

# Efficacy of Glycyrrhetic acid in the treatment of Acne Vulgaris

## through the regulation of sebogenesis and inflammatory responses

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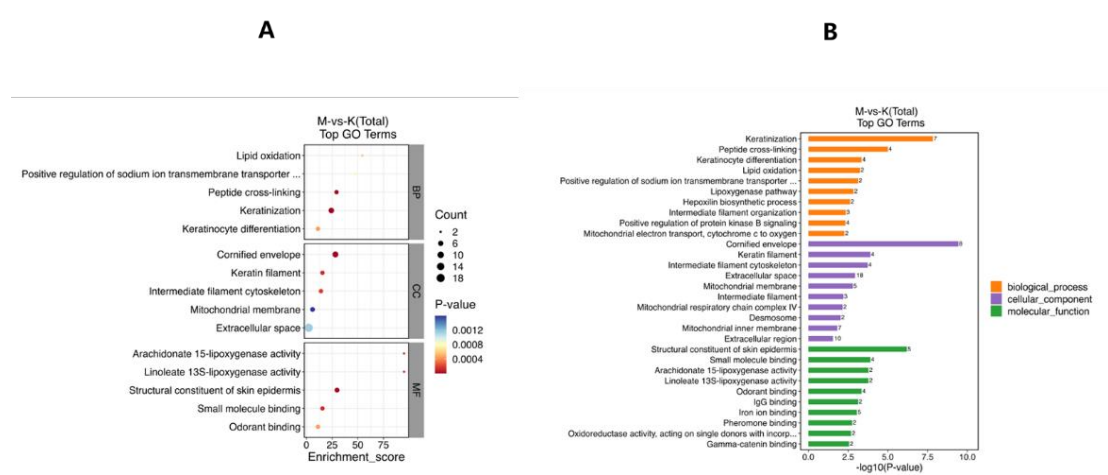


**Fig. S1.** Gene ontology annotation of DEPs between MC and BC. (A) GO analysis of DEP proteins. (B) The number of differentially expressed genes of GO.

**Table S1:** Differential proteins between MC and BC (Fold change  $\geq 1.2$  or Fold change  $\leq 1/1.2$  as well as p-value  $< 0.05$ )

| protein name | protein definition                             | FoldChange | p-value     | regulation |
|--------------|------------------------------------------------|------------|-------------|------------|
| Sprr2d       | Small proline-rich protein 2D                  | 0.41770414 | 0.002850715 | Down       |
| Il36a        | Interleukin-36 alpha                           | 0.42486115 | 0.004289882 | Down       |
| Mup1         | Major urinary protein 1                        | 0.4964258  | 0.04731588  | Down       |
| Sprr1b       | Cornifin-B                                     | 0.50667879 | 0.016256844 | Down       |
| Cdc42ep5     | Cdc42 effector protein 5                       | 0.5096846  | 0.049947698 | Down       |
| Alox8        | Polyunsaturated fatty acid lipoyxygenase ALOX8 | 0.55524254 | 0.019257919 | Down       |
| Mup17        | Major urinary protein 17                       | 0.56730769 | 0.037934468 | Down       |
| Chi3l1       | Chitinase-3-like protein 1                     | 0.60526829 | 0.045422791 | Down       |
| S100a8       | Protein S100-A8                                | 0.62890325 | 0.042789727 | Down       |

|           |                                    |            |             |      |
|-----------|------------------------------------|------------|-------------|------|
| Defb6     | Beta-defensin 6                    | 0.63719786 | 0.007092324 | Down |
| Stfa3     | Stefin-3                           | 0.66278522 | 0.045800936 | Down |
| Prss27    | Serine protease 27                 | 0.68656268 | 0.024418437 | Down |
| Ccdc61    | Centrosomal protein CCDC61         | 0.69416795 | 0.002619201 | Down |
| Znf865    | Zinc finger protein 865            | 0.70172451 | 0.016135879 | Down |
| Glrx      | Glutaredoxin-1                     | 0.70397202 | 0.048927654 | Down |
|           | U1 small nuclear ribonucleoprotein |            |             |      |
| Snrpc     | C                                  | 0.71672256 | 0.011183278 | Down |
| Tmem14c   | Transmembrane protein 14C          | 0.72053646 | 0.028858171 | Down |
| Galk2     | N-acetylgalactosamine kinase       | 0.73535018 | 0.014824575 | Down |
|           | NADH-ubiquinone oxidoreductase     |            |             |      |
| Mtnd1     | chain 1                            | 0.74472516 | 0.025242296 | Down |
| Casp14    | Caspase-14                         | 0.76281406 | 0.027881458 | Down |
|           | Cytochrome c oxidase subunit 7A2,  |            |             |      |
| Cox7a2    | mitochondrial                      | 0.76351584 | 0.01637505  | Down |
| Mt-Cyb    | Cytochrome b                       | 0.76620021 | 0.027039748 | Down |
| Mug1      | Murinoglobulin-1                   | 0.7688958  | 0.049087931 | Down |
|           | Low affinity immunoglobulin        |            |             |      |
| Fcgr3     | gamma Fc region receptor III       | 0.76894021 | 0.016767048 | Down |
|           | High mobility group                |            |             |      |
|           | nucleosome-binding                 | 0.77173815 |             | Down |
| Hmgn3     | domain-containing protein 3        |            | 0.022998779 |      |
| Mpo       | Myeloperoxidase                    | 0.77553296 | 0.011729504 | Down |
| Rpl35     | 60S ribosomal protein L35          | 0.77612271 | 0.044201633 | Down |
| Serpina3k | Serine protease inhibitor A3K      | 0.77873804 | 0.035114983 | Down |
|           | Cytochrome c oxidase subunit 6A1,  |            |             |      |
| Cox6a1    | mitochondrial                      | 0.78057906 | 0.01065072  | Down |
|           | 3-beta-hydroxysteroid-Delta(8),Del |            |             |      |
| Ebp       | ta(7)-isomerase                    | 0.78089294 | 0.003911956 | Down |
|           | Acid sphingomyelinase-like         |            |             |      |
| Smpdl3a   | phosphodiesterase 3a               | 0.78339582 | 0.000396936 | Down |
|           | Serine/threonine-protein kinase    |            |             |      |
| Atr       | ATR                                | 0.78360038 | 0.023469103 | Down |
| Gk        | Glycerol kinase                    | 0.78804322 | 0.016573551 | Down |
| Tmem41b   | Transmembrane protein 41B          | 0.78882107 | 0.008307636 | Down |
|           | Glucose-6-phosphate exchanger      |            |             |      |
| Slc37a2   | SLC37A2                            | 0.79054345 | 0.03976601  | Down |
| Sv2c      | Synaptic vesicle glycoprotein 2C   | 0.80023927 | 0.0232147   | Down |
| Ddhd2     | Phospholipase DDHD2                | 0.80543124 | 0.027418713 | Down |
|           | 39S ribosomal protein L12,         |            |             |      |
| Mrpl12    | mitochondrial                      | 0.80621321 | 0.009992413 | Down |
|           | Regulation of nuclear pre-mRNA     |            |             |      |
| Rprd2     | domain-containing protein 2        | 0.80656349 | 0.0062639   | Down |
| Arhgef18  | Rho guanine nucleotide exchange    | 0.8131368  | 0.021631537 | Down |

