UBERON:0001003 skin epidermis

(Unique DEGs among top-100 found by the distance-based method, 48 genes)
2 genes are specifically directly related to skin epidermis
3 additional genes are related to skin epidermis

dynlt1a: dynein light chain Tctex-type 1A:

slc5a10: solute carrier family 5 (sodium/glucose cotransporter), member 10:
High capacity transporter for mannose and fructose and, to a lesser extent, glucose, AMG, and galactose.

bex3: brain expressed X-linked 3.

cacybp: calcyclin binding protein:
May be involved in calcium-dependent ubiquitination and subsequent proteasomal degradation of target proteins. Probably serves as a molecular bridge in ubiquitin E3 complexes. Participates in the ubiquitin-mediated degradation of beta-catenin (CTNNB1)

car2: carbonic anhydrase 2:
Essential for bone resorption and osteoclast differentiation. Reversible hydration of carbon dioxide. Contributes to intracellular pH regulation in the duodenal upper villous epithelium during proton-coupled peptide absorption. Stimulates the chloride-bicarbonate exchange activity of SLC26A6.

dnmt3b: DNA methyltransferase 3B:
This is one of two related genes encoding de novo DNA methyltransferases, which are **responsible for the establishment of DNA methylation patterns in embryos**. Loss of function of this gene results in severe developmental defects and loss of viability. Mutation of the related gene in humans causes immunodeficiency-centromeric instability-facial anomalies (ICF) syndrome. There is a pseudogene for this gene located adjacent to this gene in the same region of chromosome 2.
Required for genome-wide de novo methylation and is essential for the establishment of DNA methylation patterns during development. DNA methylation is coordinated with methylation of histones. May preferentially methylates nucleosomal DNA within the nucleosome core region. May function as transcriptional co- repressor by associating with CBX4 and independently of DNA methylation. Seems to be involved in gene silencing. In association with DNMT1 and via the recruitment of CTCFL/BORIS, involved in activation of BAG1 gene expression by modulating dimethylation of…

egfr: **epidermal** growth factor receptor:
Receptor tyrosine kinase binding ligands of the EGF family and activating several signaling cascades to convert extracellular cues into appropriate cellular responses. Known ligands include EGF, TGFA/TGF-alpha, amphiregulin, epigen/EPGN, BTC/betacellulin, epiregulin/EREG and HBEGF/heparin-binding EGF. Ligand binding triggers receptor homo- and/or heterodimerization and autophosphorylation on key

cytoplasmic residues. The phosphorylated receptor recruits adapter proteins like GRB2 which in turn activates complex downstream signaling cascades.

emp2: **epithelial** membrane protein 2:
Functions as **a key regulator of cell membrane composition** by regulating proteins surface expression. Also, plays a role in regulation of processes including cell migration, cell proliferation, cell contraction and cell adhesion. Negatively regulates caveolae formation by reducing CAV1 expression and CAV1 amount by increasing lysosomal degradation (PubMed-17609206, PubMed-14978215). Facilitates surface trafficking and the formation of lipid rafts bearing GPI-anchor proteins (PubMed-14978215). Regulates surface expression of MHC1 and ICAM1 proteins.

fabp3: fatty acid binding protein 3, muscle and heart:
ABP are thought to **play a role in the intracellular transport of long-chain fatty acids** and their acyl-CoA esters

ftl1: ferritin light polypeptide 1:

spsb2: splA/ryanodine receptor domain and SOCS box containing 2:

igfbp2: insulin-like growth factor binding protein 2:
The protein encoded by this gene is one of several similar proteins that bind insulin-like growth factors I and II (Igf-I and Igf-II). The encoded protein can be secreted into the bloodstream, where it binds Igf-I and Igf-II with high affinity, or it can remain intracellular, interacting with many different ligands.
RNA-binding factor that recruits target transcripts to cytoplasmic protein-RNA complexes (mRNPs). This transcript 'caging' into mRNPs allows mRNA transport and transient storage. It also modulates the rate and location at which target transcripts encounter the translational apparatus and shields them from endonuclease attacks or microRNA-mediated degradation (By similarity). **Binds to the 5'-UTR of the insulin-like growth factor 2** (IGF2) mRNAs. Binding is isoform-specific. Binds to beta-actin/ACTB and MYC transcripts.

