**Supplementary Table S1.** List of targets in the spectrum screen

|  |
| --- |
| **Targets** (receptors, ion channels and kinases) |
| Adenosine A1 receptor |
| Adenosine A2A receptor |
| Adenosine A3 receptor |
| Adrenergic receptor α1A |
| Adrenergic receptor α1B |
| Adrenergic receptor α1D |
| Adrenergic receptor α2A |
| Adrenergic receptor α2C |
| Adrenergic receptor β1 |
| Adrenergic receptor β2 |
| Adrenergic receptor β3 |
| Adrenomedullin receptor AM1 |
| Adrenomedullin receptor AM2 |
| Aldosterone receptor |
| Anaphylatoxin receptor C5a |
| Androgen receptor (AR) |
| Angiotensin receptor AT1 |
| Angiotensin receptor AT2 |
| Apelin receptor (APJ) |
| Atrial Natriuretic Factor (ANF) receptor |
| Bombesin receptor BB1 |
| Bombesin receptor BB2 |
| Bombesin receptor BB3 |
| Bradykinin receptor B1 |
| Bradykinin receptor B2 |
| Calcitonin receptor |
| Calcitonin Gene-Related Peptide (CGRP) 1 |
| Calcium Channel L-Type, Benzothiazepine |
| Calcium Channel L-Type, Dihydropyridine |
| Calcium Channel L-Type, Phenylalkylamine |
| Calcium Channel N-Type |
| Cannabinoid receptor CB1 |
| Cannabinoid receptor CB2 |
| Chemokine receptor CCR1 |
| Chemokine receptor CCR2B |
| Chemokine receptor CCR4 |
| Chemokine receptor CCR5 |
| Chemokine receptor CX3CR1 |
| Chemokine receptor CXCR2 (IL-8RB) |
| Cholecystokinin receptor CCK1 (CCKA) |
| Cholecystokinin receptor CCK2 (CCKB) |
| Colchicine receptor |
| Corticotropin Releasing Factor (CRF) receptor 1 |
| Dopamine receptor D1 |
| Dopamine receptor D2s |
| Dopamine receptor D3 |
| Dopamine receptor D4.2 |
| Dopamine receptor D5 |
| Endothelin receptor ETA |
| Endothelin receptor ETB |
| Epidermal Growth Factor (EGF) receptor |
| Erythropoietin (EPO) receptor |
| Estrogen receptor (ER) α |
| Estrogen receptor (ER) β |
| G Protein-Coupled Receptor GPR103 |
| G Protein-Coupled Receptor GPR8 |
| GABAA receptor, Chloride Channel, TBOB |
| GABAA receptor, Flunitrazepam, Central |
| GABAA receptor, Muscimol, Central |
| GABAB1A receptor |
| GABAB1B receptor |
| Gabapentin receptor |
| Galanin receptor GAL1 |
| Galanin receptor GAL2 |
| Glucocorticoid receptor (GR) |
| Glutamate receptor, AMPA |
| Glutamate receptor, Kainate |
| Glutamate receptor, NMDA, Agonism |
| Glutamate receptor, NMDA, Glycine |
| Glutamate receptor, NMDA, Phencyclidine |
| Glutamate receptor, NMDA, Polyamine |
| Glycine receptor, Strychnine-Sensitive |
| Growth hormone receptor, Secretagogue (GHS, Ghrelin) |
| Histamine receptor H1 |
| Histamine receptor H2 |
| Histamine receptor H3 |
| Histamine receptor H4 |
| Imidazoline receptor I2, Central |
| Inositol trisphosphate (IP3) receptor |
| Insulin receptor |
| Interleukin IL-2 receptor |
| Interleukin IL-6 receptor |
| Leptin receptor |
| Leukotriene receptor, BLT (LTB4) |
| Leukotriene receptor, Cysteinyl CysLT1 |
