

# Supplementary data:

Table S1. Basic characteristic of LAGE3 gene on Oncomine database

| Gene         | Dataset                    | group comparison   | fold change | p-value   | number of patients |
|--------------|----------------------------|--|-------------|-----------|--------------------|
| <b>LAGE3</b> | Curtis breast (n=2136)     | Invasive Lobular Breast Carcinoma vs. Normal                     | 2.986       | 3.89E-72  | 148/292            |
|              |                            | Invasive Ductal and Invasive Lobular Breast Carcinoma vs. Normal | 2.984       | 7.40E-39  | 90/234             |
|              |                            | Invasive Breast Carcinoma vs. Normal                             | 2.516       | 5.24E-09  | 21/165             |
|              |                            | Tubular Breast Carcinoma vs. Normal                              | 2.844       | 1.17E-34  | 67/211             |
|              |                            | Invasive Ductal Breast Carcinoma vs. Normal                      | 3.042       | 9.69E-102 | 1556/1700          |
|              |                            | Breast Carcinoma vs. Normal                                      | 2.648       | 2.91E-06  | 14/158             |
|              |                            | Medullary Breast Carcinoma vs. Normal                            | 2.803       | 2.64E-12  | 32/176             |
|              |                            | Ductal Breast Carcinoma in Situ vs. Normal                       | 2.851       | 8.94E-05  | 10/154             |
|              |                            | Invasive Ductal Breast Carcinoma vs. Normal                      | 2.686       | 1.91E-69  | 389/450            |
|              |                            | Invasive Breast Carcinoma vs. Normal                             | 2.387       | 1.22E-34  | 76/137             |
|              | TCGA breast (n=593)        | Invasive Lobular Breast Carcinoma vs. Normal                     | 2.648       | 5.03E-17  | 36/97              |
|              |                            | Male Breast Carcinoma vs. Normal                                 | 4.033       | 1.99E-08  | 3/64               |
|              |                            | Mixed Lobular and Ductal Breast Carcinoma vs. Normal             | 2.504       | 9.74E-05  | 7/68               |
|              |                            | Lobular Breast Carcinoma vs. Normal                              | 3.01        | 2.04E-09  | 21/24              |
|              |                            | Invasive Ductal Breast Carcinoma vs. Normal                      | 3.073       | 1.12E-10  | 38/41              |
|              | Zhao Breast (n=64)         | Ductal Breast Carcinoma vs. Normal                               | 2.313       | 1.15E-07  | 36/39              |
|              | Perou Breast (n=65)        | Ductal Breast Carcinoma vs. Normal                               | 3.254       | 1.00E-11  | 40/47              |
|              | Richardson Breast 2 (n=47) | Ductal Breast Carcinoma vs. Normal                               | 2.734       | 5.62E-05  | 65/69              |
|              | Sorlie breast (n=85)       | Lobular Breast Carcinoma vs. Normal                              |             |           |                    |

