

**Supplementary Table 4.** Upstream Regulator Analysis (IPA) of theca interna 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.

Upstream Transcriptional Regulator	Predicted Activation State in Theca Interna	Activation z-score	Overlap p-value	Target Genes in Dataset
PTGER2	activated	2.887	1.56E-05	<i>ASPM,CENPE,CENPF,CEP55,DEPDC1,ECT2,EGR1,KIF11,MKI67,PTGES, SPAG5,THBS1,TPX2</i>
CDKN1B	activated	2.774	0.0051	<i>BCL2,CCND3,CDKN1A,EGR1,FHL1,GAB2,MEIS2,RUNX1,TMEFF2</i>
RABL6	activated	2.646	0.00486	<i>CENPF,DUT,NCAPG,NDC80,TPX2,UBE2C</i>
NR5A1	activated	2.629	0.000375	<i>CYP11A1,CYP17A1,GSTA3,HSD3B2,INHA,INSL3,LHCGR,SCARB1</i>
miR-17-5p (and other miRNAs w/seed AAAGUGC)	activated	2.558	0.00331	<i>BAMBI,BCL2,BIRC5,CDKN1A,ESR1,ITGB8,RUNX1</i>
FOXA2	activated	2.387	7.31E-06	<i>A2M,APOA1,ASTN1,CHI3L1,CNN1,GFRA4,GSTM3,HHIP,HPGD,IGFBP5,LPL, MYH11,MYOCD,NR4A2,PTGDS,TF,TNNI1,WNT5A</i>
SREBF2	activated	2.241	0.000369	<i>CDKN1A,EBP,ELOVL6,HMGCR,IDH1,LRP1,NSDHL,PTCH1,RARRES2</i>
MMP14	activated	2.213	0.000261	<i>CDKN1A,JAG1,LRP1,MMP14,NNT,SLCO2A1</i>
TFRC	activated	2.186	0.000233	<i>CDKN1A,GAS7,ID2,JUN,SULF2,TGFB2,TGFB3</i>
FSH	activated	2.164	2.58E-07	<i>ADAMTS1,AKAP12,ALPL,AR,ATP9A,CAMK4,CH25H,CITED1,COL15A1, CYP11A1,CYP17A1,DAB2,ESR1,FDX1,FOSL2,FST,GEM,HSD3B2,INHA,INHBA, JUN,LHCGR,LOX,NR4A1,RGS4,SCARB1,TF,TGFB2,THBS1,VEGFC,WT1,ZEB1</i>
MTOR	activated	2.025	1.05E-05	<i>AR,BCL2,BIRC5,CCND3,CDKN1A,CEBPD,CYP11A1,CYP17A1,FST,INHA, LHCGR,MAP2,MDH1,NAB2,NCAM1,OAS1,PECAM1,PGP,RAP1GDS1,SLC12A2, SOD1,SOX4,UBE2C</i>
Mamld1	activated	2.000	6.81E-06	<i>CYP11A1,CYP17A1,HSD3B2,INSL3</i>
RARA	activated	2.000	0.00103	<i>ALDH1A1,ALDH1A2,APOA1,ASPM,BIRC5,CD9,CDKN1A,CENPA,CENPF,EGR1, FOSL2,JUN,MALL,MAOB,NCAPG,NRP1,OAS1,RUNX1,SLC16A2,SMC4</i>
DUSP5	activated	2.000	0.00233	<i>CH25H,EGR1,ID2,ZFP36</i>

