

**Table 1.** The up-regulated DEGs in SCR-AGS

| Gene    | P.Value  | logFC  | Gene title                                                      |
|---------|----------|--------|-----------------------------------------------------------------|
| ALDH1A1 | 1.51E-13 | -2.998 | aldehyde dehydrogenase 1 family member A1                       |
| ALDH1A1 | 1.21E-12 | -2.758 | aldehyde dehydrogenase 1 family member A1                       |
| IFI27   | 1.04E-08 | -2.203 | interferon alpha inducible protein 27                           |
| PI3     | 9.08E-07 | -1.877 | peptidase inhibitor 3                                           |
| OAS2    | 9.37E-07 | -1.851 | 2'-5'-oligoadenylate synthetase 2                               |
| GCNT3   | 3.63E-09 | -1.673 | glucosaminyl (N-acetyl) transferase 3, mucin type               |
| GDF15   | 2.40E-04 | -1.649 | growth differentiation factor 15                                |
| IFI6    | 1.34E-06 | -1.627 | interferon alpha inducible protein 6                            |
| IFI44   | 1.11E-06 | -1.503 | interferon induced protein 44                                   |
| MALL    | 7.51E-08 | -1.491 | mal, T-cell differentiation protein like                        |
| IFIT1   | 1.13E-06 | -1.468 | interferon induced protein with tetratricopeptide repeats 1     |
| OAS1    | 1.78E-07 | -1.461 | 2'-5'-oligoadenylate synthetase 1                               |
| STAT1   | 1.01E-08 | -1.423 | signal transducer and activator of transcription 1              |
| MX2     | 2.62E-07 | -1.411 | MX dynamin like GTPase 2                                        |
| SLPI    | 1.27E-05 | -1.411 | secretory leukocyte peptidase inhibitor                         |
| SAMD9   | 1.66E-08 | -1.4   | sterile alpha motif domain containing 9                         |
| BST2    | 2.60E-04 | -1.393 | bone marrow stromal cell antigen 2                              |
| GSDMB   | 7.21E-07 | -1.359 | gasdermin B                                                     |
| ISG15   | 1.52E-08 | -1.353 | ISG15 ubiquitin-like modifier                                   |
| AGR2    | 3.96E-06 | -1.348 | anterior gradient 2, protein disulphide isomerase family member |
| C4BPB   | 1.97E-08 | -1.335 | complement component 4 binding protein beta                     |
| DDX60   | 3.38E-06 | -1.315 | DEXD/H-box helicase 60                                          |
| EPSTI1  | 7.48E-07 | -1.297 | epithelial stromal interaction 1 (breast)                       |
| P4HB    | 4.81E-08 | -1.291 | prolyl 4-hydroxylase subunit beta                               |
| S100A9  | 4.11E-05 | -1.287 | S100 calcium binding protein A9                                 |
| OAS1    | 1.18E-07 | -1.286 | 2'-5'-oligoadenylate synthetase 1                               |
| SIPA1L2 | 6.79E-07 | -1.283 | signal induced proliferation associated 1 like 2                |
| GSDMB   | 2.49E-06 | -1.265 | gasdermin B                                                     |
| PTPRO   | 5.47E-08 | -1.256 | protein tyrosine phosphatase, receptor type O                   |
| MUC13   | 3.24E-08 | -1.237 | mucin 13, cell surface associated                               |
| REG1A   | 8.08E-08 | -1.234 | regenerating family member 1 alpha                              |
| PTPRO   | 9.06E-08 | -1.219 | protein tyrosine phosphatase, receptor type O                   |
| IFI6    | 7.30E-08 | -1.218 | interferon alpha inducible protein 6                            |
| STAT1   | 3.07E-07 | -1.2   | signal transducer and activator of transcription 1              |
| IFIT3   | 2.75E-06 | -1.151 | interferon induced protein with tetratricopeptide repeats 3     |
| CLDN1   | 3.05E-05 | -1.139 | claudin 1                                                       |
| RGS16   | 3.10E-04 | -1.137 | regulator of G-protein signaling 16                             |
| CEACAM6 | 1.52E-05 | -1.136 | carcinoembryonic antigen related cell adhesion molecule 6       |
| PIM1    | 1.83E-05 | -1.131 | Pim-1 proto-oncogene, serine/threonine kinase                   |
| BST2    | 3.35E-04 | -1.128 | bone marrow stromal cell antigen 2                              |
| IFIT3   | 1.18E-06 | -1.1   | interferon induced protein with tetratricopeptide repeats 3     |
| SYTL2   | 2.47E-07 | -1.091 | synaptotagmin like 2                                            |