| factor 18 |                                      |            |             |      |
|-----------|--------------------------------------|------------|-------------|------|
|           | SPRY domain-containing SOCS          |            |             |      |
| Spsb2     | box protein 2                        | 0.81361603 | 0.001897452 | Down |
| Ptma      | Prothymosin alpha                    | 0.81508363 | 0.031840756 | Down |
| Ivl       | Involucrin                           | 0.81799277 | 0.009400323 | Down |
|           | Intraflagellar transport protein 140 |            |             |      |
| Ift140    | homolog                              | 0.81956295 | 0.036490498 | Down |
| Nrm       | Nurim                                | 0.81961029 | 0.001916618 | Down |
| Sprr1a    | Cornifin-A                           | 0.82086488 | 0.038577487 | Down |
|           | Probable tRNA                        |            |             |      |
| Trmt44    | (uracil-O(2)-)-methyltransferase     | 0.82297281 | 0.025068847 | Down |
| Dynlrb1   | Dynein light chain roadblock-type 1  | 0.82379275 | 0.042710357 | Down |
| Dcp2      | m7GpppN-mRNA hydrolase               | 0.82580897 | 0.030897405 | Down |
| Fam162a   | Protein FAM162A                      | 0.82662601 | 0.029528111 | Down |
|           | Gamma-tubulin complex                |            |             |      |
| Tubgcp2   | component 2                          | 0.82791429 | 0.007986618 | Down |
| Bnc2      | Zinc finger protein basonuclein-2    | 0.82829313 | 0.046541406 | Down |
| Znf706    | Zinc finger protein 706              | 0.82971245 | 0.006207667 | Down |
| Rasip1    | Ras-interacting protein 1            | 0.83138003 | 0.009050863 | Down |
|           | V-type proton ATPase 16 kDa          |            |             |      |
| Atp6v0c   | proteolipid subunit c                | 0.83209876 | 0.049371639 | Down |
| Dst       | Dystonin                             | 1.20161384 | 0.003310097 | Up   |
| Bpifb9a   | Vomeromodulin                        | 1.20389814 | 0.009260888 | Up   |
| Krt80     | Keratin, type II cytoskeletal 80     | 1.20569918 | 0.016043604 | Up   |
| Mamdc2    | MAM domain-containing protein 2      | 1.20714864 | 0.002461499 | Up   |
| Cyp2b10   | Cytochrome P450 2B10                 | 1.21196105 | 0.031246535 | Up   |
|           | DENN domain-containing protein       |            |             |      |
| Dennd10   | 10                                   | 1.21447265 | 0.037845194 | Up   |
| Dsg1a     | Desmoglein-1-alpha                   | 1.21919875 | 0.01942447  | Up   |
| Cyp4b1    | Cytochrome P450 4B1                  | 1.21991729 | 0.007083344 | Up   |
| Flg2      | Filaggrin-2                          | 1.22147133 | 0.021134433 | Up   |
| Kprp      | Keratinocyte proline-rich protein    | 1.22245667 | 0.013687904 | Up   |
| Mt4       | Metallothionein-4                    | 1.22380469 | 0.031357549 | Up   |
| Krt84     | Keratin, type II cuticular Hb4       | 1.22509475 | 0.019164254 | Up   |
| Dsc3      | Desmocollin-3                        | 1.22532971 | 0.011617008 | Up   |
| Epha4     | Ephrin type-A receptor 4             | 1.22897026 | 0.012255972 | Up   |
|           | CB1 cannabinoid                      |            |             |      |
| Cnrip1    | receptor-interacting protein 1       | 1.20969766 | 0.031644409 | Up   |
|           | Prolactin-inducible protein          |            |             |      |
| Pip       | homolog                              | 1.23475944 | 0.037781913 | Up   |
|           | FHF complex subunit HOOK             |            |             |      |
| Fhip1a    | interacting protein 1A               | 1.24633624 | 0.007121315 | Up   |
| Obp1b     | Odorant-binding protein 1b           | 1.25306391 | 0.02378033  | Up   |
| Nrbf2     | Nuclear receptor-binding factor 2    | 1.20060491 | 0.041177047 | Up   |

|          |                                                         |            |             |    |
|----------|---------------------------------------------------------|------------|-------------|----|
| Bbox1    | Gamma-butyrobetaine dioxygenase                         | 1.26819799 | 0.012070902 | Up |
| Tnnt1    | Troponin T, slow skeletal muscle                        | 1.27788676 | 0.00398389  | Up |
| Npl      | N-acetylneuraminate lyase                               | 1.27832972 | 0.027811521 | Up |
| Krt24    | Keratin, type I cytoskeletal 24                         | 1.28236474 | 0.005893034 | Up |
|          | Polyunsaturated fatty acid<br>(12S)/(13S)-lipoxygenase, | 1.29315332 |             | Up |
| Alox12e  | epidermal-type                                          |            | 0.018297865 |    |
| F3       | Tissue factor                                           | 1.2986056  | 0.009238786 | Up |
| Cds2     | Phosphatidate cytidyltransferase 2                      | 1.31272677 | 0.02149196  | Up |
| Scd1     | Acyl-CoA desaturase 1                                   | 1.17949284 | 0.020399987 | Up |
| Plxna4   | Plexin-A4                                               | 1.37611083 | 0.044238202 | Up |
|          | Secretoglobin family 2B member                          | 1.42868051 |             | Up |
| Scgb2b24 | 24                                                      |            | 0.037693634 |    |
|          | Keratin, type II cytoskeletal 2                         | 1.43651527 |             | Up |
| Krt2     | epidermal                                               |            | 0.031367576 |    |
| Ighv3-6  | Ig heavy chain V region 3-6                             | 1.50429759 | 0.02869161  | Up |
| Obp1a    | Odorant-binding protein 1a                              | 1.59567481 | 0.029756899 | Up |
| Scgb2b2  | Secretoglobin family 2B member 2                        | 1.61772906 | 0.023615293 | Up |

