C, PTAFR, FCGR2A, FCGR2B, FCGR3A, FCGR3B, SELP, SELPLG, FPR1, FPR2,</i> | 39.3 |

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| s aureus infection | <i>FPR3, HLA-DQA2, HLA-DQB1, ICAM1, IL10, ITGAM, ITGB2, KRT10</i> | |
| 10. Signaling by Interleukins 3.05E -11 | <i>MCL1, CCR2, MMP1, MMP9, ALOX5, ANXA1, CCL3L3, MYC, IL18RAP, SOCS3, OSM, IL1RL1, OSMR, CDKN1A, CEBPD, PIM1, CCR1, CCR5, APBB1IP, MAP3K8, PPP2CA, CSF1R, CSF3, CSF3R, IL20, PTAFR, IL22RA1, PTGS2, HBEGF, DUSP1, DUSP2, DUSP5, DUSP6, SPRED1, PSMD14, EREG, CCL2, CCL3, FGF7, CCL4, CCL19, BATF, FOS, FPR1, IL36B, IL37, STAT3, NOD2, CXCL1, CXCL2, TIMP1, TNF, IL36G, HCKHCK, IL34, HIF1A, HMOX1, HSPA8, VCAM1, HSP90AA1, ICAM1, IL1B, IL1R1, IL4R, IL6, IL7R, IL10, IL18, IRF4, ITGAM, ITGAX, ITGB2, ITGB3, JUNB, LYN</i> | 14.1 |

*Percentage of genes in the named pathway that were found to be upregulated in the dataset.

Supplementary Table 3. Selected upregulated ToppGene and KEGG pathways in CSU lesional skin versus healthy control skin.

| Pathway | Meth od | Q- Value | Genes Upregulated | Percentage* (%) |
|--|--------------|-------------|--|-----------------|
| IL-6 Mediated Signaling Events | Topp Gene | 8.28E -4 | <i>MCL1, MYC, SOCS3, CEBPD, FOS, STAT3, TIMP1, HCKHCK, IL6, IRF1, JUNB</i> | 25.6 |
| IL-12 Mediated Signaling Events | Topp Gene | 3.80E -3 | <i>GADD45B, IL18RAP, CCR5, MAP2K3, CCL3, CCL4, FOS, STAT3, GZMB, IL1B, IL1R1, IL18</i> | 19.7 |
| IL-18 Mediated Signaling Events | Topp Gene | 2.05E -7 | <i>MMP1, MMP9, BIRC3, FAS, ARL4D, ARG1, ATF3, NCF2, IL18RAP, IER3, SOCS3, CXCL16, CLDN1, TNFRSF11B, CYCS, CD83, CLDN4, PTGS2, PTX3, RGS16, NCF1, CCL2, CCL3, CCL4, CCL18, CCL19, ZC3H12A, FOS, SPP1, IL37, CXCL2, TIMP1, TNF, TNFAIP3, HMOX1, HSPB1, ICAM1, IL1B, IL6, IL10, IL18, IRF1, LTB</i> | 15.4 |
| IL-23 Mediated Signaling Events | Topp Gene | 1.04E -3 | <i>ALOX12B, IL18RAP, SOCS3, CCL2, STAT3, CXCL1, TNF, IL1B, IL6, IL18</i> | 27.0 |

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| IL-17 Signaling | Topp Gene | 3.60E -6 | <i>MMP1, MMP9, CSF3, MAPK6, MAPK13, PTGS2, DEFB4A, S100A7, S100A8, S100A9, CCL2, FOS, FOSB, CXCL1, CXCL2, TNF, TNFAIP3, HSP90AA1, IL1B, IL6, FOSL1</i> | 22.6 |
| IL-17 Signaling | KEG G | 3.75E -8 | <i>CSF3, HSP90AA1, MMP1, TNFAIP3, CXCL1, FOS, PTGS2, CXCL2, TNF, MMP9, MAPK13, S100A7A, FOSL1, IL6, IL1B, CCL2, FOSB, DEFB4A, MAPK6, S100A9, S100A8, S100A7</i> | 23.4 |
| Th17 Differentiation on | KEG G | 0.017 | <i>HSP90AA1, IL4R, IL1R1, STAT3, FOS, HIF1A, MAPK13, IL6, IRF4, IL1B, HLA-DQA2, NFKBIB, HLA-DQBI</i> | 12.1 |

*Percentage of genes in the named pathway that were found to be upregulated in the dataset.

