# Supplementary information

## The long non-coding RNA *GHSROS* reprograms prostate cancer cell lines toward a more aggressive phenotype

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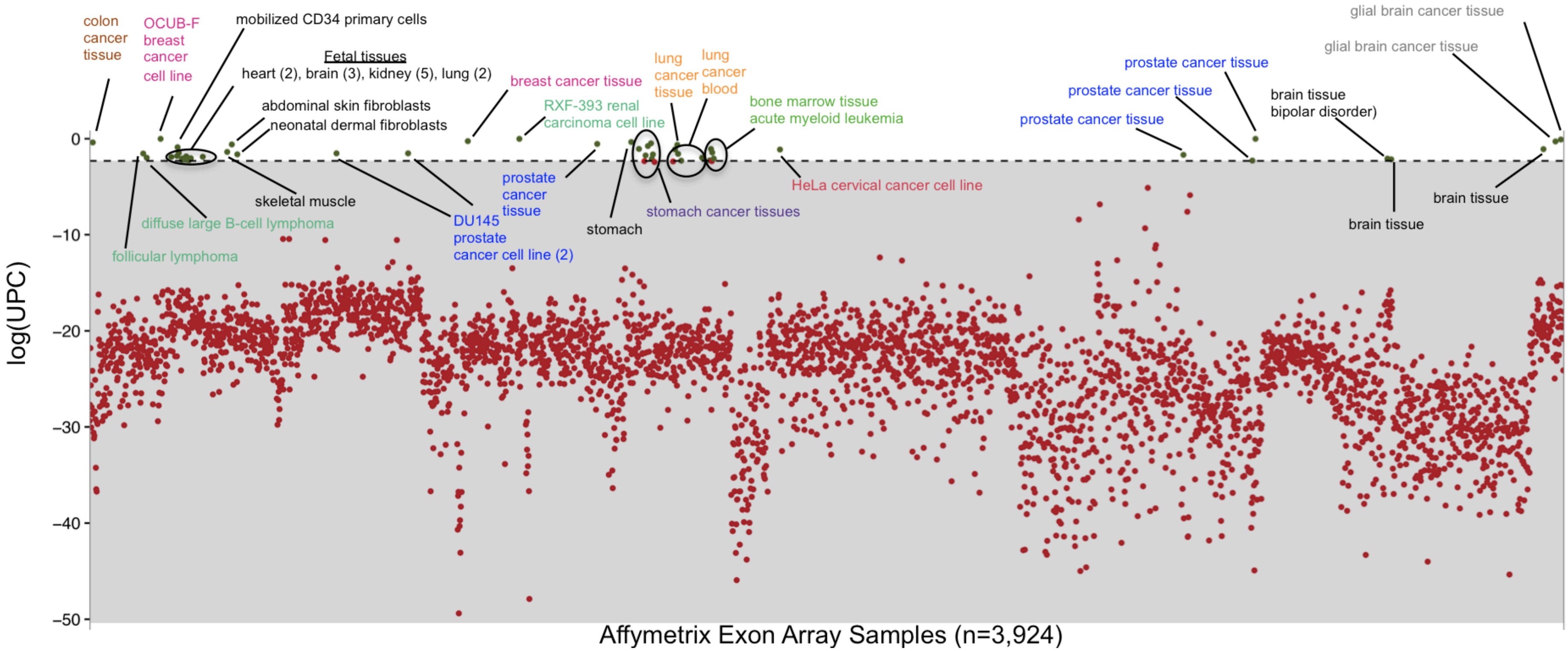
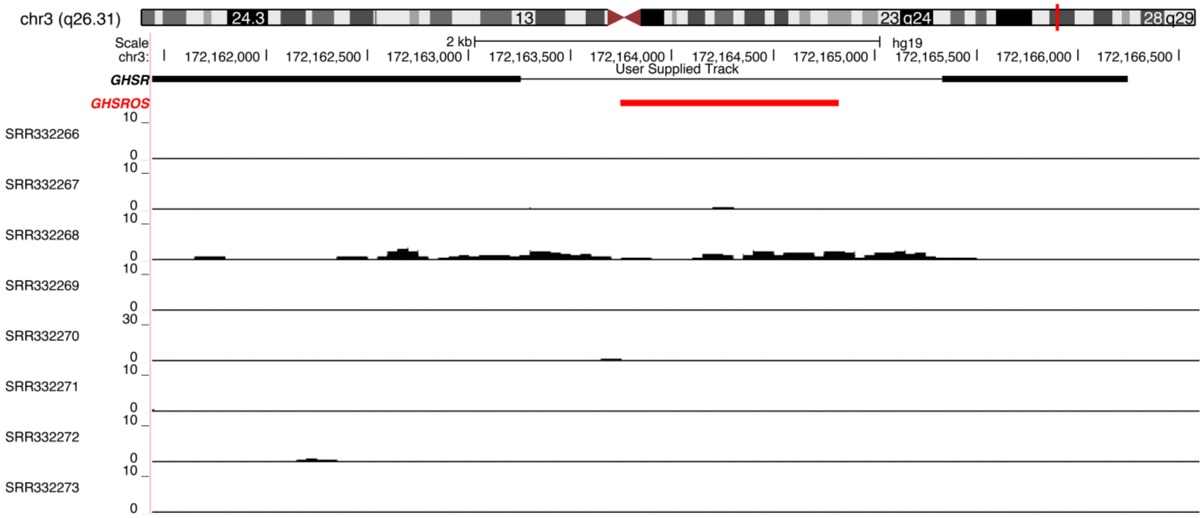
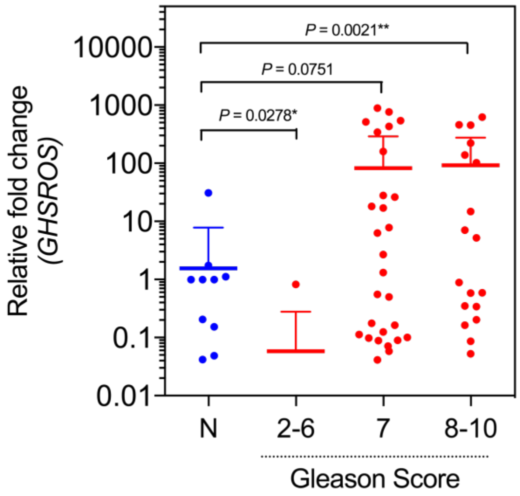


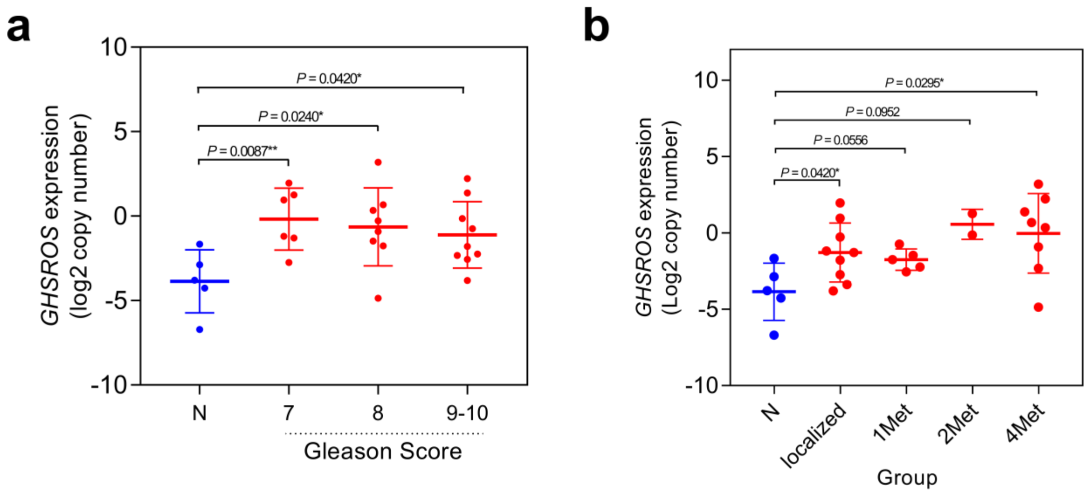
**Supplementary Fig. S1. Scatterplot of *GHSROS* Universal exPression Code values in publicly available exon array datasets.** The scatter plot shows the log of Universal exPression Code (UPC) values, an estimate on whether a gene is actively transcribed in exon array samples. The dotted horizontal line separates samples with a UPC ≥ 0.1.



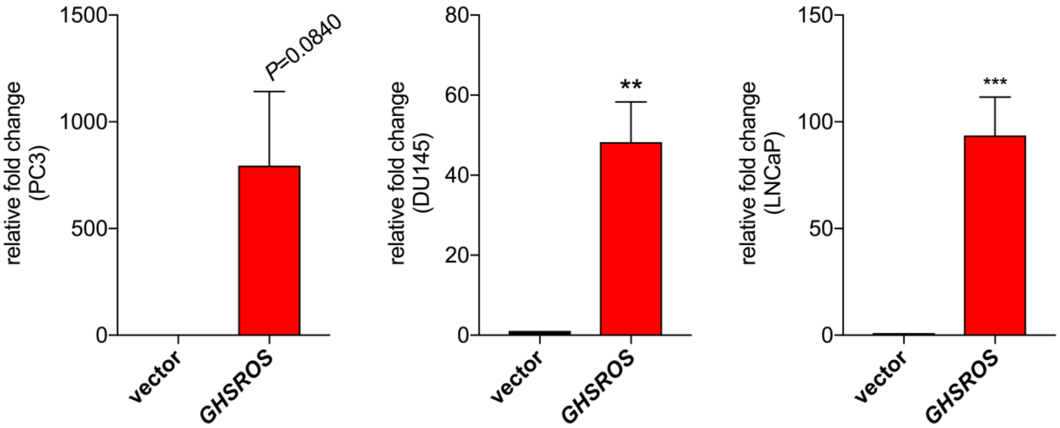
**Supplementary Fig. S2.** UCSC genome browser visualization of *GHSR*/*GHSROS* locus expression in castration-resistant prostate cancer. *GHSR* exons (black), antisense *GHSROS* exon (red). SRR332266 to SRR332273 denote NCBI Sequence Read Archive (SRA) database accession numbers. The *y*-axis represents read counts normalized to sequencing depth.



**Supplementary Fig. S3. *GHSROS* expression in OriGene TissueScan Prostate Cancer Tissue qPCR panels stratified by Gleason score.** *$P \leq 0.05$, **$P \leq 0.01$, Mann-Whitney-Wilcoxon test. Expression was normalized to the housekeeping gene *RPL32* and relative to a normal prostate sample.



**Supplementary Fig. S4. *GHSROS* expression in the Andalusian Biobank prostate tissue cohort.** *GHSROS* expression in the Andalusian Biobank prostate tissue cohort stratified by **(a)** Gleason score and **(b)** number of metastatic sites. 1 Met denotes one and ≥ 2 Met two or more metastatic sites. Absolute expression levels were determined by qRT-PCR and adjusted by a normalization factor calculated from the expression levels of three housekeeping genes (*HPRT*, *ACTB*, and *GAPDH*). N denotes normal prostate. *$P \leq 0.05$, **$P \leq 0.01$, Mann-Whitney-Wilcoxon test.



**Supplementary Fig. S5. Confirmation of *GHSROS* overexpression in prostate cancer-derived cell lines.** Bar graphs show qRT-PCR quantification of the relative expression levels of *GHSROS* when overexpressed in prostate-derived (PC3, DU145, and LNCaP) cancer cell lines. Expression was normalized to the housekeeping gene *RPL32* using the comparative $2^{-\Delta\Delta Ct}$ method of quantification. Results are relative to the respective vector control. Mean ± s.e.m., $n$=3, $^{**}P \leq 0.01$, $^{***}P \leq 0.001$, Student's $t$-test.

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GUUUCACAGAGGAUUGAAUAUACAGUUAGGAUUAAGAAUCACUGAGAUGAAUGAUUCUAU 60
GCCACUUACAAUAGACAUAAGUAAGGCUAUUAUUAAACCAACUCAUAUAAAUUAUCAUCC 120
AUCCAAGUCUUCAUUUUGCCUAUGUAAGAUAAUUUUUAAUGAUGUCUAAAUGUUUAGAUU 180
GUUUUAAAUUCAGAAAUCAGGGAAAAAUAAUAACAAAUAAUUUUUUAGUCGUUGUAACAC 240
UUUAGUGAUCCCCUUCAAAUUGUCAAGGAAGAAGAAAGUUAACAUUGGUGUUGAGACACC 300
AAUGAAGAAAUUAAUGGCUUGAAAAUAAAAUUGGAGGAAAUUAUUAAACUUAUCCUUAAA 360
ACUAAGUUGUAUAGUAGCAACUUAACUGCCACAGUAACAAUGUGACUCUCGUAGGUGAGA 420
GCUUAGGAUCCCUUGGAGGACACUAGCAGGUUUAUAACCUAUGAGUCAUAUCACGAGAAU 480
CACCGGUCCAGAAAAUAAAAUCUUUGACAUUCCUUGAAUAAACUCUAUCACUUUAAUAUG 540
GAGGAUCCAGGAACUGUAAAAUUGGAAAUAUGAAAUCAUCCUGGAAUGGCUUCUAAGAAG 600
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AGACCUUGGUUUUGAAAAUGCAAGUAGAGUUAAUAUUUUGCUGGGCUGUAACCAUAUUUA 720
UUAUUACUUCACUUGUACCAAACACAUAUACUUAAAGAAGCUGAAUUUGUGCAAUAAACA 780
UUCAGCAAAUCCAGUUAUGACAUUGUGCCCAGAUGUUCCUGAAGGGUCAUUUGGGGAAGU 840
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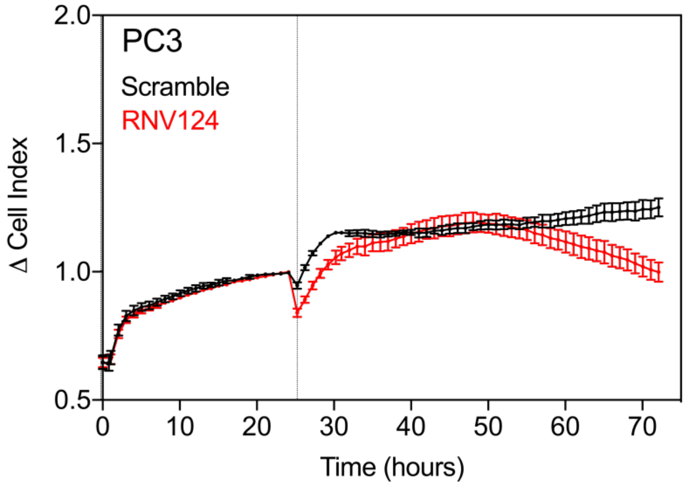
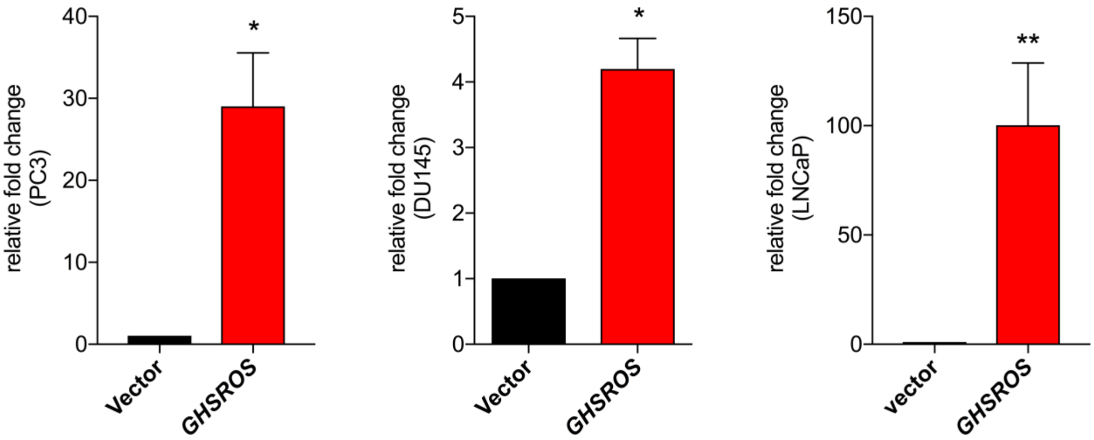
UAAACAGAAUUGAUGCAAUUAUCUGAAAAAAUGCAGGGCAGAAAACAAAUCACAAUAUUG 1080
AAAGAAAAAUGAAUAAUCUC                                         1100
```

ASO LNA RNV104L and RNV124
qRT-PCR amplicon

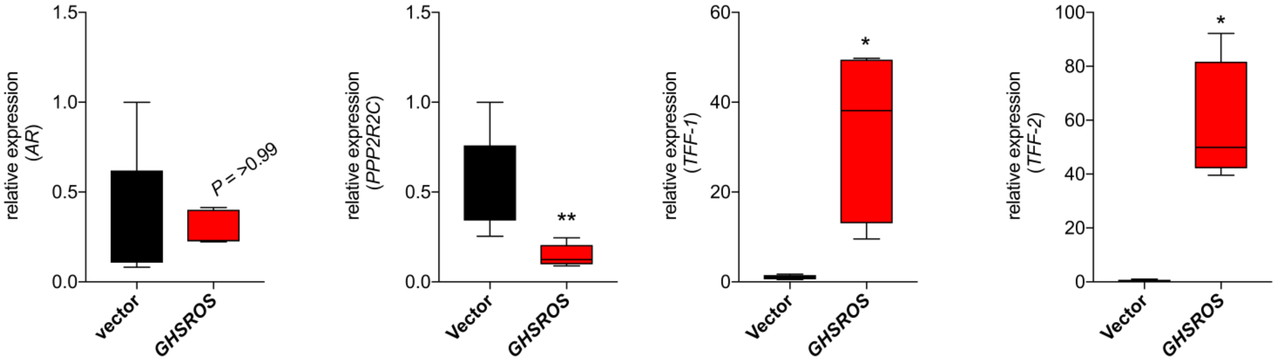
**Supplementary Fig. S6. Sequence of the lncRNA *GHSROS* and regions targeted by oligonucleotides**. The 1.1kb *GHSROS* sequence. Locked nucleic antisense oligonucleotide (LNA-ASO) locations are highlighted in red and the qRT-PCR amplicon in yellow.



