

Table S5. Upstream regulators and their potential targets in summer granulosa cells

Upstream Regulator	Molecule Type	Predicted		p-value of overlap	Target molecules in dataset
		Activation / Inhibition State	Activation z-score		
<b>Upstream regulators showing significantly different expression in summer granulosa cells</b>					
↓↓MAFB	other			6.70×10 <sup>-3</sup>	↓↓AKR1B10, ↓↓MAFB
<b>Upstream regulators (not showing significantly different expression in summer granulosa cells) with predicted activation/inhibition state ( z &gt;1.96)</b>					
OSM	cytokine	Inhibited	-2.236	3.59×10 <sup>-2</sup>	↓↓AKR1B10, ↑↑AKR1C1/AKR1C2, ↓↓PYGL, ↑↑RORA, ↑↑SYNE1
<b>Upstream regulators (not showing significantly different expression in summer granulosa cells) with uncharacterized activation/inhibition state ( z &lt;1.96)</b>					
Vegf	group		1.408	5.48×10 <sup>-4</sup>	↑↑HOPX, ↑↑MID1, ↓↓MYCN, ↓↓SHISA2, ↑↑SLC20A1, ↑↑TJP1, ↑↑VWF
hydrogen peroxide	chemical - endogenous mammalian		1.387	1.71×10 <sup>-2</sup>	↑↑AKR1C1/AKR1C2, ↑↑EZR, ↓↓F2RL1, ↑↑SLC20A1, ↑↑TGFB3
PDLIM2	other		1.342	1.71×10 <sup>-5</sup>	↓↓F2RL1, ↑↑KCTD12, ↓↓NAV1, ↓↓STC2, ↓↓SUSD3
TP53	transcription regulator		1.276	3.64×10 <sup>-2</sup>	↑↑ACSL3, ↑↑ALDH9A1, ↑↑ANXA4, ↑↑COL14A1, ↑↑EZR, ↑↑H2AFY, ↑↑INPP4A, ↑↑PTPRM, ↑↑TJP1
TGFB1	growth factor		1.086	3.60×10 <sup>-3</sup>	↑↑ACSL3, ↑↑AKR1C1/AKR1C2, ↑↑ARID5B, ↓↓F2RL1, ↑↑MID1, ↓↓MYCN, ↑↑RBMS3, ↑↑RORA, ↑↑SLC20A1, ↓↓STC2, ↑↑TGFB3, ↓↓VAT1L, ↑↑VWF
CEBPA	transcription regulator		1.000	4.08×10 <sup>-2</sup>	↓↓AKR1B10, ↑↑AKR1C1/AKR1C2, ↓↓MYCN, ↑↑RORA
IGF1	growth factor		0.789	4.90×10 <sup>-2</sup>	↑↑AKR1C1/AKR1C2, ↓↓MYCN, ↑↑SLC20A1, ↑↑TJP1
HOXA10	transcription regulator		0.762	4.30×10 <sup>-4</sup>	↓↓KCNA1, ↓↓LYZ, ↓↓MYCN, ↓↓PTGER3, ↑↑TGFB3
EGF	growth factor		0.555	2.35×10 <sup>-2</sup>	↑↑ALCAM, ↑↑EZR, ↑↑MT3, ↓↓MYCN, ↑↑TJP1
F2	peptidase		0.343	1.21×10 <sup>-2</sup>	↓↓F2RL1, ↑↑TFPI, ↑↑TJP1, ↑↑VWF
Cg	complex		-0.152	7.05×10 <sup>-3</sup>	↓↓AKR1B10, ↓↓F2RL1, ↑↑RORA, ↑↑SLC20A1, ↑↑TGFB3
STAT4	transcription regulator		-0.132	6.93×10 <sup>-3</sup>	↑↑MLLT3, ↓↓PYGL, ↑↑RORA, ↓↓STC2
HOXD10	transcription regulator		0.000	6.68×10 <sup>-5</sup>	↑↑EZR, ↑↑TFPI, ↑↑TJP1, ↑↑USP15
FOXP2	transcription regulator			1.20×10 <sup>-4</sup>	↑↑HOPX, ↓↓MYCN
LONP1	peptidase			5.36×10 <sup>-4</sup>	↓↓MT-ATP8, ↓↓MT-ND4L
PI3K (family)	group			6.80×10 <sup>-4</sup>	↓↓AKR1B10, ↑↑AKR1C1/AKR1C2, ↑↑TJP1
CAV1	transmembrane receptor			6.97×10 <sup>-4</sup>	↑↑SLC20A1, ↑↑TFPI, ↑↑TJP1, ↑↑TMEM87A
FOXP1	transcription regulator			2.44×10 <sup>-3</sup>	↑↑HOPX, ↓↓MYCN
SBDS	other			3.33×10 <sup>-3</sup>	↑↑AKR1C1/AKR1C2, ↑↑COL14A1, ↓↓MAFB