kif1c: kinesin family member 1C:
Motor required for the retrograde transport of Golgi vesicles to the endoplasmic reticulum. Has a microtubule plus end- directed motility

ly6d: lymphocyte antigen 6 complex, locus D:
May act as a specification marker at earliest stage **specification of lymphocytes between B- and T-cell development**. Marks the earliest stage of B-cell specification.

mif: macrophage migration inhibitory factor (glycosylation-inhibiting factor):
Pro-inflammatory cytokine. **Involved in the innate immune response to bacterial pathogens**. The expression of MIF at sites of inflammation suggests a role as mediator in regulating the function of macrophages in host defense. Counteracts the anti-inflammatory activity of glucocorticoids. Has phenylpyruvate tautomerase and

dopachrome tautomerase activity (in vitro), but the physiological substrate is not known. It is not clear whether the tautomerase activity has any physiological relevance, and whether it is important for cytokine activity.

mdh2: malate dehydrogenase 2, NAD (mitochondrial).

myo7a: myosin VIIA:

Myosins are actin-based motor molecules with ATPase activity. Unconventional myosins serve in intracellular movements. Their highly divergent tails bind to membranous compartments, which are then moved relative to actin filaments. **In the retina**, plays an important role in the renewal of the outer photoreceptor disks. Plays an important role in the distribution and migration of retinal pigment epithelial (RPE) melanosomes and phagosomes, and in the regulation of opsin transport in retinal photoreceptors. Mediates intracellular transport of RPE65 in the retina pigment

nefl: neurofilament, light polypeptide:

Neurofilaments usually contain three intermediate filament proteins- L, M, and H which are involved in **the maintenance of neuronal caliber**.

npm1: nucleophosmin 1:

Involved in diverse **cellular processes such as ribosome biogenesis, centrosome duplication, protein chaperoning, histone assembly, cell proliferation, and regulation of tumor suppressors** p53/TP53 and ARF. Binds ribosome presumably to drive ribosome nuclear export. Associated with nucleolar ribonucleoprotein structures and bind single-stranded nucleic acids. Acts as a chaperonin for the core histones H3, H2B and H4. Stimulates APEX1 endonuclease activity on apurinic/apyrimidinic (AP) double- stranded DNA but inhibits APEX1 endonuclease activity on AP single-stranded RNA.

pou5f1: POU domain, class 5, transcription factor 1:

Transcription factor that binds to the octamer motif (5'-ATTTGCAT-3'). Forms a trimeric complex with SOX2 on DNA and controls the expression of a number of genes involved in embryonic development such as YES1, FGF4, UTF1 and ZFP206. **Critical for early embryogenesis and for embryonic stem cell pluripotency**.

ppl: periplakin:

Component of the cornified envelope of keratinocytes. May link the cornified envelope to desmosomes and intermediate filaments. May act as a localization signal in PKB/AKT-mediated signaling.

ran: RAN, member RAS oncogene family:

GTP-binding protein involved in nucleocytoplasmic transport. **Required for the import of protein into the nucleus and also for RNA export**. Involved in chromatin condensation and control of cell cycle. The complex with BIRC5/survivin plays a role in mitotic spindle formation by serving as a physical scaffold to help deliver the RAN

effector molecule TPX2 to microtubules. Acts as a negative regulator of the kinase activity of VRK1 and VRK2.

ranbp1: RAN binding protein 1:

Inhibits GTP exchange on Ran. **Forms a Ran-GTP-RANBP1 trimeric complex**. Increase GTP hydrolysis induced by the Ran GTPase activating protein RANGAP1. May act in an intracellular signaling pathway which may control the progression through the cell cycle by regulating the transport of protein and nucleic acids across the nuclear membrane.