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|         |          |        |                                            |
|---------|----------|--------|--------------------------------------------|
| ANXA1   | 2.14E-07 | -1.081 | annexin A1                                 |
| FBXO30  | 2.33E-07 | -1.078 | F-box protein 30                           |
| TLDC2   | 2.23E-06 | -1.071 | TBC/LysM-associated domain containing 2    |
| RASGRP3 | 1.42E-05 | -1.068 | RAS guanyl releasing protein 3             |
| EMP1    | 5.70E-06 | -1.051 | epithelial membrane protein 1              |
| IRF7    | 6.32E-06 | -1.049 | interferon regulatory factor 7             |
| PTRF    | 7.45E-05 | -1.048 | polymerase I and transcript release factor |
| CD68    | 4.03E-06 | -1.047 | CD68 molecule                              |
| CPS1    | 3.16E-06 | -1.032 | carbamoyl-phosphate synthase 1             |
| PCED1B  | 5.31E-06 | -1.027 | PC-esterase domain containing 1B           |
| OAS3    | 7.14E-05 | -1.016 | 2'-5'-oligoadenylate synthetase 3          |

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**Table 2.** The up-regulated DEGs in KD-AGS

| Gene      | P.Value  | logFC | Gene title                                                                |
|-----------|----------|-------|---------------------------------------------------------------------------|
| FAM46C    | 1.17E-04 | 1.036 | family with sequence similarity 46 member C                               |
| GCNT2     | 8.72E-07 | 1.049 | glucosaminyl (N-acetyl) transferase 2, I-branching enzyme (I blood group) |
| PGC       | 2.42E-04 | 1.069 | progastricsin                                                             |
| ERO1B     | 1.77E-06 | 1.071 | endoplasmic reticulum oxidoreductase 1 beta                               |
| COPS8     | 3.90E-07 | 1.075 | COP9 signalosome subunit 8                                                |
| GSTA1     | 2.70E-04 | 1.097 | glutathione S-transferase alpha 1                                         |
| NREP      | 3.09E-06 | 1.135 | neuronal regeneration related protein                                     |
| CA2       | 2.16E-06 | 1.209 | carbonic anhydrase 2                                                      |
| CA2       | 6.44E-06 | 1.317 | carbonic anhydrase 2                                                      |
| NLRP7     | 2.26E-07 | 1.356 | NLR family pyrin domain containing 7                                      |
| EFHD2     | 4.33E-07 | 1.366 | EF-hand domain family member D2                                           |
| MYCN      | 7.78E-09 | 1.391 | v-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog |
| C14orf159 | 1.58E-08 | 1.395 | chromosome 14 open reading frame 159                                      |
| SEPP1     | 7.82E-08 | 1.395 | selenoprotein P, plasma, 1                                                |
| TMED6     | 1.26E-08 | 1.416 | transmembrane p24 trafficking protein 6                                   |
| SULT2A1   | 4.60E-08 | 1.463 | sulfotransferase family 2A member 1                                       |
| CALM1     | 1.13E-07 | 1.496 | calmodulin 1                                                              |
| HIF1A     | 1.81E-07 | 1.498 | hypoxia inducible factor 1 alpha subunit                                  |
| ESRRG     | 5.15E-08 | 1.502 | estrogen related receptor gamma                                           |
| TFF1      | 5.54E-06 | 1.543 | trefoil factor 1                                                          |
| HMGCS2    | 3.99E-08 | 1.583 | 3-hydroxy-3-methylglutaryl-CoA synthase 2                                 |
| HIF1A     | 5.98E-07 | 1.62  | hypoxia inducible factor 1 alpha subunit                                  |
| SLC9A4    | 1.48E-09 | 1.627 | solute carrier family 9 member A4                                         |
| ESRRG     | 8.83E-08 | 1.627 | estrogen related receptor gamma                                           |
| SGPP2     | 1.34E-07 | 1.685 | sphingosine-1-phosphate phosphatase 2                                     |
| NTN4      | 4.24E-10 | 1.801 | netrin 4                                                                  |
| IGFBP2    | 2.96E-10 | 1.815 | insulin like growth factor binding protein 2                              |
| HIF1A     | 4.59E-08 | 1.839 | hypoxia inducible factor 1 alpha subunit                                  |
| PUDP      | 3.67E-11 | 2.155 | pseudouridine 5'-phosphatase                                              |
| SLCO2A1   | 4.77E-11 | 2.215 | solute carrier organic anion transporter family member 2A1                |
| ATP4A     | 1.32E-12 | 2.564 | ATPase H+/K+ transporting alpha subunit                                   |
| GIF       | 1.91E-10 | 2.594 | gastric intrinsic factor                                                  |