Supplementary Table 4. Top 10 upregulated KEGG pathways in CSU lesional skin versus healthy control skin.

| Pathway | Q-Value | Genes Upregulated | Percentage * (%) |
|--|-----------|---|---------------------|
| 1. Staphylococcus aureus infection | 4.42 E-15 | <i>C1QB, DEFB103B, ITGAM, SELPLG, ITGB2, C5AR1, PTAFR, FPR1, KRT23, FPR3, FPR2, ICAM1, KRT33B, KRT33A, FCGR3A, FCGR3B, KRT26, C3AR1, HLA-DQA2, IL10, KRT34, DEFA3, KRT10, SELP, FCGR2A, KRT16, DEFB4A, FCGR2B, FCGR2C, CFB, HLA-DQBI</i> | 32.6 |
| 2. Viral protein interaction with cytokine and cytokine receptor | 1.16E-14 | <i>CSF1R, CCL13, IL20, CCL3L3, CXCR4, CXCL1, TNF, CXCL2, IL18RAP, CCL8, CXCR1, CCL4, CXCR2, CCL3, CCL2, CCR7, CCL19, CCR5, CCL18, CCR3, CCR2, CCR1, IL10, TNFSF14, IL37, IL34, TNFRSF10C, IL18, IL22RA1, IL6, CCL27</i> | 31.0 |
| 3. Cytokine-cytokine receptor interaction | 3.05E-12 | <i>CSF3, IL20, CSF3R, CXCL1, TNF, CXCL2, CXCL16, IL18RAP, IL36B, CCR7, CCR5, CCR3, CCR2, IL10, IFNAR2, IL4R, TNFRSF12A, IL1R1, IL18, OSMR, IL1B, LTB, CCL13, CSF1R, CCL3L3, CXCR4, TNFRSF11B, IL1RL1, CCL8, CXCR1, CXCR2, CCL4, CCL3, CCL2, IL36RN, CCL19, CCL18, CCRI, TNFSF14, GDF15, IL37,</i> | 16.9 |