**Table S2.** Differential proteins between GA and MC (Fold change  $\geq 1.2$  or Fold change  $\leq 1/1.2$  as well as p-value  $< 0.05$ )

| protein name | protein definition                                           | FoldChange  | p-value   | regulation |
|--------------|--------------------------------------------------------------|-------------|-----------|------------|
| Tmod1        | Tropomodulin-1                                               | 0.460078943 | 0.0003524 | Down       |
|              | Ig heavy chain V region 3-6                                  |             |           |            |
| Ighv3-6      | OS=Mus musculus                                              | 0.653725404 | 0.0310983 | Down       |
|              | Keratin-associated protein 6-5                               |             |           |            |
| Krtap6-5     | OS=Mus musculus                                              | 0.680624033 | 0.0482403 | Down       |
| Ypel5        | Protein yippee-like 5                                        | 0.681201413 | 0.0168121 | Down       |
| Nrbf2        | Nuclear receptor-binding factor 2                            | 0.71613658  | 0.0130472 | Down       |
| Prg4         | Proteoglycan 4                                               | 0.757676199 | 0.0192882 | Down       |
| Dock10       | Dedicator of cytokinesis protein 10                          | 0.758399543 | 0.006042  | Down       |
|              | Serine/threonine-protein<br>phosphatase 4 regulatory subunit |             |           |            |
| Ppp4r3b      | 3B                                                           | 0.772269696 | 0.0117442 | Down       |
| Tor3a        | Torsin-3A                                                    | 0.779096173 | 4.743E-05 | Down       |
| Vangl1       | Vang-like protein 1                                          | 0.78905075  | 0.045815  | Down       |
|              | A-kinase anchor protein 10,                                  |             |           |            |
| Akap10       | mitochondrial                                                | 0.797973827 | 0.0131154 | Down       |
|              | Oligosaccharyltransferase complex                            |             |           |            |
| Ostc         | subunit OSTC                                                 | 0.819805363 | 0.0460532 | Down       |
| Cnr1p1       | CB1 cannabinoid                                              | 0.826641291 | 0.0249413 | Down       |

|          |                                  |             |           |      |
|----------|----------------------------------|-------------|-----------|------|
|          | receptor-interacting protein 1   |             |           |      |
|          | H-2 class I histocompatibility   |             |           |      |
| H2-L     | antigen, L-D alpha chain         | 0.829329127 | 0.041222  | Down |
| Scd1     | Acyl-CoA desaturase 1            | 0.830775168 | 0.0047461 | Down |
|          | UPF0449 protein C19orf25         |             |           |      |
| C19orf25 | homolog                          | 1.200512146 | 0.0392879 | UP   |
|          | Gamma-tubulin complex            |             |           |      |
| Tubgcp2  | component 2                      | 1.222329578 | 0.0401076 | UP   |
|          | DNA polymerase alpha catalytic   |             |           |      |
| Pola1    | subunit                          | 1.234999108 | 0.0015736 | UP   |
| Yod1     | Ubiquitin thioesterase OTU1      | 1.240332282 | 0.0131235 | UP   |
| Hspa12b  | Heat shock 70 kDa protein 12B    | 1.241189445 | 0.0104855 | UP   |
| Patj     | InaD-like protein                | 1.266695713 | 0.0014815 | UP   |
| Ddhd2    | Phospholipase DDHD2              | 1.382922204 | 0.0202587 | UP   |
| Rasal1   | RasGAP-activating-like protein 1 | 1.43397844  | 0.004211  | UP   |

**Table S3.** Proteins of Trusted proteins in skin between GA and MC (Fold change  $\geq 1.2$  or Fold change  $\leq 1/1.2$ ).

| Protein Name                                                   | Gene Name | UniProt ID | LogFC    | P.values |
|----------------------------------------------------------------|-----------|------------|----------|----------|
| Tropomodulin-1                                                 | Tmod1     | P49813     | -1.12005 | 0.00035  |
| Keratin, type II cytoskeletal 2 oral                           | Krt76     | Q3UV17     | -1.02514 | 0.13988  |
| Paired amphipathic helix protein Sin3b                         | Sin3b     | Q62141     | -1.02060 | 0.11420  |
| Transmembrane protease serine 13                               | Tmprss13  | Q5U405     | -0.93702 | 0.10124  |
| Ig gamma-2A chain C region,<br>membrane-bound form             | Igh-1a    | P01865     | -0.92768 | 0.05181  |
| Deubiquitinase OTUD6B                                          | Otud6b    | Q8K2H2     | -0.77006 | 0.08904  |
| Keratin-associated protein 6-2                                 | Krtap6-2  | O08884     | -0.66701 | 0.10246  |
| Keratin-associated protein 19-2                                | Krtap19-2 | Q925I0     | -0.66670 | 0.08790  |
| Interferon-induced protein with<br>tetratricopeptide repeats 1 | Ifit1     | Q64282     | -0.63485 | 0.13829  |
| Ig heavy chain V region 3-6                                    | Ighv3-6   | P18531     | -0.61324 | 0.03110  |
| Keratin, type I cuticular Ha4                                  | Krt34     | Q9D646     | -0.59875 | 0.09919  |
| Keratin-associated protein 19-4                                | Krtap19-4 | Q925H7     | -0.57011 | 0.09407  |
| Keratin-associated protein 6-5                                 | Krtap6-5  | Q925H3     | -0.55507 | 0.04824  |
| Protein yippee-like 5                                          | Ypel5     | P62700     | -0.55385 | 0.01681  |
| Keratin-associated protein 3-1                                 | Krtap3-1  | A2A591     | -0.54636 | 0.07607  |
| Keratin-associated protein 19-3                                | Krtap19-3 | Q925H6     | -0.54106 | 0.08251  |
| Keratin-associated protein 21-1                                | Krtap21-1 | Q925H4     | -0.52841 | 0.08906  |
| Protein phosphatase PTC7 homolog                               | Pptc7     | Q6NVE9     | -0.52803 | 0.21209  |
| Keratin, type II cuticular Hb6                                 | Krt86     | P97861     | -0.50838 | 0.10053  |
| DNA polymerase alpha catalytic<br>subunit                      | Pola1     | P33609     | -0.48169 | 0.01305  |