| Leukotriene receptor, Cysteinyl CysLT2 |
| Melanocortin receptor MC1 |
| Melanocortin receptor MC3 |
| Melanocortin receptor MC4 |
| Melanocortin receptor MC5 |
| Melatonin receptor MT1 |
| Melatonin receptor MT2 |
| Motilin receptor |
| Muscarinic receptor M1 |
| Muscarinic receptor M2 |
| Muscarinic receptor M3 |
| Muscarinic receptor M4 |
| Muscarinic receptor M5 |
| N-Formyl peptide receptor (FPR) 1 |
| N-Formyl peptide receptor-like (FPRL) 1 |
| Neuromedin U receptor NMU1 |
| Neuromedin U receptor NMU2 |
| Neuropeptide Y receptor Y1 |
| Neuropeptide Y receptor Y2 |
| Neurotensin receptor NT1 |
| Nicotinic acetylcholine receptor |
| Nicotinic acetylcholine receptor α1, Bungarotoxin |
| Nicotinic acetylcholine α7, Bungarotoxin |
| Opiate receptor δ (OP1, DOP) |
| Opiate receptor κ (OP2, KOP) |
| Opiate receptor μ (OP3, MOP) |
| Orphanin receptor ORL1 |
| Phorbol ester |
| Platelet-derived growth factor (PDGF) receptor |
| Potassium channel [KATP] |
| Potassium channel [SKCA] |
| Potassium channel hERG |
| Progesterone receptor (PR)-B |
| Prostanoid receptor CRTH2 |
| Prostanoid receptor DP |
| Prostanoid receptor EP2 |
| Prostanoid receptor EP4 |
| Prostanoid receptor, Thromboxane A2 |
| Purinergic receptor P2x |
| Purinergic receptor P2γ |
| Retinoid X receptor (RXR) α |
| Rolipram |
| Ryanodine receptor RyR3 |
| Serotonin receptor (5-Hydroxytryptamine) 5-HT1A |
| Serotonin receptor (5-Hydroxytryptamine) 5-HT1B |
| Serotonin receptor (5-Hydroxytryptamine) 5-HT2B |
| Serotonin receptor (5-Hydroxytryptamine) 5-HT2C |
| Serotonin receptor (5-Hydroxytryptamine) 5-HT3 |
| Serotonin receptor (5-Hydroxytryptamine) 5-HT4 |
| Serotonin receptor (5-Hydroxytryptamine) 5-HT5A |
| Serotonin receptor (5-Hydroxytryptamine) 5-HT6 |
| Sigma receptor σ1 |
| Sigma receptor σ2 |
| Sodium channel, site 2 |
| Somatostatin receptor sst1 |
| Somatostatin receptor sst2 |
| Somatostatin receptor sst3 |
| Somatostatin receptor sst4 |
| Somatostatin receptor sst5 |
| Tachykinin receptor NK1 |
| Tachykinin receptor NK2 |
| Tachykinin receptor NK3 |
| Thyroid hormone receptor (TR) |
| Thyrotropin-releasing hormone (TRH) receptor |
| Transforming growth factor (TGF) β receptor |
| Transporter, Adenosine |
| Transporter, Choline |
| Transporter, Dopamine (DAT) |
| Transporter, GABA |
| Transporter, Monoamine |
| Transporter, Norepinephrine (NET) |
| Transporter, Serotonin (5-Hydroxytryptamine) (SERT) |
| Tumor necrosis factor (TNF) receptor, non-Selective |
| Urotensin II receptor |
| Vanilloid receptor |
| Vasoactive intestinal peptide (VIP1) receptor |
| Vasopressin receptor V1A |
| Vasopressin receptor V1B |
| Vasopressin receptor V2 |
| Vitamin D3 receptor |

**Supplementary Table S2.** Characteristics of the breast cancer PDX models

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **ER** | | **PR** | | **AR** | | **HER2** | **Treatment History** |
