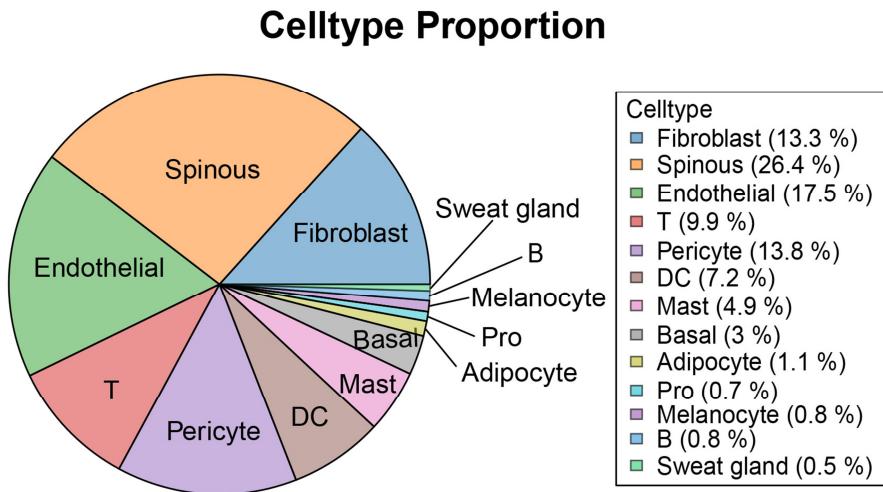


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## Supplemental Data

### 2 Supplemental Figures

#### 3 Supplemental Figure 1



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5 The relative abundance and distribution of major cell populations in KN and KD  
6 skins.

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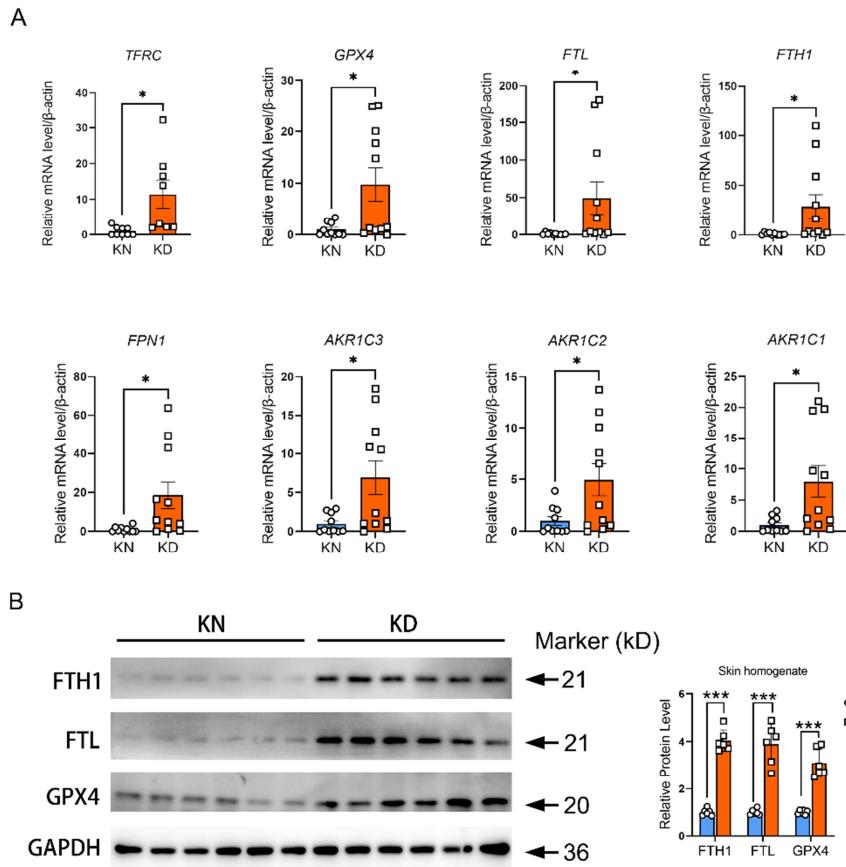
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1    **Supplemental Figure 2**



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3    **Supplementary Figure 2. Increased iron metabolism and antioxidant genes in**  
4    **skin tissue homogenate. (A)** mRNA levels of iron metabolism and antioxidant genes  
5    in skin tissue homogenate.  $N \geq 10$  per group. **(B)** FTH1, FTL, and GPX4 protein  
6    levels in skin tissue homogenate.  $N = 6$  per group. The student's t-test calculates data  
7    in A. Data in B are evaluated using the Student's t-test and corrected using the  
8    Benjamini-Hochberg procedure. Data are represented as mean  $\pm$  SEM. \* $P < 0.05$ ; \*\* $P$   
9     $< 0.001$ ; \*\*\* $P < 0.001$ .

