

Supplementary Table 5. Upstream Regulator Analysis (IPA) tunica albuginea versus stroma. Only those upstream transcriptional regulators with a predicted activation state (activated or inhibited), a z-score > 2.0 or <-2.0, and an overlap-value of < 0.01 are shown. The overlap p-value measures whether there is a statistically significant overlap between the dataset genes and the genes that are regulated by a transcriptional regulator. It is calculated using Fisher's Exact Test, and significance is generally attributed to p-values < 0.01. The activation z-score is used to infer likely activation states of upstream regulators based on comparison with a model that assigns random regulation directions. The mechanistic network column shows the number of dataset molecules targeted by the network followed in parenthesis by the number of regulators in the network.

| Upstream Transcriptional Regulator | Predicted Activation State in Tunica Albuginea | Activation z-score | Overlap p-value | Target Genes in Dataset |
|---|---|---------------------------|------------------------|--|
| TGFB1 | activated | 3.635 | 6.07E-17 | <i>ADGRG2,ADRA2A,ANKH,ARL4A,BCL2,BGN,BMP6,CCL5,CD44,CKS1B,CKS2,COL1A1,COL1A2,COL8A1,CSRP2,CTGF,CTPS1,CTSH,CTSK,CX3CL1,CXADR,CYR61,DAB2,DKK3,DOCK4,DPYSL3,ECM1,EDNRA,EDNRB,ENPP1,EPCAM,FLII,FXD5,GATA3,GNAO1,GNG2,HDAC9,HES1,HGF,HSPG2,HTRA1,ID3,IGF1,IL18,ITGB3,ITIH5,KDR,LEF1,LIFR,LOX,LOXL1,LOXL2,MET,NCAM1,NEDD9,NOG,NOV,OSR2,PCOLCE2,PECAM1,PHACTR1,PPARG,PTGER2,PTGES,RARG,SGK1,TFPI,TGFBR3,TGM2,THBS1,THY1,TNFRSF11B,VEGFC,WNT5A,XDH</i> |
| Lipopoly-saccharide | activated | 2.937 | 2.45E-10 | <i>ABCF2,ADRA2A,AGTR1,ARL4C,BCL2,BGN,CCL5,CD200,CD44,CD9,CLDN5,COL1A1,COL1A2,CTGF,CTSK,CX3CL1,CXADR,CXCL16,CYR61,DKK3,ETV5,FLII,GJA5,HDAC9,HES1,HGF,HSPA4L,HTRA1,ID3,IGF1,IL18,IL21R,KANK1,KDR,LIFR,MET,ODC1,PCOLCE,PCOLCE2,PECAM1,PENK,PPARG,PTGER2,PTGES,RASL11A,RGS16,SCUBE2,SLC29A1,TEK,TFPI,TGM2,THBS1,THBS2,THY1,TNFSF18,TNNI3,TSPO,VEGFC,XDH</i> |
| Mek | activated | 2.929 | 0.000165 | <i>CD200,COL1A2,CTGF,ETV5,ITGB3,KDR,MANSC1,PLPP3,SORL1,SPRY4,THBS1,VEGFC</i> |
| Tgf beta | activated | 2.895 | 1.9E-10 | <i>ANKH,BCL2,BGN,CCL5,COL1A1,COL1A2,CTGF,CTSK,CYR61,DAB2,GATA3,HSPG2,IGF1,ITGB3,LOX,MET,NEDD9,PLPP3,PTGER2,RYR2,TNFRSF11B</i> |
| BMP2 | activated | 2.741 | 0.000506 | <i>BCL2,COL1A1,COL1A2,CTSK,ID3,NOG,PPARG,SLC26A2,TGM2,TNFRSF11B,TNNI3</i> |
| TLR4 | activated | 2.728 | 0.000157 | <i>BCL2,CCL5,CD200,CD44,CERS6,CTSK,CYR61,DAB2,HTRA1,IL18,MET,PPARG,PTGES,RGS16,TSPO</i> |
| CXCL12 | activated | 2.577 | 0.0000533 | <i>BCL2,BMP6,CCL5,CD44,CD9,COL1A1,CTSK,CX3CL1,ITGB3,LOXL2,RYR2,TNFRSF11B</i> |