| **IHC Result** | **Intensity** | **Proportion** | **Intensity** | **Proportion** | **Intensity** | **Proportion** |
| **HBCx-22** | 2 | 3 | 2 | 3 | 2 | 5 | +/equivocal | naïve |
| **HBCx-3** | 1 | 2 | 1 | 2 | 2 | 4 | - | naïve |
| **HBCx-21** | 2 | 5 | 3 | 5 | 2 | 5 | - | naïve |
| **ST897** | 2 | 5 | 2 | 2 | 1 | 3 | - | naïve |

Intensity, 0-3 scale (median of three individual samples); Proportion of positive cells, 0-5 scale (median of three individual samples)

**Supplementary Table S3.** List of genes upregulated by more than 2-fold in RAD140-treated HBCx-22 xenografts

|  |  |
| --- | --- |
| Gene | Description |
| UGT2B28 | UDP glucuronosyltransferase 2 family, polypeptide B28 (UGT2B28) |
| UGT2B11 | UDP glucuronosyltransferase 2 family, polypeptide B11 (UGT2B11), mRNA |
| B3GAT1 | beta-1,3-glucuronyltransferase 1 (glucuronosyltransferase P) (B3GAT1) |
| HSD3B2 | hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 2 (HSD3B2) |
| DDC | dopa decarboxylase (aromatic L-amino acid decarboxylase) (DDC) |
| ST6GALNAC1 | ST6 (alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1, 3)-N-acetylgalactosaminide alpha-2,6-sialyltransferase 1 (ST6GALNAC1), mRNA |
| ABCC4 | ATP-binding cassette, sub-family C (CFTR/MRP), member 4 (ABCC4) |
| CYP4F8 | cytochrome P450, family 4, subfamily F, polypeptide 8 (CYP4F8), mRNA |
| LOC100129427 | uncharacterized LOC100129427 (LOC100129427), non-coding RNA |
| HSD3B1 | hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 1 (HSD3B1), mRNA |
| SULT1C3 | sulfotransferase family, cytosolic, 1C, member 3 (SULT1C3), mRNA |
| PGC | progastricsin (pepsinogen C) (PGC) |
| MYBPC1 | myosin binding protein C, slow type (MYBPC1) |
| HSD17B2 | hydroxysteroid (17-beta) dehydrogenase 2 (HSD17B2), mRNA |
| PIGR | polymeric immunoglobulin receptor (PIGR), mRNA |
| STAC2 | SH3 and cysteine rich domain 2 (STAC2), mRNA |
| NANOGP1 | SubName: Full=Putative homeobox protein NANOG2 |
| IQGAP2 | IQ motif containing GTPase activating protein 2 (IQGAP2), mRNA |
| ACE2 | angiotensin I converting enzyme (peptidyl-dipeptidase A) 2 (ACE2), mRNA |
| AQP3 | aquaporin 3 (Gill blood group) (AQP3), mRNA |
| SBSN | suprabasin (SBSN) |
| FAM107A | family with sequence similarity 107, member A (FAM107A) |
| CPVL | carboxypeptidase, vitellogenic-like (CPVL) |
| SLPI | secretory leukocyte peptidase inhibitor (SLPI), mRNA |
| PLA2G5 | phospholipase A2, group V (PLA2G5), mRNA |
| ACSS1 | acyl-CoA synthetase short-chain family member 1 (ACSS1), nuclear gene encoding mitochondrial protein;acyl-CoA synthetase short-chain family member 1 (ACSS1) |
| CLEC7A | C-type lectin domain family 7, member A (CLEC7A) |
| MAP1B | microtubule-associated protein 1B (MAP1B), mRNA |
| FMO5 | flavin containing monooxygenase 5 (FMO5) |