sox2: SRY (sex determining region Y)-box 2

This intronless gene encodes a member of the SRY-related HMG-box (SOX) family of transcription factors **involved in the regulation of embryonic development and in the determination of cell fate**. The product of this gene is required for stem-cell maintenance in the central nervous system, and also regulates gene expression in the stomach. Mutations in a similar gene in human have been associated with optic nerve hypoplasia and with syndromic microphthalmia, a severe form of structural eye malformation. This gene lies within an intron of another gene called SOX2 overlapping transcript.

spp1: secreted phosphoprotein 1:

Binds tightly to hydroxyapatite. Appears to form an integral part of the mineralized matrix. Probably important to cell-matrix interaction.

esrp1: epithelial splicing regulatory protein 1:

mRNA splicing factor that **regulates the formation of epithelial cell-specific isoforms**. Specifically regulates the expression of FGFR2-IIIb, an epithelial cell-specific isoform of FGFR2. Also regulates the splicing of CD44, CTNND1, ENAH, 3 transcripts that undergo changes in splicing during the epithelial-to-mesenchymal transition (EMT). Acts by directly binding specific sequences in mRNAs. Binds the GU-rich sequence motifs in the ISE/ISS-3, a cis-element regulatory region present in the mRNA of FGFR2

sdc4: syndecan 4:

Cell surface proteoglycan that bears heparan sulfate. **Regulates exosome biogenesis** in concert with SDCBP and PDCD6IP.

dynlt1b: dynein light chain Tctex-type 1B:

Acts as one of several non-catalytic accessory components of the cytoplasmic dynein 1 complex that are thought to be involved in linking dynein to cargos and to adapter proteins that regulate dynein function. Cytoplasmic dynein 1 acts as a motor for the intracellular retrograde motility of vesicles and organelles along microtubules. Binds to transport cargos and **is involved in apical cargo transport such as rhodopsin-bearing vesicles in polarized epithelia**. Is involved in intracellular targeting of D-type retrovirus gag polyproteins to the cytoplasmic.

tgtp1: T cell specific GTPase 1:

trh: thyrotropin releasing hormone:

This gene encodes a member of the thyrotropin-releasing hormone family. Cleavage of the encoded proprotein releases mature thyrotropin-releasing hormone, which is a tripeptide hypothalamic regulatory hormone. The mouse proprotein contains five thyrotropin-releasing hormone tripeptides. Thyrotropin-releasing hormone **is involved in the regulation and release of thyroid-stimulating hormone**, as well as prolactin. Disruption of this gene results in hypothyroidism, elevated thyroid-stimulating hormone levels, and hyperglycemia.

Functions as a regulator of the biosynthesis of TSH in the anterior pituitary gland and as a neurotransmitter/ neuromodulator in the central and peripheral nervous systems.

trp63: transformation related protein 63:

This gene encodes **tumor protein p63**, a member of the p53 family of transcription factors involved in cellular responses to stress and development. The family members include tumor proteins p53, p63, and p73, which have high sequence similarity to one another. This similarity allows p63 and p73 to transactivate p53-responsive genes causing cell cycle arrest and apoptosis. The family members can interact with each other in many ways, including direct and indirect protein interactions. This results in mutual regulation of target gene promoters. Tumor protein p63 -/- mice have several developmental defects which include the lack of limbs and other tissues, such as teeth and mammary glands, which develop as a result of interactions between mesenchyme and epithelium.

Acts as a sequence specific DNA binding transcriptional activator or repressor. The isoforms contain a varying set of transactivation and auto-regulating transactivation inhibiting domains thus showing an isoform specific activity. May be required in conjunction with TP73/p73 for initiation of p53/TP53 dependent apoptosis in response to genotoxic insults and the presence of activated oncogenes. Involved in Notch signaling by probably inducing JAG1 and JAG2. Activates transcription of the p21 promoter (By similarity). Activates RIPK4 transcription.

upp1: uridine phosphorylase 1:

Catalyzes the reversible phosphorylytic cleavage of uridine and deoxyuridine to uracil and ribose- or deoxyribose-1- phosphate (PubMed-7744869). The produced molecules are then utilized as carbon and energy sources or in the rescue of pyrimidine bases for nucleotide synthesis.

zfp42: zinc finger protein 42:

Involved in the **reprogramming of X-chromosome inactivation during the acquisition of pluripotency**. Required for efficient elongation of TSIX, a non-coding RNA antisense to XIST. Binds DXPas34 enhancer within the TSIX promoter. Involved in ES cell self-renewal.

zfp57: zinc finger protein 57:

Transcription regulator required to **maintain maternal and paternal gene imprinting**, a process by which gene expression is restricted in a parent of origin-specific manner by epigenetic modification of genomic DNA and chromatin, including DNA methylation.