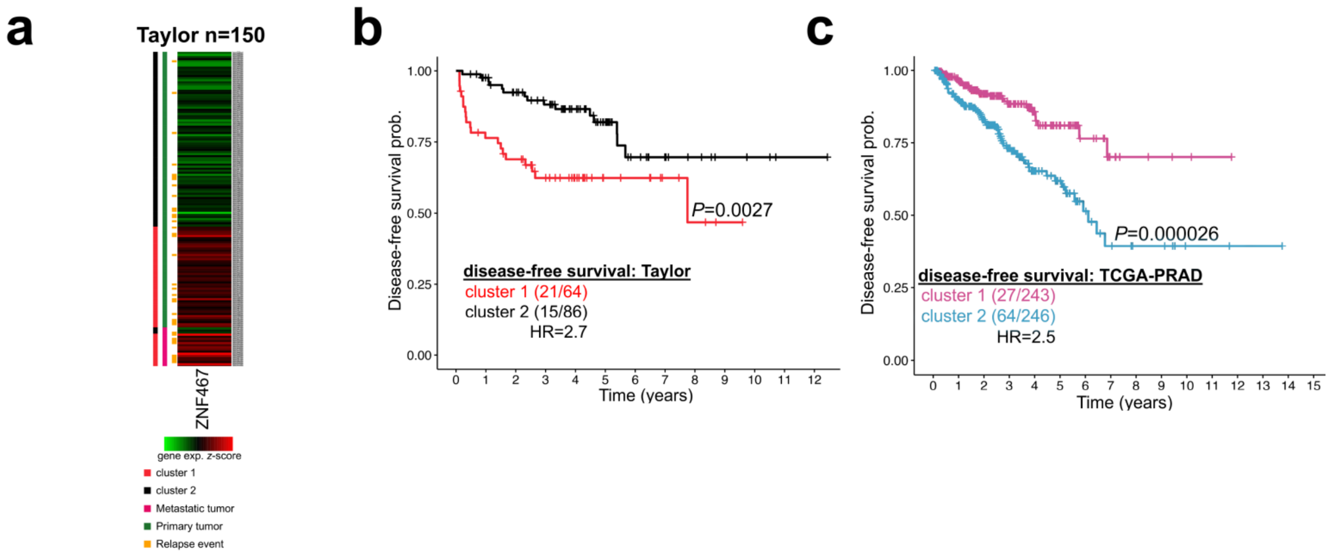
**Supplementary Fig. S7. *GHSROS* knockdown attenuates PC3 cell survival upon serum starvation.** Cells were transfected with the LNA-ASO RNV124 and grown for 24 hours (indicated by a vertical dotted line) prior to serum starvation. Results are relative to scrambled control. Mean ± s.e.m., *n*=3. At 48 hours after serum starvation, (72 hours after cells transfected as indicated on the x-axis), there was a significant difference in survival (*P* = 0.049, Student's *t*-test).



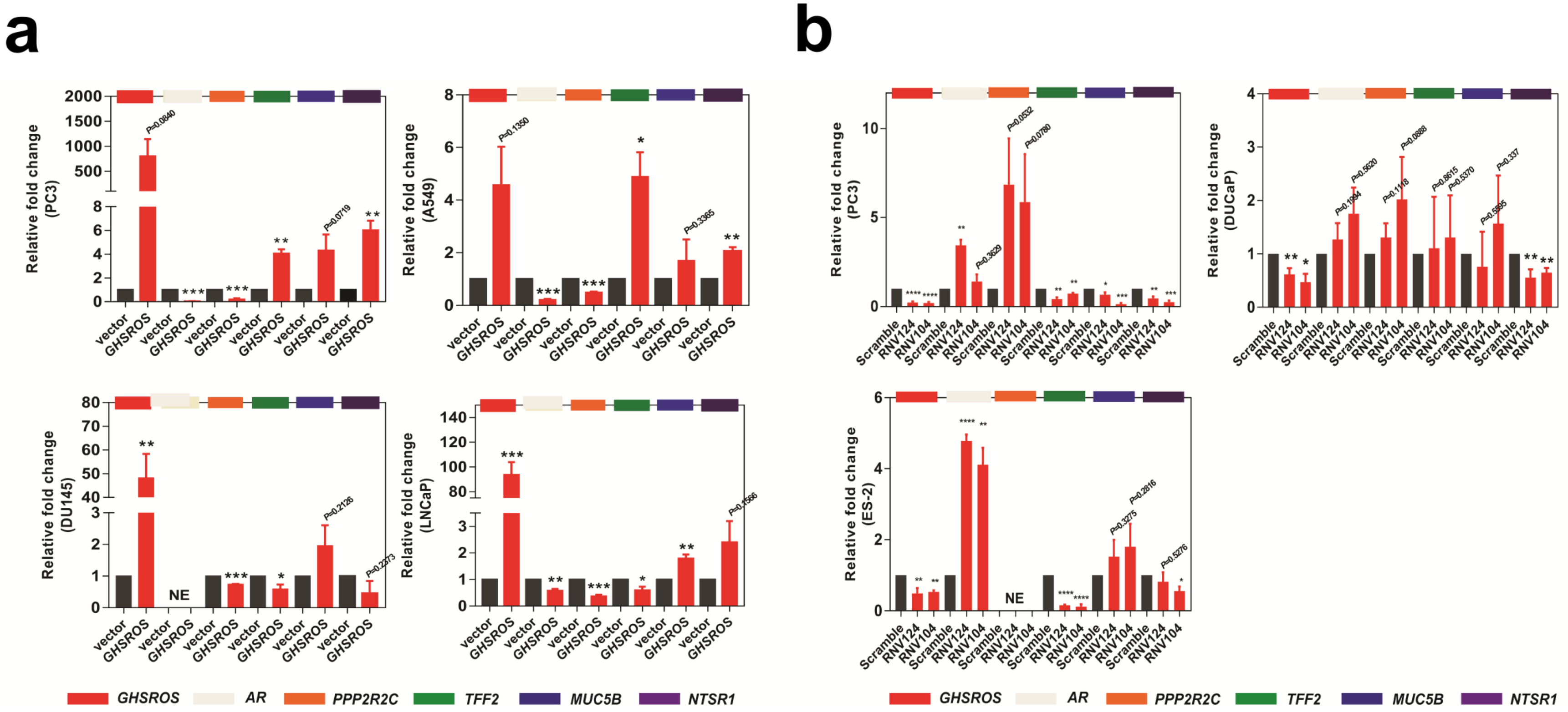
**Supplementary Fig. S8. Validation of *GHSROS* overexpression in PC3, DU145, and LNCaP tumor xenografts by qRT-PCR.** Expression changes were measured from excised PC3 (*n*=2 vector, *n*=3 *GHSROS*)*,* DU145 (*n*=2 vector, *n*=3 *GHSROS*), and LNCaP xenografts (*n*=8 vector, *n*=5 *GHSROS*) at *in vivo* endpoint. Expression was normalized to the housekeeping gene *RPL32*. Results are relative to the respective vector control. Mean ± s.e.m., *n*=3, *$P \leq 0.05$, **$P \leq 0.01$, Student's *t*-test.



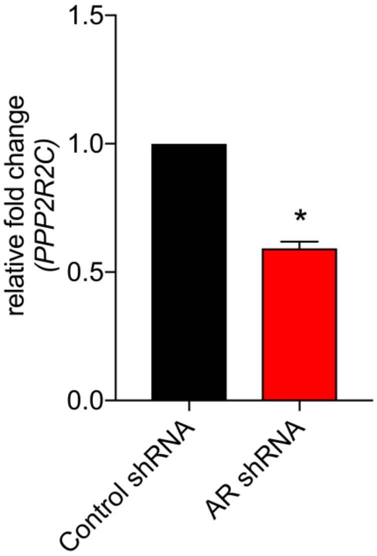
**Supplementary Fig. S9. Expression of selected genes in LNCaP tumor xenografts overexpressing *GHSROS*.** Expression changes were measured by qRT-PCR from excised LNCaP (*n*=4-8 vector, *n*=4-5 *GHSROS*) at *in vivo* endpoint. Expression was normalized to the housekeeping gene *RPL32*. Results are relative to the respective vector control. Mean, $n=3$, *$P \le 0.05$, ***$P \le 0.01$, Student's *t*-test.



**Supplementary Fig. S10. Zinc finger protein 467 (*ZNF467*), a gene induced by forced *GHSROS*-overexpression, is upregulated by metastatic tumors and associated with adverse relapse outcome. (a)** Heat map of *ZNF467* expression in the Taylor cohort normalized to depict relative values within rows (samples) with high (red) and low expression (green). Vertical bars show patient grouping by *k*-means clustering (cluster 1, red; cluster 2, black), tumor type (primary, green; metastatic pink), and relapse status (relapse event, orange). **(b)** Kaplan-Meier analyses of *ZNF467* in the Taylor cohort. Patients were stratified by *k*-means clustering, as described in (a). **(c)** Kaplan-Meier analyses of *ZNF467* in the TCGA-PRAD cohort of 489 localized prostate tumors. Patients were stratified by *k*-means clustering (cluster 1, purple; cluster 2, turquoise).



**Supplementary Fig. S11. Effects of *GHSROS* perturbation in cultured cells assessed by qRT-PCR. (a)** qRT-PCR validation of 5 genes regulated by *GHSROS*. Expression was normalized to the housekeeping gene RPL32. Results are relative to the respective vector control. Coloured bars indicate individual genes. Genes that were not expressed represented as no expression (NE). Mean ± s.e.m., *n*=3, **P* ≤ 0.05, ***P* ≤ 0.01, ****P* ≤ 0.001, Student's *t*-test. **(b)** qRT-PCR validation of regulated genes following knockdown of *GHSROS* by transfection with LNA-ASOs for 48 hours. Expression was normalized to the housekeeping gene *RPL32*. Results are relative to the respective scrambled control. Annotated as in (a).



**Supplementary Fig. S12. Effect of androgen receptor (AR) perturbation in LP50 prostate cancer cells on *PPP2R2C* expression.** Assessed by microarray (NCBI GEO accession no. GSE22483). Mean ± s.e.m. $n$=2, *$Q \leq 0.05$, moderated $t$-test.

**Supplementary Table S1. Correlation between *GHSROS* expression and clinicopathological parameters in OriGene TissueScan Prostate Cancer Tissue qPCR panels.** Six samples were excluded due to missing clinical information. Relative *GHSROS* expression in tumors (T) stratified by clinical stage and Gleason score was compared to a normal prostate sample (N). *P*-values were calculated using the Mann-Whitney-Wilcoxon test. NA = not applicable, PD = other prostatic diseases.

| **Clinicopathological parameters** | **Sample number (*n*)** | ***P*-value** |
|---|---|---|
| **Age at diagnosis (mean ± SD)** | 62.2 ± 7.80 | |
| | | |
| N/ T | 24/88 | 0.1413 |
| PD/ T | 31/88 | 0.8001 |
| N/ PD | 24/31 | 0.0691 |
| | | |
| **Clinical stage** | | |
| N (normal prostate) | 24 | |
| I | 0 | NA |
| II | 47 | 0.311 |
| III | 33 | 0.0855 |
| IV | 3 | 0.0185 |
| | | |
| **Gleason score** | | |
| N (normal prostate) | 24 | |
| 2-6 | 15 | 0.0278 |
| 7 | 47 | 0.0751 |
| 8-10 | 25 | 0.00210 |

**Supplementary Table S2. Correlation between *GHSROS* expression and clinicopathological parameters in the Andalusian Biobank prostate tissue cohort.** Absolute levels of *GHSROS* expression in tumors were stratified by Gleason score and the number of metastatic tumor sites were compared to normal prostate (N). Tumors positive or negative for extraprostatic extension and perineural infiltration were compared to each other. *P*-values were calculated using the Mann-Whitney-Wilcoxon test. NA = not applicable.

| **Clinicopathological parameters** | **Sample number (*n*)** | ***P*-value** |
|---|---|---|
| **Age at diagnosis (mean ± SD)** | 73.7 ± 9.81 | |
| | | |
| **Gleason score** | | |
| N (normal prostate) | 8 | |
| 7 | 6 | 0.00870 |
| 8 | 9 | 0.0240 |
| 9-10 | 13 | 0.0420 |
| | | |
| **Number of metastatic sites** | | |
| N (normal prostate) | 8 | |
| primary prostate tumor: 0/localized | 10 | 0.0420 |
| primary prostate tumor: 1 metastatic site | 6 | 0.0556 |
| primary prostate tumor: ≥2 metastatic sites | 12 | 0.0127 |
| | | |
| **Extraprostatic extension** | | |
| - | 16 | 0.379 |
| + | 11 | |
| | | |
| **Perineural infiltration** | | |
| - | 8 | 0.415 |
| + | 20 | |

**Supplementary Table S3. Differentially expressed genes in PC3-GHSROS cells** compared to empty vector control. Red: higher expression in PC3-GHSROS cells; Black: lower expression in PC3-GHSROS cells. Fold-changes are $\log_2$ transformed; *Q*-value denotes the false discovery rate (FDR; Benjamini-Hochberg)-adjusted *P*-value (cutoff ≤ 0.05).