| TMCC3 | transmembrane and coiled-coil domain family 3 (TMCC3), mRNA |
| ACSM1 | acyl-CoA synthetase medium-chain family member 1 (ACSM1), mRNA |
| LPXN | leupaxin (LPXN) |
| SORD | sorbitol dehydrogenase (SORD) |
| DCST1 | DC-STAMP domain containing 1 (DCST1) |
| AADAC | arylacetamide deacetylase (AADAC), mRNA |
| FKBP5 | FK506 binding protein 5 (FKBP5) |
| DOCK3 | dedicator of cytokinesis 3 (DOCK3), mRNA |
| ANKH | ankylosis, progressive homolog (mouse) (ANKH), mRNA |
| ATP6V1C2 | ATPase, H+ transporting, lysosomal 42kDa, V1 subunit C2 (ATP6V1C2) |
| SORBS1 | sorbin and SH3 domain containing 1 (SORBS1) |
| C1orf116 | chromosome 1 open reading frame 116 (C1orf116) |
| C3orf58 | chromosome 3 open reading frame 58 (C3orf58) |
| LRIG3 | leucine-rich repeats and immunoglobulin-like domains 3 (LRIG3) |
| EMP1 | epithelial membrane protein 1 (EMP1), mRNA |
| ARHGEF6 | Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6 (ARHGEF6), mRNA |
| F3 | coagulation factor III (thromboplastin, tissue factor) (F3) |
| CYP21A1P | cytochrome P450, family 21, subfamily A, polypeptide 1 pseudogene (CYP21A1P), non-coding RNA |
| ACSL1 | acyl-CoA synthetase long-chain family member 1 (ACSL1), mRNA |
| PPARG | peroxisome proliferator-activated receptor gamma (PPARG) |
| SLC15A2 | solute carrier family 15 (H+/peptide transporter), member 2 (SLC15A2) |
| ST6GAL1 | ST6 beta-galactosamide alpha-2,6-sialyltranferase 1 (ST6GAL1) |
| GLB1L2 | galactosidase, beta 1-like 2 (GLB1L2), mRNA |
| AL832891 | cDNA FLJ39101 fis, clone NTONG2002807, highly similar to CYR61 PROTEIN PRECURSOR |
| BC016015 | cDNA FLJ36665 fis, clone UTERU2003035 |
| SDC1 | syndecan 1 (SDC1) |
| HERC3 | HECT and RLD domain containing E3 ubiquitin protein ligase 3 (HERC3) |
| TNFRSF21 | tumor necrosis factor receptor superfamily, member 21 (TNFRSF21), mRNA |
| MGAT4A | mannosyl (alpha-1,3-)-glycoprotein beta-1,4-N-acetylglucosaminyltransferase, isozyme A (MGAT4A) |
| TNFSF10 | tumor necrosis factor (ligand) superfamily, member 10 (TNFSF10) |
| NFIB | nuclear factor I/B (NFIB) |
| TSPAN6 | tetraspanin 6 (TSPAN6), mRNA |
| LPIN1 | lipin 1 (LPIN1) |
| SPTBN5 | spectrin, beta, non-erythrocytic 5 (SPTBN5), mRNA |
| SOD2 | superoxide dismutase 2, mitochondrial (SOD2), nuclear gene encoding mitochondrial protein |
| GPR137B | G protein-coupled receptor 137B (GPR137B), mRNA |
| CACNB1 | calcium channel, voltage-dependent, beta 1 subunit (CACNB1) |
| ZNF518B | zinc finger protein 518B (ZNF518B), mRNA |
| TMEM62 | transmembrane protein 62 (TMEM62), mRNA |
| APMAP | adipocyte plasma membrane associated protein (APMAP), mRNA |
| SECISBP2L | SECIS binding protein 2-like (SECISBP2L) |
| TMEM63C | transmembrane protein 63C (TMEM63C), mRNA |
| SAMD12 | sterile alpha motif domain containing 12 (SAMD12) |
| NCEH1 | neutral cholesterol ester hydrolase 1 (NCEH1) |