NUPR1	inhibited	-3.674	0.00803	<i>ADGRL3,AKAP12,ARHGAP11A,AS3MT,ASB9,ASPM,B3GNT5,CDCA3,COL1A2,DHCR24,GAB2,GRAMD2B,HIST1H3C,HIST1H3J,HJURP,KIF11,LRP8,MKI67,NR1D1,NR1D2,NUPR1,RAB38,SPAG5,SPC24,ZFP36L1</i>
F2	inhibited	-3.125	0.00016	<i>ADAMTS9,B3GNT5,CDKN1A,CLU,COL4A1,EGR1,ENTPD1,FAM46A,FHL1,FOSL2,IGFBP5,JUN,MYH11,NR4A3,SDC4,SERPINC1,TGFB2,TGFB3,THBS1</i>
PTH	inhibited	-2.663	2.12E-06	<i>ADAMTS1,BCL2,CDKN1A,COL1A2,FOSL2,GNG12,IGFBP5,JUN,NR4A1,NR4A2,POSTN,RUNX1,SDC4,SFRP2,SFRP4,STC1,WNT4</i>
CDKN2A	inhibited	-2.663	0.000121	<i>A2M,BCL2,BIRC5,CCND3,CDKN1A,CDKN2C,CEBPD,CENPK,CXCL14,EGR1,FST,GAS7,HOXC4,IGFBP5,JUN,MKI67,PMEPA1,PSMB9,RRM2,TGIF1,TP53INP1</i>
BNIP3L	inhibited	-2.630	0.00106	<i>CCND3,CENPE,CENPF,CKAP2,KIF11,RRM2,TOP2A</i>
BMP4	inhibited	-2.462	2.29E-06	<i>ALDH1A2,BCL2,CDKN1A,CNN1,COCH,ID2,JUN,MITF,MMP14,NCAM1,POSTN,PTCH1,SCARB1,SMAD9,SULF1,WNT5A</i>
IL1	inhibited	-2.456	9.02E-05	<i>ADAMTS1,AR,BCL2,CDKN1A,CEBPD,CHI3L1,CTSC,CYP17A1,FST,HGF,HMGCR,INHBA,JUN,LOX,LRP1,PLD1,RBP4,SDC4,TGFB3,WNT5A,XDH</i>
NPPB	inhibited	-2.425	0.0001	<i>ACAT2,EBP,FDX1,GSTA3,HMGCR,SCARB1</i>
CREM	inhibited	-2.424	0.000443	<i>BCL2,CAMK4,CAMP,CH25H,EGR1,HMGCR,INHA,NAB2,NR4A1,NR4A2,SMC4,THBS1,TIPARP</i>
ERK	inhibited	-2.423	9.67E-07	<i>BCL2,BGN,CAV1,CCND3,CD1D,CDKN1A,CEBPD,CLU,EGR1,ESR1,FOSL2,FST,JAG1,JUN,MMP14,PECAM1,PTGES,RGS4,SOX4,THBS1,ZFP36,ZFP36L1</i>
ELK1	inhibited	-2.404	0.000811	<i>CDKN1A,EGR1,JUN,NUPR1,THBS1,TIPARP,ZFP36</i>
TNF	inhibited	-2.375	5.44E-14	<i>A2M,A4GALT,ADORA1,AKAP12,APOA1,AR,ARHGAP18,ARID5B,ASS1,BAMBI,BCL2,BGN,BIRC5,C1QTNF1,CAV1,CCND3,CD36,CDH5,CDKN1A,CDKN2C,CDO1,CEBPD,CH25H,CHI3L1,CLU,CMBL,CNN1,COL15A1,COL1A2,CTSC,CYP11A1,CYP17A1,DAG1,DCHS1,EGR1,ESR1,FBXO32,FOSL2,FST,GABRB2,GEM,HGF,HMGCR,HPGD,HSD3B2,IGFBP5,INHA,INHBA,ITGB8,JAG1,JUN,LAMA4, LGALS9,LHCGR,LOX,LPL,MALL,MEOX2,MET,MMP14,MSH2,NCAM1,NOSTRIN,NR4A1,NR4A2,NR4A3,NRP1,OAS1,OGN,P4HB,PARP14,PECAM1,POSTN,PPP1R3C,PRSS23,PSMB9,PTGES,RAPGEF5,RARRES2,RGS4,RNASE4,RRM2,SCARB1,SDC4,SLC16A2,SLC5A8,SOD1,SOX4,TF,TGFB2,TGFB3,TGIF1,THBS1,TMEM176B,TP53INP1,TRAF5,USP2,VEGFC,VEGFD,WNT5A,XDH,ZFP36,ZNF330</i>
GH1	inhibited	-2.237	7.13E-05	<i>BCL2,CCND3,CEBPD,CLU,EGR1,ID2,IGFBP5,JUN,LPL,NRAS,PRDX3,SOD1,STC1,TF,TKT,XDH,ZFP36</i>
SMARCA2	inhibited	-2.236	0.0065	<i>ALPL,BCL2,CD36,DES,IGFBP5,RRM2</i>
HSPA5	inhibited	-2.200	0.00263	<i>BCL2,BIRC5,CLU,ESR1,ID2,P4HB</i>
SMARCB1	inhibited	-2.184	0.000077	<i>A2M,CDKN1A,CDKN2C,CENPA,CENPE,COL1A2,CYP39A1,KIF11,OAS1,POSTN,PPP1R3C,SMC4,TCF21,TMOD1,WASF3</i>

PAX3	inhibited	-2.175	0.00243	<i>ASS1,CDKN1A,CLU,COL1A2,FABP7,FHL1,ID2,MET,MITF,PCSK2,RARRES2,SOX4,TGFB2,TNNI1</i>
NFKB1	inhibited	-2.151	0.00884	<i>A2M,ADORA1,AR,BAMBI,BCL2,CDKN1A,CHI3L1,COL1A2,EGR1,GNAO1,JAG1,NR4A1,SDC4,WT1</i>
CREB1	inhibited	-2.148	3.38E-09	<i>AQP11,BCL2,BIRC5,CAMK4,CCND3,CD9,CDKN1A,CEBPD,CH25H,CNN1,COCH,CPEB1,CYP11A1,EBP,EGR1,ENTPD1,FAM46A,FGL2,GEM,HMGCR,HPGD,IGSF10,INHA,INHBA,ITGBL1,JPT1,JUN,LPL,MKI67,NAB2,NR4A1,NR4A2,NR4A3,NRP1,RASGEF1B,RBP4,SCG2,SFRP4,STC1,TF,TGIF1,TIPARP,TMEFF2,ZFP36</i>
CYP51A1	inhibited	-2.000	0.000555	<i>DHCR24,EBP,HMGCR,NSDHL</i>
NFYA	inhibited	-2.000	0.00274	<i>BCL2,CDKN1A,COL1A2,EGR1,JUN,RGS4,RRM2,TOP2A</i>
Pkg	inhibited	-2.000	0.00436	<i>BCL2,EGR1,JUN,PTGES</i>
CR1L	inhibited	-2.000	0.00735	<i>BGN,COL15A1,COL1A2,COL4A1</i>
CAMK4	inhibited	-2.000	0.00995	<i>BCL2,CAMK4,FOSL2,JUN</i>