|                                                                                                                     |           |        |          |         |
|---------------------------------------------------------------------------------------------------------------------|-----------|--------|----------|---------|
| Keratin-associated protein 19-5                                                                                     | Krtap19-5 | O08632 | -0.47794 | 0.09745 |
| Keratin, type II cytoskeletal 1b                                                                                    | Krt77     | Q6IFZ6 | -0.44363 | 0.35087 |
| Keratin, type II cuticular 87                                                                                       | Krt87     | Q6IMF0 | -0.43930 | 0.12388 |
| Keratin, type II cuticular Hb1                                                                                      | Krt81     | Q9ERE2 | -0.43783 | 0.09640 |
| Keratin, type I cuticular Ha3-I                                                                                     | Krt33a    | Q8K0Y2 | -0.41794 | 0.10489 |
| Keratin, type I cuticular Ha3-II                                                                                    | Krt33b    | Q61897 | -0.40698 | 0.10389 |
| Proteoglycan 4                                                                                                      | Prg4      | Q9JM99 | -0.40035 | 0.01929 |
| Dedicator of cytokinesis protein 10                                                                                 | Dock10    | Q8BZN6 | -0.39897 | 0.00604 |
| Dual specificity protein phosphatase 14                                                                             | Dusp14    | Q9JLY7 | -0.38406 | 0.06769 |
| Serine/threonine-protein phosphatase 4<br>regulatory subunit 3B OS=Mus<br>musculus OX=10090 GN=Ppp4r3b<br>PE=1 SV=2 | Ppp4r3b   | Q922R5 | -0.37282 | 0.01174 |
| Keratin-associated protein 14                                                                                       | Krtap14   | O08640 | -0.37194 | 0.26308 |
| Alpha-1,6-mannosyl-glycoprotein<br>1-beta-N-acetylglucosaminyltransferase                                           | Mgat1     | Q921V5 | -0.36108 | 0.09741 |
| Torsin-3A                                                                                                           | Tor3a     | Q9ER38 | -0.36013 | 0.00005 |
| Odorant-binding protein 1a                                                                                          | Obp1a     | Q9D3H2 | -0.35845 | 0.22990 |
| G-protein coupled receptor family C<br>group 5 member D                                                             | Gprc5d    | Q9JIL6 | -0.34793 | 0.13028 |
| Ubiquitin-like protein ISG15                                                                                        | Isg15     | Q64339 | -0.34678 | 0.15813 |
| Keratin, type II cytoskeletal 8                                                                                     | Krt8      | P11679 | -0.34429 | 0.52322 |
| Vang-like protein 1                                                                                                 | Vangl1    | Q80Z96 | -0.34181 | 0.04582 |
| THAP domain-containing protein 11                                                                                   | Thap11    | Q9JJD0 | -0.34115 | 0.05393 |
| Nucleolar protein 16                                                                                                | Nop16     | Q9CPT5 | -0.32729 | 0.08143 |
| Keratin, type I cuticular Ha1                                                                                       | Krt31     | Q61765 | -0.32586 | 0.17668 |
| A-kinase anchor protein 10,<br>mitochondrial                                                                        | Akap10    | O88845 | -0.32559 | 0.01312 |
| Interferon-induced protein 44-like                                                                                  | Ifi44l    | Q9BDB7 | -0.31835 | 0.19422 |
| Secretoglobin family 2B member 2                                                                                    | Scgb2b2   | Q6UGQ3 | -0.31666 | 0.33570 |
| Hemoglobin subunit alpha =2                                                                                         | Hba       | P01942 | -0.31113 | 0.07083 |
| Tenomodulin                                                                                                         | Tnmd      | Q9EP64 | -0.30269 | 0.13153 |
| Hemoglobin subunit beta-2                                                                                           | Hbb-b2    | P02089 | -0.30260 | 0.16145 |
| Keratin-associated protein 7-1                                                                                      | Krtap7-1  | Q9D3I6 | -0.29986 | 0.06255 |
| Polyunsaturated fatty acid lipoxygenase<br>ALOX8                                                                    | Alox8     | O35936 | -0.28896 | 0.14990 |
| Oligosaccharyltransferase complex<br>subunit OSTC                                                                   | Ostc      | Q78XF5 | -0.28665 | 0.04605 |
| Keratin, type II cuticular Hb5                                                                                      | Krt85     | Q9Z2T6 | -0.28589 | 0.23906 |
| ATP-binding cassette sub-family C<br>member 9                                                                       | Abcc9     | P70170 | -0.28455 | 0.48742 |
| Hemoglobin subunit beta-1                                                                                           | Hbb-b1    | P02088 | -0.28285 | 0.10200 |
| E3 ubiquitin-protein ligase KCMF1                                                                                   | Kcmf1     | Q80UY2 | -0.27988 | 0.44668 |
| Myelin proteolipid protein                                                                                          | Plp1      | P60202 | -0.27615 | 0.37613 |