| ***Gene Symbol*** | **Gene Name** | **$\log_2$ Fold Change** | ***P*-value** | ***Q*-value** |
|---|---|---|---|---|
| *AADACP1* | arylacetamide deacetylase pseudogene 1 | -1.9 | 8.2E-08 | 1.3E-06 |
| *AASS* | aminoadipate-semialdehyde synthase | -2.4 | 2.5E-08 | 5.3E-07 |
| *AATK* | apoptosis associated tyrosine kinase | 1.8 | 5.1E-08 | 8.9E-07 |
| *ABCC3* | ATP binding cassette subfamily C member 3 | 1.8 | 7.7E-13 | 7.1E-10 |
| *ABCG1* | ATP binding cassette subfamily G member 1 | 2.1 | 1.7E-09 | 7.5E-08 |
| *ACHE* | acetylcholinesterase (Cartwright blood group) | 2.5 | 4.3E-10 | 3.0E-08 |
| *ACSS1* | acyl-CoA synthetase short-chain family member 1 | -1.9 | 7.4E-11 | 9.6E-09 |
| *ADAM23* | ADAM metallopeptidase domain 23 | -2.7 | 5.3E-10 | 3.5E-08 |
| *ADAM8* | ADAM metallopeptidase domain 8 | 2.7 | 5.5E-14 | 1.5E-10 |
| *ADD2* | adducin 2 | -3.2 | 2.1E-09 | 8.8E-08 |
| *ADSSL1* | adenylosuccinate synthase like 1 | 1.5 | 6.2E-08 | 1.0E-06 |
| *AFF2* | AF4/FMR2 family member 2 | -3.9 | 1.1E-11 | 3.0E-09 |
| *AGR2* | anterior gradient 2, protein disulphide isomerase family member | 2.1 | 3.9E-12 | 1.7E-09 |
| *AGTR1* | angiotensin II receptor type 1 | -2.1 | 3.6E-08 | 7.0E-07 |
| *AIF1L* | allograft inflammatory factor 1 like | 1.6 | 2.7E-08 | 5.6E-07 |
| *AMOT* | angiomotin | -3.1 | 2.3E-11 | 4.7E-09 |
| *ANGPT1* | angiopoietin 1 | -2.8 | 1.0E-08 | 2.7E-07 |
| *ANGPTL4* | angiopoietin like 4 | 1.6 | 2.0E-08 | 4.5E-07 |
| *ANK1* | ankyrin 1 | 1.5 | 9.3E-06 | 5.5E-05 |
| *ANK2* | ankyrin 2, neuronal | -3.1 | 2.4E-09 | 9.5E-08 |
| *ANOS1* | anosmin 1 | 1.9 | 6.1E-09 | 1.8E-07 |
| *ANXA10* | annexin A10 | -2.3 | 1.1E-09 | 5.7E-08 |
| *APOBEC3G* | apolipoprotein B mRNA editing enzyme catalytic subunit 3G | 2.0 | 3.3E-08 | 6.5E-07 |
| *AR* | androgen receptor | -3.6 | 1.4E-09 | 6.6E-08 |
| *ARHGAP44* | Rho GTPase activating protein 44 | -2.1 | 1.6E-08 | 3.8E-07 |
| *ARHGDIB* | Rho GDP dissociation inhibitor beta | -3.4 | 5.3E-11 | 7.7E-09 |
| *ARHGEF16* | Rho guanine nucleotide exchange factor 16 | 2.4 | 7.8E-10 | 4.6E-08 |
| *ARNT2* | aryl hydrocarbon receptor nuclear translocator 2 | -1.6 | 1.0E-07 | 1.5E-06 |
| *ASS1* | argininosuccinate synthase 1 | 1.8 | 2.2E-08 | 4.8E-07 |
| *B3GALT5* | beta-1,3-galactosyltransferase 5 | -2.0 | 2.1E-06 | 1.7E-05 |

| | | | | |
|---|---|---|---|---|
| *B3GALT5-AS1* | B3GALT5 antisense RNA 1 | -2.2 | 6.1E-09 | 1.8E-07 |
| *B3GNT7* | UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 7 | 1.6 | 4.2E-09 | 1.4E-07 |
| *B4GALNT1* | beta-1,4-N-acetyl-galactosaminyltransferase 1 | -1.8 | 8.8E-11 | 1.1E-08 |
| *BCAT1* | branched chain amino acid transaminase 1 | -3.9 | 1.5E-11 | 3.4E-09 |
| *BEX2* | brain expressed X-linked 2 | -1.8 | 4.2E-07 | 4.4E-06 |
| *BEX4* | brain expressed X-linked 4 | -1.8 | 1.1E-08 | 2.9E-07 |
| *BEX5* | brain expressed X-linked 5 | -1.7 | 8.1E-07 | 7.5E-06 |
| *BIK* | BCL2 interacting killer | 1.8 | 2.1E-06 | 1.6E-05 |
| *BLMH* | bleomycin hydrolase | -1.8 | 6.6E-13 | 6.5E-10 |
| *BMP6* | bone morphogenetic protein 6 | -2.3 | 5.1E-09 | 1.6E-07 |
| *BTBD11* | BTB domain containing 11 | -3.1 | 5.7E-10 | 3.6E-08 |
| *BTG3* | BTG family member 3 | -2.0 | 1.1E-10 | 1.3E-08 |
| *C11orf45* | chromosome 11 open reading frame 45 | -1.8 | 2.0E-08 | 4.5E-07 |
| *C20orf166-AS1* | C20orf166 antisense RNA 1 | 1.8 | 3.0E-07 | 3.5E-06 |
| *C9orf152* | chromosome 9 open reading frame 152 | 1.8 | 5.3E-07 | 5.4E-06 |
| *CA9* | carbonic anhydrase 9 | 2.5 | 3.1E-08 | 6.2E-07 |
| *CACNA2D2* | calcium voltage-gated channel auxiliary subunit alpha2delta 2 | -1.6 | 2.6E-08 | 5.5E-07 |
| *CADM4* | cell adhesion molecule 4 | 2.3 | 8.8E-10 | 5.0E-08 |
| *CADPS2* | calcium dependent secretion activator 2 | -2.0 | 8.9E-12 | 2.6E-09 |
| *CALB1* | calbindin 1 | 3.3 | 2.1E-10 | 1.9E-08 |
| *CAMK2N1* | calcium/calmodulin dependent protein kinase II inhibitor 1 | 3.3 | 4.1E-12 | 1.7E-09 |
| *CAPN6* | calpain 6 | -2.5 | 3.3E-08 | 6.5E-07 |
| *CAV1* | caveolin 1 | 1.6 | 5.2E-13 | 6.0E-10 |
| *CBLC* | Cbl proto-oncogene C | 1.8 | 2.8E-07 | 3.3E-06 |
| *CCBE1* | collagen and calcium binding EGF domains 1 | 1.5 | 1.5E-08 | 3.7E-07 |
| *CCDC160* | coiled-coil domain containing 160 | -2.5 | 1.6E-08 | 3.8E-07 |
| *CCNB3* | cyclin B3 | -2.1 | 5.3E-08 | 9.2E-07 |
| *CD24* | CD24 molecule | 1.5 | 2.9E-12 | 1.5E-09 |
| *CD33* | CD33 molecule | -2.0 | 5.7E-08 | 9.7E-07 |
| *CD70* | CD70 molecule | -2.1 | 6.3E-07 | 6.2E-06 |
| *CDH1* | cadherin 1 | 2.2 | 4.1E-08 | 7.8E-07 |
| *CDH12* | cadherin 12 | -1.6 | 8.8E-10 | 5.0E-08 |
| *CDH3* | cadherin 3 | 2.0 | 1.5E-07 | 2.1E-06 |
| *CEACAM6* | carcinoembryonic antigen related cell adhesion molecule 6 | 1.7 | 6.2E-07 | 6.1E-06 |
| *CEND1* | cell cycle exit and neuronal differentiation 1 | -2.0 | 2.4E-07 | 2.9E-06 |
| *CHD7* | chromodomain helicase DNA binding protein 7 | -1.6 | 1.1E-06 | 9.6E-06 |
| *CHRDL1* | chordin-like 1 | -3.0 | 5.4E-10 | 3.5E-08 |
| *CKB* | creatine kinase B | 1.8 | 2.6E-11 | 5.0E-09 |
| *CLDN7* | claudin 7 | 2.1 | 1.4E-07 | 1.9E-06 |
| *CLMN* | calmin (calponin-like, transmembrane) | -2.4 | 4.9E-09 | 1.6E-07 |

| | | | | |
|---|---|---|---|---|
| *CNKSR2* | connector enhancer of kinase suppressor of Ras 2 | -2.4 | 9.2E-09 | 2.5E-07 |
| *CNTN1* | contactin 1 | -4.4 | 4.2E-11 | 6.6E-09 |
| *COBL* | cordon-bleu WH2 repeat protein | -4.6 | 1.0E-11 | 2.9E-09 |
| *COL21A1* | collagen type XXI alpha 1 chain | -1.9 | 1.2E-07 | 1.7E-06 |
| *COL5A1* | collagen type V alpha 1 | 2.1 | 1.9E-09 | 8.2E-08 |
| *COX7B2* | cytochrome c oxidase subunit 7B2 | 3.8 | 1.8E-09 | 7.6E-08 |
| *CPA6* | carboxypeptidase A6 | -2.3 | 1.5E-08 | 3.5E-07 |
| *CPEB1* | cytoplasmic polyadenylation element binding protein 1 | -2.5 | 5.4E-11 | 7.7E-09 |
| *CPZ* | carboxypeptidase Z | 1.6 | 1.7E-09 | 7.5E-08 |
| *CRABP1* | cellular retinoic acid binding protein 1 | 4.1 | 1.1E-11 | 3.0E-09 |
| *CRABP2* | cellular retinoic acid binding protein 2 | 2.4 | 1.1E-12 | 7.8E-10 |
| *CREB3L1* | cAMP responsive element binding protein 3 like 1 | 4.0 | 2.4E-13 | 3.4E-10 |
| *CRIP1* | cysteine rich protein 1 | 2.2 | 1.4E-10 | 1.5E-08 |
| *CRIP2* | cysteine rich protein 2 | 2.3 | 9.6E-12 | 2.8E-09 |
| *CSMD2* | CUB and Sushi multiple domains 2 | -2.5 | 7.9E-09 | 2.2E-07 |
| *CST1* | cystatin SN | -3.3 | 1.3E-10 | 1.4E-08 |
| *CST4* | cystatin S | -2.6 | 1.8E-09 | 7.6E-08 |
| *CXADR* | coxsackie virus and adenovirus receptor | -2.8 | 4.0E-11 | 6.5E-09 |
| *CXADRP2* | coxsackie virus and adenovirus receptor pseudogene 2 | -1.8 | 3.5E-07 | 3.9E-06 |
| *CXCL5* | C-X-C motif chemokine ligand 5 | 1.5 | 1.0E-06 | 9.0E-06 |
| *CXorf57* | chromosome X open reading frame 57 | -3.0 | 4.7E-10 | 3.2E-08 |
| *CYP4F35P* | cytochrome P450 family 4 subfamily F member 35, pseudogene | -1.5 | 1.4E-07 | 2.0E-06 |
| *CYP4V2* | cytochrome P450 family 4 subfamily V member 2 | -2.6 | 2.3E-09 | 9.1E-08 |
| *CYP7B1* | cytochrome P450 family 7 subfamily B member 1 | -2.3 | 2.2E-08 | 4.8E-07 |
| *DEPTOR* | DEP domain containing MTOR-interacting protein | -1.7 | 6.7E-08 | 1.1E-06 |
| *DGKG* | diacylglycerol kinase gamma | -2.7 | 1.0E-10 | 1.2E-08 |
| *DIRAS1* | DIRAS family GTPase 1 | 2.2 | 2.8E-10 | 2.2E-08 |
| *DLX3* | distal-less homeobox 3 | -1.6 | 1.7E-06 | 1.4E-05 |
| *DMD* | dystrophin | -3.0 | 4.0E-10 | 2.8E-08 |
| *DNAH5* | dynein axonemal heavy chain 5 | -1.7 | 3.3E-09 | 1.2E-07 |
| *DNAJA4* | DnaJ heat shock protein family (Hsp40) member A4 | -2.0 | 1.8E-08 | 4.1E-07 |
| *DNAJC6* | DnaJ heat shock protein family (Hsp40) member C6 | -2.4 | 4.6E-10 | 3.1E-08 |
| *DOCK3* | dedicator of cytokinesis 3 | -1.5 | 9.4E-09 | 2.6E-07 |
| *DPY19L2P1* | DPY19L2 pseudogene 1 | -1.9 | 1.2E-06 | 1.1E-05 |
| *DTX4* | deltex 4, E3 ubiquitin ligase | -1.8 | 1.1E-08 | 2.8E-07 |
| *DYSF* | dysferlin | -2.0 | 5.9E-11 | 8.3E-09 |
| *EDA* | ectodysplasin A | -3.0 | 6.2E-09 | 1.8E-07 |
| *EGF* | epidermal growth factor | -2.5 | 9.1E-10 | 5.1E-08 |
| *EGLN3* | egl-9 family hypoxia inducible factor 3 | -1.8 | 1.3E-07 | 1.8E-06 |
| *EHD2* | EH domain containing 2 | 2.3 | 9.7E-09 | 2.6E-07 |
| *EHF* | ETS homologous factor | 1.9 | 8.5E-09 | 2.4E-07 |
| *ENTPD3* | ectonucleoside triphosphate diphosphohydrolase 3 | -1.8 | 1.1E-08 | 2.8E-07 |

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|---|---|---|---|---|
| *EOMES* | eomesodermin | -2.1 | 1.2E-09 | 6.1E-08 |
| *EPHB2* | EPH receptor B2 | -1.5 | 2.6E-10 | 2.1E-08 |
| *EPHB6* | EPH receptor B6 | 1.7 | 1.4E-10 | 1.5E-08 |
| *ESM1* | endothelial cell specific molecule 1 | -1.8 | 4.3E-11 | 6.7E-09 |
| *EYA1* | EYA transcriptional coactivator and phosphatase 1 | -3.5 | 1.5E-10 | 1.6E-08 |
| *F2RL2* | coagulation factor II thrombin receptor like 2 | -1.6 | 2.0E-07 | 2.6E-06 |
| *FAM110C* | family with sequence similarity 110 member C | -3.0 | 1.6E-10 | 1.6E-08 |
| *FAM131B* | family with sequence similarity 131 member B | 1.5 | 1.7E-11 | 3.6E-09 |
| *FAM134B* | family with sequence similarity 134 member B | -1.5 | 6.3E-08 | 1.0E-06 |
| *FAM20A* | family with sequence similarity 20 member A | 2.0 | 1.3E-07 | 1.9E-06 |
| *FAM50B* | family with sequence similarity 50 member B | 1.7 | 8.5E-08 | 1.3E-06 |
| *FAM89A* | family with sequence similarity 89 member A | -1.6 | 5.1E-08 | 8.9E-07 |
| *FBP1* | fructose-bisphosphatase 1 | 2.5 | 3.1E-11 | 5.6E-09 |
| *FBXL16* | F-box and leucine rich repeat protein 16 | 2.0 | 1.4E-08 | 3.5E-07 |
| *FBXL7* | F-box and leucine rich repeat protein 7 | -1.7 | 1.6E-08 | 3.7E-07 |
| *FCGBP* | Fc fragment of IgG binding protein | -3.1 | 1.5E-10 | 1.6E-08 |
| *FEZF1-AS1* | FEZF1 antisense RNA 1 | -2.0 | 1.1E-06 | 9.8E-06 |
| *FGF13* | fibroblast growth factor 13 | -1.8 | 1.7E-08 | 4.0E-07 |
| *FNDC4* | fibronectin type III domain containing 4 | 2.0 | 4.2E-08 | 7.9E-07 |
| *FOXL1* | forkhead box L1 | 1.6 | 4.1E-10 | 2.9E-08 |
| *FOXRED2* | FAD dependent oxidoreductase domain containing 2 | 3.6 | 2.3E-12 | 1.5E-09 |
| *FRMD4B* | FERM domain containing 4B | -1.9 | 5.5E-09 | 1.7E-07 |
| *GAL* | galanin and GMAP prepropeptide | -3.2 | 1.5E-09 | 6.7E-08 |