| ABRACL | ABRA C-terminal like (ABRACL), mRNA |
| ZNF652 | zinc finger protein 652 (ZNF652) |
| HIF1A | hypoxia-inducible factor 1 alpha subunit;hypoxia inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor) (HIF1A) |
| YPEL2 | yippee-like 2 (Drosophila) (YPEL2), mRNA |
| APLP2 | amyloid beta (A4) precursor-like protein 2 (APLP2) |
| DNAJC3 | DnaJ (Hsp40) homolog, subfamily C, member 3 (DNAJC3), mRNA |
| CCPG1 | cell cycle progression 1 (CCPG1) |
| ERO1LB | ERO1-like beta (S. cerevisiae) (ERO1LB), mRNA |
| ACAT1 | acetyl-CoA acetyltransferase 1 (ACAT1), nuclear gene encoding mitochondrial protein, mRNA |
| FAM172A | family with sequence similarity 172, member A (FAM172A) |
| ZCCHC6 | zinc finger, CCHC domain containing 6 (ZCCHC6) |
| TRIL | TLR4 interactor with leucine-rich repeats (TRIL), mRNA |
| AFMID | arylformamidase (AFMID) |

**Supplementary Table S4.** List of genes downregulated by more than 2-fold in RAD140-treated HBCx-22 xenografts

|  |  |
| --- | --- |
| Gene | Description |
| TFF1 | trefoil factor 1 (TFF1), mRNA |
| PGR | progesterone receptor (PGR) |
| PLCL1 | phospholipase C-like 1 (PLCL1), mRNA |
| IGFBP2 | insulin-like growth factor binding protein 2, 36kDa (IGFBP2), mRNA |
| KIF18A | kinesin family member 18A (KIF18A), mRNA |
| RERG | RAS-like, estrogen-regulated, growth inhibitor (RERG) |
| C6orf211 | chromosome 6 open reading frame 211 (C6orf211), mRNA |
| RMND1 | required for meiotic nuclear division 1 homolog (S. cerevisiae) (RMND1);required for meiotic nuclear division 1 homolog (S. cerevisiae) (RMND1), nuclear gene encoding mitochondrial protein |
| UBE2C | ubiquitin-conjugating enzyme E2C (UBE2C) |
| KIFC1 | kinesin family member C1 (KIFC1), mRNA |
| KIF2C | kinesin family member 2C (KIF2C), mRNA |
| CASC5 | cancer susceptibility candidate 5 (CASC5) |
| AURKB | aurora kinase B (AURKB) |
| UHRF1 | ubiquitin-like with PHD and ring finger domains 1 (UHRF1) |
| MYBL2 | v-myb myeloblastosis viral oncogene homolog (avian)-like 2 (MYBL2), mRNA |
| CDC20 | cell division cycle 20 (CDC20), mRNA |
| FAM64A | family with sequence similarity 64, member A (FAM64A) |
| ZWINT | ZW10 interacting kinetochore protein (ZWINT) |
| CENPI | centromere protein I (CENPI), mRNA |
| BIRC5 | baculoviral IAP repeat containing 5 (BIRC5) |
| SPC25 | SPC25, NDC80 kinetochore complex component (SPC25), mRNA |
| CDCA3 | cell division cycle associated 3 (CDCA3), mRNA |
| PLK1 | polo-like kinase 1 (PLK1), mRNA |
| NUSAP1 | nucleolar and spindle associated protein 1 (NUSAP1) |
| LMNB1 | lamin B1 (LMNB1) |
| BLM | Bloom syndrome, RecQ helicase-like (BLM), mRNA |
| IQGAP3 | IQ motif containing GTPase activating protein 3 (IQGAP3), mRNA |
| MELK | maternal embryonic leucine zipper kinase (MELK) |
| KIF4A | kinesin family member 4A (KIF4A), mRNA |
