

Supplementary Figure S1. Correlations of *CALD1* alterations and expression with poor prognosis and *AR* in PCa patient data sets.

(A) Kaplan-Meier overall survival curves between patients with *CALD1* amplifications (n = 2) and unaltered *CALD1* (n = 46) (70).

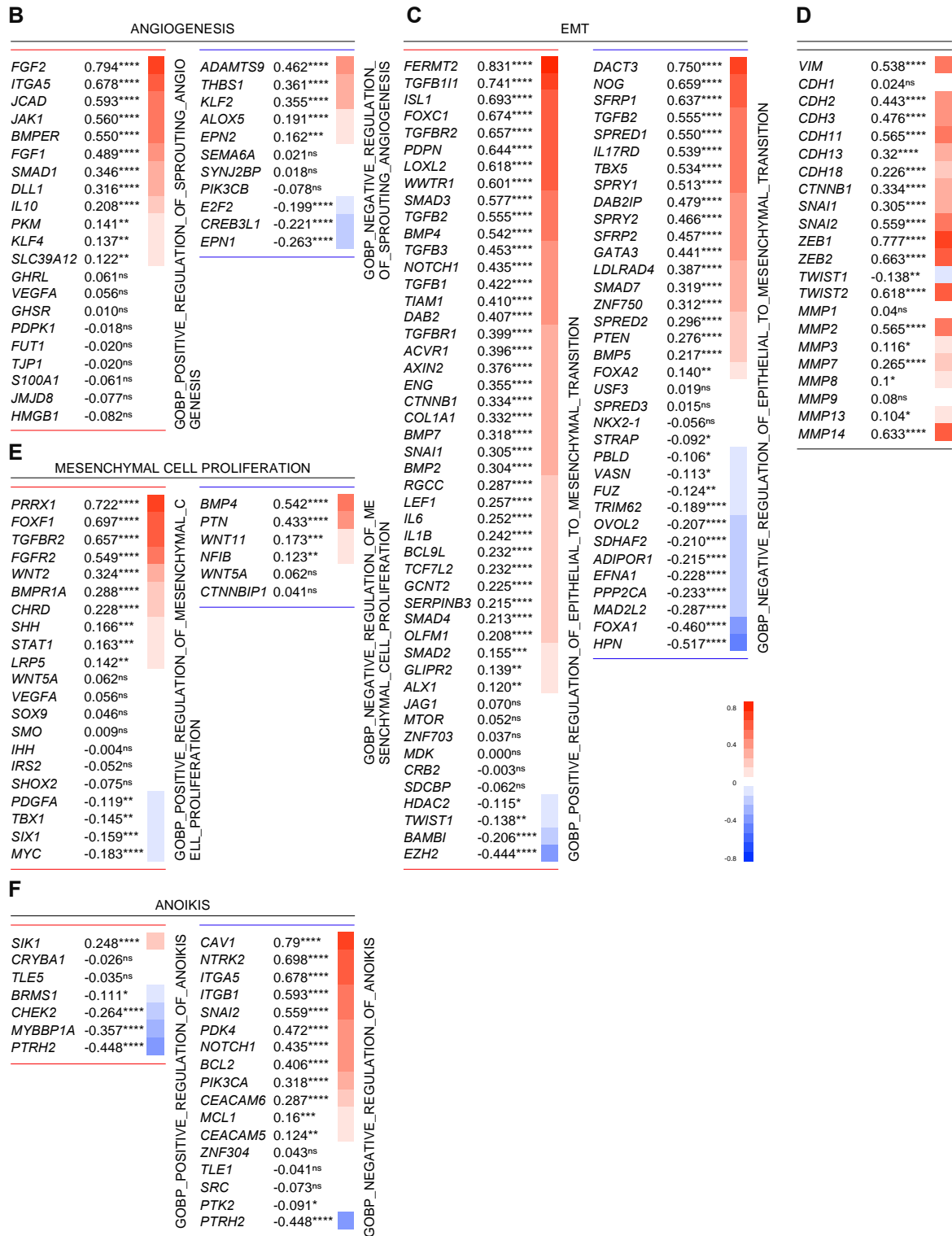
(B) Kaplan-Meier overall survival curves between patients with *CALD1* alterations (n = 10) and unaltered *CALD1* (n = 118) (68).