| IFNG | activated | 2.526 | 2.28E-14 | <i>ADCY5,ADGRG2,ADRA2A,AGTR1,ALDH1A3,BCL2,BMP6,BUD23,CCL5,CD200,CD44,CERS6,COL1A1,COL1A2,CTGF,CTSH,CTSK,CX3CL1,CXADR,CXCL16,EDNRA,EDNRB,F11R,FKBP5,GATA3,GJA5,GNAO1,GNG2,HDAC9,</i> |

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| | | | | <i>HSPG2,HTRA1,IGF1,IL18,ITGB3,KDR,LAMB2,LIFR,LOX,NCAM1,NEDD9,ODCI,PCSK2,PECAM1,PENK,PHACTR1,PPARG,PTGES,RAB27A,RARRES1,SERPING1,SLC29A1,SMC1B,TGFBR3,THBS1,THY1,TNFRSF11B,VEGFC, WNT5A</i> |
| P38 MAPK | activated | 2.480 | 0.000118 | <i>BCL2,BGN,CCL5,CD44,CLDN5,CTGF,CTSK,EDNRB,HTRA1,ID3,ITGB3,PPARG,SGK1,THBS1,VEGFC,WNT5A</i> |
| SP1 | activated | 2.409 | 0.0000564 | <i>AEBPI,AGTR1,ANKH,BCL2,CCL5,CHRNA3,COL1A1,COL1A2,COL8A1,CTGF,CYP1B1,HGF,IGF1,IL21R,KDR,MET,PENK,PRKCB,PTTG1,SGK1,TGFBR3, TSPO</i> |
| HIF1A | activated | 2.352 | 0.00000211 | <i>ABCF2,AURKA,BCL2,BGN,CD44,CTGF,CTPS1,CYR61,EPAS1,IGF1,ITGB3,LIFR,LOX,LOXL2,MET,NOV,SLC29A1,THBS1,TMEM45A,TNFRSF11B,VEGFC</i> |
| bleomycin | activated | 2.334 | 0.00000349 | <i>BCL2,CCL5,COL1A1,COL1A2,CTGF,CTSK,IGF1,IL18,PTGER2,PTTG1,STK17B,THBS1,WNT5A</i> |
| ERK1/2 | activated | 2.295 | 0.000132 | <i>BCL2,CCL5,CD44,CDC42EP5,COL1A1,CTGF,FKBP5,ID3,IL17RD,ITGB3,PTGER2,PTGES,SGK1,SPRY4</i> |
| TNFSF11 | activated | 2.289 | 0.000824 | <i>AURKA,BCL2,CCL5,CD44,CTSK,DAB2,IGF1,ITGB3,PTGER2,RGS16, TNFRSF11B,TSPAN13</i> |
| F2 | activated | 2.250 | 0.0000032 | <i>CD44,COL1A1,CTGF,CTPS1,CX3CL1,CYR61,DKK3,EDNRB,HDAC9,IGF1,KDR,LOXL2,PROS1,TEK,TFPI,THBS1</i> |
| SEMA7A | activated | 2.219 | 0.0000219 | <i>COL1A1,COL1A2,CTGF,IL18,NOV</i> |
| gefitinib | activated | 2.216 | 0.000278 | <i>ALDH1A1,AURKA,BCL2,COL1A1,COL8A1,IGF1,LIFR,PPARG,PTTG1,S100A14</i> |
| calcium chloride | activated | 2.213 | 1.38E-08 | <i>ANKH,ENPP1,ID3,STC1,TNFRSF11B</i> |
| IL1A | activated | 2.209 | 4.02E-08 | <i>ALDH1A1,ALDH1A3,BCL2,CCL5,CD44,CTSK,CYR61,HSPG2,IGF1,IL18,ITGB3,LOX,PPARG,PTGES,TNFRSF11B,VEGFC,WNT5A</i> |
| TGFBR1 | activated | 2.178 | 0.0000263 | <i>ALX1,BGN,CLDN5,COL1A1,COL1A2,CTGF,DOCK4,VEGFC</i> |
| IL10RA | activated | 2.138 | 0.000276 | <i>ANKH,BCL2,CCL5,CSRP2,CYR61,ECM1,EDNRB,HGF,NOV,PCOLCE,PDE2A,TGM2,TMEM30B,TNNI3</i> |
| TGFB3 | activated | 2.111 | 8.87E-09 | <i>BCL2,COL1A1,COL1A2,CTGF,CYR61,HTRA1,ITGB3,LEF1,NOV,TGFBR3,THBS1,TNFRSF11B,TSPAN13</i> |
| TP53 | activated | 2.080 | 0.000000135 | <i>ADAMTSL4,AGTR1,ANKH,AURKA,BCL2,CD44,CERS6,CKS1B,COL1A1,COL1A2,CTGF,CTSH,CTSK,CX3CL1,CYR61,DKK3,EPHX1,F11R,FAT1,FKBP5,GLB1,GNAI1,HDAC9,HSPA4L,HSPG2,ID3,IGF1,IL21R,KDR,KPNA2,LAMB2,LOX,MET,NR2F1,PDE2A,PDLIM1,PECAM1,PPARG,PRKCB,PTTG1,RGS16,SERPING1,SFRP2,SGK1,SPATA18,SRGAP3,TGM2,THBS1,THBS2,THY1,TSPO</i> |