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| | | <i>IL34, OSM, TNFRSF10C, IL36G, IL22RA1, IL6, FAS, IL7R, CCL27</i> | |
| 4. Phagosome | 2.62E-10 | <i>ITGAM, NCF1, NCF2, ITGB3, NCF4, ITGB2, CORO1A, THBS1, CTSS, TUBB8, TUBA1C, FCGR3A, FCGR3B, CTS, SEC61G, MRC1, CD14, HLA-DQA2, CYBB, HLA-C, TUBB4B, TUBA4A, MARCO, TUBB2A, FCGR2A, CD209, ATP6VIB2, FCGR2B, TLR4, FCGR2C, HLA-DQB1, TLR2</i> | 21.1 |
| 5. Osteoclast differentiation | 2.62E-10 | <i>LILRA6, CSF1R, NCF1, NCF2, ITGB3, NCF4, TNFRSF11B, TNF, LILRA4, SOCS3, FCGR3A, FCGR3B, JUNB, IFNAR2, IL1R1, LILRB1, FOS, LILRB2, LILRB3, LILRB4, MAPK13, FOSL1, TYROBP, FCGR2A, IL1B, FOSB, LCP2, FCGR2B, FCGR2C</i> | 22.8 |
| 6. Lipid and atherosclerosis | 5.12E-10 | <i>CALML5, NCF1, NCF2, CCL3L3, NCF4, CXCL1, TNF, CXCL2, ICAM1, HSPD1, CCL3, CCL2, CD14, LDLR, LYN, MAP2K3, CYP2J2, HSPA8, HSP90AA1, VCAM1, HSPA5, HSPA4, MMP1, STAT3, IL18, CYBB, FOS, SOD2, SELE, MMP9, MAPK13, SELP, IL6, IL1B, FAS, CYCS, TLR4, TLR2</i> | 17.7 |
| 7. Leishmaniasis | 4.76E-9 | <i>IL10, ITGAM, NCF1, NCF2, ITGB2, NCF4, CYBB, FOS, PTGS2, TNF, MAPK13, FCGR3A, FCGR3B, FCGR2A, IL1B, TLR4, HLA-DQA2, FCGR2C, HLA-DQB1, TLR2, NFKBIB</i> | 27.3 |
| 8. IL-17 signaling pathway | 3.75E-8 | <i>CSF3, HSP90AA1, MMP1, TNFAIP3, CXCL1, FOS, PTGS2, CXCL2, TNF, MMP9, MAPK13, S100A7A, FOSL1, IL6, IL1B, CCL2, FOSB, DEFB4A, MAPK6, S100A9, S100A8, S100A7</i> | 23.4 |
| 9. TNF signaling pathway | 4.02E-8 | <i>MAP2K3, VCAM1, TNFAIP3, CXCL1, FOS, NOD2, PTGS2, TNF, SELE, CXCL2, MMP9, ICAM1, MAPK13, RPS6KA4, SOCS3, IL6, CREB3L4, IL1B, IRF1, CCL2, FAS, MAP3K8, JUNB, BIRC3</i> | 21.4 |
| 10. Rheumatoid arthritis | 1.43E-7 | <i>MMP1, CCL3L3, ITGB2, IL18, CXCL1, FOS, CXCL2, TNF, ICAM1, IL6, CTS, IL1B, ATP6VIB2, CCL3, CTLA4, CCL2, LTB, TLR4, HLA-DQA2, HLA-DQB1, TLR2</i> | 22.6 |

*Percentage of genes in the named pathway that were found to be upregulated in the dataset.

Supplementary Table 5. Top 10 upregulated ToppGene pathways in CSU lesional skin versus non-lesional skin.