|                                                                |          |        |          |         |
|----------------------------------------------------------------|----------|--------|----------|---------|
| CB1 cannabinoid receptor-interacting protein 1                 | Cnrip1   | Q5M8N0 | -0.27467 | 0.02494 |
| Serum amyloid P-component                                      | Apcs     | P12246 | -0.27045 | 0.14013 |
| H-2 class I histocompatibility antigen, L-D alpha chain        | H2-L     | P01897 | -0.26998 | 0.04122 |
| Ferroxidase HEPHL1                                             | Heph11   | Q3V1H3 | -0.26967 | 0.17757 |
| Keratin, type I cytoskeletal 16                                | Krt16    | Q9Z2K1 | -0.26874 | 0.42289 |
| Keratin, type II cytoskeletal 6A                               | Krt6a    | P50446 | -0.26801 | 0.28358 |
| Acyl-CoA desaturase 1                                          | Scd1     | P13516 | -0.26747 | 0.00475 |
| Interferon-induced protein with tetratricopeptide repeats 3    | Ifit3    | Q64345 | -0.26622 | 0.11035 |
| Keratin, type II cytoskeletal 6B                               | Krt6b    | Q9Z331 | -0.26560 | 0.53080 |
| Keratin, type II cytoskeletal 72                               | Krt72    | Q6IME9 | -0.26542 | 0.23331 |
| Keratin, type II cuticular Hb4                                 | Krt84    | Q99M73 | -0.26471 | 0.07547 |
| UPF0449 protein C19orf25 homolog                               | /        | Q9D7E4 | 0.26365  | 0.03929 |
| Haloacid dehalogenase-like hydrolase domain-containing 5       | Hdhd5    | Q91WM2 | 0.26457  | 0.37094 |
| Rootletin                                                      | Crocc    | Q8CJ40 | 0.27597  | 0.09549 |
| Troponin T, slow skeletal muscle                               | Tnnt1    | O88346 | 0.27728  | 0.08731 |
| Zinc finger protein basonuclin-2                               | Bnc2     | Q8BMQ3 | 0.27892  | 0.10682 |
| Seminal vesicle secretory protein 4                            | Svs4     | P18419 | 0.28155  | 0.14199 |
| Kinesin-like protein KIF13A                                    | Kif13a   | Q9EQW7 | 0.28386  | 0.06780 |
| Phosphofurin acidic cluster sorting protein 2                  | Pacs2    | Q3V3Q7 | 0.28586  | 0.05661 |
| Cytosolic phospholipase A2 epsilon                             | Pla2g4e  | Q50L42 | 0.28875  | 0.27782 |
| Gamma-tubulin complex component 2                              | Tubgcp2  | Q921G8 | 0.28963  | 0.04011 |
| Lipolysis-stimulated lipoprotein receptor                      | Lsr      | Q99KG5 | 0.29875  | 0.06916 |
| Eukaryotic translation initiation factor 2 subunit 3, Y-linked | Eif2s3y  | Q9Z0N2 | 0.30223  | 0.15176 |
| Nuclear receptor-binding factor 2                              | Nrbf2    | Q8VCQ3 | 0.30451  | 0.00157 |
| Ubiquitin thioesterase OTU1                                    | Yod1     | Q8CB27 | 0.31073  | 0.01312 |
| Heat shock 70 kDa protein 12B                                  | Hspa12b  | Q9CZJ2 | 0.31172  | 0.01049 |
| Anillin OS=Mus musculus                                        | Anln     | Q8K298 | 0.31463  | 0.24838 |
| Protein FAM91A1                                                | Fam91a1  | Q3UVG3 | 0.31986  | 0.21999 |
| FHF complex subunit HOOK interacting protein 1A                | Fhip1a   | Q505K2 | 0.32544  | 0.10872 |
| InaD-like protein                                              | Patj     | Q63ZW7 | 0.34107  | 0.00148 |
| Cdc42 effector protein 5                                       | Cdc42ep5 | Q9Z0X0 | 0.34983  | 0.40324 |
| Cyclin-dependent kinase 4                                      | Cdk4     | P30285 | 0.36038  | 0.45719 |
| FAST kinase domain-containing protein 4                        | Tbrg4    | Q91YM4 | 0.36279  | 0.07446 |
| E3 ubiquitin-protein ligase DTX3L                              | Dtx3l    | Q3UIR3 | 0.39155  | 0.36608 |
| Protein N-terminal glutamine                                   | Ntaq1    | Q80WB5 | 0.40577  | 0.07478 |

|                                                                   |        |        |         |         |
|-------------------------------------------------------------------|--------|--------|---------|---------|
| amidohydrolase                                                    |        |        |         |         |
| Serine/threonine-protein kinase RIO1                              | Riok1  | Q922Q2 | 0.43559 | 0.17357 |
| Phospholipase DDHD2                                               | Ddhd2  | Q80Y98 | 0.46772 | 0.02026 |
| Disintegrin and metalloproteinase domain-containing protein 17    | Adam17 | Q9Z0F8 | 0.50090 | 0.06697 |
| RasGAP-activating-like protein 1                                  | Rasal1 | Q9Z268 | 0.52002 | 0.00421 |
| Dehydrogenase/reductase SDR family member on chromosome X homolog | Dhrsx  | Q8VBZ0 | 0.52449 | 0.06761 |
| Platelet-activating factor acetylhydrolase 2, cytoplasmic         | Pafah2 | Q8VDG7 | 0.55420 | 0.18817 |
| Protein mono-ADP-ribosyltransferase                               |        |        |         |         |
| PARP4                                                             | Parp4  | E9PYK3 | 0.59002 | 0.37570 |
| Uricase                                                           | Uox    | P25688 | 0.60856 | 0.56363 |
| Ribokinase                                                        | Rbks   | Q8R1Q9 | 0.65071 | 0.37526 |
| Polyphosphoinositide phosphatase                                  | Fig4   | Q91WF7 | 0.65380 | 0.19794 |
| Major urinary protein 3                                           | Mup3   | P04939 | 0.70052 | 0.23418 |
| Major urinary protein 17                                          | Mup17  | B5X0G2 | 0.95580 | 0.11504 |
| Major urinary protein 2                                           | Mup2   | P11589 | 0.99134 | 0.19731 |
| Major urinary protein 1                                           | Mup1   | P11588 | 1.36602 | 0.12425 |

**Table S4.** Proteins of Trusted proteins in skin between MC and BC (Fold change  $\geq 1.2$  or Fold change  $\leq 1/1.2$ ).

| Protein Name                                  | Gene Name | UniProt ID | LogFC    | P.values |
|-----------------------------------------------|-----------|------------|----------|----------|
| Repetin                                       | Rptn      | P97347     | -1.32120 | 0.05716  |
| Small proline-rich protein 2D                 | Sprr2d    | O70555     | -1.25945 | 0.00285  |
| Interleukin-36 alpha                          | Il36a     | Q9JLA2     | -1.23494 | 0.00429  |
| Major urinary protein 1                       | Mup1      | P11588     | -1.01035 | 0.04732  |
| Cornifin-B                                    | Sprr1b    | Q62267     | -0.98086 | 0.01626  |
| Cdc42 effector protein 5                      | Cdc42ep5  | Q9Z0X0     | -0.97232 | 0.04995  |
| Polyunsaturated fatty acid lipoxigenase ALOX8 | Alox8     | O35936     | -0.84881 | 0.01926  |
| Major urinary protein 17                      | Mup17     | B5X0G2     | -0.81780 | 0.03793  |
| Insulin receptor-related protein              | Insrr     | Q9WTL4     | -0.77527 | 0.34749  |
| Protein S100-A9                               | S100a9    | P31725     | -0.77261 | 0.06355  |
| Chitinase-3-like protein 1                    | Chi3l1    | Q61362     | -0.72435 | 0.04542  |
| Major urinary protein 2                       | Mup2      | P11589     | -0.72366 | 0.08720  |
| Neutrophilic granule protein                  | Ngp       | O08692     | -0.68083 | 0.05195  |
| Protein S100-A8                               | S100a8    | P27005     | -0.66909 | 0.04279  |
| Filaggrin (Fragment)                          | Flg       | P11088     | -0.66019 | 0.06776  |
| Beta-defensin 6                               | Defb6     | Q91VD6     | -0.65019 | 0.00709  |
| Stefin-3                                      | Stfa3     | P35173     | -0.59339 | 0.04580  |
| Serine protease 27                            | Prss27    | Q8BJR6     | -0.54254 | 0.02442  |
| LIM domain-containing protein 2               | Limd2     | Q8BGB5     | -0.53273 | 0.16534  |
| Centrosomal protein CCDC61                    | Ccdc61    | Q3UJV1     | -0.52664 | 0.00262  |