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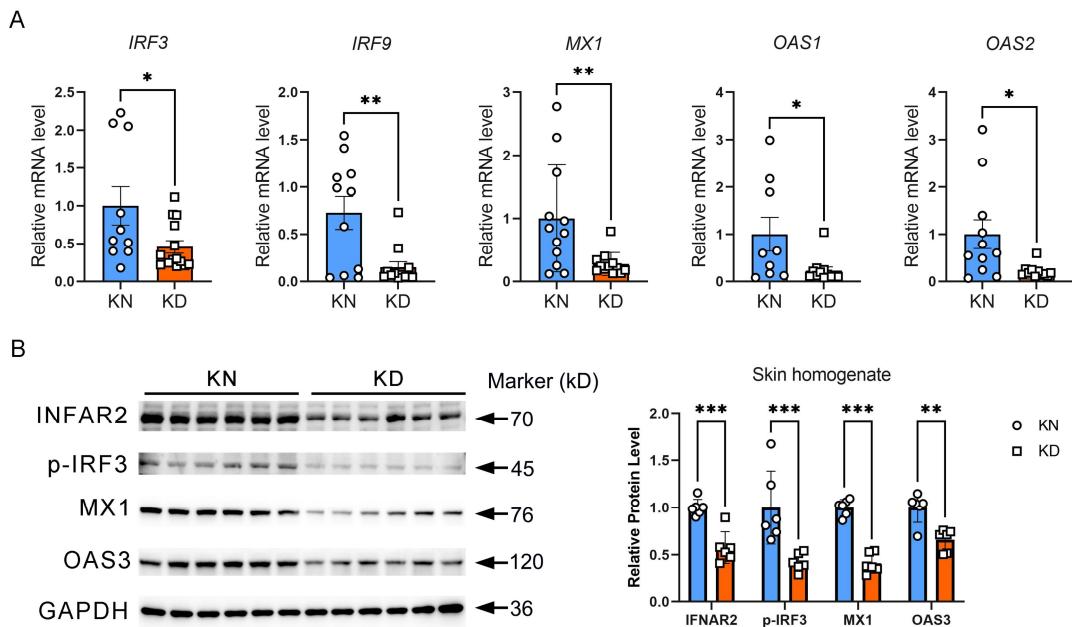
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1    **Supplemental Figure 3**



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3    **Supplementary Figure 3. Decreased interferon signaling in skin tissue**  
4    **homogenate.** (A) mRNA levels of *IRF3*, *IRF9*, *MX1*, *OAS1*, and *OAS2* genes in skin  
5    tissue homogenate. N ≥ 10 per group. (B) IFNAR2, p-IRF3, MX1, and OAS3 protein  
6    levels in skin tissue homogenate. N = 6 per group. The student's t-test calculates all  
7    the data in A. Data are represented as mean ± SEM. \*P < 0.05; \*\*P < 0.001; \*\*\*P <  
8    0.001.

1 **Supplemental Tables**

2 **Supplemental Table S1 Gene panel for evaluating ferroptosis resistance scores.**