Acts by controlling DNA methylation during the earliest multicellular stages of development at multiple imprinting control regions. Required for the establishment of maternal methylation imprints at SNRPN locus. Acts as a transcriptional repressor in Schwann cells. Binds to a 5'-TGCCGC- 3' consensus sequence a

ccnb1: cyclin B1:

Essential for the control of the cell cycle at the G2/M (mitosis) transition.

asns: asparagine synthetase:

eno1b: enolase 1B, retrotransposed:

This gene may represent an evolving pseudogene of the alpha-enolase (enolase 1, alpha non-neuron) gene, which has multiple pseudogenes. This gene has an intact open reading frame as well as strong transcriptional support. The length of encoded protein is conserved, compared to the original enolase 1 protein. The exact function of this gene is unknown.

dppa5a: developmental pluripotency associated 5A:

Involved in the **maintenance of embryonic stem (ES) cell pluripotency**. Dispensable for self-renewal of pluripotent ES cells and establishment of germ cells. Associates with specific target mRNAs

amt: aminomethyltransferase:

The glycine cleavage system **catalyzes the degradation of glycine**.

h2afz: H2A histone family, member Z:

Histones are basic nuclear proteins that are responsible for the nucleosome structure of the chromosomal fiber in eukaryotes. Nucleosomes consist of approximately 146 bp of DNA wrapped around a histone octamer composed of pairs of each of the four core histones (H2A, H2B, H3, and H4). The chromatin fiber is further compacted through the interaction of a linker histone, H1, with the DNA between the nucleosomes to form higher order chromatin structures. This gene encodes a replication-independent member of the histone H2A family that is distinct from other members of the family. Studies in mice have shown that **this particular histone is required for embryonic development** and indicate that lack of functional histone H2A leads to embryonic lethality.
Variant histone H2A which replaces conventional H2A in a subset of nucleosomes. Nucleosomes wrap and compact DNA into chromatin, limiting DNA accessibility to the cellular machineries which require DNA as a template. Histones thereby play a central role in transcription regulation, DNA repair, DNA replication and chromosomal stability. DNA accessibility is regulated via a complex set of post-translational modifications of histones, also called histone code, and nucleosome remodeling. May be involved in the formation of constitutive heterochromatin.

pkp3: plakophilin 3:

May play a role in junctional plaques.

ahnak: AHNAK nucleoprotein (desmoyokin).

slc25a53: solute carrier family 25, member 53.

zfp605: zinc finger protein 605:

s100a16: S100 calcium binding protein A16:

ssfa2: sperm specific antigen 2:

selenoh: selenoprotein H:

> This gene encodes a nucleolar protein, which belongs to the SelWTH family. It functions as an oxidoreductase, and has been shown to protect neurons against UVB-induced damage by inhibiting apoptotic cell death pathways, promote mitochondrial biogenesis and mitochondrial function, and suppress cellular senescence through genome maintenance and redox regulation. This protein is a selenoprotein, containing the rare amino acid selenocysteine (Sec) at its active site. Sec is encoded by the UGA codon, which normally signals translation termination. The 3' UTRs of selenoprotein mRNAs contain a conserved stem-loop structure, designated the Sec insertion sequence (SECIS) element, that is necessary for the recognition of UGA as a Sec codon, rather than as a stop signal.

tbc1d30: TBC1 domain family, member 30:

> GTPase-activating protein (GAP) with broad specificity. Acts as a GAP for RAB3A. Also exhibits significant GAP activity toward RAB22A, RAB27A, and RAB35 in vitro.