(C) Scatterplot depicting the Spearman's rank correlation between *CALD1* and *AR* in TCGA PCa data set.

A

EPITHELIAL CELL PROLIFERATION

GOBP_POSITIVE_REGULATION_OF_EPITHELIAL_CELL_PROLIFERATION				GOBP_NEGATIVE_REGULATION_OF_EPITHELIAL_CELL_PROLIFERATION					
ITGB3	0.811****	PKHD1	0.202****	ZNF580	-0.225****	CAV1	0.79****	NFIB	0.123**
FGF2	0.794****	VASH2	0.2****	HRAS	-0.246****	CAV2	0.763****	IFT52	0.118**
FZD7	0.788****	PDGFB	0.189****	BAD	-0.247****	TGFBR3	0.752****	DUSP10	0.112*
CAV7	0.763****	THBS4	0.189****	MYDGF	-0.255****	GJA1	0.744****	CDK6	0.1*
NRP2	0.763****	PTPRN	0.188****	SIRT6	-0.258****	LIMS2	0.703****	SAV1	0.093*
FGFR1	0.69****	HIF1A	0.184****	AKT1	-0.273****	WFDC1	0.697****	XDH	0.077**
NOG	0.659****	CCR3	0.183****	APLN	-0.285****	ISL1	0.693****	IL12B	0.064 ^{ns}
SFRP1	0.637****	NOTCH2	0.173***	EMC10	-0.291****	MEF2C	0.674****	WNT5A	0.062 ^{ns}
SCN5A	0.63****	ODAM	0.173***	IQGAP3	-0.291****	RGN	0.661****	GHRL	0.061 ^{ns}
FGF7	0.627****	SP1	0.171***	PDCL3	-0.335****	SERPINF1	0.651****	DLG1	0.048 ^{ns}
FGF10	0.615****	CYP7B1	0.168***	GATA2	-0.342****	MCC	0.647****	SOX9	0.046 ^{ns}
SEMA5A	0.597****	SHH	0.166***	NME2	-0.356****	SFRP1	0.637****	AR	0.044 ^{ns}
HTRA1	0.593****	ADAM17	0.162***	ESRP2	-0.371****	SULF1	0.623****	MED1	0.044 ^{ns}
JCAD	0.593****	VIP	0.151***	MST1	-0.373****	SNAI2	0.559****	SUZ12	0.025 ^{ns}
KDR	0.589****	SCG2	0.15**	SRSF6	-0.413****	NR2F2	0.555****	SYNJ2BP	0.018 ^{ns}
YAP1	0.579****	APLNR	0.146**	PDCD6	-0.424****	TGFB2	0.555****	GDF2	0.012 ^{ns}
TLR4	0.568****	MMP12	0.14**	NME1	-0.465****	FGFR2	0.549****	IL26	0.011 ^{ns}
FGFR2	0.549****	NR4A1	0.138**	HPN	-0.517****	ROBO1	0.549****	KRIT1	0.009 ^{ns}
TEK	0.545****	GRN	0.135**			GDF5	0.548****	INTU	0.004 ^{ns}
STAT5A	0.544****	CCL24	0.131**			BMP4	0.542****	IFT172	-0.018 ^{ns}