| *GALNT12* | polypeptide N-acetylgalactosaminyltransferase 12 | 2.1 | 9.9E-10 | 5.3E-08 |
| *GALNT14* | polypeptide N-acetylgalactosaminyltransferase 14 | -1.6 | 1.3E-08 | 3.3E-07 |
| *GALNT16* | polypeptide N-acetylgalactosaminyltransferase 16 | -1.7 | 1.2E-06 | 1.0E-05 |
| *GAS6* | growth arrest specific 6 | 1.6 | 2.1E-09 | 8.8E-08 |
| *GBP7* | guanylate binding protein 7 | -1.5 | 2.9E-06 | 2.1E-05 |
| *GCNT1* | glucosaminyl (N-acetyl) transferase 1, core 2 | -1.6 | 1.4E-07 | 1.9E-06 |
| *GCNT3* | glucosaminyl (N-acetyl) transferase 3, mucin type | -2.4 | 6.8E-09 | 2.0E-07 |
| *GDF15* | growth differentiation factor 15 | 1.5 | 1.5E-08 | 3.6E-07 |
| *GHSROS* | Growth Hormone Secretagogue Receptor Opposite Strand | 5.3 | 3.4E-13 | 4.3E-10 |
| *GJB3* | gap junction protein beta 3 | 1.7 | 6.0E-10 | 3.8E-08 |
| *GNAI1* | G protein subunit alpha i1 | 1.5 | 1.6E-10 | 1.6E-08 |
| *GPR153* | G protein-coupled receptor 153 | 1.6 | 5.7E-13 | 6.1E-10 |
| *GPR63* | G protein-coupled receptor 63 | -2.3 | 2.5E-09 | 9.7E-08 |
| *GRID2* | glutamate ionotropic receptor delta type subunit 2 | 1.7 | 1.5E-07 | 2.1E-06 |
| *GRIN2D* | glutamate ionotropic receptor NMDA type subunit 2D | 2.0 | 1.6E-08 | 3.7E-07 |
| *GRTP1* | growth hormone regulated TBC protein 1 | 2.1 | 6.0E-08 | 1.0E-06 |
| *GUCA1B* | guanylate cyclase activator 1B | 1.5 | 6.7E-07 | 6.5E-06 |
| *HEPH* | hephaestin | -2.4 | 2.4E-09 | 9.3E-08 |

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|---|---|---|---|---|
| *HR* | hair growth associated | 2.2 | 5.3E-09 | 1.7E-07 |
| *HRASLS* | HRAS like suppressor | -1.9 | 2.7E-07 | 3.2E-06 |
| *HSPA12A* | heat shock protein family A (Hsp70) member 12A | -3.7 | 2.7E-11 | 5.1E-09 |
| *HSPB8* | heat shock protein family B (small) member 8 | -3.5 | 9.9E-10 | 5.3E-08 |
| *HTR7* | 5-hydroxytryptamine receptor 7 | -2.0 | 2.4E-07 | 2.9E-06 |
| *HTRA3* | HtrA serine peptidase 3 | -1.8 | 1.5E-08 | 3.6E-07 |
| *IFI16* | interferon gamma inducible protein 16 | -2.2 | 9.4E-13 | 7.5E-10 |
| *IFITM1* | interferon induced transmembrane protein 1 | 1.6 | 3.6E-06 | 2.5E-05 |
| *IGFBP5* | insulin like growth factor binding protein 5 | 1.6 | 2.4E-12 | 1.5E-09 |
| *IGFBP6* | insulin like growth factor binding protein 6 | 1.9 | 3.8E-11 | 6.3E-09 |
| *IL13RA2* | interleukin 13 receptor subunit alpha 2 | -3.0 | 6.4E-10 | 4.0E-08 |
| *ITGB2* | integrin subunit beta 2 | 2.2 | 6.1E-11 | 8.4E-09 |
| *ITGB4* | integrin subunit beta 4 | 1.9 | 9.2E-13 | 7.5E-10 |
| *ITM2A* | integral membrane protein 2A | -2.7 | 7.3E-10 | 4.4E-08 |
| *JAM3* | junctional adhesion molecule 3 | -1.8 | 1.3E-08 | 3.3E-07 |
| *JUP* | junction plakoglobin | 1.5 | 5.9E-12 | 2.0E-09 |
| *KCNJ12* | potassium voltage-gated channel subfamily J member 12 | -2.2 | 4.3E-09 | 1.4E-07 |
| *KCNJ3* | potassium voltage-gated channel subfamily J member 3 | 1.5 | 2.4E-05 | 1.2E-04 |
| *KCNN3* | potassium calcium-activated channel subfamily N member 3 | -2.3 | 5.9E-07 | 5.9E-06 |
| *KIAA0319* | KIAA0319 | -3.6 | 4.6E-11 | 6.9E-09 |
| *KIAA1210* | KIAA1210 | -1.7 | 2.9E-07 | 3.4E-06 |
| *KIAA1211* | KIAA1211 | -3.8 | 2.7E-12 | 1.5E-09 |
| *KIAA1644* | KIAA1644 | 2.0 | 2.6E-07 | 3.1E-06 |
| *KIF26A* | kinesin family member 26A | -1.7 | 4.5E-08 | 8.3E-07 |
| *KIF5C* | kinesin family member 5C | -2.7 | 1.6E-11 | 3.5E-09 |
| *KLF9* | Kruppel like factor 9 | -3.3 | 2.5E-10 | 2.1E-08 |
| *KRT6B* | keratin 6B | -2.2 | 1.7E-08 | 3.9E-07 |
| *KRT7* | keratin 7 | 2.6 | 1.9E-14 | 6.7E-11 |
| *KRT75* | keratin 75 | -5.5 | 3.5E-16 | 2.5E-12 |
| *KRT81* | keratin 81 | 1.5 | 3.1E-12 | 1.5E-09 |
| *LAMA1* | laminin subunit alpha 1 | -2.1 | 1.6E-08 | 3.8E-07 |
| *LAMC3* | laminin subunit gamma 3 | -1.7 | 2.1E-09 | 8.5E-08 |
| *LARGE2* | LARGE xylosyl- and glucuronyltransferase 2 | 1.8 | 4.3E-08 | 8.0E-07 |
| *LCK* | LCK proto-oncogene, Src family tyrosine kinase | 1.5 | 2.6E-06 | 2.0E-05 |
| *LCP1* | lymphocyte cytosolic protein 1 | -2.3 | 3.4E-12 | 1.6E-09 |
| *LEF1* | lymphoid enhancer binding factor 1 | -1.5 | 6.7E-07 | 6.5E-06 |
| *LGR5* | leucine rich repeat containing G protein-coupled receptor 5 | -1.7 | 3.9E-09 | 1.3E-07 |
| *LIMCH1* | LIM and calponin homology domains 1 | 2.2 | 6.1E-10 | 3.8E-08 |
| *LIMS2* | LIM zinc finger domain containing 2 | 1.7 | 3.1E-09 | 1.2E-07 |
| *LINC00346* | long intergenic non-protein coding RNA 346 | 1.5 | 8.0E-07 | 7.4E-06 |
| *LINC01133* | long intergenic non-protein coding RNA 1133 | 1.5 | 4.1E-06 | 2.8E-05 |
| *LITAF* | lipopolysaccharide induced TNF factor | 3.1 | 1.1E-10 | 1.3E-08 |

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|---|---|---|---|---|
| *LOC100506123* | uncharacterized LOC100506123 | -1.6 | 1.4E-09 | 6.7E-08 |
| *LOC101927870* | uncharacterized LOC101927870 | 1.5 | 5.2E-09 | 1.6E-07 |
| *LOXL4* | lysyl oxidase like 4 | 1.7 | 4.4E-12 | 1.8E-09 |
| *LRCH2* | leucine rich repeats and calponin homology domain containing 2 | -2.4 | 3.7E-09 | 1.3E-07 |
| *LRIG1* | leucine rich repeats and immunoglobulin like domains 1 | -2.0 | 1.6E-08 | 3.7E-07 |
| *LRP4* | LDL receptor related protein 4 | -1.5 | 1.8E-05 | 9.3E-05 |
| *LRRN2* | leucine rich repeat neuronal 2 | -1.5 | 8.3E-07 | 7.7E-06 |
| *MAGEH1* | MAGE family member H1 | -1.9 | 1.1E-08 | 2.8E-07 |
| *MAP2* | microtubule associated protein 2 | -1.5 | 3.0E-08 | 6.0E-07 |
| *MAP3K15* | mitogen-activated protein kinase kinase kinase 15 | -1.5 | 8.5E-09 | 2.3E-07 |
| *MARCH3* | membrane associated ring-CH-type finger 3 | 1.5 | 2.2E-06 | 1.7E-05 |
| *MARK1* | microtubule affinity regulating kinase 1 | -2.9 | 2.7E-10 | 2.2E-08 |
| *MCOLN3* | mucolipin 3 | -1.8 | 2.1E-06 | 1.7E-05 |
| *MCTP2* | multiple C2 domains, transmembrane 2 | -3.0 | 3.1E-10 | 2.3E-08 |
| *MEGF6* | multiple EGF like domains 6 | 2.0 | 4.0E-12 | 1.7E-09 |
| *MEST* | mesoderm specific transcript | 1.7 | 7.0E-09 | 2.0E-07 |
| *MFAP3L* | microfibrillar associated protein 3 like | -2.5 | 1.3E-09 | 6.3E-08 |
| *MIR31HG* | MIR31 host gene | 1.7 | 2.4E-09 | 9.3E-08 |
| *MISP* | mitotic spindle positioning | 1.7 | 1.0E-10 | 1.2E-08 |
| *MLLT11* | myeloid/lymphoid or mixed-lineage leukemia; translocated to, 11 | -3.2 | 3.1E-16 | 2.5E-12 |
| *MMRN1* | multimerin 1 | -1.8 | 1.1E-08 | 2.9E-07 |
| *MN1* | meningioma (disrupted in balanced translocation) 1 | -2.6 | 1.2E-10 | 1.3E-08 |
| *MSX2* | msh homeobox 2 | -2.1 | 1.3E-08 | 3.3E-07 |
| *MTSS1* | metastasis suppressor 1 | -1.5 | 4.2E-07 | 4.4E-06 |
| *MUC2* | mucin 2, oligomeric mucus/gel-forming | 2.0 | 1.3E-08 | 3.3E-07 |
| *MUC3A* | mucin 3A, cell surface associated | 3.7 | 7.5E-12 | 2.4E-09 |
| *MUC5B* | mucin 5B, oligomeric mucus/gel-forming | 2.8 | 2.3E-09 | 9.2E-08 |
| *MUM1L1* | MUM1 like 1 | -3.5 | 1.1E-09 | 5.6E-08 |
| *MYT1* | myelin transcription factor 1 | -1.6 | 4.8E-06 | 3.2E-05 |
| *NACAD* | NAC alpha domain containing | 2.9 | 4.0E-09 | 1.4E-07 |
| *NAP1L2* | nucleosome assembly protein 1 like 2 | -1.7 | 1.4E-11 | 3.3E-09 |
| *NAP1L6* | nucleosome assembly protein 1 like 6 | -1.8 | 2.0E-06 | 1.6E-05 |
| *NAV3* | neuron navigator 3 | -1.6 | 4.3E-07 | 4.6E-06 |
| *NBEAP1* | neurobeachin pseudogene 1 | -1.8 | 6.9E-07 | 6.6E-06 |
| *NCR3LG1* | natural killer cell cytotoxicity receptor 3 ligand 1 | -1.7 | 8.9E-06 | 5.3E-05 |
| *NEK3* | NIMA related kinase 3 | 2.0 | 1.4E-08 | 3.4E-07 |
| *NELL2* | neural EGFL like 2 | -4.3 | 2.6E-12 | 1.5E-09 |
| *NEO1* | neogenin 1 | -1.5 | 3.2E-06 | 2.3E-05 |
| *NFASC* | neurofascin | -2.3 | 7.1E-11 | 9.5E-09 |
| *NLGN1* | neuroligin 1 | -1.7 | 1.9E-06 | 1.5E-05 |
| *NLRC5* | NLR family CARD domain containing 5 | -1.5 | 3.9E-07 | 4.2E-06 |
| *NOG* | noggin | -1.5 | 1.3E-09 | 6.4E-08 |
| *NPR3* | natriuretic peptide receptor 3 | 1.6 | 1.2E-07 | 1.7E-06 |

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|---|---|---|---|---|
| *NPY1R* | neuropeptide Y receptor Y1 | 1.9 | 3.0E-11 | 5.4E-09 |
| *NRXN3* | neurexin 3 | -1.9 | 1.2E-07 | 1.7E-06 |
| *NTSR1* | neurotensin receptor 1 (high affinity) | 4.0 | 1.4E-14 | 6.3E-11 |
| *NUDT10* | nudix hydrolase 10 | -2.6 | 9.7E-10 | 5.3E-08 |
| *NUDT11* | nudix hydrolase 11 | -4.9 | 2.4E-13 | 3.4E-10 |
| *OASL* | 2'-5'-oligoadenylate synthetase like | -1.6 | 1.8E-10 | 1.6E-08 |
| *OCLN* | occludin | 1.7 | 4.0E-09 | 1.4E-07 |
| *OPN3* | opsin 3 | 1.5 | 5.9E-09 | 1.8E-07 |
| *OSBP2* | oxysterol binding protein 2 | 1.8 | 1.5E-12 | 1.0E-09 |
| *OXTR* | oxytocin receptor | 1.7 | 7.0E-12 | 2.3E-09 |
| *PALD1* | phosphatase domain containing, paladin 1 | -2.2 | 2.0E-08 | 4.5E-07 |
| *PALM2* | paralemmin 2 | -2.1 | 5.0E-07 | 5.2E-06 |
| *PAQR8* | progestin and adipoQ receptor family member 8 | 1.7 | 3.1E-09 | 1.1E-07 |
| *PARM1* | prostate androgen-regulated mucin-like protein 1 | -4.4 | 3.2E-12 | 1.5E-09 |
| *PARP8* | poly(ADP-ribose) polymerase family member 8 | -1.9 | 4.0E-09 | 1.4E-07 |
| *PCDH19* | protocadherin 19 | -1.7 | 2.0E-06 | 1.6E-05 |
| *PCDHGB2* | protocadherin gamma subfamily B, 2 | 1.7 | 3.4E-07 | 3.8E-06 |
| *PCSK5* | proprotein convertase subtilisin/kexin type 5 | -1.9 | 2.4E-07 | 2.9E-06 |
| *PCSK9* | proprotein convertase subtilisin/kexin type 9 | 1.7 | 4.8E-08 | 8.7E-07 |
| *PDGFA* | platelet derived growth factor subunit A | 1.6 | 1.9E-08 | 4.3E-07 |
| *PDLIM2* | PDZ and LIM domain 2 | 1.9 | 8.0E-09 | 2.3E-07 |
| *PELI2* | pellino E3 ubiquitin protein ligase family member 2 | -1.6 | 2.3E-06 | 1.8E-05 |
| *PI3* | peptidase inhibitor 3 | 1.7 | 5.8E-10 | 3.7E-08 |
| *PIANP* | PILR alpha associated neural protein | 1.6 | 8.1E-07 | 7.5E-06 |
| *PLAT* | plasminogen activator, tissue type | 1.8 | 1.9E-13 | 3.4E-10 |
| *PLBD1* | phospholipase B domain containing 1 | -1.5 | 4.1E-06 | 2.8E-05 |
| *PLCH2* | phospholipase C eta 2 | 1.7 | 8.4E-10 | 4.8E-08 |
| *PLD5* | phospholipase D family member 5 | -2.1 | 4.5E-08 | 8.2E-07 |
| *PLEKHG6* | pleckstrin homology and RhoGEF domain containing G6 | 1.5 | 3.3E-06 | 2.3E-05 |
| *PLLP* | plasmolipin | 1.5 | 9.7E-07 | 8.7E-06 |
| *PLXNA4* | plexin A4 | 2.6 | 1.9E-07 | 2.4E-06 |
| *POF1B* | premature ovarian failure, 1B | -1.5 | 1.6E-06 | 1.3E-05 |