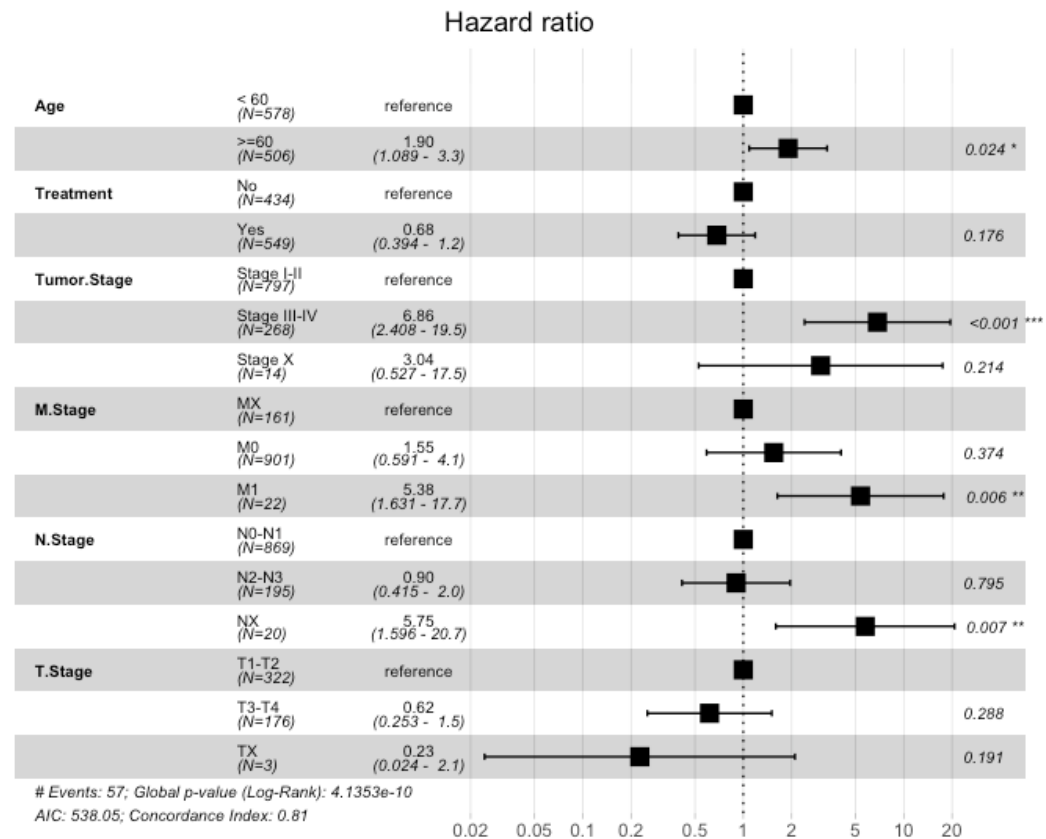


Figure S1. Multivariate analysis of LAGE3 expression and the relationship between it and clinicopathological parameters (Age, Treatment, Stage, TNM stage)

**Table S2.** Univariate of LAGE3 expression and its clinicopathological parameters

|           | <b>element</b> | <b>number of samples</b> | <b>P-value</b> | <b>Hazard ratio</b> | <b>95% CI low</b> | <b>95% CI high</b> |
|-----------|----------------|--------------------------|----------------|---------------------|-------------------|--------------------|
| Age       | <60            | 578                      | 3.84E-05       | 1.97                | 1.427             | 2.721              |
|           | >=60           | 506                      |                |                     |                   |                    |
| Gender    | Female         | 1072                     | 0.85           | 0.83                | 0.1155            | 5.927              |
|           | Male           | 12                       |                |                     |                   |                    |
| Treatment | No             | 434                      | 0.0352         | 0.57                | 0.3915            | 0.8318             |
|           | Yes            | 549                      |                |                     |                   |                    |
| Stage     | Stage I-II     | 797                      | 6.87E-09       | 2.671               | 1.916             | 3.723              |
|           | Stage III-IV   | 268                      |                |                     |                   |                    |
|           | Stage X        | 14                       |                |                     |                   |                    |
| M Stage   | MX             | 161                      | 0.73           | 0.9064              | 0.5188            | 1.584              |
|           | M0             | 901                      |                |                     |                   |                    |
|           | M1             | 22                       |                |                     |                   |                    |
| N Stage   | N0-N1          | 869                      | 1.34E-05       | 2.32                | 1.588             | 3.39               |
|           | N2-N3          | 195                      |                |                     |                   |                    |
|           | NX             | 20                       |                |                     |                   |                    |
| T Stage   | T1-T2          | 322                      | 3.81E-03       | 1.9385              | 1.23814           | 3.035              |
|           | T3-T4          | 176                      |                |                     |                   |                    |
|           | TX             | 3                        |                |                     |                   |                    |