BMP4	0.542****	RICTOR	0.13**			COL4A3	0.515****	PRL	-0.018 ^{ns}
ECM1	0.531****	CCL26	0.128**			SPARC	0.5****	IFT57	-0.019 ^{ns}
PRKCA	0.512****	EGFL7	0.125**			DAB2IP	0.479****	SLURP1	-0.025 ^{ns}
FGF1	0.489****	HMOX1	0.116*			NGFR	0.457****	APOE	-0.028 ^{ns}
OSR1	0.483****	F3	0.112*			SFRP2	0.457****	CPB2	-0.04 ^{ns}
CDH3	0.476****	CCL11	0.109*			GATA3	0.441****	PDCD10	-0.044 ^{ns}
PIK3CD	0.474****	EPGN	0.1*			CD109	0.433****	IFT80	-0.056 ^{ns}
TP63	0.458****	VEGFB	0.1*			PTN	0.433****	MARVELD3	-0.082 ^{ns}
CXCL12	0.454****	CDC42	0.097*			TGFB1	0.422****	STRAP	-0.092*
IGF2	0.443****	CCND1	0.092*			GPC3	0.412****	TINF2	-0.101*
NOTCH1	0.435****	NRP1	0.089*			CDKN2B	0.405****	APOH	-0.106*
PTN	0.433****	EGF	0.086 ^{ns}			TGFB1	0.399****	PBLD	-0.106*
HYAL1	0.43****	SIRT1	0.084 ^{ns}			KLF9	0.395****	WNT10B	-0.111*
FLT4	0.429****	LACRT	0.083 ^{ns}			ATOH8	0.389****	PEX2	-0.115*
HAS2	0.425****	CRNN	0.077 ^{ns}			TNMD	0.386****	AQP11	-0.127**
LAMB1	0.414****	VEGFD	0.071 ^{ns}			FLT1	0.375****	ATP5F1A	-0.16**
NOD2	0.407****	REG3G	0.068 ^{ns}			THBS1	0.361****	NUPR1	-0.184****
TGFBR1	0.399****	WNT5A	0.062 ^{ns}			CEACAM1	0.359****	NKX3-1	-0.194****
TNFAIP3	0.394****	GHRL	0.061 ^{ns}			DLL4	0.338****	MAGED1	-0.219****
OSR2	0.389****	VEGFA	0.056 ^{ns}			SOX2	0.333****	PHB2	-0.228****
B4GALT1	0.368****	PLCG1	0.055 ^{ns}			MTSS1	0.326****	STK11	-0.232****
PGF	0.366****	MTOR	0.052 ^{ns}			KRT4	0.325****	IFT74	-0.251****
PROX1	0.366****	SOX9	0.046 ^{ns}			B2M	0.294****	AIMP1	-0.306****
TGM1	0.366****	AR	0.044 ^{ns}			RGCC	0.287****	WDR13	-0.317****
ITGA4	0.361****	MED1	0.044 ^{ns}			PPARG	0.282****	ATP5IF1	-0.365****
RPTOR	0.359****	ZNF304	0.043 ^{ns}			PTEN	0.276****	WDR77	-0.396****
JAML	0.354****	MAP2K5	0.04 ^{ns}			IL12A	0.274****	KDF1	-0.485****