| *POU3F2* | POU class 3 homeobox 2 | -3.6 | 2.7E-11 | 5.1E-09 |
| *PPL* | periplakin | 2.2 | 1.7E-10 | 1.6E-08 |
| *PPP1R1B* | protein phosphatase 1 regulatory inhibitor subunit 1B | 3.2 | 5.9E-10 | 3.7E-08 |
| *PPP1R3G* | protein phosphatase 1 regulatory subunit 3G | 2.3 | 4.3E-09 | 1.4E-07 |
| *PPP2R2C* | protein phosphatase 2 regulatory subunit Bgamma | -4.9 | 1.9E-13 | 3.4E-10 |
| *PREX2* | phosphatidylinositol-3,4,5-trisphosphate dependent Rac exchange factor 2 | -1.6 | 8.3E-07 | 7.7E-06 |
| *PRKXP1* | protein kinase, X-linked, pseudogene 1 | -1.5 | 6.6E-06 | 4.2E-05 |
| *PRR15* | proline rich 15 | 1.8 | 4.8E-08 | 8.6E-07 |
| *PTGER2* | prostaglandin E receptor 2 | 1.9 | 1.5E-09 | 6.9E-08 |

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|---|---|---|---|---|
| *PTGFRN* | prostaglandin F2 receptor inhibitor | -1.6 | 4.6E-10 | 3.2E-08 |
| *PTGS2* | prostaglandin-endoperoxide synthase 2 | 1.7 | 4.9E-07 | 5.1E-06 |
| *PTPN20* | protein tyrosine phosphatase, non-receptor type 20 | 1.8 | 5.1E-08 | 9.0E-07 |
| *PTPRG* | protein tyrosine phosphatase, receptor type G | -2.5 | 5.3E-09 | 1.7E-07 |
| *RAB39B* | RAB39B, member RAS oncogene family | -2.1 | 9.3E-08 | 1.4E-06 |
| *RASD1* | ras related dexamethasone induced 1 | 2.4 | 4.9E-09 | 1.6E-07 |
| *RASEF* | RAS and EF-hand domain containing | -1.8 | 3.6E-07 | 4.0E-06 |
| *RASL11A* | RAS like family 11 member A | 1.9 | 6.8E-11 | 9.2E-09 |
| *RBM11* | RNA binding motif protein 11 | -3.2 | 1.4E-10 | 1.5E-08 |
| *RBP4* | retinol binding protein 4 | 1.6 | 1.3E-11 | 3.2E-09 |
| *RCOR2* | REST corepressor 2 | 1.6 | 1.3E-06 | 1.1E-05 |
| *REG4* | regenerating family member 4 | 2.2 | 5.1E-09 | 1.6E-07 |
| *RFTN1* | raftlin, lipid raft linker 1 | -1.8 | 6.6E-09 | 1.9E-07 |
| *RGAG4* | retrotransposon gag domain containing 4 | -1.6 | 5.0E-06 | 3.3E-05 |
| *RGCC* | regulator of cell cycle | 1.7 | 3.3E-06 | 2.3E-05 |
| *RHOU* | ras homolog family member U | 1.7 | 1.5E-07 | 2.0E-06 |
| *RIMKLB* | ribosomal modification protein rimK-like family member B | -1.6 | 1.5E-08 | 3.6E-07 |
| *RNASEL* | ribonuclease L | -2.4 | 1.4E-09 | 6.6E-08 |
| *RNF128* | ring finger protein 128, E3 ubiquitin protein ligase | -3.8 | 1.5E-11 | 3.5E-09 |
| *RNF152* | ring finger protein 152 | -1.5 | 2.7E-06 | 2.0E-05 |
| *ROBO4* | roundabout guidance receptor 4 | -2.1 | 2.0E-11 | 4.1E-09 |
| *RPS6KA2* | ribosomal protein S6 kinase A2 | 1.5 | 6.3E-08 | 1.0E-06 |
| *RRAGD* | Ras related GTP binding D | -3.0 | 8.0E-11 | 1.0E-08 |
| *RUNDC3B* | RUN domain containing 3B | -1.8 | 2.8E-06 | 2.0E-05 |
| *RYR2* | ryanodine receptor 2 | -2.9 | 3.2E-09 | 1.2E-07 |
| *S100A2* | S100 calcium binding protein A2 | 2.1 | 5.4E-11 | 7.7E-09 |
| *S100A9* | S100 calcium binding protein A9 | -1.5 | 8.9E-06 | 5.3E-05 |
| *S100P* | S100 calcium binding protein P | 1.9 | 9.6E-07 | 8.6E-06 |
| *SCIN* | scinderin | 1.5 | 7.2E-07 | 6.8E-06 |
| *SCN3A* | sodium voltage-gated channel alpha subunit 3 | -1.9 | 2.4E-08 | 5.1E-07 |
| *SEMA3B* | semaphorin 3B | 1.9 | 3.4E-10 | 2.5E-08 |
| *SEMA6B* | semaphorin 6B | 2.3 | 5.3E-10 | 3.5E-08 |
| *SERPINA1* | serpin family A member 1 | -2.1 | 3.2E-08 | 6.4E-07 |
| *SERPINB2* | serpin family B member 2 | -2.9 | 2.4E-11 | 4.7E-09 |
| *SERTAD4* | SERTA domain containing 4 | -1.6 | 2.3E-06 | 1.7E-05 |
| *SESN3* | sestrin 3 | -2.6 | 5.4E-10 | 3.5E-08 |
| *SGK494* | uncharacterized serine/threonine-protein kinase SgK494 | -1.5 | 3.1E-08 | 6.2E-07 |
| *SH2D1B* | SH2 domain containing 1B | -2.2 | 1.5E-08 | 3.5E-07 |
| *SIRPB1* | signal regulatory protein beta 1 | -2.3 | 6.3E-11 | 8.7E-09 |
| *SIRPB2* | signal regulatory protein beta 2 | -1.6 | 3.2E-06 | 2.3E-05 |
| *SLC16A9* | solute carrier family 16 member 9 | 1.7 | 4.0E-11 | 6.5E-09 |
| *SLC1A3* | solute carrier family 1 member 3 | -3.7 | 4.2E-11 | 6.6E-09 |
| *SLC25A25-AS1* | SLC25A25 antisense RNA 1 | -1.5 | 3.2E-08 | 6.3E-07 |
| *SLC26A10* | solute carrier family 26 member 10 | -1.8 | 1.6E-10 | 1.6E-08 |
| *SLC26A5* | solute carrier family 26 member 5 | 1.5 | 1.4E-05 | 7.6E-05 |
| *SLC29A4* | solute carrier family 29 member 4 | 1.6 | 2.6E-08 | 5.4E-07 |

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|---|---|---|---|---|
| *SLC38A11* | solute carrier family 38 member 11 | 1.7 | 2.7E-07 | 3.2E-06 |
| *SLC44A5* | solute carrier family 44 member 5 | -2.1 | 6.3E-08 | 1.1E-06 |
| *SLC47A1* | solute carrier family 47 member 1 | 1.8 | 2.6E-07 | 3.1E-06 |
| *SLC6A11* | solute carrier family 6 member 11 | -2.3 | 4.9E-08 | 8.8E-07 |
| *SLC7A8* | solute carrier family 7 member 8 | -3.4 | 4.0E-10 | 2.8E-08 |
| *SLC9A2* | solute carrier family 9 member A2 | -3.6 | 2.1E-11 | 4.2E-09 |
| *SLFN13* | schlafen family member 13 | -2.3 | 2.9E-10 | 2.2E-08 |
| *SLITRK4* | SLIT and NTRK like family member 4 | -1.8 | 1.7E-09 | 7.5E-08 |
| *SOD3* | superoxide dismutase 3, extracellular | 1.7 | 7.5E-09 | 2.1E-07 |
| *SPDEF* | SAM pointed domain containing ETS transcription factor | 1.5 | 2.3E-10 | 2.0E-08 |
| *SPOCK3* | sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 3 | 1.5 | 7.9E-08 | 1.3E-06 |
| *SPTB* | spectrin beta, erythrocytic | -1.7 | 1.0E-09 | 5.5E-08 |
| *SRPX* | sushi repeat containing protein, X-linked | -1.5 | 1.2E-09 | 6.1E-08 |
| *ST6GAL1* | ST6 beta-galactoside alpha-2,6-sialyltransferase 1 | -3.8 | 2.8E-12 | 1.5E-09 |
| *ST6GAL2* | ST6 beta-galactoside alpha-2,6-sialyltransferase 2 | 2.0 | 9.2E-09 | 2.5E-07 |
| *ST6GALNAC2* | ST6 N-acetylgalactosaminide alpha-2,6-sialyltransferase 2 | 2.4 | 1.6E-09 | 7.2E-08 |
| *STARD8* | StAR related lipid transfer domain containing 8 | -1.8 | 1.7E-07 | 2.2E-06 |
| *STAT6* | signal transducer and activator of transcription 6 | 1.9 | 1.3E-11 | 3.2E-09 |
| *STC1* | stanniocalcin 1 | -1.5 | 4.5E-08 | 8.3E-07 |
| *STMN3* | stathmin 3 | 1.5 | 3.8E-08 | 7.3E-07 |
| *STOX2* | storkhead box 2 | -2.6 | 5.3E-09 | 1.7E-07 |
| *SUSD3* | sushi domain containing 3 | 1.8 | 1.9E-07 | 2.5E-06 |
| *SYT14* | synaptotagmin 14 | -2.2 | 1.0E-07 | 1.5E-06 |
| *TACSTD2* | tumor-associated calcium signal transducer 2 | -2.0 | 3.0E-09 | 1.1E-07 |
| *TAGLN3* | transgelin 3 | -1.5 | 5.2E-09 | 1.6E-07 |
| *TBC1D30* | TBC1 domain family member 30 | -1.8 | 7.1E-08 | 1.2E-06 |
| *TCN1* | transcobalamin 1 | -5.4 | 1.7E-13 | 3.4E-10 |
| *TDO2* | tryptophan 2,3-dioxygenase | -2.0 | 1.3E-06 | 1.1E-05 |
| *TENM1* | teneurin transmembrane protein 1 | -1.8 | 7.8E-09 | 2.2E-07 |
| *TFF1* | trefoil factor 1 | 3.6 | 5.2E-12 | 1.9E-09 |
| *TFF2* | trefoil factor 2 | 3.4 | 3.4E-10 | 2.5E-08 |
| *TGFBI* | transforming growth factor beta induced | -1.6 | 2.2E-07 | 2.7E-06 |
| *THBS1* | thrombospondin 1 | 1.5 | 5.5E-09 | 1.7E-07 |
| *TLR3* | toll like receptor 3 | -1.9 | 2.1E-07 | 2.6E-06 |
| *TMC6* | transmembrane channel like 6 | 1.7 | 2.4E-09 | 9.3E-08 |
| *TMEM108-AS1* | TMEM108 antisense RNA 1 | -3.1 | 9.8E-11 | 1.2E-08 |
| *TMEM229B* | transmembrane protein 229B | -1.5 | 8.4E-08 | 1.3E-06 |
| *TMEM27* | transmembrane protein 27 | -1.7 | 4.4E-11 | 6.8E-09 |
| *TMEM74* | transmembrane protein 74 | -1.8 | 1.7E-07 | 2.2E-06 |
| *TMOD2* | tropomodulin 2 | -2.3 | 3.0E-10 | 2.3E-08 |
| *TMPRSS15* | transmembrane protease, serine 15 | 2.4 | 2.8E-08 | 5.7E-07 |
| *TMPRSS3* | transmembrane protease, serine 3 | 2.1 | 3.3E-07 | 3.8E-06 |
| *TMX4* | thioredoxin related transmembrane protein 4 | -1.7 | 8.7E-12 | 2.6E-09 |

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|---|---|---|---|---|
| *TNFRSF11B* | tumor necrosis factor receptor superfamily member 11b | -1.9 | 8.9E-08 | 1.4E-06 |
| *TNFRSF14* | tumor necrosis factor receptor superfamily member 14 | 1.7 | 1.0E-08 | 2.7E-07 |
| *TNFSF9* | tumor necrosis factor superfamily member 9 | -1.5 | 1.5E-07 | 2.0E-06 |
| *TNXB* | tenascin XB | 2.6 | 2.8E-10 | 2.2E-08 |
| *TP53I11* | tumor protein p53 inducible protein 11 | 2.5 | 1.0E-08 | 2.7E-07 |
| *TPTE* | transmembrane phosphatase with tensin homology | -2.1 | 2.4E-08 | 5.1E-07 |
| *TSPEAR* | thrombospondin type laminin G domain and EAR repeats | 1.9 | 3.8E-08 | 7.2E-07 |
| *TSPOAP1* | TSPO associated protein 1 | 1.7 | 4.7E-07 | 4.9E-06 |
| *TTC3P1* | tetratricopeptide repeat domain 3 pseudogene 1 | -1.8 | 9.6E-08 | 1.5E-06 |
| *TTC9* | tetratricopeptide repeat domain 9 | 1.6 | 6.7E-07 | 6.5E-06 |
| *UBE2QL1* | ubiquitin conjugating enzyme E2 Q family like 1 | -2.4 | 1.3E-11 | 3.2E-09 |
| *UNC80* | unc-80 homolog, NALCN activator | -3.6 | 3.0E-11 | 5.4E-09 |
| *VASH1* | vasohibin 1 | -1.6 | 2.8E-10 | 2.2E-08 |
| *VAV3* | vav guanine nucleotide exchange factor 3 | -1.6 | 2.5E-07 | 3.0E-06 |
| *VSTM2L* | V-set and transmembrane domain containing 2 like | 2.0 | 1.2E-08 | 3.1E-07 |
| *VWA5A* | von Willebrand factor A domain containing 5A | -3.4 | 1.5E-10 | 1.6E-08 |
| *WDR72* | WD repeat domain 72 | -3.2 | 3.7E-11 | 6.2E-09 |
| *WNT2B* | Wnt family member 2B | -1.5 | 2.1E-06 | 1.7E-05 |
| *YPEL2* | yippee like 2 | -1.5 | 1.7E-07 | 2.3E-06 |
| *ZFPM2* | zinc finger protein, FOG family member 2 | -3.8 | 5.1E-12 | 1.9E-09 |
| *ZG16B* | zymogen granule protein 16B | 1.6 | 8.2E-08 | 1.3E-06 |
| *ZNF334* | zinc finger protein 334 | 3.1 | 4.5E-09 | 1.5E-07 |
| *ZNF415* | zinc finger protein 415 | 2.5 | 2.0E-10 | 1.8E-08 |
| *ZNF43* | zinc finger protein 43 | 2.0 | 2.5E-07 | 3.0E-06 |
| *ZNF467* | zinc finger protein 467 | 3.5 | 1.7E-10 | 1.6E-08 |
| *ZNF470* | zinc finger protein 470 | 2.5 | 5.3E-09 | 1.7E-07 |
| *ZNF521* | zinc finger protein 521 | -1.5 | 7.8E-07 | 7.3E-06 |
| *ZNF585B* | zinc finger protein 585B | -2.3 | 2.9E-08 | 5.9E-07 |
| *ZNF607* | zinc finger protein 607 | 2.4 | 3.0E-09 | 1.1E-07 |
| *ZNF702P* | zinc finger protein 702, pseudogene | 2.2 | 3.2E-09 | 1.2E-07 |
| *ZNF818P* | zinc finger protein 818, pseudogene | 2.0 | 1.5E-07 | 2.0E-06 |
| *ZNF85* | zinc finger protein 85 | 3.9 | 1.6E-11 | 3.5E-09 |

**Supplementary Table S4. Enrichment for GO terms in the category 'biological process' for genes upregulated in PC3-GHSROS cells (compared to empty-vector control).** $P \leq 0.01$, Fisher's exact test.