| <b>Gene Symbol</b> | <b>Official Full Name (NCBI)</b>                   |
|--------------------|--|
| SLC7A11            | solute carrier family 7 member 11                  |
| GPX4               | glutathione peroxidase 4                           |
| AKR1C1             | aldo-keto reductase family 1 member C1             |
| AKR1C2             | aldo-keto reductase family 1 member C2             |
| AKR1C3             | aldo-keto reductase family 1 member C3             |
| RB1                | RB transcriptional corepressor 1                   |
| HSPB1              | heat shock protein family B (small) member 1       |
| HSF1               | heat shock transcription factor 1                  |
| GCLC               | glutamate-cysteine ligase catalytic subunit        |
| NFE2L2             | nuclear factor, erythroid 2 like 2                 |
| SQSTM1             | sequestosome 1                                     |
| NQO1               | NAD(P)H quinone dehydrogenase 1                    |
| HMOX1              | heme oxygenase 1                                   |
| FTH1               | ferritin heavy chain 1                             |
| MUC1               | mucin 1, cell surface associated                   |
| SLC3A2             | solute carrier family 3 member 2                   |
| MT1G               | metallothionein 1G                                 |
| SLC40A1            | solute carrier family 40 member 1                  |
| CISD1              | CDGSH iron sulfur domain 1                         |
| FANCD2             | FA complementation group D2                        |
| FTMT               | ferritin mitochondrial                             |
| HSPA5              | heat shock protein family A (Hsp70) member 5       |
| ATF4               | activating transcription factor 4                  |
| TP53               | tumor protein p53                                  |
| HELLS              | helicase, lymphoid-specific                        |
| SCD                | stearoyl-CoA desaturase                            |
| FADS2              | fatty acid desaturase 2                            |
| SRC                | SRC proto-oncogene, non-receptor tyrosine kinase   |
| STAT3              | signal transducer and activator of transcription 3 |
| PML                | promyelocytic leukemia                             |
| MTOR               | mechanistic target of rapamycin kinase             |
| NFS1               | NFS1 cysteine desulfurase                          |
| TP63               | tumor protein p63                                  |
| CDKN1A             | cyclin dependent kinase inhibitor 1A               |
| ENPP2              | ectonucleotide pyrophosphatase/phosphodiesterase 2 |
| VDAC2              | voltage dependent anion channel 2                  |
| FH                 | fumarate hydratase                                 |
| CISD2              | CDGSH iron sulfur domain 2                         |

|         |  |
|---------|--|
| CBS     | cystathionine beta-synthase  |
| ISCU    | iron-sulfur cluster assembly enzyme                                    |
| ACSL3   | acyl-CoA synthetase long chain family member 3                         |
| OTUB1   | OTU deubiquitinase, ubiquitin aldehyde binding 1                       |
| CD44    | CD44 molecule  |
| BRD4    | bromodomain containing 4   |
| PRDX6   | peroxiredoxin 6  |
| SESN2   | sestrin 2  |
| NF2     | NF2, moesin-ezrin-radixin like (MERLIN) tumor suppressor               |
| ARNTL   | aryl hydrocarbon receptor nuclear translocator like                    |
| HIF1A   | hypoxia inducible factor 1 subunit alpha                               |
| JUN     | Jun proto-oncogene, AP-1 transcription factor subunit                  |
| CA9     | carbonic anhydrase 9   |
| TMBIM4  | transmembrane BAX inhibitor motif containing 4                         |
| PLIN2   | perilipin 2  |
| AIFM2   | apoptosis inducing factor mitochondria associated 2                    |
| LAMP2   | lysosomal associated membrane protein 2                                |
| ZFP36   | ZFP36 ring finger protein  |
| PROM2   | prominin 2   |
| CHMP5   | charged multivesicular body protein 5                                  |
| CHMP6   | charged multivesicular body protein 6                                  |
| CAV1    | caveolin 1   |
| GCH1    | GTP cyclohydrolase 1   |
| SIRT3   | sirtuin 3  |
| DAZAP1  | DAZ associated protein 1   |
| PIR     | pirin  |
| FTL     | ferritin light chain   |
| HCAR1   | hydroxycarboxylic acid receptor 1                                      |
| SLC16A1 | solute carrier family 16 member 1                                      |
| RRM2    | ribonucleotide reductase regulatory subunit M2                         |
| NR4A1   | nuclear receptor subfamily 4 group A member 1                          |
| PIK3CA  | phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha |
| RPTOR   | regulatory associated protein of MTOR complex 1                        |
| SREBF1  | sterol regulatory element binding transcription factor 1               |
| SREBF2  | sterol regulatory element binding transcription factor 2               |
| FZD7    | frizzled class receptor 7  |
| P4HB    | prolyl 4-hydroxylase subunit beta                                      |
| NT5DC2  | 5'-nucleotidase domain containing 2                                    |
| BCAT2   | branched chain amino acid transaminase 2                               |
| PLA2G6  | phospholipase A2 group VI  |
| PARK7   | Parkinsonism associated deglycase                                      |
| FXN     | frataxin   |