| Pathway | Q-Value | Genes Upregulated | Perce ntage * (%) |
|--|----------|--|-------------------------|
| 1. Interleukin-10 signaling | 1.05E-14 | <i>CCL2, CCL3, CCL4, CCL19, FPR1, ICAM1, CCL3L3, CSF3, IL1B, IL1R1, IL6, IL10, PTAFR, PTGS2, STAT3, CXCL1, CXCL2, TIMP1</i> | 36.7 |
| 2. Cytokine Signaling in Immune system | 1.70E-10 | <i>CDKN1A, SEH1L, HIF1A, TNFRSF12A, FCGR1B, PIM1, IFI30, CCL2, CCL3, CCL4, MMP1, CCL19, HSPA8, VCAM1, FPR1, PIK3R3, ICAM1, CCL3L3, MT2A, CSF3, IL20, IL1B, IL1R1, IL4R, IL6, IL7R, MYC, IL10, EIF4A3, IRF1, PTAFR, ITGB3, PTGS2, STAT3, JUNB, NFKB1, KPNA2, HBEGF, DUSP2, DUSP5, DUSP6, SOCS3, CXCL1, CXCL2, OSM, TIMP1, EGR1, EIF4A1, SPRED1, IL1RL1, OSMR, LYN</i> | 6.8 |
| 3. Signaling by Interleukins | 2.60E-10 | <i>CDKN1A, HIF1A, PIM1, CCL2, CCL3, CCL4, MMP1, CCL19, HSPA8, VCAM1, FPR1, PIK3R3, ICAM1, CCL3L3, CSF3, IL20, IL1B, IL1R1, IL4R, IL6, IL7R, MYC, IL10, PTAFR, ITGB3, PTGS2, STAT3, JUNB, NFKB1, HBEGF, DUSP2, DUSP5, DUSP6, SOCS3, CXCL1, CXCL2, OSM, TIMP1, SPRED1, IL1RL1, OSMR, LYN</i> | 7.9 |
| 4. Neutrophil degranulation | 1.38E-9 | <i>SERPINA3, FABP5, S100A7, S100A8, S100A9, S100A12, SERPINA1, FCGR2A, FCGR3B, SERPINB3, GCA, PLAU, HSPA8, SELL, ANPEP, FPR1, FPR2, CCT2, SLC2A3, CD93, CXCR1, CXCR2, PTAFR, FGL2, PTPRC, PTX3, ADGRE3, NFKB1, C5AR1, PNP, CRISPLD2, LILRB3, CXCL1, FCGR2C, PA2G4, CD53, SERPINB1, TNFAIP6, STOM</i> | 7.9 |
| 5. Interleukin-4 and 13 signaling | 2.15E-9 | <i>CDKN1A, HIF1A, PIM1, CCL2, MMP1, HSPA8, VCAM1, ICAM1, IL1B, IL4R, IL6, MYC, IL10, PTGS2, STAT3, JUNB, SOCS3, OSM, TIMP1</i> | 16.7 |
| 6. AP-1 transcription factor network | 7.68E-9 | <i>HIF1A, CCL2, PLAU, MMP1, FOSB, MT2A, CCNI, ATF3, IL6, MYC, IL10, JUNB, FOSL1, TIMP1, EGR1</i> | 21.4 |
| 7. rRNA modification in | 1.84E-8 | <i>UTP15, WDR36, NOP58, NOP14, PDCD11, UTP14A, WDR43, WDR3, DKC1, UTP20, NOP2, HEATR1, UTP4, NAT10</i> | 22.2 |

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| the nucleus and cytosol | | | |
| 8. Ribosome biogenesis in eukaryotes | 3.43E-8 | <i>GTPBP4, LSG1, UTP15, GNL2, XRN2, WDR36, NOP58, UTP14A, WDR43, WDR3, DKC1, GNL3, RAN, RIOK1, HEATR1, UTP4, NAT10</i> | 16.0 |
| 9. Ensemble of genes encoding ECM- associated proteins including ECM-affiliated proteins, ECM regulators and secreted factors | 1.43E-7 | <i>SERPINA3, S100A2, S100A3, S100A7, S100A8, S100A9, S100A12, SERPINA1, PI3, SERPINE2, CLC, SERPINB13, SERPINB3, SERPINB4, CCL2, CCL3, CCL4, PLAU, CCL8, CCL13, MMP1, CCL19, MMP12, PLOD2, ADAMTS4, ADAMTS1, CCL3L3, AREG, CSF3, IL20, IL1B, CTSL, IL6, IL10, ADAMTS9, CLEC4A, FGFBP1, HBEGF, CXCL1, CXCL2, OSM, TIMP1, SERPINE1, SERPINB1, GREM1</i> | 6.0 |
| 10. Lung fibrosis | 1.61E-7 | <i>SERPINA1, CCL2, CCL3, CCL4, PLAU, MT2A, CSF3, IL1B, IL6, PTX3, CXCL2, TIMP1, GREM1</i> | 20.6 |

*Percentage of genes in the named pathway that were found to be upregulated in the dataset.

Supplementary Table 6. Selected upregulated ToppGene and KEGG pathways in lesional versus non-lesional CSU samples.

| Pathway | Meth | Q- od | Value | Genes Upregulated | Percentage* (%) |
|--|--------------|-------------|-------|---|-----------------|
| IL-18 Signaling | Topp Gene | 1.72E -4 | | <i>CCL2, CCL3, CCL4, MMP1, CCL19, ZC3H12A, ICAM1, ATF3, IL1B, IL6, IL10, IRF1, NCF2, PTGS2, PTX3, NFKB1, SOCS3, CXCL2, RGS16, TIMP1</i> | 7.2 |
| IL-6 Mediated Signaling Events | Topp Gene | 1.28E -3 | | <i>IL6, MYC, IRF1, STAT3, JUNB, SOCS3, TIMP1</i> | 16.3 |
| IL-12 Mediated Signaling Events | Topp Gene | 2.57E -2 | | <i>CCL3, CCL4, IL1B, IL1R1, STAT3, NFKB1</i> | 9.8 |