| GO term | Description | Count | % | Genes | Fold Enrichment | Fisher Exact P-value |
|---|---|---|---|---|---|---|
| GO:0010669 | epithelial structure maintenance | 4 | 2.6 | *MUC2, RBP4, MUC3A, TFF1* | 70 | 1.1E-07 |
| GO:0030277 | maintenance of gastrointestinal epithelium | 4 | 2.6 | *MUC2, RBP4, MUC3A, TFF1* | 70 | 1.1E-07 |
| GO:0070482 | response to oxygen levels | 9 | 5.9 | *PLAT, CAV1, CA9, PDGFA, OXTR, CD24, THBS1, SOD3, ANGPTL4* | 7 | 7.5E-06 |
| GO:0009725 | response to hormone stimulus | 13 | 8.5 | *RBP4, CAV1, PTGS2, PDGFA, FBP1, OXTR, NPY1R, ABCG1, CA9, PCSK9, CD24, TFF1, THBS1* | 4 | 4.4E-05 |
| GO:0001666 | response to hypoxia | 8 | 5.2 | *PLAT, CAV1, CA9, PDGFA, CD24, THBS1, SOD3, ANGPTL4* | 6 | 4.0E-05 |
| GO:0022600 | digestive system process | 5 | 3.3 | *MUC2, RBP4, MUC3A, OXTR, TFF1* | 16 | 1.6E-05 |
| GO:0009719 | response to endogenous stimulus | 13 | 8.5 | *RBP4, CAV1, PTGS2, PDGFA, FBP1, OXTR, NPY1R, ABCG1, CA9, PCSK9, CD24, TFF1, THBS1* | 3 | 1.2E-04 |
| GO:0048545 | response to steroid hormone stimulus | 9 | 5.9 | *CAV1, PTGS2, CA9, PDGFA, OXTR, TFF1, NPY1R, CD24, THBS1* | 5 | 8.6E-05 |
| GO:0043627 | response to estrogen stimulus | 7 | 4.6 |  | 7 | 6.1E-05 |
| GO:0008285 | negative regulation of cell proliferation | 12 | 7.8 | *MUC2, RBP4, CAV1, TP53I11, IFITM1, PTGS2, IGFBP6, SCIN, TNFRSF14, CD24, THBS1, IGFBP5* | 4 | 1.6E-04 |
| GO:0051241 | negative regulation of multicellular organismal process | 8 | 5.2 | *RBP4, CAV1, ACHE, PTGS2, PDGFA, PCSK9, CD24, THBS1* | 5 | 1.6E-04 |
| GO:0042493 | response to drug | 9 | 5.9 | *CAV1, PTGS2, CA9, PDGFA, LCK, OXTR, CDH1, CDH3, SLC47A1* | 4 | 2.1E-04 |
| GO:0032355 | response to estradiol stimulus | 5 | 3.3 | *PTGS2, PDGFA, OXTR, TFF1, NPY1R* | 10 | 1.5E-04 |
| GO:0007586 | digestion | 6 | 3.9 | *MUC2, RBP4, MUC3A, TFF2, OXTR, TFF1* | 7 | 2.2E-04 |
| GO:0042127 | regulation of cell proliferation | 17 | 11.1 | *MUC2, RBP4, CAV1, PTGER2, TP53I11, PTGS2, IFITM1, CXCL5, PDGFA, CRIP2, IGFBP6, TNFRSF14, STAT6, SCIN, CD24, THBS1, IGFBP5* | 2 | 1.2E-03 |

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|---|---|---|---|---|---|---|
| GO:0010033 | response to organic substance | 16 | 10.5 | *RBP4, CAV1, PTGS2, PDGFA, FBP1, OXTR, CDH1, NPY1R, ABCG1, STAT6, CA9, PCSK9, CREB3L1, CD24, TFF1, THBS1* | 2 | 1.3E-03 |
| GO:0031644 | regulation of neurological system process | 7 | 4.6 | *PLAT, ACHE, S100P, PTGS2, GRIN2D, OXTR, CALB1* | 5 | 6.2E-04 |
| GO:0050730 | regulation of peptidyl-tyrosine phosphorylation | 5 | 3.3 | *CAV1, PDGFA, TNFRSF14, ITGB2, CD24* | 8 | 4.5E-04 |
| GO:0007267 | cell-cell signaling | 14 | 9.2 | *PLAT, GUCA1B, ACHE, CXCL5, PDGFA, OXTR, ITGB2, NTSR1, GRIN2D, GRID2, CEACAM6, SEMA3B, CD24, GDF15* | 2 | 1.6E-03 |
| GO:0042632 | cholesterol homeostasis | 4 | 2.6 | *CAV1, PCSK9, CD24, ABCG1* | 11 | 4.4E-04 |
| GO:0055092 | sterol homeostasis | 4 | 2.6 | *CAV1, PCSK9, CD24, ABCG1* | 11 | 4.4E-04 |
| GO:0007155 | cell adhesion | 15 | 9.8 | *CLDN7, ACHE, CADM4, TNXB, ITGB4, ITGB2, CDH1, CDH3, PCDHGB2, COL5A1, JUP, CD24, ADAM8, THBS1, MUC5B* | 2 | 2.5E-03 |
| GO:0022610 | biological adhesion | 15 | 9.8 | *CLDN7, ACHE, CADM4, TNXB, ITGB4, ITGB2, CDH1, CDH3, PCDHGB2, COL5A1, JUP, CD24, ADAM8, THBS1, MUC5B* | 2 | 2.6E-03 |
| GO:0045907 | positive regulation of vasoconstriction | 3 | 2.0 | *CAV1, PTGS2, NPY1R* | 24 | 2.2E-04 |
| GO:0035249 | synaptic transmission, glutamatergic | 3 | 2.0 | *PLAT, GRIN2D, GRID2* | 23 | 2.8E-04 |
| GO:0044057 | regulation of system process | 9 | 5.9 | *PLAT, CAV1, ACHE, S100P, PTGS2, GRIN2D, OXTR, NPY1R, CALB1* | 3 | 2.7E-03 |
| GO:0048878 | chemical homeostasis | 12 | 7.8 | *RBP4, CAV1, LCK, GRID2, PCSK9, OXTR, PLLP, NPY1R, CD24, ABCG1, TMPRSS3, CKB* | 2 | 3.4E-03 |
| GO:0050804 | regulation of synaptic transmission | 6 | 3.9 | *PLAT, ACHE, S100P, PTGS2, OXTR, CALB1* | 5 | 1.8E-03 |
| GO:0042592 | homeostatic process | 15 | 9.8 | *RBP4, MUC2, CAV1, OXTR, NPY1R, TMPRSS3, ABCG1, CKB, MUC3A, LCK, GRID2, PCSK9, PLLP, CD24, TFF1* | 2 | 4.9E-03 |

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|---|---|---|---|---|---|---|
| GO:0055088 | lipid homeostasis | 4 | 2.6 | *CAV1, PCSK9, CD24, ABCG1* | 8 | 1.4E-03 |
| GO:0051969 | regulation of transmission of nerve impulse | 6 | 3.9 | *PLAT, ACHE, S100P, PTGS2, OXTR, CALB1* | 4 | 2.7E-03 |
| GO:0007610 | behavior | 11 | 7.2 | *S100P, PTGS2, CXCL5, PDGFA, PPP1R1B, GRIN2D, OXTR, ITGB2, NPY1R, NTSR1, CALB1* | 2 | 4.9E-03 |
| GO:0032570 | response to progesterone stimulus | 3 | 2.0 | *CAV1, OXTR, THBS1* | 16 | 8.4E-04 |
| GO:0016337 | cell-cell adhesion | 8 | 5.2 | *JUP, CLDN7, CDH1, ITGB2, CD24, ADAM8, CDH3, PCDHGB2* | 3 | 4.7E-03 |
| GO:0032101 | regulation of response to external stimulus | 6 | 3.9 | *CAV1, PTGS2, PDGFA, GRID2, CD24, THBS1* | 4 | 4.0E-03 |
| GO:0051050 | positive regulation of transport | 7 | 4.6 | *RBP4, CAV1, ACHE, SCIN, PCSK9, OXTR, CDH1* | 3 | 5.3E-03 |
| GO:0001894 | tissue homeostasis | 4 | 2.6 | *MUC2, RBP4, MUC3A, TFF1* | 7 | 3.0E-03 |
| GO:0048167 | regulation of synaptic plasticity | 4 | 2.6 | *PLAT, S100P, PTGS2, CALB1* | 7 | 3.1E-03 |
| GO:0033273 | response to vitamin | 4 | 2.6 | *RBP4, PTGS2, PDGFA, MEST* | 6 | 3.5E-03 |
| GO:0050865 | regulation of cell activation | 6 | 3.9 | *STAT6, PDGFA, LCK, TNFRSF14, CD24, THBS1* | 4 | 6.4E-03 |
| GO:0006873 | cellular ion homeostasis | 9 | 5.9 | *CAV1, LCK, GRID2, OXTR, PLLP, NPY1R, CD24, TMPRSS3, CKB* | 3 | 9.1E-03 |
| GO:0051480 | cytosolic calcium ion homeostasis | 5 | 3.3 | *CAV1, LCK, OXTR, NPY1R, CD24* | 4 | 5.2E-03 |
| GO:0007618 | mating | 3 | 2.0 | *PPP1R1B, PI3, OXTR* | 12 | 2.0E-03 |
| GO:0055082 | cellular chemical homeostasis | 9 | 5.9 | *CAV1, LCK, GRID2, OXTR, PLLP, NPY1R, CD24, TMPRSS3, CKB* | 3 | 1.0E-02 |
| GO:0001568 | blood vessel development | 7 | 4.6 | *PLAT, CAV1, PDGFA, CCBE1, THBS1, COL5A1, ANGPTL4* | 3 | 8.7E-03 |
| GO:0010648 | negative regulation of cell communication | 7 | 4.6 | *CBLC, CAV1, ACHE, PTGS2, STMN3, THBS1, IGFBP5* | 3 | 9.3E-03 |
| GO:0008544 | epidermis development | 6 | 3.9 | *PTGS2, PDGFA, PPL, CRABP2, GJB3, COL5A1* | 3 | 8.1E-03 |
| GO:0043588 | skin development | 3 | 2.0 | *PDGFA, GJB3, COL5A1* | 11 | 2.5E-03 |
| GO:0001944 | vasculature development | 7 | 4.6 | *PLAT, CAV1, PDGFA, CCBE1, THBS1, COL5A1, ANGPTL4* | 3 | 9.9E-03 |
| GO:0010038 | response to metal ion | 5 | 3.3 | *CAV1, PTGS2, TFF1, THBS1, SOD3* | 4 | 7.6E-03 |
| GO:0007270 | nerve-nerve synaptic transmission | 3 | 2.0 | *PLAT, GRIN2D, GRID2* | 10 | 3.1E-03 |

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|---|---|---|---|---|---|---|
| GO:0006875 | cellular metal ion homeostasis | 6 | 3.9 | *CAV1, LCK, OXTR, NPY1R, CD24, TMPRSS3* | 3 | 1.1E-02 |
| GO:0044092 | negative regulation of molecular function | 8 | 5.2 | *CBLC, CAV1, GNAI1, HR, PCSK9, NPY1R, NPR3, ANGPTL4* | 3 | 1.4E-02 |
| GO:0031667 | response to nutrient levels | 6 | 3.9 | *RBP4, CAV1, PTGS2, PDGFA, PCSK9, MEST* | 3 | 1.1E-02 |
| GO:0032526 | response to retinoic acid | 3 | 2.0 | *RBP4, PDGFA, MEST* | 10 | 3.7E-03 |

**Supplementary Table S5. Enrichment for GO terms in the category 'biological process' for genes downregulated in PC3-GHSROS cells (compared to empty-vector control).** $P \leq 0.01$, Fisher's exact test.

| GO term | Description | Count | % | Genes | Fold Enrichment | Fisher Exact *P*-value |
|---|---|---|---|---|---|---|
| GO:0007155 | cell adhesion | 22 | 1.1 | *MTSS1, COL21A1, ADAM23, NRXN3, LRRN2, NELL2, NLGN1, NFASC, LEF1, NEO1, MMRN1, CXADR, PCDH19, CDH12, LAMA1, SRPX, LAMC3, CD33, TGFBI, CNTN1, FCGBP, CXADRP2, EDA* | 3 | 5.8E-06 |
| GO:0022610 | biological adhesion | 22 | 1.1 | *MTSS1, COL21A1, ADAM23, NRXN3, LRRN2, NELL2, NLGN1, NFASC, LEF1, NEO1, MMRN1, CXADR, PCDH19, CDH12, LAMA1, SRPX, LAMC3, CD33, TGFBI, CNTN1, FCGBP, CXADRP2, EDA* | 3 | 6.0E-06 |
| GO:0007267 | cell-cell signaling | 16 | 0.8 | *AR, NRXN3, S100A9, NLGN1, CD70, FGF13, GAL, TNFSF9, SLC1A3, KCNN3, HTR7, CD33, DMD, TMOD2, STC1, PCSK5* | 2 | 7.6E-04 |
| GO:0000904 | cell morphogenesis involved in differentiation | 9 | 0.4 | *NOG, SLITRK4, SLC1A3, NRXN3, KIF5C, NFASC, EOMES, LEF1, EPHB2* | 3 | 1.3E-03 |
| GO:0000902 | cell morphogenesis | 11 | 0.5 | *LAMA1, NOG, SLITRK4, SLC1A3, NRXN3, DMD, KIF5C, NFASC, EOMES, LEF1, EPHB2* | 3 | 1.7E-03 |
| GO:0001655 | urogenital system development | 6 | 0.3 | *AGTR1, EYA1, AR, NOG, LEF1, PCSK5* | 5 | 1.2E-03 |
| GO:0043009 | chordate embryonic development | 10 | 0.5 | *EYA1, AR, NOG, CHD7, ARNT2,* | 3 | 3.2E-03 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | *EOMES, LEF1, AMOT, ZFPM2, PCSK5* | | |
| GO:0009792 | embryonic development ending in birth or egg hatching | 10 | 0.5 | *EYA1, AR, NOG, CHD7, ARNT2, EOMES, LEF1, AMOT, ZFPM2, PCSK5* | 3 | 3.4E-03 |
| GO:0032989 | cellular component morphogenesis | 11 | 0.5 | *LAMA1, NOG, SLITRK4, SLC1A3, NRXN3, DMD, KIF5C, NFASC, EOMES, LEF1, EPHB2* | 3 | 3.8E-03 |
| GO:0030509 | BMP signaling pathway | 4 | 0.2 | *MSX2, NOG, CHRDL1, BMP6* | 8 | 1.3E-03 |
| GO:0006928 | cell motion | 12 | 0.6 | *LAMA1, MTSS1, VAV3, NRXN3, KIF5C, S100A9, NFASC, AMOT, POU3F2, DNAH5, EPHB2, ARHGDIB* | 2 | 5.4E-03 |
| GO:0003013 | circulatory system process | 7 | 0.3 | *AGTR1, CHD7, HTR7, RYR2, AMOT, KCNJ12, PCSK5* | 3 | 4.0E-03 |
| GO:0008015 | blood circulation | 7 | 0.3 | *AGTR1, CHD7, HTR7, RYR2, AMOT, KCNJ12, PCSK5* | 3 | 4.0E-03 |
| GO:0048732 | gland development | 6 | 0.3 | *EYA1, AR, NOG, LEF1, POU3F2, EDA* | 4 | 3.4E-03 |
| GO:0001837 | epithelial to mesenchymal transition | 3 | 0.1 | *NOG, EOMES, LEF1* | 15 | 8.9E-04 |
| GO:0021545 | cranial nerve development | 3 | 0.1 | *SLC1A3, CHD7, EPHB2* | 15 | 1.1E-03 |
| GO:0030182 | neuron differentiation | 11 | 0.5 | *SLITRK4, SLC1A3, MCOLN3, NRXN3, DGKG, DMD, KIF5C, MAP2, NFASC, POU3F2, EPHB2* | 2 | 7.9E-03 |
| GO:0001822 | kidney development | 5 | 0.2 | *AGTR1, EYA1, NOG, LEF1, PCSK5* | 5 | 3.8E-03 |
| GO:0001501 | skeletal system development | 9 | 0.4 | *MSX2, EYA1, TNFRSF11B, NOG, CHD7, CHRDL1, STC1, PCSK5, BMP6* | 3 | 7.8E-03 |
| GO:0035108 | limb morphogenesis | 5 | 0.2 | *MSX2, NOG, CHD7, LEF1, PCSK5* | 5 | 4.3E-03 |
| GO:0035107 | appendage morphogenesis | 5 | 0.2 | *MSX2, NOG, CHD7, LEF1, PCSK5* | 5 | 4.3E-03 |

| | | | | | | |
|---|---|---|---|---|---|---|
| GO:0048736 | appendage development | 5 | 0.2 | *MSX2, NOG, CHD7, LEF1, PCSK5* | 4 | 5.1E-03 |
| GO:0060173 | limb development | 5 | 0.2 | *MSX2, NOG, CHD7, LEF1, PCSK5* | 4 | 5.1E-03 |
| GO:0043627 | response to estrogen stimulus | 5 | 0.2 | *TNFRSF11B, ARNT2, ANGPT1, SERPINA1, GAL* | 4 | 5.6E-03 |
| GO:0021675 | nerve development | 3 | 0.1 | *SLC1A3, CHD7, EPHB2* | 11 | 2.4E-03 |

**Supplementary Table S6. Oncomine concepts analysis of positively and negatively correlated PC3-*GHSROS* gene signature.** Red: positively correlated gene signature; Black: negatively correlated gene signature. $P \leq 0.01$, Fisher's exact test.