|                                                                       |           |        |          |         |
|-----------------------------------------------------------------------|-----------|--------|----------|---------|
| NADH-ubiquinone oxidoreductase chain 2                                | mt-Nd2    | P03893 | -0.52283 | 0.05550 |
| Zinc finger protein 865                                               | Znf865    | Q3U3I9 | -0.51102 | 0.01614 |
| Glutaredoxin-1                                                        | Glrx      | Q9QUH0 | -0.50641 | 0.04893 |
| U1 small nuclear ribonucleoprotein C                                  | Snrpc     | Q62241 | -0.48051 | 0.01118 |
| Isochorismatase domain-containing protein 2A                          | Isoc2a    | P85094 | -0.47313 | 0.10965 |
| Transmembrane protein 14C                                             | Tmem14c   | Q9CQN6 | -0.47286 | 0.02886 |
| Major urinary protein 3                                               | Mup3      | P04939 | -0.44858 | 0.16736 |
| Myoglobin                                                             | Mb        | P04247 | -0.44370 | 0.08915 |
| N-acetylgalactosamine kinase                                          | Galk2     | Q68FH4 | -0.44350 | 0.01482 |
| Cyclin-T2                                                             | Ccnt2     | Q7TQK0 | -0.42832 | 0.07144 |
| NADH-ubiquinone oxidoreductase chain 1                                | Mtnd1     | P03888 | -0.42522 | 0.02524 |
| Prostaglandin E synthase                                              | Ptges     | Q9JM51 | -0.40536 | 0.06421 |
| Caspase-14                                                            | Casp14    | O89094 | -0.39060 | 0.02788 |
| Cytochrome c oxidase subunit 7A2, mitochondrial                       | Cox7a2    | P48771 | -0.38927 | 0.01638 |
| Cytochrome b                                                          | Mt-Cyb    | P00158 | -0.38421 | 0.02704 |
| Murinoglobulin-1                                                      | Mug1      | P28665 | -0.37914 | 0.04909 |
| Low affinity immunoglobulin gamma Fc region<br>receptor III           | Fcgr3     | P08508 | -0.37906 | 0.01677 |
| Lactotransferrin                                                      | Ltf       | P08071 | -0.37758 | 0.05270 |
| PRKC apoptosis WT1 regulator protein                                  | Pawr      | Q925B0 | -0.37747 | 0.05345 |
| High mobility group nucleosome-binding<br>domain-containing protein 3 | Hmgn3     | Q9DCB1 | -0.37382 | 0.02300 |
| Sodium/glucose cotransporter 1                                        | Slc5a1    | Q8C3K6 | -0.37019 | 0.06936 |
| Tapasin-related protein                                               | Tapbp1    | Q8VD31 | -0.36892 | 0.37303 |
| Leptin receptor gene-related protein                                  | Leprot    | O89013 | -0.36708 | 0.07831 |
| Myeloperoxidase                                                       | Mpo       | P11247 | -0.36674 | 0.01173 |
| 60S ribosomal protein L35                                             | Rpl35     | Q6ZWV7 | -0.36564 | 0.04420 |
| Serine protease inhibitor A3K                                         | Serpina3k | P07759 | -0.36079 | 0.03511 |
| Cytochrome c oxidase subunit NDUF44                                   | Ndufa4    | Q62425 | -0.35854 | 0.12794 |
| Seminal vesicle secretory protein 4                                   | Svs4      | P18419 | -0.35839 | 0.08775 |
| Cytochrome c oxidase subunit 6A1, mitochondrial                       | Cox6a1    | P43024 | -0.35738 | 0.01065 |
| 3-beta-hydroxysteroid-Delta(8),Delta(7)-isomerase                     | Ebp       | P70245 | -0.35680 | 0.00391 |
| Vitamin K epoxide reductase complex subunit 1                         | Vkorc1    | Q9CRC0 | -0.35272 | 0.12525 |
| Arginase-1                                                            | Arg1      | Q61176 | -0.35262 | 0.32047 |
| Acid sphingomyelinase-like phosphodiesterase 3a                       | Smpdl3a   | P70158 | -0.35219 | 0.00040 |
| Serine/threonine-protein kinase ATR                                   | Atr       | Q9JJK8 | -0.35181 | 0.02347 |
| Zinc finger MYM-type protein 2                                        | Zmym2     | Q9CU65 | -0.35132 | 0.15783 |
| Thymosin beta-10                                                      | Tmsb10    | Q6ZWY8 | -0.35118 | 0.18368 |
| Putative peptidyl-tRNA hydrolase PTRHD1                               | Ptrhd1    | D3Z4S3 | -0.34639 | 0.05284 |
| Gasdermin-C                                                           | Gsdmc     | Q99NB5 | -0.34439 | 0.15433 |
| Glycerol kinase                                                       | Gk        | Q64516 | -0.34365 | 0.01657 |