WNT3A	0.351****	ATP7A	0.038 ^{ns}			RUNX3	0.274****	HPN	-0.517****
BMPR2	0.349****	ZNF703	0.037 ^{ns}			CDKN1C	0.271****		
TGFA	0.349****	RREB1	0.033 ^{ns}			NF1	0.252****		
EGFR	0.343****	REG3A	0.026 ^{ns}			CCL2	0.25****		
TNFSF12	0.341****	ARG1	0.022 ^{ns}			EREG	0.244****		
WNT2	0.324****	PRKD1	0.018 ^{ns}			VASH1	0.24****		
CDH13	0.32****	GDF2	0.012 ^{ns}			PTPRK	0.225****		
STXBP4	0.319****	GHSR	0.01 ^{ns}			CNMD	0.222****		
ID1	0.315****	SMO	0.009 ^{ns}			TNF	0.217****		
FGF9	0.313****	AGGF1	0.008 ^{ns}			VDR	0.204****		
PPP1R16B	0.305****	DLX5	0.003 ^{ns}			ATF2	0.196****		
BMP2	0.304****	DLX6	0.001 ^{ns}			ALOX5	0.191****		
CLDN1	0.303****	MDK	0 ^{ns}			RB1	0.189****		
ARNT	0.299****	NRAS	0 ^{ns}			NLRC3	0.186****		
AKT3	0.294****	IHH	-0.004 ^{ns}			A4GNT	0.183****		
WDR48	0.292****	LRG1	-0.004 ^{ns}			PTPRM	0.183****		
BMPR1A	0.288****	PDPK1	-0.018 ^{ns}			SFN	0.169****		
NR4A3	0.28****	XBP1	-0.027 ^{ns}			PPARD	0.164****		
CFLAR	0.278****	PRKD2	-0.047 ^{ns}			STAT1	0.163****		
FGFBP1	0.277****	REG1A	-0.05 ^{ns}			PTCH1	0.161****		
GPBAR1	0.272****	SOX11	-0.057 ^{ns}			EPPK1	0.151****		
RTN4	0.265****	HMGB2	-0.061 ^{ns}			SCG2	0.15**		
ANG	0.251****	ERBB2	-0.067 ^{ns}			BRCA2	0.148**		
LAMC1	0.25****	HMGB1	-0.082 ^{ns}			NKX2-8	0.146**		
WNT7A	0.25****	KDM5B	-0.085 ^{ns}			CDC73	0.143**		
C5AR2	0.247****	BMP6	-0.093*			CASK	0.142**		
IGF1	0.245****	AGTR1	-0.096*			FBXW7	0.123**		
VEGFC	0.24****	PAX2	-0.122**						
TCF7L2	0.232****	ZBED9	-0.137**						
NODAL	0.226****	TWIST1	-0.138**						
EGR3	0.225****	MST1L	-0.142**						
C5AR1	0.218****	TBX1	-0.145**						
BMP5	0.217****	FOXE3	-0.156***						
AREG	0.213****	NRARP	-0.169***						
IL10	0.208****	MYC	-0.183****						
HTR2B	0.205****	PLXNB3	-0.218****						