| Concept 1 ID | Concept 1 Name | Concept 2 ID | Concept 2 Name | P-value | Odds Ratio | Overlap Size |
|---|---|---|---|---|---|---|
| C41610 | PC3 GHSROS downregulated gene list | 17697 | Cancer Type: Prostate Cancer - Top 10% Over-expressed (Bittner Multi-cancer) | 2.17E-08 | 3.7 | 32 |
| C41610 | PC3 GHSROS downregulated gene list | 122189617 | Prostate Cancer - Metastasis - Top 10% Under-expressed (Taylor Prostate 3) | 3.14E-06 | 3.1 | 28 |
| C41610 | PC3 GHSROS downregulated gene list | 122210891 | Cancer Type: Prostate Cancer - Top 5% Under-expressed (Garnett CellLine) | 3.94E-06 | 4.5 | 16 |
| C41610 | PC3 GHSROS downregulated gene list | 122208916 | Cancer Type: Prostate Cancer - Top 5% Under-expressed (Barretina CellLine) | 3.55E-05 | 3.5 | 17 |
| C41610 | PC3 GHSROS downregulated gene list | 122213069 | Prostate Cancer - Metastasis - Top 5% Under-expressed (Grasso Prostate) | 9.84E-05 | 3.3 | 16 |
| C41610 | PC3 GHSROS downregulated gene list | 28483 | Prostate Cancer - Metastasis - Top 5% Under-expressed (Varambally Prostate) | 4.13E-04 | 3 | 15 |
| C41610 | PC3 GHSROS downregulated gene list | 23100 | Prostate Cancer - Metastasis - Top 10% Under-expressed (LaTulippe Prostate) | 4.20E-04 | 3 | 16 |
| C41610 | PC3 GHSROS downregulated gene list | 28344 | Prostate Cancer - Metastasis - Top 10% Under-expressed (Vanaja Prostate) | 0.001 | 2.3 | 21 |
| 17697 | Cancer Type: Prostate Cancer - Top 10% Over-expressed (Bittner Multi-cancer) | 122189617 | Prostate Cancer - Metastasis - Top 10% Under-expressed (Taylor Prostate 3) | 1.55E-120 | 4.2 | 559 |
| 17697 | Cancer Type: Prostate Cancer - Top 10% Over-expressed (Bittner Multi-cancer) | 122213069 | Prostate Cancer - Metastasis - Top 5% Under-expressed (Grasso Prostate) | 1.33E-120 | 6.4 | 356 |
| 17697 | Cancer Type: Prostate Cancer - Top 10% Over-expressed (Bittner Multi-cancer) | 28483 | Prostate Cancer - Metastasis - Top 5% Under-expressed (Varambally Prostate) | 3.67E-134 | 6.8 | 377 |
| 17697 | Cancer Type: Prostate Cancer - Top 10% Over-expressed (Bittner Multi-cancer) | 23100 | Prostate Cancer - Metastasis - Top 10% Under-expressed (LaTulippe Prostate) | 1.22E-54 | 4.1 | 250 |
| 17697 | Cancer Type: Prostate Cancer - Top 10% Over-expressed (Bittner Multi-cancer) | 28344 | Prostate Cancer - Metastasis - Top 10% Under-expressed (Vanaja Prostate) | 3.10E-189 | 6.1 | 619 |
| 122189617 | Prostate Cancer - Metastasis - Top 10% Under-expressed (Taylor Prostate 3) | 122210891 | Cancer Type: Prostate Cancer - Top 5% Under-expressed (Garnett CellLine) | 1.63E-12 | 2.1 | 143 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 122189617 | Prostate Cancer - Metastasis - Top 10% Under-expressed (Taylor Prostate 3) | 122208916 | Cancer Type: Prostate Cancer - Top 5% Under-expressed (Barretina CellLine) | 1.94E-26 | 2.5 | 218 |
| 122189617 | Prostate Cancer - Metastasis - Top 10% Under-expressed (Taylor Prostate 3) | 122213069 | Prostate Cancer - Metastasis - Top 5% Under-expressed (Grasso Prostate) | 6.85E-300 | 15.4 | 554 |
| 122189617 | Prostate Cancer - Metastasis - Top 10% Under-expressed (Taylor Prostate 3) | 28483 | Prostate Cancer - Metastasis - Top 5% Under-expressed (Varambally Prostate) | 1.26E-181 | 8.7 | 446 |
| 122189617 | Prostate Cancer - Metastasis - Top 10% Under-expressed (Taylor Prostate 3) | 23100 | Prostate Cancer - Metastasis - Top 10% Under-expressed (LaTulippe Prostate) | 7.69E-149 | 8.1 | 422 |
| 122189617 | Prostate Cancer - Metastasis - Top 10% Under-expressed (Taylor Prostate 3) | 28344 | Prostate Cancer - Metastasis - Top 10% Under-expressed (Vanaja Prostate) | 1.66E-141 | 4.8 | 574 |
| 122210891 | Cancer Type: Prostate Cancer - Top 5% Under-expressed (Garnett CellLine) | 122208916 | Cancer Type: Prostate Cancer - Top 5% Under-expressed (Barretina CellLine) | 6.57E-135 | 13.7 | 232 |
| 122210891 | Cancer Type: Prostate Cancer - Top 5% Under-expressed (Garnett CellLine) | 122213069 | Prostate Cancer - Metastasis - Top 5% Under-expressed (Grasso Prostate) | 4.37E-06 | 1.9 | 65 |
| 122210891 | Cancer Type: Prostate Cancer - Top 5% Under-expressed (Garnett CellLine) | 23100 | Prostate Cancer - Metastasis - Top 10% Under-expressed (LaTulippe Prostate) | 3.26E-04 | 1.6 | 73 |
| 122208916 | Cancer Type: Prostate Cancer - Top 5% Under-expressed (Barretina CellLine) | 122213069 | Prostate Cancer - Metastasis - Top 5% Under-expressed (Grasso Prostate) | 9.74E-20 | 2.9 | 118 |
| 122208916 | Cancer Type: Prostate Cancer - Top 5% Under-expressed (Barretina CellLine) | 28483 | Prostate Cancer - Metastasis - Top 5% Under-expressed (Varambally Prostate) | 1.44E-09 | 2.1 | 93 |
| 122208916 | Cancer Type: Prostate Cancer - Top 5% Under-expressed (Barretina CellLine) | 23100 | Prostate Cancer - Metastasis - Top 10% Under-expressed (LaTulippe Prostate) | 1.04E-05 | 1.7 | 87 |
| 122213069 | Prostate Cancer - Metastasis - Top 5% Under-expressed (Grasso Prostate) | 28483 | Prostate Cancer - Metastasis - Top 5% Under-expressed (Varambally Prostate) | 1.06E-199 | 14.8 | 332 |
| 122213069 | Prostate Cancer - Metastasis - Top 5% Under-expressed (Grasso Prostate) | 23100 | Prostate Cancer - Metastasis - Top 10% Under-expressed (LaTulippe Prostate) | 5.82E-85 | 7.7 | 221 |
| 122213069 | Prostate Cancer - Metastasis - Top 5% Under-expressed (Grasso Prostate) | 28344 | Prostate Cancer - Metastasis - Top 10% Under-expressed (Vanaja Prostate) | 1.21E-75 | 4.7 | 288 |
| 28483 | Prostate Cancer - Metastasis - Top 5% | 23100 | Prostate Cancer - Metastasis - Top 10% | 1.59E-59 | 5.7 | 192 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Under-expressed (Varambally Prostate) | | Under-expressed (LaTulippe Prostate) | | | |
| 28483 | Prostate Cancer - Metastasis - Top 5% Under-expressed (Varambally Prostate) | 28344 | Prostate Cancer - Metastasis - Top 10% Under-expressed (Vanaja Prostate) | 3.84E-80 | 4.7 | 302 |
| 23100 | Prostate Cancer - Metastasis - Top 10% Under-expressed (LaTulippe Prostate) | 28344 | Prostate Cancer - Metastasis - Top 10% Under-expressed (Vanaja Prostate) | 2.79E-54 | 4 | 258 |
| C41610 | PC3 GHSROS downregulated gene list | 122199554 | Prostate Carcinoma - Dead at 3 Years - Top 10% Under-expressed (Setlur Prostate) | 0.003 | 2.9 | 12 |
| C41610 | PC3 GHSROS downregulated gene list | 122189630 | Prostate Carcinoma - Advanced Gleason Score - Top 5% Under-expressed (Taylor Prostate 3) | 0.004 | 2.5 | 13 |
| C41610 | PC3 GHSROS downregulated gene list | 122189606 | Prostate Carcinoma - Recurrence at 5 Years - Top 5% Under-expressed (Taylor Prostate 3) | 0.004 | 2.5 | 13 |
| 122199554 | Prostate Carcinoma - Dead at 3 Years - Top 10% Under-expressed (Setlur Prostate) | 122189630 | Prostate Carcinoma - Advanced Gleason Score - Top 5% Under-expressed (Taylor Prostate 3) | 3.07E-37 | 4.7 | 141 |
| 122199554 | Prostate Carcinoma - Dead at 3 Years - Top 10% Under-expressed (Setlur Prostate) | 122189606 | Prostate Carcinoma - Recurrence at 5 Years - Top 5% Under-expressed (Taylor Prostate 3) | 3.29E-24 | 3.4 | 130 |
| 122189630 | Prostate Carcinoma - Advanced Gleason Score - Top 5% Under-expressed (Taylor Prostate 3) | 122189606 | Prostate Carcinoma - Recurrence at 5 Years - Top 5% Under-expressed (Taylor Prostate 3) | 0.00E+00 | 26.5 | 493 |
| C41601 | PC3 GHSROS upregulated gene list_RNAseq | 29459 | Prostate Carcinoma vs. Normal - Top 1% Over-expressed (Yu Prostate) | 4.78E-04 | 12.5 | 4 |
| C41602 | PC3 GHSROS upregulated gene list_RNAseq | 122189633 | Prostate Carcinoma - Advanced N Stage - Top 5% Over-expressed (Taylor Prostate 3) | 0.002 | 3.5 | 9 |
| C41603 | PC3 GHSROS upregulated gene list_RNAseq | 17807 | Prostate Adenocarcinoma - Advanced Stage - Top 1% Over-expressed (Bittner Prostate) | 0.003 | 7.5 | 4 |
| C41604 | PC3 GHSROS upregulated gene list_RNAseq | 23091 | Prostate Carcinoma vs. Normal - Top 10% Over-expressed (LaTulippe Prostate) | 0.003 | 3.4 | 10 |
| 29459 | Prostate Carcinoma vs. Normal - Top 1% Over-expressed (Yu Prostate) | 17807 | Prostate Adenocarcinoma - Advanced Stage - Top 1% Over-expressed (Bittner Prostate) | 3.33E-04 | 7.2 | 6 |
| 29459 | Prostate Carcinoma vs. Normal - Top 1% Over-expressed (Yu Prostate) | 23091 | Prostate Carcinoma vs. Normal - Top 10% Over-expressed (LaTulippe Prostate) | 5.61E-07 | 3.8 | 25 |
| 122189633 | Prostate Carcinoma - Advanced N Stage - Top 5% Over- | 23091 | Prostate Carcinoma vs. Normal - Top 10% Over- | 3.73E-06 | 2 | 61 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | expressed (Taylor Prostate 3) | | expressed (LaTulippe Prostate) | | | |
| 17807 | Prostate Adenocarinoma - Advanced Stage - Top 1% Over-expressed (Bittner Prostate) | 23091 | Prostate Carcinoma vs. Normal - Top 10% Over-expressed (LaTulippe Prostate) | 6.07E-04 | 2.5 | 20 |

**Supplementary Table S7. Differentially expressed genes in PC3-GHSROS and LNCaP-GHSROS cells compared to the Grasso Oncomine dataset.** The Grasso dataset includes 59 localized and 35 metastatic prostate tumors. Red: higher expression in metastatic tumors; Black: lower expression in metastatic tumors. Fold-changes are $\log_2$ transformed; *Q*-value denotes the false discovery rate (FDR; Benjamini-Hochberg)-adjusted *P*-value.

| ***Gene Symbol*** | **Gene Name** | **Reporter ID** | **Fold Change** | ***P*-value** | ***Q*-value** |
|---|---|---|---|---|---|
| *AASS* | aminoadipate-semialdehyde synthase | A_23_P8754 | -1.5 | 6.0E-03 | 2.5E-02 |
| *CHRDL1* | chordin-like 1 | A_24_P168925 | -48.0 | 3.6E-21 | 2.9E-18 |
| *CNTN1* | contactin 1 | A_23_P204541 | -19.3 | 1.6E-16 | 3.4E-14 |
| *DIRAS1* | DIRAS family, GTP-binding RAS-like 1 | A_23_P386942 | 2.2 | 3.5E-07 | 4.4E-06 |
| *FBXL16* | F-box and leucine-rich repeat protein 16 | A_23_P406385 | 6.0 | 2.5E-08 | 4.7E-07 |
| *IFI16* | interferon, gamma-inducible protein 16 | A_23_P160025 | -2.2 | 1.1E-05 | 8.8E-05 |
| *MUM1L1* | melanoma associated antigen (mutated) 1-like 1 | A_23_P73571 | -8.8 | 7.9E-11 | 2.5E-09 |
| *TFF2* | trefoil factor 2 | A_23_P57364 | 1.3 | 6.4E-04 | 3.1E-03 |
| *TP53I11* | tumor protein p53 inducible protein 11 | A_23_P150281 | 1.5 | 4.8E-05 | 3.1E-04 |
| *ZNF467* | zinc finger protein 467 | A_23_P59470 | 3.5 | 5.4E-07 | 6.3E-06 |

**Supplementary Table S8. Differentially expressed genes in PC3-GHSROS and LNCaP-GHSROS cells compared to the Taylor Oncomine dataset.** The Taylor dataset includes 123 localized and 35 metastatic prostate tumors. Red: higher expression in metastatic tumors; Black: lower expression in metastatic tumors. Fold-changes are $\log_2$ transformed; *Q*-value denotes the false discovery rate (FDR; Benjamini-Hochberg)-adjusted *P*-value.

| ***Gene Symbol*** | **Gene Name** | **Reported ID** | **Fold Change** | ***P*-value** | ***Q*-value** |
|---|---|---|---|---|---|
| *AASS* | aminoadipate-semialdehyde synthase | 10093 | -1.5 | 3.9E-05 | 1.7E-03 |
| *CHRDL1* | chordin-like 1 | 20828 | -5.0 | 1.6E-18 | 1.3E-15 |
| *CNTN1* | contactin 1 | 6403 | -3.5 | 4.2E-22 | 6.8E-19 |
| *DIRAS1* | DIRAS family, GTP-binding RAS-like 1 | 20799 | 1.1 | 1.2E-02 | 1.4E-01 |
| *FBXL16* | F-box and leucine-rich repeat protein 16 | 21824 | 1.1 | 8.0E-03 | 1.2E-01 |
| *IFI16* | interferon, gamma-inducible protein 16 | 9878 | -1.5 | 8.4E-05 | 3.3E-03 |
| *MUM1L1* | melanoma associated antigen (mutated) 1-like 1 | 21313 | -1.3 | 1.0E-02 | 1.3E-01 |
| *TFF2* | trefoil factor 2 | 9774 | 1.1 | 3.6E-02 | 2.4E-01 |
| *TP53I11* | tumor protein p53 inducible protein 11 | 4038 | 1.1 | 2.2E-02 | 1.9E-01 |
| *ZNF467* | zinc finger protein 467 | 25037 | 1.3 | 2.8E-04 | 1.7E-02 |

**Supplementary Table S9. Disease-free survival (DFS) analysis of differentially expressed genes (in PC3-GHSROS cells, LNCaP-GHSROS cells and clinical metastatic tumors) in human datasets.** Patients, in the Taylor (*N*=150; *n*=123 localized and *n*=27 metastatic tumors) and TCGA-PRAD (*N*=489; localized tumors) datasets, were stratified into two groups by *k*-means clustering of gene expression (*k*=2). The log-rank test, was used to assign statistical significance, with $P \leq 0.05$ considered significant (shown in bold). The Cox *P*-value and absolute hazard ratio (HR) between *k*-means cluster 1 and 2 for each gene are indicated. Overall median disease-free survival (DFS) in days are indicated for each cluster.

| | **Taylor (*N*=150)** | | | | | **TCGA-PRAD (*N*=489)** | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **gene** | **log-rank *P*** | **Cox *P*** | **Absolute HR** | **Overall median DFS cluster 1** | **Overall median DFS cluster 2** | **log-rank *P*** | **Cox *P*** | **Absolute HR** | **Overall median DFS cluster 1** | **Overall median DFS cluster 2** |
| *ZNF467* | **0.0027** | **0.0039** | 2.7 | 174 | 871 | **0.000050** | **0.000026** | 2.5 | 546 | 685 |
| *CHRDL1* | **0.0047** | **0.0062** | 2.5 | 840 | 402 | **0.0079** | **0.0071** | 1.8 | 649 | 640 |
| *FBXL16* | **0.017** | **0.020** | 2.2 | 300 | 871 | 0.089 | 0.087 | 1.5 | 627 | 663 |
| *DIRAS1* | 0.09 | 0.099 | 1.7 | 709 | 329 | **0.012** | **0.011** | 1.7 | 425 | 723 |
| *TFF2* | 0.11 | 0.11 | 1.7 | 840 | 125 | 0.84 | 0.089 | 1.1 | 648 | 896 |
| *CNTN1* | 0.13 | 0.14 | 1.6 | 701 | 457 | 0.10 | 0.094 | 1.4 | 627 | 691 |
| *IFI16* | 0.27 | 0.28 | 1.5 | 579 | 181 | 0.95 | 0.95 | 1.0 | 671 | 648 |
| *AASS* | 0.62 | 0.63 | 1.2 | 843 | 348 | 0.35 | 0.35 | 1.2 | 552 | 697 |
| *MUM1L1* | 0.78 | 0.78 | 1.1 | 472 | 676 | 0.14 | 0.14 | 1.4 | 765 | 426 |
| *TP53I11* | 0.98 | 0.98 | 1.0 | 122 | 843 | 0.57 | 0.57 | 1.1 | 533 | 751 |