**Table S3.** Pathway analysis of LAGE1-coexpressed genes from public breast cancer databases using the MetaCore database (p<0.01 set as the cutoff value)

| # | Maps   | p-value  | Network Objects from Active Data   |
|---|--|----------|--|
| 1 | Role of tumor-infiltrating B cells in anti-tumor immunity                              | 3.73E-07 | MAGEB2, MAGE-4 antigen, XAGE1, MAGEA10, NXF2, CT47A, CD20, GAGE2, T-bet                        |
| 2 | Cell adhesion_Gap junctions  | 2.43E-06 | Tubulin beta, Tubulin alpha, Actin cytoskeletal, Tubulin (in microtubules), Actin              |
| 3 | Inhibition of remyelination in multiple sclerosis: regulation of cytoskeleton proteins | 5.38E-06 | Tubulin beta, MARCKS, Tubulin alpha, p190RhoGAP, Actin cytoskeletal, Tubulin (in microtubules) |
| 4 | Cytoskeleton remodeling_Reverse signaling by Ephrin-B                                  | 1.71E-05 | Ephrin-B receptors, Tubulin alpha, Actin cytoskeletal, F-Actin, Tubulin (in microtubules)      |
| 5 | Tau pathology in Alzheimer disease   | 2.02E-05 | p38 MAPK, Caspase-6, p38gamma (MAPK12), PP2C, DYRK1a, Tubulin (in microtubules)                |

|    |  |          |  |
|----|--|----------|--|
| 6  | Cell adhesion_Tight junctions  | 8.37E-05 | Tubulin alpha, Actin cytoskeletal, F-Actin, Tubulin (in microtubules), Actin           |
| 7  | Cytoskeleton remodeling_Neurofilaments   | 0.000114 | Tubulin beta, Tubulin alpha, Actin cytoskeletal, Tubulin (in microtubules)             |
| 8  | Cell cycle_Role of Nek in cell cycle regulation  | 0.000307 | Insulin receptor, Tubulin beta, Tubulin alpha, Tubulin (in microtubules)               |
| 9  | Development_Regulation of cytoskeleton proteins in oligodendrocyte differentiation and myelination | 0.000341 | Tubulin beta, Tubulin alpha, p190RhoGAP, Actin cytoskeletal, Tubulin (in microtubules) |
| 10 | Cytoskeleton remodeling_Keratin filaments  | 0.000487 | Tubulin beta, Tubulin alpha, Actin cytoskeletal, Tubulin (in microtubules)             |
| 11 | Inhibition of apoptosis in gastric cancer  | 0.000882 | Gastrin 17, Gastrin 17-Gly, HGF receptor (Met), Progastrin                             |
| 12 | wtCFTR and deltaF508-CFTR traffic / Clathrin coated vesicles formation (normal and CF)             | 0.001065 | Myosin I, Actin cytoskeletal, Actin  |
| 13 | Immune response _CCR3 signaling in eosinophils   | 0.001162 | p38 MAPK, Profilin I, Profilin, FGR, Actin cytoskeletal                                |
| 14 | High shear stress-induced platelet activation  | 0.001246 | GP-IB alpha, Tyro3, Ephrin-B receptor 1, Actin cytoskeletal                            |
| 15 | Defective macrophage-mediated bacterial phagocytosis in COPD                                       | 0.00207  | Tubulin alpha, MANR, Tubulin (in microtubules)   |
| 16 | Cell adhesion_Classical cadherin-mediated cell adhesion  | 0.002322 | F-Actin cytoskeleton, Actin cytoskeletal, F-Actin                                      |
| 17 | Muscle contraction_nNOS signaling in skeletal muscle   | 0.002883 | Syntrophin A, CACNA1C, Actin   |
| 18 | Inhibition of Ephrin receptors in colorectal cancer  | 0.003519 | Ephrin-B receptors, Ephrin-B receptor 2, Ephrin-B receptor 1                           |
| 19 | Protein folding and maturation_Bradykinin / Kallidin maturation                                    | 0.004236 | Aminopeptidase P2, Tissue kallikreins, CPB2  |
| 20 | LRRK2 in neurons in Parkinson's disease  | 0.004625 | ACTB, Actin cytoskeletal, Tubulin (in microtubules)                                    |
| 21 | Anti-apoptotic action of Gastrin in gastric cancer   | 0.005466 | Gastrin 17, Gastrin 17-Gly, Progastrin   |
| 22 | Neurophysiological process_Ephrin-B receptors in dendritic spine morphogenesis and synaptogenesis  | 0.005466 | Ephrin-B receptors, Ephrin-B receptor 2, Actin cytoskeletal                            |
| 23 | CHDI_Correlations from Discovery data_Causal network (positive)                                    | 0.005918 | Ephrin-B receptors, Actin cytoskeletal, Actin  |
| 24 | Transport_Clathrin-coated vesicle cycle  | 0.006092 | Myosin I, Actin cytoskeletal, VAMP8, Actin   |
| 25 | Transport_Macropinocytosis   | 0.006472 | Actin cytoskeletal, Tubulin (in microtubules)  |
| 26 | Development_SLIT-ROBO1 signaling   | 0.00795  | F-Actin cytoskeleton, ACTB, p190RhoGAP   |
| 27 | Cytoskeleton remodeling_Hyaluronic acid/ CD44 signaling pathways                                   | 0.009711 | HGF receptor (Met), Actin cytoskeletal, Actin  |
| 28 | Role of platelets in allograft rejection   | 0.009711 | GP-IB alpha, Glycoprotein VI, Kainate receptor   |