|                                                                  |          |        |          |         |
|------------------------------------------------------------------|----------|--------|----------|---------|
| ATP synthase subunit ATP5MPL, mitochondrial                      | Atp5mpl  | P56379 | -0.34337 | 0.07887 |
| Transmembrane protein 41B                                        | Tmem41b  | Q8K1A5 | -0.34223 | 0.00831 |
| Calreticulin                                                     | Calr     | P14211 | -0.34190 | 0.06704 |
| TRAF-type zinc finger domain-containing protein 1                | Trafd1   | Q3UDK1 | -0.34033 | 0.31849 |
| Glucose-6-phosphate exchanger SLC37A2                            | Slc37a2  | Q9WU81 | -0.33908 | 0.03977 |
| Dehydrogenase/reductase SDR family member 7C                     | Dhrs7c   | Q8CHS7 | -0.33454 | 0.33543 |
| Acyl-coenzyme A thioesterase 13                                  | Acot13   | Q9CQR4 | -0.33336 | 0.07306 |
| ATP synthase membrane subunit K, mitochondrial                   | Atp5mk   | Q78IK2 | -0.33269 | 0.07003 |
| Solute carrier organic anion transporter family member 1A1       | Slco1a1  | Q9QXZ6 | -0.33201 | 0.17202 |
| Thymosin beta-4                                                  | Tmsb4x   | P20065 | -0.32934 | 0.09989 |
| Polyribonucleotide 5'-hydroxyl-kinase Clp1                       | Clp1     | Q99LI9 | -0.32257 | 0.50562 |
| Synaptic vesicle glycoprotein 2C                                 | Sv2c     | Q69ZS6 | -0.32150 | 0.02321 |
| NGFI-A-binding protein 2                                         | Nab2     | Q61127 | -0.31685 | 0.11095 |
| Nucleoporin Nup43                                                | Nup43    | P59235 | -0.31545 | 0.26700 |
| Activating molecule in BECN1-regulated autophagy protein 1       | Ambra1   | A2AH22 | -0.31397 | 0.08915 |
| Phospholipase DDHD2                                              | Ddhd2    | Q80Y98 | -0.31217 | 0.02742 |
| ADP-ribosylation factor-like protein 6-interacting protein 4     | Arl6ip4  | Q9JM93 | -0.31117 | 0.10193 |
| Y-box-binding protein 1                                          | Ybx1     | P62960 | -0.31112 | 0.09388 |
| 39S ribosomal protein L12, mitochondrial                         | Mrpl12   | Q9DB15 | -0.31077 | 0.00999 |
| Phosphofurin acidic cluster sorting protein 2                    | Pacs2    | Q3V3Q7 | -0.31123 | 0.05661 |
| Glutathione S-transferase Mu 4                                   | Gstm4    | Q8R5I6 | -0.29946 | 0.37750 |
| Rho guanine nucleotide exchange factor 18                        | Arhgef18 | Q6P9R4 | -0.29843 | 0.02163 |
| SPRY domain-containing SOCS box protein 2                        | Spsb2    | O88838 | -0.29758 | 0.00190 |
| Prothymosin alpha                                                | Ptma     | P26350 | -0.29498 | 0.03184 |
| Transient receptor potential cation channel subfamily M member 7 | Trpm7    | Q923J1 | -0.29399 | 0.32487 |
| Vasorin                                                          | Vasn     | Q9CZT5 | -0.29274 | 0.12629 |
| Involucrin                                                       | Ivl      | P48997 | -0.28984 | 0.00940 |
| Keratin, type I cytoskeletal 16                                  | Krt16    | Q9Z2K1 | -0.28979 | 0.44332 |
| Tyrosine-protein kinase BTK                                      | Btk      | P35991 | -0.28843 | 0.05958 |
| Interferon-inducible GTPase 1                                    | Iigp1    | Q9QZ85 | -0.28784 | 0.30825 |
| Intraflagellar transport protein 140 homolog                     | Ift140   | E9PY46 | -0.28707 | 0.03649 |
| Nurim                                                            | Nrm      | Q8VC65 | -0.28699 | 0.00192 |
| Chromodomain Y-like protein 2                                    | Cdy12    | Q9D5D8 | -0.28608 | 0.26104 |
| Cornifin-A                                                       | Sprr1a   | Q62266 | -0.28478 | 0.03858 |
| NADH dehydrogenase [ubiquinone] flavoprotein                     | Ndufv3   | Q8BK30 | -0.28477 | 0.07683 |

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3, mitochondrial

|                                                 |          |        |          |         |
|-------------------------------------------------|----------|--------|----------|---------|
| Probable tRNA (uracil-O(2)-)-methyltransferase  | Trmt44   | Q9D2Q2 | -0.28108 | 0.02507 |
| Alpha-actinin-3                                 | Actn3    | O88990 | -0.28100 | 0.16148 |
| Stefin-1                                        | Stfa1    | P35175 | -0.28021 | 0.25389 |
| Dynein light chain roadblock-type 1             | Dynlrb1  | P62627 | -0.27965 | 0.04271 |
| CDP-diacylglycerol--inositol                    |          |        | -0.27801 | 0.06824 |
| 3-phosphatidyltransferase                       | Cdipt    | Q8VDP6 |          |         |
| Mitochondrial fission 1 protein                 | Fis1     | Q9CQ92 | -0.27666 | 0.09273 |
| m7GpppN-mRNA hydrolase                          | Dcp2     | Q9CYC6 | -0.27612 | 0.03090 |
| NADH-ubiquinone oxidoreductase chain 5          | Mtnd5    | P03921 | -0.27576 | 0.06021 |
| Protein FAM162A                                 | Fam162a  | Q9D6U8 | -0.27469 | 0.02953 |
| Nuclear receptor-binding factor 2               | Nrbf2    | Q8VCQ3 | -0.27245 | 0.00799 |
| Apolipoprotein A-II                             | Apoa2    | P09813 | -0.27200 | 0.06764 |
| Zinc finger protein basonuclin-2                | Bnc2     | Q8BMQ3 | -0.27179 | 0.04654 |
| Microsomal glutathione S-transferase 1          | Mgst1    | Q91VS7 | -0.27171 | 0.08888 |
| Superoxide dismutase [Mn], mitochondrial        | Sod2     | P09671 | -0.27064 | 0.05566 |
| Zinc finger protein 706                         | Znf706   | Q9D115 | -0.26932 | 0.00621 |
| ATP synthase-coupling factor 6, mitochondrial   | Atp5pf   | P97450 | -0.26904 | 0.08897 |
| Interleukin-36 beta                             | Il36b    | Q9D6Z6 | -0.26676 | 0.06795 |
| Ras-interacting protein 1                       | Rasip1   | Q3U0S6 | -0.26642 | 0.00905 |
| Kallikrein-1                                    | Klk1     | P15947 | -0.26624 | 0.48929 |
| V-type proton ATPase 16 kDa proteolipid subunit |          |        | -0.26517 | 0.04937 |
| c                                               | Atp6v0c  | P63082 |          |         |
| Keratin, type I cytoskeletal 13                 | Krt13    | P08730 | 0.26430  | 0.08659 |
| Dystonin                                        | Dst      | Q91ZU6 | 0.26497  | 0.00331 |
| Vomeromodulin                                   | Bpifb9a  | Q80X17 | 0.26771  | 0.00926 |
| Secretoglobulin family                          | Scgb2b20 | Q9JI02 | 0.26799  | 0.12458 |
| Keratin, type II cuticular 87                   | Krt87    | Q6IMF0 | 0.26803  | 0.24727 |
| Keratin, type II cytoskeletal 80                | Krt80    | Q0VBK2 | 0.26987  | 0.01604 |
| MAM domain-containing protein 2                 | Mamdc2   | Q8CG85 | 0.27160  | 0.00246 |
| Keratin, type II cuticular Hb6                  | Krt86    | P97861 | 0.27323  | 0.25496 |
| Odorant-binding protein 2a                      | Obp2a    | Q8K1H9 | 0.27475  | 0.10890 |
| Non-homologous end-joining factor 1             | Nhej1    | Q3KNJ2 | 0.27608  | 0.29525 |
| Cytochrome P450 2B10                            | Cyp2b10  | P12791 | 0.27734  | 0.03125 |
| Keratin, type I cuticular Ha4                   | Krt34    | Q9D646 | 0.27902  | 0.31634 |
| Keratin-associated protein 6-5                  | Krtap6-5 | Q925H3 | 0.27993  | 0.21757 |
| Gamma-tubulin complex component 2               | Tubgcp2  | Q921G8 | 0.27992  | 0.01305 |
| Protein phosphatase PTC7 homolog                | Pptc7    | Q6NVE9 | 0.28545  | 0.53432 |
| Desmoglein-1-alpha                              | Dsg1a    | Q61495 | 0.28593  | 0.01942 |
| Cytochrome P450 4B1                             | Cyp4b1   | Q64462 | 0.28678  | 0.00708 |
| Keratin-associated protein 5-5                  | Krtap5-5 | Q2TA51 | 0.28793  | 0.44164 |
| Filaggrin-2                                     | Flg2     | Q2VIS4 | 0.28862  | 0.02113 |
| Keratinocyte proline-rich protein               | Kprp     | B2RUR4 | 0.28978  | 0.01369 |