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|--|--------------|-------------|---|------|
| IL-17 Signaling | Topp Gene | 1.04E -3 | <i>S100A7, S100A8, S100A9, CCL2, MMP1, FOSB, CSF3, IL1B, IL6, PTGS2, NFKB1, CXCL1, CXCL2, FOSL1</i> | 15.1 |
| IL-23 Mediated Signaling Events | Topp Gene | 5.59E -4 | <i>CCL2, IL1B, IL6, STAT3, NFKB1, SOCS3, CXCL1</i> | 18.9 |
| IL-4 Mediated Signaling Events | Topp Gene | 0.029 | <i>SELP, IL4R, IL10, ITGB3, SOCS3, EGR2</i> | 9.50 |
| IL-17 Signaling | KEG G | 9.20E -8 | <i>CSF3, MMP1, CXCL1, PTGS2, CXCL2, NFKB1, FOSL1, IL6, IL1B, CCL2, FOSB, S100A9, S100A8, S100A7</i> | 14.9 |
| Th17 Differentiation | KEG G | 0.019 | <i>IL6, IL4R, IL1R1, IL1B, STAT3, HIF1A, NFKB1</i> | 6.5 |

*Percentage of genes in the named pathway that were found to be upregulated in the dataset.

Supplementary Table 7. Top 10 upregulated KEGG pathways in CSU lesional skin versus non-lesional skin.

| Pathway | Q-Value | Genes Upregulated | Perce ntage * (%) |
|--|---------|--|-------------------------|
| 1. Lipid and atherosclerosis | 1.36E-9 | <i>LYN, HSPA8, VCAM1, HSPA5, NCF2, MMP1, CCL3L3, STAT3, PIK3R3, CXCL1, SOD2, EIF2S1, SELE, CXCL2, NFKB1, ICAM1, HSPD1, SELP, IL6, IL1B, CCL3, CCL2, LDLR</i> | 10.7 |
| 2. Ribosome biogenesis in eukaryotes | 1.36E-9 | <i>UTP15, WDR36, NOP58, UTP4, WDR3, HEATR1, NAT10, GNL2, GTPBP4, WDR43, GNL3, LSG1, DKC1, XRN2, RIOK1, UTP14A, RAN</i> | 15.7 |
| 3. Osteoclast differentiation | 1.28E-8 | <i>NCF2, IL1R1, ITGB3, PIK3R3, LILRB3, NFKB1, FOSL1, SOCS3, FCGR3A, FCGR3B, FCGR2A, IL1B, FOSB, LCP2, FCGR2B, JUNB, FCGR2C</i> | 13.4 |

