

**SUPPLEMENTARY MATERIALS**

Supplementary Tables 1-3: Please see pages below.

**Supplementary Table S1. Description of variables and parameters comprising the high-dimensional regression model.**

Symbol	Dimension	Description	Symbol	Dimension	Description
$n$	scalar	sample size	$\mathbf{G}$	$q \times q$	conditional independence graph
$p$	scalar	number of predictor variables	$\mathbf{B}\boldsymbol{\gamma}$	$p\boldsymbol{\gamma} \times q$	matrix of regression coefficients
$q$	scalar	number of response variables	$\mathbf{Y}$	$n \times q$	matrix of responses
$p\boldsymbol{\gamma}$	scalar	number of selected predictor variables	$\mathbf{E}$	$n \times q$	matrix of regression errors
$\boldsymbol{\gamma}$	$p$	vector of indicators for selecting predictors	$\boldsymbol{\Sigma}\mathbf{G}$	$q \times q$	column covariance for errors
$\mathbf{X}$	$n \times p$	matrix of available predictors	$\mathbf{W}$	$q \times q$	symmetric matrix of edge weights
$\mathbf{X}\boldsymbol{\gamma}$	$n \times p\boldsymbol{\gamma}$	matrix of selected predictors	$\mathbf{T}\boldsymbol{\gamma}$	$n \times q$	matrix of marginal data distribution

**Supplementary Table S2. Significantly-associated RPPA molecules.** Multiple response regression was applied to the combined BRCA imaging feature set and RPPA dataset from 82 patients, and the results were filtered to include only molecules significantly correlated with each imaging feature after multiple-testing correction.

<b>Imaging Feature</b>	<b>Positively correlated proteins</b>	<b>Negatively correlated proteins</b>
<i>T2 Signal Intensity</i>	RB1, YAP1, BAD, PDCC4, KDR	RAD51, BAK1, ERBB3
<i>T2 Heterogeneity</i>	None	ACACA ACACB, FASN, NF2, PIK3CA, PRKCA, MTOR, SQSTM1
<i>Skin Thickening</i>	EIF4EBP1, CASP3, DVL3, CDH1, MYH9, PEA15, RPS6, YBX1, CTNNB1	EGFR, FOXO3, STK11, NOTCH1, RAD51, STMN1, MET, CDKN1B, CHEK1
<i>Skin Invasion</i>	YWHAZ, EIF4EBP1, PRDX1	EIF4EBP1, BAD, CHEK1, CHEK2, PRKCD, AKT1S1, SCD, JUN, MET, RPS6KA1
<i>Irregular Shape</i>	None	ANXA1, EGFR, NDRG1, SRC, YAP1, MAPK14, PEA15
<i>Rim Enhancement</i>	EIF4EBP1, BECN1, CHEK1, CHEK2, EGFR, ERCC1, FOXO3, STK11, MRE11A, SERPINE1, PDCC4, AKT1S1, RICTOR, ABL1, JUN, PRKCA, STMN1, CDKN1A	ACACA, ANXA7, NRG1, ACACA ACACB, MAPK14, BAP1, ESR1, FASN
<i>Pectoral Invasion</i>	YWHAB, YWHAE, MS4A1, ITGA2, CASP8, CAV1, CHEK1, COL6A1, CCND1, EGFR, ERCC1, FOXO3, ERBB3, MYH11, PARP1, PRKCA, RAD51, RB1, SHC1, SNAI1, STMN1, XBP1, MET, STMN1	BRD4, BAP1, DVL3, JAK2, PDK1, RBM15, EIF4G1, MTOR, RPS6KB1, DPP4
<i>Non-Mass Heterogeneous Internal Enhancement</i>	YWHAB, ACVRL1, DIRAS3, FOXO3, FN1, RAB11A RAB11B	TP53BP1, CDH1, GSK3A GSK3B, RPTOR, CTNNB1, MTOR, BRAF, BAP1
<i>Non-Mass Clustered Ring Internal Enhancement</i>	PDK1, TGM2, MAPK14	ABL1
<i>Non-Mass Clumped Internal Enhancement</i>	ATM, YAP1	ERRFI1
<i>Regional Non-Mass Distribution</i>	PDK1, KIT	AKT1 AKT2 AKT3, ADAR, INPP4B, MTOR
<i>Multiple Regions Non-Mass Distribution</i>	PIK3R1 PIK3R2	EIF4EBP1, BCL2L1, PXN
<i>Linear Non-Mass Distribution</i>	BRAF, CCNE1	AKT1 AKT2 AKT3, ERBB3, PTPN11, JUN
<i>Focal Non-Mass Distribution</i>	EIF4EBP1, RAF1, CHEK1, EGFR, FOXO3, GSK3A GSK3B, NDRG1, PIK3R1 PIK3R2, AKT1S1, RICTOR, SRC, STMN1, YBX1	TP53BP1, ARAF, ACACA, ADAR, ATM, BRD4, COG3, MAPK1, FASN, GATA3, INPP4B, MAPK9, XRCC5, PDK1, RAB25, AKT1 AKT2 AKT3
<i>Diffuse Non-Mass Distribution</i>	MAPK14	BRCA2, MRE11A, MET, CDKN1B
<i>Nipple Retraction</i>	MYH11, PIK3CA, RICTOR	EIF4EBP1, DPP4, MTOR, CDKN1B
<i>Nipple Invasion</i>	ESR1, DIABLO, XRCC1	GUSP4, PDCC4, RPS6
<i>Margin</i>	PRKAA1, INPP4B, PEA15	ASNS, CASP7, CCNE1, CDH1, FOXM1, IGF1R1
<i>Lesion Size</i>	CHEK2, CCNB1, GUSP4, FOXM1, MSH2, MSH6, NOTCH1, EIF4EBP1, TSC1, EIF4G1,	BCL2, PARK7, ESR1, MAPK8, NRAS, COL6A1,