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|----|---|----------|---|
| 29 | Proliferative action of Gastrin in pancreatic cancer  | 0.010344 | Gastrin 17, Gastrin 17-Gly, Progastrin                              |
| 30 | Cytoskeleton remodeling_Substance P mediated membrane blebbing  | 0.011455 | Tubulin alpha, Tubulin (in microtubules)                            |
| 31 | Neurophysiological process_Receptor-mediated axon growth repulsion                                    | 0.011682 | F-Actin cytoskeleton, Actin cytoskeletal, Tubulin (in microtubules) |
| 32 | Signal transduction_Intracellular calcium increase  | 0.011682 | CACNA1C, RAP-2B, PLC-delta 1  |
| 33 | Cytoskeleton remodeling_Regulation of actin cytoskeleton nucleation and polymerization by Rho GTPases | 0.011682 | F-Actin cytoskeleton, Profilin, Actin cytoskeletal                  |
| 34 | Chemotaxis_Lipoxin inhibitory action on Formyl-Met-Leu-Phe-induced neutrophil chemotaxis              | 0.012386 | p38 MAPK, F-Actin cytoskeleton, Actin cytoskeletal                  |
| 35 | Immune response_Fc gamma R-mediated phagocytosis in macrophages                                       | 0.012386 | F-Actin cytoskeleton, Profilin, Actin cytoskeletal                  |
| 36 | Transcription_Transcription factor Tubby signaling pathways   | 0.012896 | Insulin receptor, HTR2C (HTR1C)                                     |
| 37 | Involvement of VEGF signaling in the progression of lung cancer                                       | 0.012896 | p38 MAPK, p190RhoGAP  |
| 38 | PI3K signaling in gastric cancer  | 0.014643 | Gastrin 17, HGF receptor (Met), Progastrin                          |
| 39 | DNA damage_ATM/ATR regulation of G2/M checkpoint: cytoplasmic signaling                               | 0.015444 | p38 MAPK, p38gamma (MAPK12), PLK1                                   |
| 40 | Proliferative action of Gastrin in gastric cancer   | 0.017118 | Gastrin 17, Gastrin 17-Gly, Progastrin                              |
| 41 | Immune response_CCL2 signaling  | 0.017991 | CCBP2 (CCR9), Actin cytoskeletal, CDH19                             |
| 42 | Cell cycle_Chromosome condensation in prometaphase  | 0.019388 | BRRN1, CAP-H/H2   |
| 43 | Platelet activation as a result of endothelial dysfunction after stenting                             | 0.019812 | Prostacyclin receptor, Glycoprotein VI, Actin cytoskeletal          |
| 44 | CCR7 signaling pathways in dendritic cells in allergic contact dermatitis                             | 0.020759 | p38 MAPK, Profilin, Actin cytoskeletal                              |
| 45 | Development_H3K9 demethylases in pluripotency maintenance of stem cells                               | 0.021185 | Oct-3/4, ZFP57  |
| 46 | NMDA-independent presynaptic long-term potentiation in Huntington's disease                           | 0.021731 | MARCKS, GluR7, Actin cytoskeletal                                   |
| 47 | Cytoskeleton remodeling_CDC42 in cellular processes   | 0.023048 | F-Actin cytoskeleton, Actin cytoskeletal                            |
| 48 | Oxidative stress_ROS-mediated MAPK activation via canonical pathways                                  | 0.023747 | p38 MAPK, TRPM2, SFK  |
| 49 | Stimulation of gastric acid secretion in gastric cancer   | 0.023747 | Gastrin 17, Gastrin 17-Gly, Progastrin                              |