|          |  |
|----------|--|
| SUV39H1  | suppressor of variegation 3-9 homolog 1                |
| ATF2     | activating transcription factor 2                      |
| ACOT1    | acyl-CoA thioesterase 1                                |
| ALDH3A2  | aldehyde dehydrogenase 3 family member A2              |
| STK11    | serine/threonine kinase 11                             |
| FNDC5    | fibronectin type III domain containing 5               |
| CDH1     | cadherin 1   |
| NEDD4L   | NEDD4 like E3 ubiquitin protein ligase                 |
| TF       | transferrin  |
| BRD2     | bromodomain containing 2                               |
| BRD3     | bromodomain containing 3                               |
| BRDT     | bromodomain testis associated                          |
| DECR1    | 2,4-dienoyl-CoA reductase 1                            |
| GLRX5    | glutaredoxin 5   |
| NCOA3    | nuclear receptor coactivator 3                         |
| NR5A2    | nuclear receptor subfamily 5 group A member 2          |
| PANX2    | pannexin 2   |
| TFAP2A   | transcription factor AP-2 alpha                        |
| CP       | ceruloplasmin  |
| ARF6     | ADP ribosylation factor 6                              |
| GDF15    | growth differentiation factor 15                       |
| ABHD12   | abhydrolase domain containing 12                       |
| PPP1R13L | protein phosphatase 1 regulatory subunit 13 like       |
| TFAM     | transcription factor A, mitochondrial                  |
| KDM3B    | lysine demethylase 3B                                  |
| AHCY     | adenosylhomocysteinase                                 |
| IDH2     | isocitrate dehydrogenase (NADP(+)) 2                   |
| PPARA    | peroxisome proliferator activated receptor alpha       |
| NOS2     | nitric oxide synthase 2                                |
| SIAH2    | siah E3 ubiquitin protein ligase 2                     |
| RELA     | RELA proto-oncogene, NF-kB subunit                     |
| PRKAA2   | protein kinase AMP-activated catalytic subunit alpha 2 |
| VDR      | vitamin D receptor                                     |
| NEDD4    | NEDD4 E3 ubiquitin protein ligase                      |
| PRDX1    | peroxiredoxin 1  |
| AR       | androgen receptor                                      |
| MTF1     | metal regulatory transcription factor 1                |
| COPZ1    | COPI coat complex subunit zeta 1                       |
| NUPR1    | nuclear protein 1, transcriptional regulator           |
| USP35    | ubiquitin specific peptidase 35                        |
| NEAT1    | nuclear paraspeckle assembly transcript 1              |
| PARP1    | poly(ADP-ribose) polymerase 1                          |
| PARP2    | poly(ADP-ribose) polymerase 2                          |

|          |   |
|----------|---|
| PARP3    | poly(ADP-ribose) polymerase 3                           |
| PARP4    | poly(ADP-ribose) polymerase family member 4             |
| PARP6    | poly(ADP-ribose) polymerase family member 6             |
| PARP8    | poly(ADP-ribose) polymerase family member 8             |
| PARP9    | poly (ADP-ribose) polymerase family member 9            |
| PARP10   | poly(ADP-ribose) polymerase family member 10            |
| PARP11   | poly(ADP-ribose) polymerase family member 11            |
| PARP12   | poly(ADP-ribose) polymerase family member 12            |
| PARP14   | poly(ADP-ribose) polymerase family member 14            |
| PARP15   | poly(ADP-ribose) polymerase family member 15            |
| PARP16   | poly(ADP-ribose) polymerase family member 16            |
| PDSS2    | decaprenyl diphosphate synthase subunit 2               |
| TXN      | thioredoxin   |
| SENP1    | SUMO specific peptidase 1                               |
| OIP5-AS1 | OIP5 antisense RNA 1                                    |
| CREB1    | cAMP responsive element binding protein 1               |
| CREB3    | cAMP responsive element binding protein 3               |
| CREB5    | cAMP responsive element binding protein 5               |
| GOT1     | glutamic-oxaloacetic transaminase 1                     |
| TFRC     | transferrin receptor                                    |
| BEX1     | brain expressed X-linked 1                              |
| ASAH2    | N-acylsphingosine amidohydrolase 2                      |
| FABP4    | fatty acid binding protein 4                            |
| AKT1S1   | AKT1 substrate 1  |
| MLST8    | MTOR associated protein, LST8 homolog                   |
| SIRT1    | sirtuin 1   |
| TYRO3    | TYRO3 protein tyrosine kinase                           |
| SIRT6    | sirtuin 6   |
| TMSB4X   | thymosin beta 4, X-linked                               |
| TMSB4Y   | thymosin beta 4, Y-linked                               |
| KIF20A   | kinesin family member 20A                               |
| ECH1     | enoyl-CoA hydratase 1                                   |
| ETV4     | ETS variant transcription factor 4                      |
| MEG8     | maternally expressed 8                                  |
| VCP      | valosin containing protein                              |
| RBMS1    | RNA binding motif single stranded interacting protein 1 |
| KDM4A    | lysine demethylase 4A                                   |
| MGST1    | microsomal glutathione S-transferase 1                  |
| MPC1     | mitochondrial pyruvate carrier 1                        |
| CHMP1A   | charged multivesicular body protein 1A                  |
| CAMKK2   | calcium/calmodulin dependent protein kinase kinase 2    |
| SOX2     | SRY-box transcription factor 2                          |
| SRSF9    | serine and arginine rich splicing factor 9              |