| Doxorubicin | activated | 2.054 | 0.00155 | <i>ABCF2,AURKA,BCL2,CD44,CTGF,CYR61,GLB1,GSTM3,HSPB6,MET,NCAM1,PTTG1,RGS16,RYR2,TNNI3</i> |
| ETS1 | activated | 2.048 | 0.00193 | <i>ARL4C,CCL5,CD44,COL1A2,CTGF,FLI1,HGF,ITGB3,MET,THY1</i> |

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|---------------------------|-----------|--------|-------------|--|
| TGFB2 | activated | 2.029 | 0.000000904 | <i>ALX1, COL1A1, COL1A2, CTGF, DOCK4, HSPG2, KDR, PECAM1, TGFB3, THBS1, TNFRSF11B</i> |
| MIR101 | activated | 2.000 | 0.0000783 | <i>BCL2, CLDN5, IGF1, MET</i> |
| SP600125 | inhibited | -2.815 | 0.000141 | <i>BCL2, CCL5, CD44, COL1A1, COL8A1, CTGF, CXCL16, CYR61, PPARG, PTGES, THBS1, THBS2</i> |
| Docosa-hexaenoic acid | inhibited | -2.612 | 0.00000902 | <i>BCL2, CD44, COL1A1, CTGF, LOX, LOXL1, LOXL2, PDE5A, PTGES, SORL1, THBS1, THBS2</i> |
| 8-bromo-cAMP | inhibited | -2.592 | 0.000331 | <i>CTGF, CYP1B1, GNAI1, IGF1, KDR, LOX, ODC1, SGK1, TGFB3, VEGFC</i> |
| SPDEF | inhibited | -2.449 | 0.000579 | <i>COL1A1, CTGF, DKK3, LAMB2, LEF1, WNT5A</i> |
| SAFB | inhibited | -2.433 | 0.000147 | <i>CCL5, CX3CL1, IGF1, NEDD9, NOV, TNFRSF11B</i> |
| APLN | inhibited | -2.414 | 0.0000374 | <i>BCL2, CTGF, KDR, NOSTRIN, PECAM1, TEK</i> |
| NR3C1 | inhibited | -2.395 | 0.00593 | <i>BCL2, C1QTNF1, CCL5, CKS1B, CLDN5, CYR61, ENC1, FKBP5, GATA3, HIFOO, IGF1, IL18, PPARG, PPP1R14C, PRKCB, SGK1, STK17B, THBS1, TNFRSF11B, WNT5A</i> |
| Growth hormone | inhibited | -2.355 | 0.000701 | <i>BCL2, COL1A1, CX3CL1, FKBP5, IGF1, NEDD9, PPARG, SGK1</i> |
| FOXM1 | inhibited | -2.236 | 0.000194 | <i>CKS1B, CKS2, GLB1, IGF1, KDR, LEF1, LOX, MET, PECAM1</i> |
| DKK1 | inhibited | -2.209 | 0.00000629 | <i>BMP6, CD44, COL1A1, EPCAM, GATA3, LEF1, PPARG, WNT5A</i> |
| CR1L | inhibited | -2.200 | 0.0000595 | <i>BGN, COL1A1, COL1A2, COL8A1, CTGF</i> |
| GW3965 | inhibited | -2.200 | 0.00816 | <i>ADRA2A, CCL5, EDNRA, GNAI1, GNG2</i> |
| Dehydro-isoandrosterone | inhibited | -2.190 | 0.00376 | <i>BCL2, ECM1, FKBP5, IGF1, PPARG</i> |
| Epigallo-catechin-gallate | inhibited | -2.178 | 0.00156 | <i>BCL2, CCL5, CLDN5, CTGF, CTSK, CYR61, IL18, ITGB3, KDR, VEGFC</i> |
| estrogen receptor | inhibited | -2.164 | 0.000396 | <i>BCL2, CD44, CTGF, F11R, GATA3, IGF1, LOXL2, NEDD9, PDGFD, TGFB3, VEGFC, WNT5A</i> |
| ESR1 | inhibited | -2.009 | 0.000836 | <i>AURKA, BCL2, CENPU, CHRM2, COL8A1, CPM, CXADR, CYP1B1, DAB2, DOCK4, GATA3, GLB1, HTRA1, IGF1, IL20RA, LAMB2, NEB, NEDD9, NOV, PDGFD, PROS1, PTTG1, RAB27A, RAMP3, RGS16, SCUBE2, SGK1, SLC26A2, SPRY4, TEK, TGM2, TNFRSF11B, TNNT3, TNS3, TSPO, VEGFC</i> |