ADTRP	other	$3.51 \times 10^{-3}$	↑↑TFPI
CLDN9	other	$3.51 \times 10^{-3}$	↑↑TJP1
SYMPK	other	$3.51 \times 10^{-3}$	↑↑TJP1
MYT1L	transcription regulator	$3.51 \times 10^{-3}$	↑↑RBFOX1
LRRN1	other	$3.51 \times 10^{-3}$	↓↓MYCN
B4GALNT2	enzyme	$3.51 \times 10^{-3}$	↑↑VWF
WASF1	other	$3.51 \times 10^{-3}$	↑↑EZR
TGFB3	growth factor	$4.16 \times 10^{-3}$	↓↓F2RL1, ↑↑TGFB3, ↑↑TJP1
FGF2	growth factor	$6.88 \times 10^{-3}$	↓↓AKR1B10, ↑↑SLC20A1, ↑↑TFPI, ↑↑TGFB3, ↑↑VWF
NTN4	other	$7.00 \times 10^{-3}$	↑↑TJP1
VANGL2	other	$7.00 \times 10^{-3}$	↑↑PRICKLE2
IL15	cytokine	$7.84 \times 10^{-3}$	↑↑H2AFY, ↓↓HMCN1, ↑↑MLLT3, ↓↓PYGL, ↑↑TJP1
mir-34	microRNA	$7.86 \times 10^{-3}$	↑↑MLLT3, ↓↓MYCN
NKX2-5	transcription regulator	$7.86 \times 10^{-3}$	↑↑HOPX, ↓↓MYCN
ETV5	transcription regulator	$9.54 \times 10^{-3}$	↑↑ALCAM, ↑↑TJP1
GDP	chemical - endogenous mammalian	$1.05 \times 10^{-2}$	↑↑TGFB3
Vacuolar H+ ATPase gelatinase	complex group	$1.05 \times 10^{-2}$	↓↓TMEM106B
MZB1	other	$1.05 \times 10^{-2}$	↑↑TJP1
NPHS1	other	$1.05 \times 10^{-2}$	↑↑TJP1
Ptger2	G-protein coupled receptor	$1.05 \times 10^{-2}$	↓↓PTGER3
GIPC1	other	$1.05 \times 10^{-2}$	↑↑TGFB3
KIRREL	other	$1.05 \times 10^{-2}$	↑↑TJP1
NPHS2	other	$1.05 \times 10^{-2}$	↑↑TJP1
VEZF1	transcription regulator	$1.05 \times 10^{-2}$	↑↑USP15
MXD3	transcription regulator	$1.05 \times 10^{-2}$	↓↓MYCN
hydrocortisone	chemical - endogenous mammalian	$1.06 \times 10^{-2}$	↑↑EZR, ↑↑MT3, ↓↓STC2
IL11	cytokine	$1.14 \times 10^{-2}$	↑↑EZR, ↑↑VWF
IGFBP2	other	$1.14 \times 10^{-2}$	↑↑COL14A1, ↑↑RBMS3
RXRA	ligand-dependent nuclear receptor	$1.14 \times 10^{-2}$	↑↑ACSL3, ↑↑AKR1C1/AKR1C2, ↓↓MYCN, ↑↑RORA
SYVN1	transporter	$1.15 \times 10^{-2}$	↑↑ACSL3, ↑↑SLC20A1, ↓↓TMEM106B
WT1	transcription regulator	$1.29 \times 10^{-2}$	↑↑EZR, ↓↓MYCN, ↑↑SLC20A1
PML	transcription regulator	$1.33 \times 10^{-2}$	↑↑ANXA4, ↓↓LYZ