	ADAR, PRKAA1, GSK3A GSK3B, YBX1, EEF2	DIRAS3, RB1, SRC, JUN
<i>Heterogeneous Enhancement Intensity</i>	IRF1, ERCC1	PGR, PTPN11, STAT3, MAPK14
<i>Fibroglandular</i>	PECAM1, ITGA2, CHEK2, STK11, MRE11A, NRAS, PARP1, PRKCD, SCD, SETD2, SRSF1, STMN1, MET, TP53	EIF4EBP1, BCL2A1, EGFR, ERCC5, MAPK9, MAP2K1, NDRG1, PRKCB, RPS6, RPS6KA1, MAPK1 MAPK3, PIK3R1 PIK3R2, RPS6KA1, TP53BP1
<i>Extent Heterogeneity</i>	CCNE2, FOXM1	BAD, MTOR, GSK3A GSK3B, PTPN11
<i>Extent - Multi-focal</i>	PIK3CA, RPS6KB1	TGM2, SRC
<i>Extent - Multi-centric</i>	CLDN7	BAX, SERPINE1, PDK1
<i>Edema</i>	CCND1, FOXO3, CDH2, PEA15, RAD51, TIGAR, SQSTM1	ARID1A
<i>Dark Internal Septum</i>	HSPA1A, MAPK8, KIT	None
<i>Background</i>	EIF4EBP1, BRAF, GAPDH, GSK3A GSK3B, TSC1, KDR, SQSTM1, TUBA1B, CHEK2, MSH2	BID, MS4A1, CASP8, ERCC5, FOXO3, ERBB3, IRS1, RB1, RAB11A RAB11B, COL6A1, ERCC5, HSPA1A
<i>Axillary Lymphadenopathy</i>	EIF4EBP1, PRDX1, SRC	RAB25, SHC1, XRCC1, PARK7
<i>Associated Non-Mass Enhancement</i>	PRKAA1, MAPK9, BCL2, MAPK9, EEF2K	GSK3A GSK3B, ARAF, CCNE1, FOXM1, PIK3CA, SCD, TP53, SCD, TSC1, TGM2, CDK1, CHEK1, CHEK2

**Supplementary Table S3.** Imaging features are associated with unique biological functions in breast invasive carcinoma. Proteins and phospho-proteins with expression significantly correlated with imaging features were analyzed using Ingenuity Pathway Analysis. Values shown are  $-\log$  (Z-score).