Supplementary Figure S2. Co-expression between *CALD1* and regulators of proliferation, angiogenesis, EMT, and anoikis in the prostate TCGA data set.

(A) List of transcripts from the Gene Ontology: Biological Processes gene set for positive and negative regulators of epithelial cell proliferation sorted according to Spearman's correlation values.

(B) List of transcripts from the Gene Ontology: Biological Processes gene set for positive and negative regulators of angiogenesis sorted according to Spearman's correlation values.

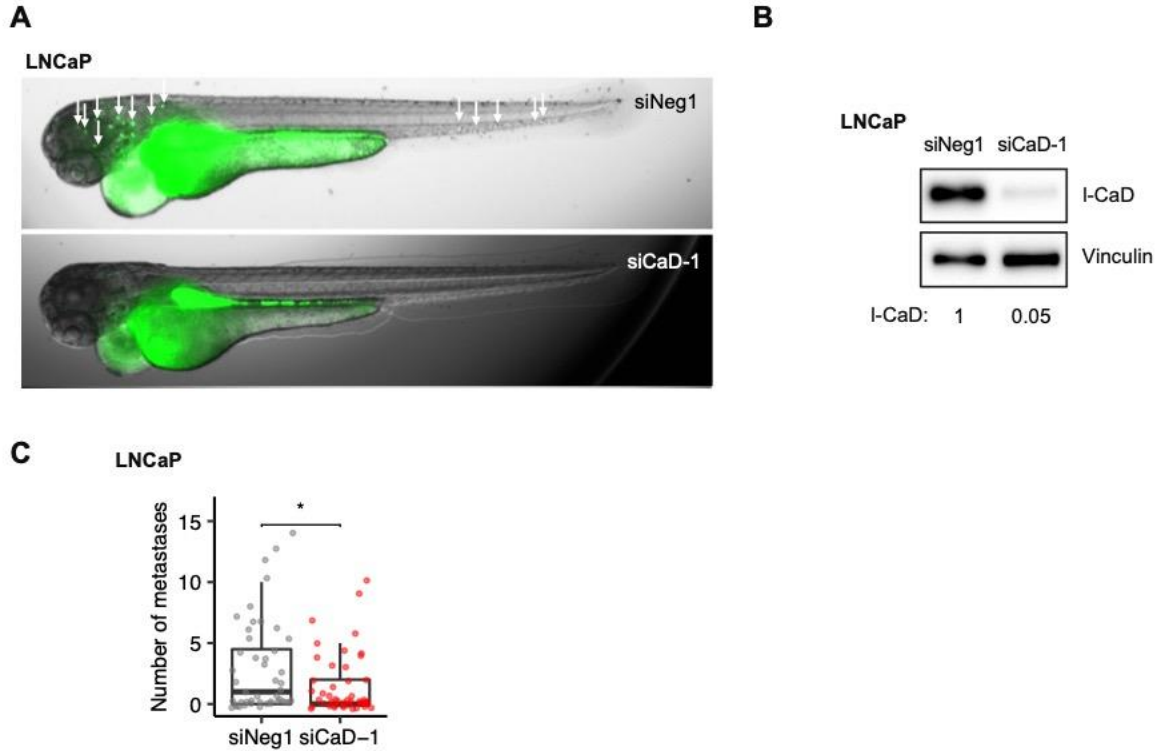
(C) List of transcripts from the Gene Ontology: Biological Processes gene set for positive and negative regulators of EMT sorted according to Spearman's correlation values.