**Table 3.** Gene ontology analysis of differentially expressed genes in scrambled AGS cells.

| Category         | Term                                                                                                                 | Count | P-Value  |
|------------------|----------------------------------------------------------------------------------------------------------------------|-------|----------|
| GOTERM_BP_DIRECT | positive regulation of epithelial to mesenchymal transition                                                          | 6     | 2.40E-03 |
| GOTERM_BP_DIRECT | epithelial cell development                                                                                          | 4     | 3.30E-03 |
| GOTERM_BP_DIRECT | negative regulation of interleukin-4 production                                                                      | 3     | 7.80E-03 |
| GOTERM_BP_DIRECT | negative regulation of interleukin-5 production                                                                      | 3     | 7.80E-03 |
| GOTERM_BP_DIRECT | neural crest cell migration                                                                                          | 6     | 9.20E-03 |
| GOTERM_BP_DIRECT | regulation of intracellular pH                                                                                       | 5     | 1.90E-02 |
| GOTERM_BP_DIRECT | membrane repolarization during ventricular cardiac muscle cell action potential                                      | 3     | 2.10E-02 |
| GOTERM_BP_DIRECT | positive regulation of transcription, DNA-templated                                                                  | 24    | 2.60E-02 |
| GOTERM_BP_DIRECT | substrate-dependent cell migration, cell extension                                                                   | 3     | 2.60E-02 |
| GOTERM_BP_DIRECT | tongue development                                                                                                   | 3     | 3.20E-02 |
| GOTERM_BP_DIRECT | protein folding                                                                                                      | 11    | 3.60E-02 |
| GOTERM_BP_DIRECT | negative regulation of axon extension                                                                                | 3     | 3.80E-02 |
| GOTERM_BP_DIRECT | cardiac muscle cell differentiation                                                                                  | 4     | 4.20E-02 |
| GOTERM_BP_DIRECT | ethanol oxidation                                                                                                    | 3     | 4.50E-02 |
| GOTERM_CC_DIRECT | basolateral plasma membrane                                                                                          | 14    | 1.70E-03 |
| GOTERM_CC_DIRECT | adherens junction                                                                                                    | 7     | 2.60E-03 |
| GOTERM_CC_DIRECT | membrane                                                                                                             | 77    | 3.10E-02 |
| GOTERM_CC_DIRECT | organelle membrane                                                                                                   | 7     | 3.50E-02 |
| GOTERM_CC_DIRECT | endoplasmic reticulum membrane                                                                                       | 34    | 4.40E-02 |
| GOTERM_CC_DIRECT | extracellular exosome                                                                                                | 94    | 4.70E-02 |
| GOTERM_MF_DIRECT | AMP binding                                                                                                          | 4     | 2.60E-03 |
| GOTERM_MF_DIRECT | identical protein binding                                                                                            | 34    | 1.40E-02 |
| GOTERM_MF_DIRECT | calcium ion binding                                                                                                  | 32    | 2.10E-02 |
| GOTERM_MF_DIRECT | voltage-gated potassium channel activity involved in ventricular cardiac muscle cell action potential repolarization | 3     | 2.10E-02 |
| GOTERM_MF_DIRECT | protein disulfide isomerase activity                                                                                 | 4     | 2.60E-02 |

|                  |                                                                                               |   |          |
|------------------|-----------------------------------------------------------------------------------------------|---|----------|
| GOTERM_MF_DIRECT | transcription factor activity, RNA polymerase II distal<br>enhancer sequence-specific binding | 6 | 4.40E-02 |
|------------------|-----------------------------------------------------------------------------------------------|---|----------|

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**Table 4.** Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis of differentially expressed genes in scrambled AGS cells.

| Category     | Term                                         | Count | P-Value  | Genes                                                                                         |
|--------------|----------------------------------------------|-------|----------|-----------------------------------------------------------------------------------------------|
| KEGG_PATHWAY | Metabolism of xenobiotics by cytochrome P450 | 10    | 4.00E-04 | <i>UGT2B17, ADH1B, ADH5, AKR7A3, CYP2F1, CYP2S1, DHDH, GSTA3, GSTM2, SULT2A1</i>              |
| KEGG_PATHWAY | Protein processing in endoplasmic reticulum  | 12    | 1.50E-02 | <i>DNAJC5G, HSPBP1, CALR, EIF2AK3, MAN1B1, P4HB, PDIA6, RRBP1, SAR1B, SSR4, SYVN1, UBE2D2</i> |
| KEGG_PATHWAY | Chemical carcinogenesis                      | 7     | 3.60E-02 | <i>NAT1, UGT2B17, ADH1B, ADH5, GSTA3, GSTM2, SULT2A1</i>                                      |
| KEGG_PATHWAY | Platelet activation                          | 9     | 4.60E-02 | <i>FCGR2A, ORAI1, ARHGEF12, COL1A1, COL3A1, COL27A1, ITPR1, ITGB1, PPP1CA</i>                 |

Figure S1: The three MCODE modules of hub genes.