|          |   |
|----------|---|
| PROK2    | prokineticin 2  |
| SIRT2    | sirtuin 2   |
| MEF2C    | myocyte enhancer factor 2C                                |
| EZH2     | enhancer of zeste 2 polycomb repressive complex 2 subunit |
| SMPD1    | sphingomyelin phosphodiesterase 1                         |
| ADAMTS13 | ADAM metallopeptidase with thrombospondin type 1 motif 13 |
| CDC25A   | cell division cycle 25A                                   |
| G6PD     | glucose-6-phosphate dehydrogenase                         |
| PPARD    | peroxisome proliferator activated receptor delta          |
| ENO3     | enolase 3   |
| LCN2     | lipocalin 2   |
| TRIB2    | tribbles pseudokinase 2                                   |
| DHODH    | dihydroorotate dehydrogenase                              |
| PDK4     | pyruvate dehydrogenase kinase 4                           |
| MIR9-3HG | MIR9-3 host gene  |
| IL6      | interleukin 6   |
| PTPN18   | protein tyrosine phosphatase non-receptor type 18         |
| ABCC5    | ATP binding cassette subfamily C member 5                 |
| CISD3    | CDGSH iron sulfur domain 3                                |
| MS4A15   | membrane spanning 4-domains A15                           |
| FURIN    | furin, paired basic amino acid cleaving enzyme            |
| GALNT14  | polypeptide N-acetylgalactosaminyltransferase 14          |
| KLHDC3   | kelch domain containing 3                                 |
| MAPKAP1  | MAPK associated protein 1                                 |
| PRR5     | proline rich 5  |
| RICTOR   | RPTOR independent companion of MTOR complex 2             |
| GSTM1    | glutathione S-transferase mu 1                            |
| RARRES2  | retinoic acid receptor responder 2                        |
| USP11    | ubiquitin specific peptidase 11                           |

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1      **Supplemental Table S2**

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**Characteristics of paired keloid patients (KD and KN)**

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**Age (years), mean ± SD**                             $35 \pm 9$

**Gender**

Female    N=7

Male    N=5

**Site of Specimen**

Ear    N=3

Chest    N=6

Shoulder    N=3

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**Characteristics of unpaired keloid patients (KD)**

