Supplemental Information files for:

E-cadherin is required for metastasis in multiple models of breast cancer

Veena Padmanaban[1], Ilona Krol[3], Yasir Suhail[2], Barbara M. Szczerba[3], Nicola Aceto[3], Joel S. Bader[2], and Andrew J. Ewald[1,2*]

Supplementary Information 1: References for apoptosis regulating transcripts

PMIDs describing the role of each differentially expressed transcript in apoptosis that is represented in red in Extended Data Fig. 8e. RNA-seq was performed by comparing transcriptomes of 4 adeno-Cre treated MMTV-PyMT; E-cad$^{+/+}$ organoids to 5 adeno-Cre treated MMTV-PyMT; E-cad$^{fl/fl}$ organoids. Statistical significance was calculated using the Wald test. Adjusted p-values reported here are corrected for multiple testing with the Benjamini-Hochberg method. Fold change is reported as experimental/control for experimental > control and as -control/experimental for control > experimental. Genome wide significance = 1.7 E-6 (FWER = 0.05).

Transcript	p-value (adj)	Fold change	PMID(s)
Wnt7b	2.24E-14	1.92	23386686
Cacna1a	1.43E-09	1.98	27342111
Bmp2	2.59E-09	1.90	22735990; 28725489
Foxj1	2.59E-09	2.49	18836996; 29434839
Adamts4	4.01E-08	1.82	24213506; 23319426
Fxyd2	4.01E-08	2.07	26910837; 15280368
Trpv4	4.30E-08	1.91	28759041; 29293584
Ptx3	4.67E-07	1.93	27625097; 25679762
Sod3	5.65E-07	2.32	24328532; 24922645
Tnfrsf12a	9.10E-07	1.34	9405449; 21525013
Id3	1.01E-06	2.06	27176047; 25693514
Nox4	1.01E-06	1.82	28806703; 28422720
Anxa3	1.34E-06	1.35	27878264
Il33	3.69E-06	-2.29	28978138; 28119694
Fam107b	4.32E-06	1.46	22825356; 24748967
Mtus1	5.41E-06	-1.70	22153618
Pappa	8.69E-06	2.15	23152806; 26020769
Pde9a	1.73E-05	-2.17	22469131; 23544068
Fgl1	3.43E-05	15.12	22566646; 26225745;
Bst2	4.31E-05	1.76	28693265, 23840623
Loxl4	5.12E-05	1.70	28060764; 25311867
Dpp4	5.92E-05	-1.54	27936466; 26816911
Rassf4	7.03E-05	1.29	15574778
Rhobtb2	7.59E-05	1.34	26131191; 21801820
Grk5	7.59E-05	1.48	19008357; 29463786
Pam	8.80E-05	1.35	29235204; 27035127
Nol3	1.35E-04	-1.48	21129150
Lactb	1.60E-04	1.34	28642719
Selenbp1	2.05E-04	-2.43	24163737; 20332323
Naf1	2.44E-04	1.55	26621032
Bmp4	2.47E-04	1.84	20951698; 10578180
Csn3	2.77E-04	-1.64	22237956; 23613978
Crip2	2.77E-04	1.27	22154084; 21540330
Tle2	2.88E-04	-1.31	27852056
Enc1	2.92E-04	1.53	15459180; 11691783

Supplementary Information 2: Cancer Hallmarks Enrichment Analysis

GSEA analysis for Cancer Hallmarks categories that are significantly altered in adeno-Cre transduced E-cad$^{fl/fl}$ organoids relative to E-cad$^{+/+}$ organoids. RNA-seq was performed by comparing transcriptomes of 4 adeno-Cre treated MMTV-PyMT; E-cad$^{+/+}$ organoids to 5 adeno-Cre treated MMTV-PyMT; E-cad$^{fl/fl}$ organoids. p-values were calculated using the t-test for the difference in mean z-scores for genes in the gene set vs those outside the gene set, with multiple testing correction applied using the Benjamini-Hochberg method. Genome wide significance = 1.7 E-6 (FWER = 0.05).

Hallmarks Term	p-value	Top contributing genes
Oxidative phosphorylation	4.29 E-33	*CPT1A, MDH1, ACAT1, NDUFA5, ATP5J2, ALDH6A1, ATP5O, ATP5I, IDH3G, NDUFA3, NDUFV2, ACAA2, UQCR11, GLUS1, SDHD, COX7B, COX7A2, NDUFC2, ATP5C1, COX7C*
TNFα signaling via NFκB	5.90 E-26	*PTGER4, NFKBIE, NFKB2, PTGS2, F2RL1, SPSB1, PDLIM5, KLF6, TNC, LITAF, TNFAIP8, BMP2, IL15RA, NR4A2, RNF19B, PMEPA1, CCL20, HBEGF, TGIF1, MAFF*
UV response	1.78 E-15	*LTBP1, CACNA1A, PDLIM5, KALRN, DLC1, SCNBA, GCNT1, RBPM5, SMAD7, GRK5, NFKB1, HAS2, NOTCH2, SMAD3, CYR61, MAP2K5, ID1, NIPBL, PTPN21, KCNMA1*
Inflammatory Response	2.96 E-14	*PTGER4, IL18RAP, BST2, TAPBP, PVR, IRF7, KLF6, RGS16, CALCRL, IL18R1, IL15RA, CCL20, HBEGF, RTP4, NFKB1, PLAUR, AXL, SGMS2, HAS2, PDPN*
TGFβ signaling	3.18 E-17	*CDH1, BMP2, PMEPA1, SMAD7, TGIF1, ID3, WWTR1, SMAD3, ID1, LTBP2, SMURF2, ACVR1, JUNB, SKIL, HIPK2, PPP1R15A, ID2, TJP1, TGFBR1, BCAR3*
EMT	3.58 E-13	*TIMP3, PVR, TNC, SPP1, NT5E, PMEPA1, PDLIM4, TNFRSF12A PLAUR, AREG, NOTCH2, PPIB, TNFRSF11B, CYR61, PTX3, VEGFC, CXCL1, CADM1, SDC4, RHOB*
Apoptosis	7.43 E-08	*LMNA, TIMP3, CLU, BMP2, CTH, EMP1, HSPB1, TNFRSF12A, SMAD7, ANXA1, APP, EREG, CYLD, CTG3, KRT18, MCL1, IGF2R, RHOB, PSEN1, BCL2L1*
P53 pathway	5.47 E-10	*RSG16, BMP2, VDR, RNF19B, HBEGF, APP, PLXNB2, NUPR1, DCXR, RPL36, SPHK1, FGF13, SOCS1, TP53, PHLDA3, LRMP, TOB1, TRAF4, ST14, RPS27L*

Supplementary Information 3

PDX model source: Jackson Laboratories
Model #: TM00089
Primary site: Breast
Patient diagnosis: Invasive ductal carcinoma
Tumor type: Primary malignancy
Stage Grade: AJCC IIA / Grade:3
Patient age: 68
Patient sex: Female
Race/ ethnicity: Asian or Pacific Islander / Not Hispanic or Latino
Treatment status: Naïve
Host strain: NSG
Sample type: Surgical resection
Mutation burden: Passage 0: 4.04

Gene expression and other information can be obtained at
http://tumor.informatics.jax.org/mtbwi/pdxDetails.do?modelID=TM00089.