| DMBX1 | diencephalon/mesencephalon homeobox 1 (DMBX1) |
| TPX2 | TPX2, microtubule-associated, homolog (Xenopus laevis) (TPX2), mRNA |
| PRR11 | proline rich 11 (PRR11), mRNA |
| FOXM1 | forkhead box M1 (FOXM1) |
| PTTG1 | pituitary tumor-transforming 1 (PTTG1), mRNA |
| CKAP2L | cytoskeleton associated protein 2-like (CKAP2L), mRNA |
| FAM83D | family with sequence similarity 83, member D (FAM83D), mRNA |
| MCM2 | minichromosome maintenance complex component 2 (MCM2) |
| RRM2 | ribonucleotide reductase M2 (RRM2) |
| PRIMA1 | proline rich membrane anchor 1 (PRIMA1), mRNA |
| RMI2 | RMI2, RecQ mediated genome instability 2, homolog (S. cerevisiae) (RMI2), mRNA |
| SHCBP1 | SHC SH2-domain binding protein 1 (SHCBP1), mRNA |
| CDK1 | cyclin-dependent kinase 1 (CDK1) |
| RACGAP1 | Rac GTPase activating protein 1 (RACGAP1) |
| CCNB2 | cyclin B2 (CCNB2), mRNA |
| ST6GALNAC2 | ST6 (alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1, 3)-N-acetylgalactosaminide alpha-2,6-sialyltransferase 2 (ST6GALNAC2), mRNA |
| KIF23 | kinesin family member 23 (KIF23) |
| TK1 | thymidine kinase 1, soluble (TK1), mRNA |
| CDCA8 | cell division cycle associated 8 (CDCA8) |
| GINS2 | GINS complex subunit 2 (Psf2 homolog) (GINS2), mRNA |
| FADS1 | fatty acid desaturase 1 (FADS1), mRNA |
| TUBA1B | tubulin, alpha 1b (TUBA1B), mRNA |
| CCNB1 | cyclin B1 (CCNB1), mRNA |
| STMN1 | stathmin 1 (STMN1) |
| CCNF | cyclin F (CCNF), mRNA |
| UBE2S | ubiquitin-conjugating enzyme E2S (UBE2S), mRNA |
| TACC3 | transforming, acidic coiled-coil containing protein 3 (TACC3), mRNA |
| SMC4 | structural maintenance of chromosomes 4 (SMC4) |
| KIF22 | kinesin family member 22 (KIF22) |
| AURKA | aurora kinase A (AURKA) |
| ECT2 | epithelial cell transforming sequence 2 oncogene (ECT2) |
| NEURL1B | neuralized homolog 1B (Drosophila) (NEURL1B), mRNA |
| LIG1 | ligase I, DNA, ATP-dependent (LIG1), mRNA |
| SKA2 | spindle and kinetochore associated complex subunit 2 (SKA2) |
| RRM1 | ribonucleotide reductase M1 (RRM1), mRNA |
| HMGN2 | high mobility group nucleosomal binding domain 2 (HMGN2), mRNA |
| BZW2 | basic leucine zipper and W2 domains 2 (BZW2) |
| DHFR | dihydrofolate reductase (DHFR), mRNA |
| KPNA2 | karyopherin alpha 2 (RAG cohort 1, importin alpha 1) (KPNA2), mRNA |
| HIRIP3 | mRNA for HIRIP3 protein (clone pH4-31, pH4-17);HIRA interacting protein 3 (HIRIP3) |
| ORC6 | origin recognition complex, subunit 6 (ORC6) |
| RPS2 | ribosomal protein S2 (RPS2), mRNA |
| IMPDH2 | IMP (inosine 5'-monophosphate) dehydrogenase 2 (IMPDH2), mRNA |
| CKAP2 | cytoskeleton associated protein 2 (CKAP2) |
| BCAS4 | breast carcinoma amplified sequence 4 (BCAS4) |
| EPS15L1 | epidermal growth factor receptor pathway substrate 15-like 1 (EPS15L1) |
| CENPN | centromere protein N (CENPN) |
| FBL | fibrillarin (FBL), mRNA |