---

**Age (years), mean ± SD**                             $40 \pm 4$

**Gender**

Female    N=10

Male    N=8

**Site of Specimen**

Chest    N=5

Ear    N=3

Hip    N=3

Shoulder    N=5

Neck    N=2

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**N, Number of patients**

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1 Supplemental Table S3

| qRT-PCR Primers | Sequence (5'-3')   |
|-----------------|--|
| <i>α-SMA</i>    | F: CTGAACGAGAACCAAGTGCG;<br>R: ACGAACCTCTGCACATTGA         |
| <i>ACSL4</i>    | F: ACTGGCCGACCTAAGGGAG;<br>R: GCCAAAGGCAAGTAGCCAATA        |
| <i>ADIPOQ</i>   | F: TGCTGGGAGCTGTTCTACTG;<br>R: TACTCCGGTTTCACCGATGTC       |
| <i>AKR1C1</i>   | F: TTCATGCCTGTCCTGGGATTT;<br>R: CTGGCTTACAGACACTGGAAAA     |
| <i>AKR1C2</i>   | F: CAACTCAACCACAGGCTGC;<br>R: GTCTGATGCGCTGCTCATTG         |
| <i>AKR1C3</i>   | F: GAGAGCAGAACGAAAGGAAAGGA;<br>R: CACAACACCACGTTATCGGG     |
| <i>COL1A1</i>   | F: GTGGGCAACGACTCTGGAC;<br>R: GCTTCGACATCAGCATTCTCA        |
| <i>COL1A2</i>   | F: GATCACCCGAATGGCTATGAAT;<br>R: GGGGTACAGTTGTCAATGTT      |
| <i>COL3A1</i>   | F: CACAACACGCTGTCGGCTA;<br>R: CGATCCTGCATCTGTAAATCGC       |
| <i>EIF2AK2</i>  | F: GCCGCTAAACTGCATATCTTCAT;<br>R: TCACACGTAGTAGCAAAAGAACCC |
| <i>FN1</i>      | F: CGGTGGCTGTCAGTCAAAG;<br>R: AACCTCGGCTTCCTCCATAA         |
| <i>FTH1</i>     | F: CCCCCATTTGTGTGACTTCAT;<br>R: GCCCAGGGCTTAGCTTCATT       |
| <i>FTL</i>      | F: CAGCCTGGTCAATTGTACCT;<br>R: GCCAATTGCGGAAGAAGTG         |
| <i>GAPDH</i>    | F: GGAGCGAGATCCCTCCAAAAT;<br>R: GGCTGTTGTCATACTTCTCATGG    |
| <i>GPX4</i>     | F: GAGGCAAGACCGAAGTAAACTAC;<br>R: CGGAACCTGGTTACACGGGAA    |
| <i>IRF3</i>     | F: AGAGGCTCGTGATGGTCAAG;<br>R: AGGTCCACAGTATTCTCCAGG       |
| <i>IRF9</i>     | F: GCCCTACAAGGTGTATCAGTTG;<br>R: TGCTGTCGCTTGATGGTACT      |
| <i>ISG15</i>    | F: CGCAGATCACCCAGAACGATCG;<br>R: TTCGTCGCATTGTCCACCA       |
| <i>MX1</i>      | F: GTTCCGAAGTGGACATCGCA;<br>R: CTGCACAGGTTGTTCTCAGC        |
| <i>MX2</i>      | F: CAGAGGCAGCGGAATCGTAA;<br>R: TGAAGCTCTAGCTCGGTGTT        |

|                |   |
|----------------|---|
| <i>NFE2L2</i>  | F: TCAGCGACGGAAAGAGTATGA;<br>R: CCACTGGTTCTGACTGGATGT     |
| <i>OAS1</i>    | F: TGTCCAAGGTGGTAAAGGGTG;<br>R: CCGGCGATTAACTGATCCTG      |
| <i>OAS2</i>    | F: CTCAGAAGCTGGGTTGGTTAT;<br>R: ACCATCTCGTCGATCAGTGTC     |
| <i>PLIN1</i>   | F: TGTGCAATGCCTATGAGAAGG;<br>R: AGGGCGGGGATCTTCCT         |
| <i>SLC3A2</i>  | F: TGAATGAGTTAGAGCCCCGAGA;<br>R: GTCTTCCGCCACCTTGATCTT    |
| <i>SLC40A1</i> | F: CTACTTGGGGAGATCGGATGT;<br>R: CTGGGCCACTTAAGTCTAGC      |
| <i>SLC7A11</i> | F: TCTCCAAAGGAGGTTACCTGC;<br>R: AGACTCCCCTCAGTAAAGTGAC    |
| <i>TFRC</i>    | F: ACCATTGTCATATAACCGGTTCA;<br>R: CAATAGCCCAAGTAGCCAATCAT |
| <i>TGF-β1</i>  | F: GGCCAGATCCTGTCCAAGC;<br>R: GTGGGTTCCACCATTAGCAC        |