50 Immune response\_Fc epsilon RI pathway: signaling through Fyn and PI3K 0.024793 Fc epsilon RI beta, FGR, VAMP8

**Table S4.** Pathway analysis of LAGE2A-coexpressed genes from public breast cancer databases using the MetaCore database (p<0.01 set as the cutoff value)

| # | Maps   | pValue   | Network Objects from Active Data  |
|---|--|----------|---|
| 1 | Development_Negative regulation of WNT/Beta-catenin signaling in the nucleus   | 1.02E-09 | TBL1X, SP7, Calcineurin A (catalytic), BACH1, HBP1, Oct-3/4, VHL, APC protein, Lef-1, PGAM5, TCF7L2 (TCF4), 14-3-3, Jade-1, Casein kinase I epsilon, VEGF-A, TLE, Dsh, KLF4, Menin, NF-AT5, GSK3 beta, Nephrocystin-4, HDAC2, HIC1, P15RS, TBLR1, TAB2, PPAR-gamma, Axin, TAK1(MAP3K7), KDM2, TRRAP, NARF, c-Cbl, Tcf(Lef), E2F1, GLI-3R, CHD8, NLK, SOX2, WNT, FOXO3A, CHIBBY, Plakoglobin, Frizzled, Histone H1, DACT1  |
| 2 | Epigenetic alterations in ovarian cancer                                       | 6.92E-09 | DNMT3B, RARbeta, ZIC4, APC protein, CDC20, GATA-4, HDAC3, p21, DAB2, ESR2 (nuclear), CTCF, WIF1, FGFR1, STAR, Bax, OBCAM, HDAC2, RASSF1, CARD5, IGF-2, AL1A1, SKP2, HSD3B2, p27KIP1, Histone H3, GATA-6, DAPK1, SF1, ErbB4, LSD1, DOK2, ZIC1, Dlec1, Claudin-4, SSTR1, SUZ12, p15, GATA-5, Aurora-B, SNAIL1, L1TD1, GLI-1, MLH1   |
| 3 | Development_SLIT-ROBO1 signaling   | 1.83E-08 | Rictor, Calcineurin A (catalytic), NCK1, VEGFR-2, LSP1, PI3K reg class IA (p85), MENA, CDC42, Fyn, AKT(PKB), Cytohesin1, CXCR4, ACTB, RhoA, SRGAP1, F-Actin cytoskeleton, p190RhoGAP, SLIT3, Myosin II, ROCK, Calmodulin, FLII, SLIT1, SSH1L, Cofilin, PREX1  |
| 4 | Development_Positive regulation of WNT/Beta-catenin signaling in the cytoplasm | 2.63E-07 | Casein kinase II, alpha chains, TBL1X, UBE2B, PP1-cat, APC protein, 14-3-3, TGIF, Makorin-1, Dsh, ZBED3, Beta-arrestin2, YAP1 (YAp65), PPP2R2A, SIAH1, USP25, Insulin receptor, GSK3 alpha/beta, TBLR1, AKT(PKB), RNF146, Axin, Tcf(Lef), 14-3-3 zeta/delta, PP2A catalytic, RNF220, ILK, DOCK4, Trabad, Tankyrases, WNT, USP7, FAK1, JNK(MAPK8-10), Parathyroid hormone, MITF, PKA-cat (cAMP-dependent), Frizzled, DACT1 |
| 5 | Development_Negative regulation of WNT/Beta-catenin signaling in the cytoplasm | 3E-07    | CXXC4, VHL, PP1-cat, APC protein, Presenilin 1, Laforin, FAF1, Casein kinase I epsilon, CYLD, PI3K cat class III (Vps34), DAB2, Dsh, YAP1 (YAp65), G-protein alpha-13, LATS1, STK4, SIAH1, Itch, GSK3 alpha/beta, Ankyrin-G, WDR26, Skp2/TrCP/FBXW, TAZ, Axin, Prickle-1, c-Cbl, Tcf(Lef), E2F1, Amer1, PP2A catalytic, JNK1(MAPK8), RNF185, YAP1/TAZ, ELAVL1 (HuR), PEG3, Malin, WNT, NEDD4L, Frizzled, DACT1            |
| 6 | Cytoskeleton remodeling_Regulation of actin cytoskeleton                       | 5E-07    | Spectrin, PRK1, Alpha-actinin, Talin, MLCP (reg), GIT1, Cdc42 subfamily, ERM proteins, RhoA-related, CDC42, Actin cytoskeletal, MLCK, BETA-PIX, RhoA, Citron,   |