## Supplementary Table S10. Overview of human Affymetrix exon array datasets interrogated.

| resource | unique ID | tissue/cell type | type | N | reference |
|---|---|---|---|---|---|
| ArrayExpress | E-MEXP-2644 | lung (18 benign and 18 cancer) | tissues | 36 | [86] |
| ArrayExpress | E-MEXP-3931 | THP1 (acute monocytic leukemia) | cell lines | 12 | [87] |
| ArrayExpress | E-MTAB-1273 | induced pluripotent stem (iPS) cells derived from glioblastoma-derived neural stem cells | primary cells | 16 | [88] |
| ArrayExpress | E-MTAB-2471 | large B-cell lymphoma | tissues | 16 | [89] |
| Affymetrix web site | goo.gl/rBWrFv | breast, cerebellum, heart, kidney, liver, muscle, pancreas, prostate, spleen, testes, thyroid, mixture | tissues | 53 | - |
| Affymetrix web site | goo.gl/Yack5K | colon cancer (10 benign and 10 cancer) | tissues | 20 | - |
| GEO | GSE11967 | thymus (4 benign and 4 cancer) | tissues | 8 | [90] |
| GEO | GSE16732 | breast (cancer) | cell lines | 41 | [91] |
| GEO | GSE18927 | NIH Epigenomics Roadmap Initiative (stem cells and primary *ex vivo* tissues) | tissues and primary cells | 99 | [92,93,94,94,96,97] |
| GEO | GSE19090 | ENCODE Project Consortium (84 cell lines and primary cells) | cell lines and primary cells | 182 | [98, 99] |
| GEO | GSE19891 | HeLa (cervical cancer) | cell lines | 15 | [100] |
| GEO | GSE20342 | MCF7 (breast cancer) | cell lines | 32 | [101] |
| GEO | GSE20567 | HL60, THP-1, U937 (myeloid leukemia) | cell lines | 17 | [102] |
| GEO | GSE21034 | prostate (cancer) | tissues | 310 | [24] |
| GEO | GSE21163 | pancreas (1 benign and 6 cancer) | cell lines | 22 | [103, 104] |
| GEO | GSE21337 | acute myeloid leukemia | tissues | 64 | [105] |
| GEO | GSE21840 | MCF7 (breast cancer) | cell lines | 6 | [106, 107] |
| GEO | GSE23361 | lung (cancer) | tissues | 12 | [108] |
| GEO | GSE23514 | HeLa S3 (cervical cancer) | cell lines | 12 | [109] |
| GEO | GSE23768 | breast, lung, ovarian and prostate cancer | tissues | 153 | [110] |
| GEO | GSE24778 | K562 (chronic myelogenous leukemia) | cell lines | 10 | [111] |
| GEO | GSE29682 | breast, central nervous system, colon, leukemia, melanoma, lung, ovary, prostate, kidney (cancer) | cell lines | 178 | [112, 113] |
| GEO | GSE29778 | HEK293 (embryonic kidney) | cell lines | 12 | [114] |
| GEO | GSE30472 | brain (cancer; glioma) | tissues | 55 | [115] |
| GEO | GSE30521 | prostate (benign and cancer) | tissues | 23 | [116] |
| GEO | GSE30727 | stomach (cancer) | tissues | 60 | [117] |
| GEO | GSE32875 | LNCaP (prostate cancer) | cell lines | 8 | [118] |
| GEO | GSE37138 | lung (cancer) | tissues | 117 | [119] |
| GEO | GSE40871 | acute myeloid leukemia | primary cells | 67 | [120] |
| GEO | GSE43107 | brain (cancer; glioma) | tissues | 95 | [121, 122] |
| GEO | GSE43754 | bone marrow stem and progenitor cells (chronic myeloid leukemia) | cells | 20 | [123] |
| GEO | GSE43830 | WI38 (fetal lung fibroblasts) | cell lines | 6 | [124] |
| GEO | GSE45379 | HeLa (cervical cancer) | cell lines | 6 | - |
| GEO | GSE46691 | prostate (cancer) | tissues | 545 | [125, 126] |

| | | | | | |
|---|---|---|---|---|---|
| GEO | GSE47032 | kidney (cancer) | tissues | 40 | [127] |
| GEO | GSE53405 | MCF10A (benign) | cell lines | 26 | - |
| GEO | GSE57076 | THP1 (acute monocytic leukemia) | cell lines | 7 | [128] |
| GEO | GSE57933 | bladder (cancer) | tissues | 199 | [129] |
| GEO | GSE58598 | breast (cancer) | tissues | 10 | - |
| GEO | GSE62116 | prostate (cancer) | tissues | 235 | [126, 130, 131] |
| GEO | GSE62667 | prostate (cancer) | tissues | 182 | [132] |
| GEO | GSE67312 | bladder (cancer) | primary xenografts | 10 | [133] |
| GEO | GSE68591 | sarcoma (84 cancer) and 5 benign | cell lines | 75 | [134] |
| GEO | GSE71010 | neutrophils (cystic fibrosis and healthy controls) | cells | 93 | [135] |
| GEO | GSE72291 | prostate (cancer) | tissues | 139 | [136] |
| GEO | GSE78246 | brain (schizophrenia, bipolar disorder, major depressive disorder, and controls) | tissues | 20 | [137] |
| GEO | GSE79956 | prostate (cancer) | tissues | 211 | - |
| GEO | GSE79957 | prostate (cancer) | tissues | 260 | - |
| GEO | GSE80683 | prostate (cancer) | tissues | 17 | - |
| GEO | GSE9342 | T-cell acute lymphoblastic leukaemia | cell lines | 17 | - |
| GEO | GSE9385 | brain (26 glioblastomas, 22 oligodendrogliomas and 6 control brain samples) | tissues | 55 | [138] |

## Supplementary Table S11. Primers used in this study.

| **Primer** | **Gene name** | **Primer sequence (5'-3')** |
|---|---|---|
| *GHSROS* | growth hormone secretagogue receptor opposite strand | ACATTCAGCAAATCCAGTTAATGACA |
| | | CGACTGGAGCACGAGGACACTTGA |
| *GHSROS*-RT linker | | CGACTGGAGCACGAGGACACTGACAACAGAATTCACTACTTCCCCAAA |
| *AR* | androgen receptor | CTGGACACGACAACAACCAG |
| | | CAGATCAGGGGCGAAGTAGA |
| *NTSR1* | neurotensin receptor 1 (high affinity) | Proprietary – QIAGEN QuantiTect Primer Assay QT00018494 |
| *TFF1* | trefoil factor 1 | Proprietary - QIAGEN QuantiTect Primer Assay QT00209608 |
| *TFF2* | trefoil factor 2 | Proprietary - QIAGEN QuantiTect Primer Assay QT00001785 |
| *MUC5B* | mucin 5B, oligomeric mucus/ gel-forming | Proprietary - QIAGEN QuantiTect Primer Assay QT01322818 |
| *PPP2R2C* | protein phosphatase 2, regulatory subunit B, gamma | Proprietary - QIAGEN QuantiTect Primer Assay QT01006383 |
| *RPL32* | ribosomal protein L32 (housekeeping gene) | CCCCTTGTGAAGCCCAAGA |
| | | GACTGGTGCCGGATGAACTT |
| *ACTB* | actin beta (housekeeping gene) | ACTCTTCCAGCCTTCCTTCCT |
| | | CAGTGATCTCCTTCTGCATCCT |
| *GAPDH* | glyceraldehyde-3-phosphate dehydrogenase (housekeeping gene) | AATCCCATCACCATCTTCCA |
| | | AAATGAGCCCCAGCCTTC |
| *HPRT* | hypoxanthine phosphoribosyltransferase 1 (housekeeping gene) | CAGTCAACGGGGGACATAAA |
| | | AGAGGTCCTTTTCACCAGCAA |

**Supplementary Dataset 1. Differentially expressed genes in LNCaP-GHSROS cells. Compared to empty vector control**. Red: higher expression in LNCaP-GHSROS cells; Black: lower expression in LNCaP-GHSROS cells. Fold-changes are $\log_2$ transformed; *Q*-value denotes the false discovery rate (FDR; Benjamini-Hochberg)-adjusted *P*-value (cutoff $\leq 0.05$).

(provided in a separate file).

**Supplementary Dataset 2. Enrichment for GO terms in the category ‘biological process’ for genes upregulated in LNCaP-GHSROS cells (compared to empty-vector control).** $P \leq 0.01$, Fisher's exact test.

(provided in a separate file).

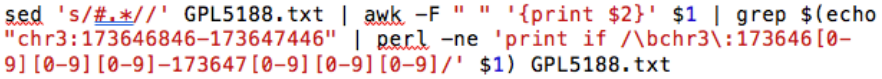
**Supplementary Dataset 3. Enrichment for GO terms in the category ‘biological process’ for genes downregulated in LNCaP-GHSROS cells (compared to empty-vector control).** $P \leq 0.01$, Fisher's exact test.

(provided in a separate file).

## SUPPLEMENTARY METHODS

### Identification of *GHSROS* transcription in exon array datasets

To assess *GHSROS* expression, we interrogated Affymetrix GeneChip Exon 1.0 ST arrays, strand-specific oligonucleotide microarrays with probes for known and predicted exons (hereafter termed exon arrays). Exon arrays are comparable to RNA-seq in experiments aimed at assessing exon expression (*i.e.* gene isoforms) and suitable for experiments where the exon of interest is known[139, 140]. In the Exon 1.0 ST array, known (genes and ESTs) and putative exons are combined to form 'transcript clusters', with each exon defined as a probe set (typically, a set of 2-4 probes). By combining all probe sets, the expression of a transcript cluster (known or putative gene) can be measured (see https://goo.gl/4RSTG3). To identify probe set(s) corresponding to *GHSROS*, we downloaded the Exon 1.0 ST probe annotation file from NCBI (NCBI Gene Expression Omnibus (GEO) accession no. GPL5188). Full-length *GHSROS* (1.1 kb) was aligned to the human genome (NCBI36/hg18; March 2006 assembly) to generate genomic coordinates compatible with the probe file (chr3:173,646,439-173,647,538). Next, the probe annotation file (GPL5188) was interrogated to reveal probe sets spanning *GHSROS* by entering the following command in a UNIX terminal window:



```
sed 's/#.*//' GPL5188.txt | awk -F " " '{print $2}' $1 | grep $(echo
"chr3:173646846-173647446" | perl -ne 'print if /\bchr3\:173646[0-
9][0-9][0-9]-173647[0-9][0-9][0-9]/' $1) GPL5188.txt
```

This revealed a probe set, 2652604, consisting of 4 probes complementary to *GHSROS*.

Cell and tissue exon array data were downloaded from NCBI GEO[141], EBI ArrayExpress[142] and the Affymetrix web site (see Supplementary Table S10). GEO datasets were bulk-downloaded using v3.6.2.117442 of the Aspera Connect Linux software (Aspera, Emeryville, CA, USA). In total, 3,924 samples were downloaded, corresponding to ~46% of all exon array data deposited in the NCBI GEO database. Arrays (individual CEL files) were normalized (output on a $\log_2$ scale, centered at 0) using the *SCAN* function in the R package 'SCAN.UPC'[143, 144]. SCAN normalizes each array (sample) individually by removing background noise (probe- and array-specific) data from within the array. Next, arrays were interrogated using the *UPC* function in 'SCAN.UPC'. UPC outputs standardized expression values (UPC value), ranging from 0 to 1, which indicate whether a gene is actively transcribed in a sample of interest: higher values indicate that a gene is 'active'[143]. UPC scores are platform-independent and allow cross-experimental and cross-platform integration.

### Evaluation of *GHSR/GHSROS* transcription in deep RNA-seq dataset

It has been estimated that reliable detection of low abundance transcripts in humans warrants very deep sequencing (> 200 million reads per sample[145]) – far beyond most current datasets. To illustrate, we considered the expression of *GHSR*/*GHSROS* in a comparable clinical dataset. Publicly available RNA-seq data (NCBI GEO accession no. GSE31528) from eight subjects with metastatic castration-resistant prostate cancer (bone marrow metastases)[146] were interrogated. Briefly, total RNA-seq was performed on random-primed paired end read libraries, to ensure consistent transcript coverage[147, 148,149], generating an average of 160M reads per sample. Paired-end FASTQ files were aligned to the human genome (UCSC build hg19) using the spliced-read mapper TopHat (v2.0.9)[148] and reference gene annotations to guide the alignment. BigWig sequencing tracks for the UCSC genome browser[150] were obtained from TopHat-generated BAM files (indexed by samtools v1.2[151]) using a local instance of the *bamCoverage* command in deepTools v2.5.4[152]. BigWig files were visualized in the UCSC genome browser (hg19). A region with less than ~10 supporting reads can be considered to have low coverage, rendering active transcription difficult to interpret[152, 153].

### RNA secondary structure prediction

The ViennaRNA web server was employed[154] to predict the secondary structure of *GHSROS* and its minimum free energy[155].

### RNA sequencing of PC3-GHSROS cells

RNA was extracted from *in vitro* cultured PC3-GHSROS cells and controls, as outlined in the manuscript body. RNA purity was analysed using an Agilent 2100 Bioanalyzer, and RNA with an RNA Integrity Number (RIN) above 7 used for RNA-seq. Strand-specific RNA-sequencing (RNA-seq) was performed by Macrogen, South Korea. A TruSeq stranded mRNA library (Illumina) was constructed and RNA sequencing performed (50 million reads) on a HiSeq 2000 instrument (Illumina) with 100bp paired end reads. Pre-processing of raw FASTQ reads, including elimination of contamination adapters, was performed with scythe v0.994 (https://github.com/vsbuffalo/scythe). Paired-end human FASTQ files were aligned to the human genome, UCSC build hg19 using the spliced-read mapper TopHat (v2.0.9)[148] and reference gene annotations to guide the alignment.

Raw gene counts were computed from TopHat-generated BAM files using featureCounts v1.4.5-p1[156], counting coding sequence (CDS) features of the UCSC hg19 gene annotation file (gtf). FeatureCounts output files were analysed using the R programming language (v.3.2.2). Briefly, raw counts were normalized by Trimmed Mean of M-values (TMM) correction[157, 158]. Library size-normalized read counts (per million; CPM) were subjected to the voom function (variance modelling at the observation-level) in limma v3.22.1 (Linear Models for Microarray Data)[159, 160], with trend=TRUE for the eBayes function and correction for multiple testing (Benjamini-Hochberg false discovery rate of cut-off, *Q*-value, set at 0.05). Genes with at least a 1.5 $\log_2$ fold-change difference in expression between PC3-GHSROS and PC3-vector (empty vector) cells were defined as differentially expressed. Although validation is not required, as RNA-seq gives very accurate measurements of relative expression across a broad dynamic range[160], selected differentially regulated genes were validated using quantitative reverse-transcription PCR (qRT-PCR) (see manuscript body and table S11). Detailed gene annotations were obtained by querying Ensembl with the R/Bioconductor package ‘biomaRt’[161].

### RNA sequencing of LNCaP-GHSROS cells

RNA was extracted from LNCaP-GHSROS xenograft tumors and controls (empty vector control lentiviral constructs), as outlined in the manuscript body. RNA purity was analysed using an Agilent 2100 Bioanalyzer, and RNA with an RNA Integrity Number (RIN) above 7 used for RNA-seq. Strand-specific RNA-seq was performed by the South Australian Health and Medical Research Institute (SAHMRI, Adelaide, SA, Australia). A TruSeq stranded mRNA library (Illumina) was constructed and RNA sequencing performed (35 million reads) on a Nextseq 500 instrument (Illumina) with 75bp single end reads. Pre-processing of raw FASTQ reads, including elimination of contamination adapters, was performed with scythe v0.994 (https://github.com/vsbuffalo/scythe). Human (xenograft tumor; the graft) and mouse (the host) RNA-seq reads were separated using Xenome[162] on the trimmed FASTQ files, leaving ~20M human reads. Reads were aligned to the human genome and processed as described for PC3-GHSROS cells above. Genes differentially expressed in LNCaP-GHSROS cells (cutoff set at $\log_2$ 1.5-fold-change and $Q \leq 0.05$) were imported into the GSEA (Gene Set Enrichment Analysis) program[163].

**Survival analysis**

Two datasets were interrogated: Taylor[23](123 localized and 27 metastatic prostate tumors) and TCGA-PRAD from The Cancer Genomics Atlas (TCGA) consortium, which contains tumors from patients with moderate- (~39% Gleason 6 and 3 + 4) and high- (~61% Gleason 4+3 and Gleason 8-10) risk localized prostate carcinoma[24]. Briefly, in the case of TCGA-PRAD, the UCSC Xena Browser[32] was used to obtain normalized gene expression values, represented as $\log_2$(normalized counts+1), from the 'TCGA TARGET GTeX' dataset consisting of ~12,000 tissue samples from 31 cancers[161]. To obtain up-to-date overall survival (OS) and disease-free survival (DFS) information, we manually queried cBioPortal for Cancer Genomics[34, 35] (last accessed 05.08.16).

We performed non-hierarchical *k*-means clustering[164, 165] to partition patients into groups with similar gene expression patterns[166]. The following 10 genes obtained by Oncomine meta-analysis (see above) were assessed: *AASS*, *CHRDL1*, *CNTN1*, *DIRAS1*, *FBXL16*, *IFI16*, *MUM1L1*, *TP53I11*, *TFF2*, and *ZNF467.* Clustering was performed using the *kmeans* function in the R package 'stats' with two clusters/groups (*k=2*) and the best cluster pair after 500 runs (*nstart=500*) was retained[167]. Kaplan-Meier survival analysis[168] was performed with the R package 'survival'[169], fitting survival curves (*survfit*) and computing log-rank *P*-values using the *survdiff* function, with *rho=0* (equivalent to the method employed by UCSC Xena; see https://goo.gl/4knf62). Survival curves were plotted when survival was significantly different between two groups (log-rank $P \leq 0.05$). We used the *coxph* function in the R package 'survival' to test the prognostic significance of genes (that is: we implemented the Cox proportional hazard model to analyze the association of gene expression with patient survival)[170], with $P \leq 0.05$ (Wald test) considered significant. Because there is a single categorical covariate (*k*-means cluster; group), the *P*-values from the log-rank and the Cox regression tests are comparable. We considered groups (clusters) that had fewer than 10 samples with a recorded event unreliable.

A scaled heat map (unsupervised hierarchical clustering by Euclidean distance) was generated in R using heatmap.3 (available at https://goo.gl/Yd9aTY) and a custom R script.

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