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|                                                                        |           |        |         |         |
|------------------------------------------------------------------------|-----------|--------|---------|---------|
| Metallothionein-4                                                      | Mt4       | P47945 | 0.29137 | 0.03136 |
| Vang-like protein 1                                                    | Vangl1    | Q80Z96 | 0.29146 | 0.04582 |
| Desmocollin-3                                                          | Dsc3      | P55850 | 0.29317 | 0.01162 |
| Adenylate cyclase type 8                                               | Adcy8     | P97490 | 0.29462 | 0.32208 |
| Ephrin type-A receptor 4                                               | Epha4     | Q03137 | 0.29745 | 0.01226 |
| Myocilin                                                               | Myoc      | O70624 | 0.29793 | 0.01394 |
| Dual specificity protein phosphatase 14                                | Dusp14    | Q9JLY7 | 0.29791 | 0.06769 |
| Loricrin                                                               | Loricrin  | P18165 | 0.31101 | 0.08398 |
| FHF complex subunit HOOK interacting protein 1A                        | Fhip1a    | Q505K2 | 0.31769 | 0.00712 |
| Keratin-associated protein 5-2                                         | Krtap5-2  | Q9D5Z7 | 0.32425 | 0.54177 |
| Interferon-induced protein with tetratricopeptide repeats 1            | Ifit1     | Q64282 | 0.32624 | 0.13829 |
| Serine/threonine-protein kinase WNK4                                   | Wnk4      | Q80UE6 | 0.32952 | 0.02410 |
| Protein yippee-like 5                                                  | Ypel5     | P62700 | 0.33780 | 0.11913 |
| Ig heavy chain V region VH558 A1/A4                                    | Gm5629    | P06327 | 0.34256 | 0.23467 |
| Gamma-butyrobetaine dioxygenase                                        | Bbox1     | Q924Y0 | 0.34278 | 0.01207 |
| Putative transferase CAF17 homolog, mitochondrial                      | Iba57     | Q8CAK1 | 0.34394 | 0.06689 |
| Ig heavy chain V-III region T957                                       | /         | P01800 | 0.34413 | 0.26008 |
| Disintegrin and metalloproteinase domain-containing protein 17         | Adam17    | Q9Z0F8 | 0.34525 | 0.15697 |
| Troponin T, slow skeletal muscle                                       | Tnnt1     | O88346 | 0.35376 | 0.00398 |
| N-acetylneuraminase lyase                                              | Npl       | Q9DCJ9 | 0.35424 | 0.02781 |
| Alpha-1,6-mannosyl-glycoprotein 1-beta-N-acetylglucosaminyltransferase | Mgat1     | Q921V5 | 0.35426 | 0.09741 |
| Keratin, type I cytoskeletal 24                                        | Krt24     | A1L317 | 0.35881 | 0.00589 |
| Immunoglobulin kappa constant                                          | Igkc      | P01837 | 0.36099 | 0.16975 |
| Polyunsaturated fatty acid (12S)/(13S)-lipoxygenase, epidermal-type    | Alox12e   | P55249 | 0.37089 | 0.01830 |
| Tissue factor                                                          | F3        | P20352 | 0.37696 | 0.00924 |
| FYVE, RhoGEF and PH domain-containing protein 4                        | Fgd4      | Q91ZT5 | 0.38005 | 0.10449 |
| Phosphatidate cytidyltransferase 2                                     | Cds2      | Q99L43 | 0.39257 | 0.02149 |
| Ig gamma-3 chain C region                                              |           | P03987 | 0.41808 | 0.03716 |
| Paired amphipathic helix protein Sin3b                                 | Sin3b     | Q62141 | 0.44475 | 0.57687 |
| Plexin-A4                                                              | Plxna4    | Q80UG2 | 0.46060 | 0.04424 |
| Keratin-associated protein 21-1                                        | Krtap21-1 | Q925H4 | 0.47485 | 0.07867 |
| Secretoglobulin family 2B member 24                                    | Scgb2b24  | Q7M747 | 0.51468 | 0.03769 |
| Acyl-CoA desaturase 1                                                  | Scd1      | P13516 | 0.46747 | 0.00475 |
| Keratin-associated protein 6-2                                         | Krtap6-2  | O08884 | 0.52512 | 0.14274 |
| Keratin, type II cytoskeletal 2 oral                                   | Krt76     | Q3UV17 | 0.58489 | 0.45623 |
| Ig heavy chain V region 3-6                                            | Ighv3-6   | P18531 | 0.58909 | 0.02869 |
| Odorant-binding protein 1a                                             | Obp1a     | Q9D3H2 | 0.67417 | 0.02976 |

|                                                 |         |        |         |         |
|-------------------------------------------------|---------|--------|---------|---------|
| Keratin, type II cytoskeletal 1b                | Krt77   | Q6IFZ6 | 0.68593 | 0.13743 |
| Secretoglobin family 2B member 2                | Scgb2b2 | Q6UGQ3 | 0.69397 | 0.02362 |
| Tropomodulin-1                                  | Tmod1   | P49813 | 0.72707 | 0.11263 |
| Ig gamma-2A chain C region, membrane-bound form | Igh-1a  | P01865 | 0.80559 | 0.09882 |
| Ribokinase                                      | Rbks    | Q8R1Q9 | 0.87657 | 0.13249 |