ZFYVE9	peptidase	1.39x10 <sup>-2</sup> ↑↑TJP1
LRP8	transmembrane receptor	1.39x10 <sup>-2</sup> ↓↓GPX4
TBX20	transcription regulator	1.39x10 <sup>-2</sup> ↓↓MYCN
GRPR	G-protein coupled receptor	1.39x10 <sup>-2</sup> ↓↓MYCN
miR-101-3p (and other miRNAs w/seed ACAGUAC)	mature microRNA	1.39x10 <sup>-2</sup> ↓↓MYCN
QKI	other	1.39x10 <sup>-2</sup> ↑↑H2AFY
F2R	G-protein coupled receptor	1.49x10 <sup>-2</sup> ↑↑TJP1, ↑↑VWF
Calmodulin	group	1.71x10 <sup>-2</sup> ↑CORO6, ↑↑MAP9
GTP	chemical - endogenous mammalian	1.74x10 <sup>-2</sup> ↑↑TGFB3
chondroitin sulfate E	chemical - endogenous mammalian	1.74x10 <sup>-2</sup> ↑↑PRICKLE1
ELAVL4	other	1.74x10 <sup>-2</sup> ↓↓MYCN
FZD5	G-protein coupled receptor	1.74x10 <sup>-2</sup> ↑↑TJP1
NAA10	enzyme	1.74x10 <sup>-2</sup> ↑↑TGFB3
PLAA	other	1.74x10 <sup>-2</sup> ↑↑ANXA4
ACTN4	other	1.74x10 <sup>-2</sup> ↓↓MYCN
succinylacetone	chemical - endogenous mammalian	1.74x10 <sup>-2</sup> ↓ALAS1
prostaglandin E2	chemical - endogenous mammalian	1.84x10 <sup>-2</sup> ↓↓F2RL1, ↓↓MAFB, ↑↑TGFB3, ↑↑TJP1
BSCL2	other	1.88x10 <sup>-2</sup> ↑MARK1, ↓↓PYGL
PRKAG3	kinase	2.03x10 <sup>-2</sup> ↓ALAS1, ↑↑REV3L, ↓↓SHISA2
PROCR	other	2.09x10 <sup>-2</sup> ↑↑TJP1
LIMS2	other	2.09x10 <sup>-2</sup> ↑↑TJP1
TNFRSF14	transmembrane receptor	2.09x10 <sup>-2</sup> ↓↓F2RL1
ERG	transcription regulator	2.13x10 <sup>-2</sup> ↓↓MYCN, ↓↓SVIL, ↑↑VWF
PKD1	ion channel	2.23x10 <sup>-2</sup> ↑↑MID1, ↑↑SYNE1, ↑↑VWF
PDX1	transcription regulator	2.30x10 <sup>-2</sup> ↑↑MDH1, ↓↓PTGER3, ↑↑TGFB3
CDX2	transcription regulator	2.32x10 <sup>-2</sup> ↑↑MLLT3, ↓↓MYCN
MYOD1	transcription regulator	2.40x10 <sup>-2</sup> ↓↓MAFB, ↑↑TGFB3, ↑↑TJP1
tryptase	group	2.43x10 <sup>-2</sup> ↓↓F2RL1
MRPL12	other	2.43x10 <sup>-2</sup> ↓↓MT-ND2

NPAS2	transcription regulator	$2.43 \times 10^{-2}$ ↓ALAS1
GLI1	transcription regulator	$2.44 \times 10^{-2}$ ↑↑EZR, ↓↓MYCN, ↑↑SYNE1
MIF	cytokine	$2.45 \times 10^{-2}$ ↓↓F2RL1, ↓↓MYCN
CCL5	cytokine	$2.65 \times 10^{-2}$ ↑↑ALCAM, ↓↓F2RL1
TCF7L1	transcription regulator	$2.77 \times 10^{-2}$ ↓↓SLC26A2
TIP60	complex	$2.77 \times 10^{-2}$ ↓↓MYCN
LIMS1	other	$2.77 \times 10^{-2}$ ↑↑TJP1
miR-203-3p (and other miRNAs w/seed UGAAAUG)	mature microRNA	$2.77 \times 10^{-2}$ ↓↓F2RL1
POU3F3	transcription regulator	$2.77 \times 10^{-2}$ ↓↓PTGER3
HBP1	transcription regulator	$2.77 \times 10^{-2}$ ↓↓MYCN
SDC2	other	$2.77 \times 10^{-2}$ ↑↑TGFB3
pepstatin	chemical - protease inhibitor	$2.77 \times 10^{-2}$ ↓↓STC2
EDN1	cytokine	$2.81 \times 10^{-2}$ ↑↑ANXA4, ↑↑EZR, ↑↑VWF
dinoprost	chemical - endogenous mammalian	$2.85 \times 10^{-2}$ ↑↑AKR1C1/AKR1C2, ↑↑ANXA4
TRAF2	enzyme	$2.85 \times 10^{-2}$ ↑↑ANXA4, ↓↓PYGL
PAX3	transcription regulator	$3.08 \times 10^{-2}$ ↓↓F2RL1, ↓↓GPX4, ↓↓PTGER3
LIN28B	other	$3.11 \times 10^{-2}$ ↓↓MYCN
MEMO1	other	$3.11 \times 10^{-2}$ ↓↓STC2
mir-214	microRNA	$3.11 \times 10^{-2}$ ↑↑ALCAM
ERP29	transporter	$3.11 \times 10^{-2}$ ↑↑TJP1
TRAF3	enzyme	$3.14 \times 10^{-2}$ ↑↑ANXA4, ↓↓PYGL
progesterone	chemical - endogenous mammalian	$3.25 \times 10^{-2}$ ↑↑HOPX, ↓↓KCNAB1, ↓↓MYCN, ↓↓PTGER3, ↑↑TGFB3
mir-210	microRNA	$3.44 \times 10^{-2}$ ↑↑H2AFY, ↓↓MRPL36
mir-130	microRNA	$3.45 \times 10^{-2}$ ↓↓MAFB
miR-130a-3p (and other miRNAs w/seed AGUGCAA)	mature microRNA	$3.45 \times 10^{-2}$ ↓↓MAFB
NMNAT1	enzyme	$3.45 \times 10^{-2}$ ↑↑TFPI
ALK	kinase	$3.45 \times 10^{-2}$ ↓↓MYCN
FLT1	kinase	$3.45 \times 10^{-2}$ ↑↑VWF
ACKR3	G-protein coupled receptor	$3.45 \times 10^{-2}$ ↑↑VWF