| | | | |
|--|---------|---|------|
| 4. IL-17 signaling pathway | 9.20E-8 | <i>CSF3, MMP1, CXCL1, PTGS2, CXCL2, NFKB1, FOSL1, IL6, IL1B, CCL2, FOSB, S100A9, S100A8, S100A7</i> | 15.2 |
| 5. TNF signaling pathway | 9.20E-8 | <i>VCAM1, PIK3R3, CXCL1, PTGS2, SELE, CXCL2, NFKB1, ICAM1, SOCS3, IL6, IL1B, IRF1, BCL3, CCL2, JUNB</i> | 13.4 |
| 6. Viral protein interaction with cytokine and cytokine receptor | 1.48E-7 | <i>IL10, CCL13, IL20, CCL3L3, CXCL1, CXCL2, IL6, CCL8, CXCR1, CCL4, CXCR2, CCL3, CCL2, CCL19</i> | 14.0 |
| 7. Cytokine- cytokine receptor interaction | 1.92E-7 | <i>IL10, CCL13, CSF3, IL20, IL4R, TNFRSF12A, IL1R1, CCL3L3, OSM, CXCL1, OSMR, CXCL2, IL1RL1, IL6, CCL8, CXCR1, IL1B, CXCR2, CCL4, CCL3, CCL2, CCL19, IL7R</i> | 7.8 |
| 8. Staphylococcus aureus infection | 5.06E-7 | <i>IL10, C5AR1, PTAFR, FPR1, FPR2, ICAM1, SELP, FCGR3A, FCGR3B, FCGR2A, KRT16, FCGR2B, FCGR2C</i> | 13.7 |
| 9. Malaria | 5.06E-7 | <i>IL10, SELP, CSF3, IL6, VCAM1, IL1B, CCL2, THBS1, SELE, ICAM1</i> | 20.0 |
| 10. AGE-RAGE signaling pathway in diabetic complications | 8.01E-7 | <i>EGRI, VCAM1, SERPINE1, STAT3, PIK3R3, SELE, NFKB1, ICAM1, THBD, IL6, IL1B, PIM1, CCL2</i> | 13.0 |

*Percentage of genes in the named pathway that were found to be upregulated in the dataset.

Supplementary Table 8. Cell-types with significant differences in the Gimenez et al. dataset.

| Cell Type | Cell-Type Enrichment Methods | Lesional Skin Mean Score | Non- Lesional Skin Mean Score | Healthy Control Skin Mean Score | Q-Value Lesional vs. Non- lesional Skin | Q-Value Lesional vs. Healthy Control Skin |
|-----------------|------------------------------------|-----------------------------------|---|--|---|--|
| Astrocytes | xCell | 0.00093 | - | 0.032 | - | 0.028 |
| Dendritic Cells | xCell | 0.18 | - | 0.056 | - | 0.024 |

| | | | | | | |
|---|-----------|--------|---|--------|---|--------|
| Endothelial Cells | xCell | 0.14 | - | 0.25 | - | 0.028 |
| Epithelial Cells | xCell | 0.040 | - | 0.012 | - | 0.045 |
| Keratinocytes | xCell | 0.079 | - | 0.031 | - | 0.037 |
| Megakaryocyte- Erythroid Progenitor Cells | xCell | 0.064 | - | 0.0070 | - | 0.040 |
| M1 Macrophages | xCell | 0.046 | - | 0.0087 | - | 0.030 |
| Mesangial cells | xCell | 0.0067 | - | 0.072 | - | 0.0013 |
| Monocytes | xCell | 0.18 | - | 0.048 | - | 0.040 |
| Neurons | xCell | 0.019 | - | 0.034 | - | 0.048 |
| Neutrophils | xCell | 0.077 | - | 0.0038 | - | 0.037 |
| Osteoblast | xCell | 0.096 | - | 0.019 | - | 0.030 |
| Pericytes | xCell | 0.0047 | - | 0.019 | - | 0.030 |
| Preadipocytes | xCell | 0.11 | - | 0.017 | - | 0.028 |
| Sebocytes | xCell | 0.014 | - | 0.0039 | - | 0.0070 |
| Tgd cells | xCell | 0.091 | - | 0.015 | - | 0.028 |
| Activated Dendritic Cells | xCell | 0.13 | - | 0.039 | - | 0.026 |
| Lymphatic Endothelial Cells | xCell | 0.12 | - | 0.22 | - | 0.028 |
| Microvascular Endothelial Cells | xCell | 0.10 | - | 0.20 | - | 0.030 |
| CD8+ T-Cells | CIBERSORT | 0.020 | - | 0.15 | - | 0.049 |

Supplementary Table 9. Cell-types with significant differences in the Patel et al. dataset.