(D) A custom list featuring markers associated with epithelial and markers associated with mesenchymal cell phenotype.

(E) List of transcripts from the Gene Ontology: Biological Processes gene set for positive and negative regulators of mesenchymal cell proliferation sorted according to Spearman's correlation values.

(F) List of transcripts from the Gene Ontology: Biological Processes gene set for positive and negative regulators of anoikis sorted according to Spearman's correlation values.

Spearman's rank correlation coefficient presented as numbers and significance indicated by asterisks (ns = not significant, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, and **** $p < 0.0001$ as obtained using cBioPortal v4.1.9).

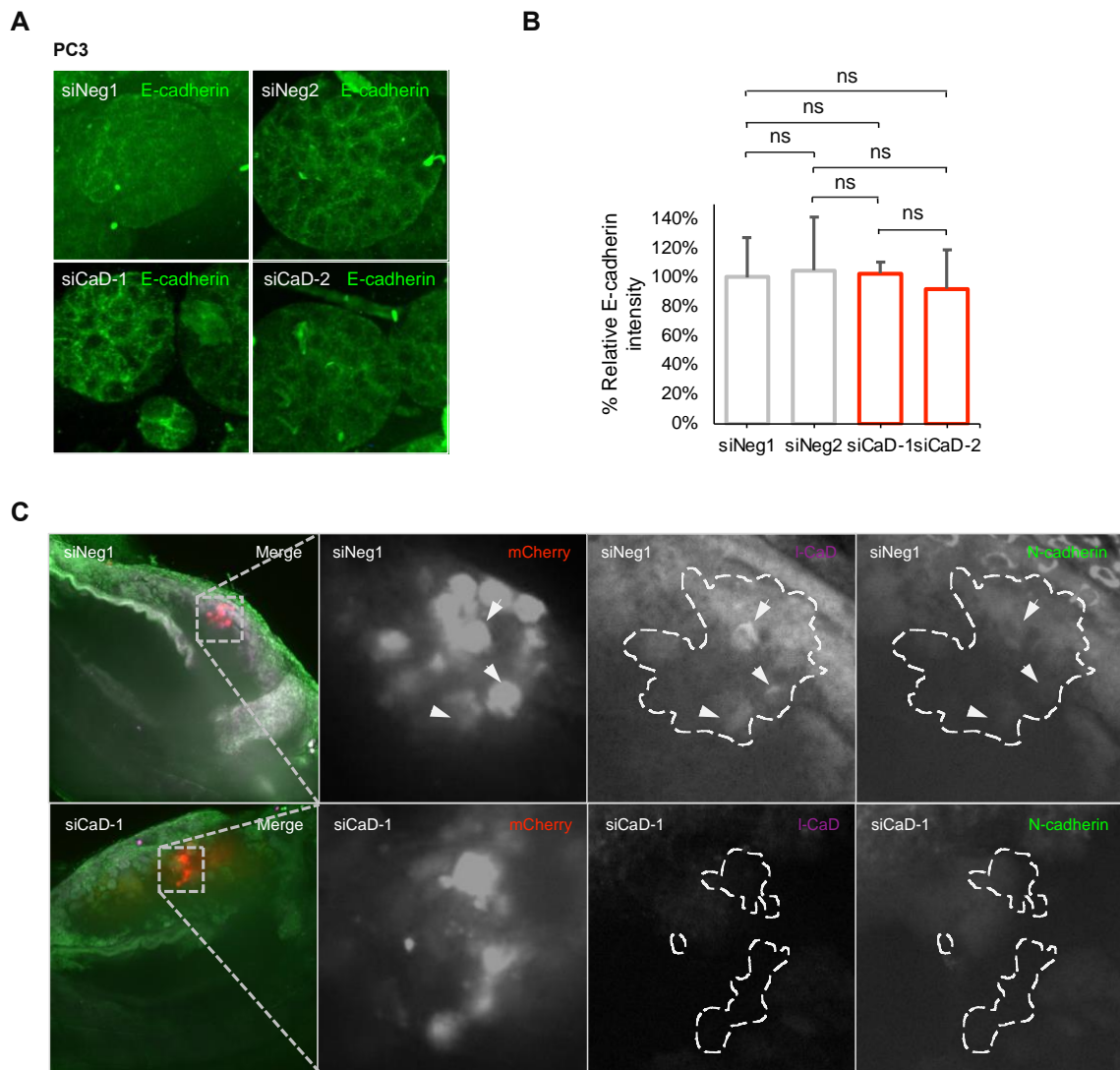


Supplementary figure S4. I-CaD knockdown impairs metastatic potential of LNCaP cells injected into zebrafish.

(A) Representative brightfield and fluorescent merge images of zebrafish embryos 1 day after microinjection of CellTracker Green labeled LNCaP cells transfected with siNeg1 or siCaD-1 to the common cardinal vein. Metastases are indicated with arrows.

(B) Expression levels of I-CaD in LNCaP cells transfected with siNeg1 or siCaD-1 48 h after transfection were analyzed by Western blotting using an anti-CaD antibody and loading was controlled using anti-vinculin.

(C) Box and jitter plots depicting the number of metastases in zebrafish embryos ($n = 96$). Boxplot indicates median, and whiskers indicate 1.5 times interquartile range (* $p < 0.05$ as determined by t -test).