<b>Imaging Feature</b>	<b>Positively-correlated Diseases and Bio-Functions</b>	<b>Negatively-correlated Diseases and Bio-Functions</b>
<i>T2 Signal Intensity</i>	cell death of tumor cell lines 0.881 cell proliferation of tumor cell lines 0.462 cell viability 0.38	organismal death -0.92 apoptosis -0.184 abnormal bone density 0
<i>T2 Heterogeneity</i>	organismal death 2.39 necrosis 1.69 apoptosis of tumor cell lines 1.309	cell viability of tumor cell lines -2.207 cell movement -2.12 cell cycle progression -1.896
<i>Skin Thickening</i>	cell movement of fibroblasts 2.228 quantity of tumor 2.219 cell proliferation of cervical cancer cell lines 1.98	development of neurons -1.949 cell viability of lung cancer cell lines -1.94 development of body trunk -1.815
<i>Skin Invasion</i>	apoptosis of tumor cells 1.446 organismal death 1.163 apoptosis of cancer cells 1.154	interphase -2.321 S phase -1.981 outgrowth of neurites -1.969
<i>Irregular Shape</i>	organismal death 2.38 apoptosis of epithelial cells 1.964 apoptosis of colorectal cancer cell lines 1.131	angiogenesis -2.225 cell proliferation of tumor cell lines -2.222 cell proliferation of breast cell lines -1.987
<i>Rim Enhancement</i>	Viral infection 2.435 cell viability 2.4 cell viability of tumor cell lines 2.255	lung tumor -2.296 organismal death -2.275 apoptosis of epithelial cells -1.964
<i>Pectoral Invasion</i>	neoplasia of tumor cell lines 3.116 migration of tumor cell lines 2.761 cell movement of tumor cell lines 2.733	necrosis -3.09 cell death -2.855 organismal death -2.443
<i>Non-Mass Heterogeneous Internal Enhancement</i>	autophagy of cells 1.982 autophagy 1.961 apoptosis of tumor cell lines 1.553	cell proliferation of kidney cell lines -1.982 cell cycle progression -1.561 vasculogenesis -1.436
<i>Non-Mass Clustered Ring Internal Enhancement</i>	cell movement of tumor cell lines 1.93 migration of cells 1.731 neuronal cell death 0.886	transmembrane potential of mitochondria -1.974 survival of organism -1.946 cell death of lymphocytes -0.762

<i>Non-Mass Clumped Internal Enhancement</i>	None	None
<i>Regional Non-Mass Distribution</i>	cell viability of lymphatic system cells 0.293	proliferation of lymphatic system cells -0.686
<i>Multiple Regions Non-Mass Distribution</i>	None	None
<i>Linear Non-Mass Distribution</i>	organismal death 0.933 necrosis of epithelial tissue 0.205 expression of RNA 0.029	quantity of cells -1.899 mitosis -1.067 transformation of fibroblast cell lines -0.972
<i>Focal Non-Mass Distribution</i>	cell viability of lung cancer cell lines 2.19 proliferation of embryonic cells 2 lymphoid cancer 1.977	differentiation of embryonic cells -2.171 autophagy of tumor cell lines -1.982 cell death of fibroblasts -1.932
<i>Diffuse Non-Mass Distribution</i>	apoptosis 2.17 apoptosis of lung cancer cell lines 1.109 migration of cells 1.041	cell viability of tumor cell lines -2.189 quantity of cells -0.75
<i>Nipple Retraction</i>	migration of cells 1.608 quantity of protein in blood 1.131 growth of tumor 0.927	Viral Infection -1.021 metabolism of protein -0.263
<i>Nipple Invasion</i>	apoptosis 0.252	None
<i>Margin</i>	organismal death 1.995 transcription 1.118 expression of RNA 0.837	cell cycle progression -1.943 quantity of cells -1.896 cell viability -1.849
<i>Lesion Size</i>	cell death of connective tissue cells 1.747 cell cycle progression 1.492 interphase 1.492	microtubule dynamics -2.519 organization of cytoplasm -2.519 organization of cytoskeleton -2.519
<i>Heterogeneous Enhancement Intensity</i>	inflammation of organ 1.964 inflammation of absolute anatomical region 1.955 apoptosis of tumor cell lines 1.811	cell proliferation of tumor cell lines -1.715 cell cycle progression -1.387 T cell development -1.039
<i>Fibroglandular</i>	apoptosis of sarcoma cell lines 2.214 apoptosis of lymphoma cell lines 2.184 autophagy 2.065	proliferation of B lymphocytes -2.426 cell movement of fibroblasts -2.375 tumorigenesis of benign tumor -2.19
<i>Extent Heterogeneity</i>	None	None
<i>Extent - Multi-focal</i>	None	None
<i>Extent - Multi-centric</i>	None	migration of cells -0.592 apoptosis -0.547 cellular homeostasis -0.343
<i>Edema</i>	cell movement of tumor cell lines 1.959	organismal death -1.795

	invasion of cells 1.948 cell proliferation of tumor cell lines 1.808	transcription of RNA -1.164 cell death -0.839
<i>Dark Internal Septum</i>	None	None
<i>Background</i>	apoptosis of cardiomyocytes 1.949 cell viability of tumor cell lines 1.758 cellular homeostasis 1.658	cell death of epithelial cell lines -2.57 apoptosis of epithelial cell lines -2.388 cell death of kidney cell lines -2.156
<i>Axillary Lymphadenopathy</i>	survival of organism 0.152 organismal death 0.046 necrosis 0.023	quantity of cells -1.414 migration of cells -0.747 cell transformation -0.587
<i>Associated Non-Mass Enhancement</i>	hypoplasia of organ 1.982 synthesis of nitric oxide 1.98 organismal death 1.643	cell cycle progression -1.85 synthesis of DNA -1.623 S phase -1.589