| Cell Type | Cell-Type Enrichment Method | Lesional Skin Mean Score | Non-Lesional Skin Mean Score | Healthy Control Skin Mean Score | Q-Value Lesional vs. Non-lesional Skin | Q-Value Lesional vs. Healthy Control Skin |
|--|-----------------------------|--------------------------|------------------------------|---------------------------------|--|---|
| CD4+ Memory T-Cells | xCell | 0.11 | 0.057 | - | 0.039 | - |
| Naïve CD8+ T-Cells | xCell | 0.0048 | 0.035 | - | 0.037 | - |
| Lymphoid Progenitor Cells | xCell | 0.031 | 0.0077 | - | 0.024 | - |
| Common Myeloid Progenitor Cell | xCell | 0.0072 | 0.059 | - | 0.019 | - |
| Chondrocytes | xCell | 0.018 | 0.071 | - | 0.024 | - |
| Dendritic Cells | xCell | 0.15 | 0.085 | - | 0.037 | - |
| Hematopoietic Stem Cells | xCell | 0.053 | 0.16 | - | 0.024 | - |
| Hepatocytes | xCell | 0 | 0.0094 | - | 0.024 | - |
| Megakaryocyte-Erythroid Progenitor Cells | xCell | 0.026 | 0.0014 | - | 0.039 | - |
| Macrophages | xCell | 0.024 | 0.051 | - | 0.039 | - |
| Neurons | xCell | 0.0085 | 0.020 | - | 0.049 | - |
| Neutrophils | xCell | 0.11 | 0.0094 | - | 0.024 | - |
| Skeletal muscle | xCell | 0.00037 | 0.011 | - | 0.024 | - |
| Activated Dendritic Cells | xCell | 0.096 | 0.051 | - | 0.019 | - |
| Immature Dendritic Cells | xCell | 0.16 | 0.093 | - | 0.039 | - |

| | | | | | | |
|------------------------------------|-----------|---------|-------|-------|-------|-------|
| Lymphatic Endothelial cells | xCell | 0.099 | 0.045 | - | 0.039 | - |
| Plasma Cells | CIBERSORT | 0.018 | 0.042 | 0.057 | 0.032 | 0.015 |
| CD8+ T-Cells | CIBERSORT | 0.035 | - | 0.090 | - | 0.028 |
| CD4+ Resting Memory T- Cells | CIBERSORT | 0.13 | 0.038 | 0.037 | 0.032 | 0.035 |
| Tregs | CIBERSORT | 0.00094 | 0.030 | 0.034 | 0.032 | 0.015 |
| Resting Mast Cells | CIBERSORT | 0.14 | 0.27 | 0.25 | 0.029 | 0.016 |

Supplementary Table 10. Cell-types with significant differences between datasets.

| Sample Type | Cell Type | Deconvolution Method | Patel et al. Mean Score | Gimenez et al. Mean Score | Q- Value |
|----------------------|---|-------------------------|----------------------------|------------------------------|-------------|
| Lesional Skin | Naïve B-Cells | CIBERSORT | 0.040 | 0.011 | 0.014 |
| Lesional Skin | Resting Dendritic Cells | CIBERSORT | 0.21 | 0.049 | 0.014 |
| Non-Lesional Skin | CD4+ Central Memory T- Cells | xCell | 0.017 | 0 | 0.029 |
| Non-Lesional Skin | CD8+ T-Cells | xCell | 0.018 | 0.072 | 0.044 |
| Non-Lesional Skin | Lymphoid Progenitor Cell | xCell | 0.0077 | 0.044 | 0.024 |
| Non-Lesional Skin | Chondrocytes | xCell | 0.071 | 0.18 | 0.018 |
| Non-Lesional Skin | Endothelial Cells | xCell | 0.033 | 0.19 | 0.0080 |
| Non-Lesional Skin | Granulocyte- Monocyte Progenitor Cells | xCell | 0.012 | 0.089 | 0.044 |