GBX2	transcription regulator	$3.45 \times 10^{-2}$	↓↓MAFB
dihydrotestosterone	chemical - endogenous mammalian	$3.47 \times 10^{-2}$	↓ALAS1, ↓↓GPX4, ↑MARK1, ↑↑TFPI, ↑↑TGFB3
FBXO32	enzyme	$3.51 \times 10^{-2}$	↓↓MYCN, ↓↓PTGER3
IGF1R	transmembrane receptor	$3.63 \times 10^{-2}$	↓↓MYCN, ↑↑TJP1, ↑TMEM87A
RAF1	kinase	$3.67 \times 10^{-2}$	↑↑FAM13A, ↑↑MT3, ↓↓SLC26A2
HNRNPAB	enzyme	$3.79 \times 10^{-2}$	↑↑TJP1
BMP6	growth factor	$3.83 \times 10^{-2}$	↓↓MYCN, ↑↑SLC20A1
TGFB2	growth factor	$3.83 \times 10^{-2}$	↑↑MLLT3, ↑↑TGFB3
phosphate	chemical - endogenous mammalian	$3.98 \times 10^{-2}$	↑↑SLC20A1, ↓↓STC2
COL18A1	other	$4.06 \times 10^{-2}$	↓↓F2RL1, ↑↑VWF
FH	enzyme	$4.13 \times 10^{-2}$	↑↑AKR1C1/AKR1C2
SATB2	transcription regulator	$4.13 \times 10^{-2}$	↑↑AUTS2
PER2	other	$4.13 \times 10^{-2}$	↓ALAS1
EPHA2	kinase	$4.13 \times 10^{-2}$	↑↑TJP1
TFF3	other	$4.13 \times 10^{-2}$	↑↑TJP1
KLF13	transcription regulator	$4.13 \times 10^{-2}$	↓ALAS1
AKT1	kinase	$4.22 \times 10^{-2}$	↓↓AKR1B10, ↑↑AKR1C1/AKR1C2, ↑↑TGFB3
HSPA9	other	$4.46 \times 10^{-2}$	↓↓MYCN
UCP1	transporter	$4.46 \times 10^{-2}$	↓ALAS1
SDCBP	enzyme	$4.46 \times 10^{-2}$	↑↑TJP1
CCND1	other	$4.51 \times 10^{-2}$	↑MARK1, ↑↑RBMS3, ↓↓TMEM219
CYP1A1	enzyme	$4.56 \times 10^{-2}$	↑↑ANXA4, ↑↑MID1
miR-30c-5p (and other miRNAs w/seed GUAAACA)	mature microRNA	$4.64 \times 10^{-2}$	↓↓GALNT7, ↑TMEM87A
PPARG	ligand-dependent nuclear receptor	$4.75 \times 10^{-2}$	↑↑ALDH9A1, ↑↑MDH1, ↓↓PYGL, ↑↑TJP1
SLC9A3R1	other	$4.80 \times 10^{-2}$	↑↑EZR
mir-122	microRNA	$4.80 \times 10^{-2}$	↑MARK1
RARA	ligand-dependent nuclear receptor	$4.90 \times 10^{-2}$	↓↓MAFB, ↓↓MYCN

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Symbols for regulators with increased (or decreased) expression and fold-change $\geq$ 2 are preceded with ↑↑ (or ↓↓). Symbols for genes with increased (or decreased) expression and fold-change $<$ 2 are preceded with ↑ (or ↓).

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