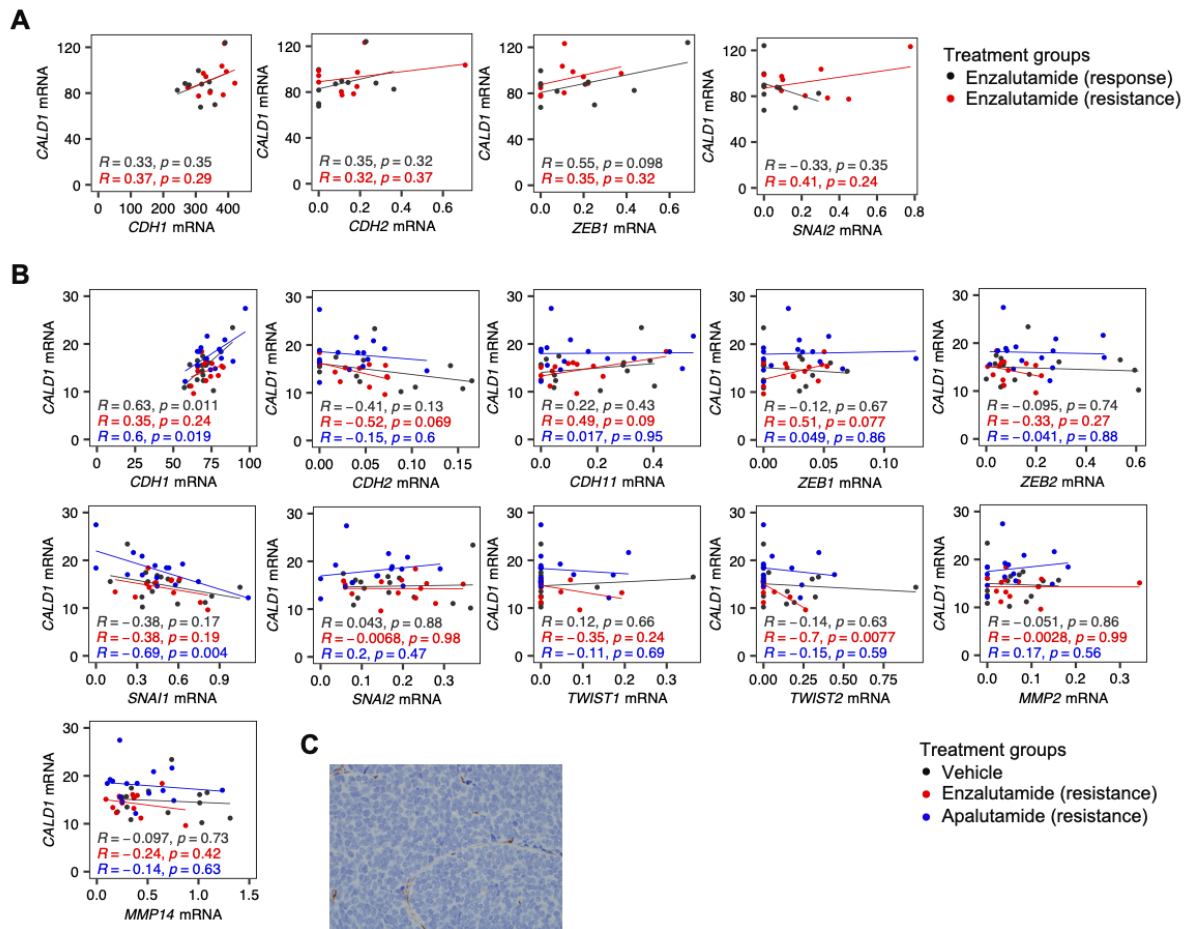


Supplementary Figure S5. E-cadherin expression in PC3 cell spheroids after l-CaD knockdown *in vitro* and N-cadherin expression in mCherry PC3 cell primary tumors after l-CaD knockdown in zebrafish xenografts *in vivo*.

(A) Representative fluorescent images of PC3 spheroids transfected with siNeg1, siNeg2, or siCaD-1, siCaD-2, stained with E-cadherin, and counterstained with DAPI.

(B) Barplots depicting E-cadherin protein intensity in spheroids formed by transfected PC3 cells shown in figure A. Average was calculated from multiple individual spheroids (N = 25) measured for mean intensity. The mean and SD are shown (ns = not significant as determined by *t*-test).

(C) Representative fluorescent images of primary tumors formed in zebrafish yolks from injected PC3 cells transfected with siNeg1 or siCaD-1 stained for l-CaD and N-cadherin. Merge image shows the primary tumor in the yolk sac of the zebrafish.



Supplementary Figure S6. EMT-related marker expression in VCaP xenograft mouse models.

- (A) Scatterplots depicting the correlation between *CALD1* and EMT marker mRNAs from enzalutamide-treated VCaP xenograft mice.
- (B) Scatterplots depicting the correlation between *CALD1* and EMT marker mRNAs from vehicle-, enzalutamide- and apalutamide-treated VCaP xenograft mice.
- (C) Representative IHC staining of vimentin from a castration-resistant subcutaneous VCaP xenograft mouse resistant to enzalutamide.