| | | | | | |
|----------------------|-----------------------------|-----------|--------|--------|--------|
| Non-Lesional Skin | Hematopoietic Stem Cells | xCell | 0.16 | 0.35 | 0.0080 |
| Non-Lesional Skin | Monocytes | xCell | 0.030 | 0.13 | 0.029 |
| Non-Lesional Skin | Myocytes | xCell | 0.0089 | 0.043 | 0.020 |
| Non-Lesional Skin | Neurons | xCell | 0.020 | 0.032 | 0.044 |
| Non-Lesional Skin | Th1 Cells | xCell | 0.054 | 0 | 0.016 |
| Non-Lesional Skin | Th2 Cells | xCell | 0 | 0.029 | 0.046 |
| Non-Lesional Skin | Lymphatic Endothelial Cells | xCell | 0.044 | 0.15 | 0.016 |
| Non-Lesional Skin | Naïve B-Cells | CIBERSORT | 0.050 | 0.0091 | 0.0058 |
| Non-Lesional Skin | Activated NK Cells | CIBERSORT | 0.070 | 0.0024 | 0.0011 |
| Non-Lesional Skin | Monocytes | CIBERSORT | 0.18 | 0.018 | 0.0011 |
| Non-Lesional Skin | M2 Macrophages | CIBERSORT | 0.010 | 0.28 | 0.011 |
| Non-Lesional Skin | Resting Dendritic Cells | CIBERSORT | 0.15 | 0.041 | 0.0058 |
| Non-Lesional Skin | Resting Mast Cells | CIBERSORT | 0.27 | 0.16 | 0.042 |
| Healthy Control Skin | Adipocytes | xCell | 0.21 | 0.074 | 0.046 |
| Healthy Control Skin | Chondrocytes | xCell | 0.025 | 0.12 | 0.014 |
| Healthy Control Skin | Endothelial Cells | xCell | 0.0080 | 0.25 | 0.0047 |

| | | | | | |
|----------------------|---------------------------------------|-----------|--------|--------|--------|
| Healthy Control Skin | Epithelial Cells | xCell | 0.074 | 0.012 | 0.0083 |
| Healthy Control Skin | Fibroblasts | xCell | 0.049 | 0.13 | 0.041 |
| Healthy Control Skin | Granulocyte-Monocyte Progenitor Cells | xCell | 0.0027 | 0.064 | 0.046 |
| Healthy Control Skin | Hematopoietic Stem Cells | xCell | 0.13 | 0.32 | 0.0047 |
| Healthy Control Skin | Keratinocytes | xCell | 0.071 | 0.031 | 0.046 |
| Healthy Control Skin | Mesangial Cells | xCell | 0.0092 | 0.072 | 0.0047 |
| Healthy Control Skin | Monocytes | xCell | 0.0038 | 0.048 | 0.041 |
| Healthy Control Skin | Myocytes | xCell | 0.0098 | 0.057 | 0.0047 |
| Healthy Control Skin | Neurons | xCell | 0.024 | 0.034 | 0.047 |
| Healthy Control Skin | Sebocytes | xCell | 0.0095 | 0.0039 | 0.046 |
| Healthy Control Skin | Th1 Cells | xCell | 0.074 | 0 | 0.0047 |
| Healthy Control Skin | Lymphatic Endothelial Cells | xCell | 0.020 | 0.22 | 0.0047 |
| Healthy Control Skin | Microvascular Endothelial Cells | xCell | 0.047 | 0.20 | 0.0057 |
| Healthy Control Skin | Naïve B-Cells | CIBERSORT | 0.058 | 0 | 0.019 |
| Healthy Control Skin | Activated NK Cells | CIBERSORT | 0.073 | 0.014 | 0.0068 |

| | | | | | |
|----------------------|-------------------------|-----------|-------|-------|--------|
| Healthy Control Skin | Monocytes | CIBERSORT | 0.21 | 0.017 | 0.0069 |
| Healthy Control Skin | M2 Macrophages | CIBERSORT | 0.067 | 0.30 | 0.030 |
| Healthy Control Skin | Resting Dendritic Cells | CIBERSORT | 0.12 | 0.012 | 0.019 |