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|----|---|----------|--|
|    | organization by the kinase effectors of Rho GTPases   |          | Destrin, F-Actin cytoskeleton, Myosin II, RhoB, MyHC, Rac3, MRCK, ROCK, Actomyosin, PAK, Rac1-related, Rhov, MRLC, Filamin A, TC10, Cofilin  |
| 7  | Tumor-stroma interactions in pancreatic cancer  | 5.81E-07 | Galectin-3, PDGF-B, VEGF-A, KIF27, Fibronectin, Smoothed, FGFR1, OSF-2, SUFU, CD147, HGF, PTCH1, HIF1A, STK36, FGF2, SHH, GLI-1, IGF-1, HGF receptor (Met)   |
| 8  | Development_Negative regulation of STK3/4 (Hippo) pathway and positive regulation of YAP/TAZ function | 9.25E-07 | ASPP1, LARG, G-protein alpha-q/11, Angiotensin II, YAP1 (YAp65), MLCP (reg), LATS1, ARHGEF2, Nephrocystin-4, FRMD4A, STK4, Itch, Actin cytoskeletal, TAZ, PDK (PDPK1), RhoA, G-protein alpha-12 family, PAR3, Citron, LPAR1, LIMD1, ASPP2, RhoGAP5, KIBRA, S1P2 receptor, NEDD4, ILK, MOBKL1A, WW45, PDZ-RhoGEF, Mol1b, JNK(MAPK8-10)  |
| 9  | Development_Embryonal epaxial myogenesis  | 9.95E-07 | FZD6, Lef-1, KIF27, Smoothed, MYOG, PAX3, SUFU, PTCH1, Myostatin, STK36, SHH, WNT1, GLI-3, HES1, WNT, Pitx2, GLI-1, Frizzled, WNT6, MYOD   |
| 10 | Role of tumor-infiltrating B cells in anti-tumor immunity   | 1.02E-06 | IL-18R1, MLANA, IP10, CD20, CTAG2, JAK1, DHFR, MAGE-1 antigen, POLR2B, Apo-2L(TNFSF10), IFN-alpha/beta receptor, Dsk2 (ubiquilin-2), ADAM-TS9, MAGE-3, IFN-alpha, GAGE2, CD27(TNFRSF7), MHC class I, MAGE-4 antigen, NXF2, MAGEB2, NF-kB, CT47A, SDF-1, CXCR4, IL-2, T-bet, G-protein alpha-i family, AID, IL4RA, IRF4, JAK3, Btk, NY-ESO-1, XAGE1, CXorf61, SOX2, FasR(CD95), KTN1, MAGEC2, MAGEA10, BLIMP1 (PRDI-BF1)      |
| 11 | Immune response_IFN-alpha/beta signaling via PI3K and NF-kB pathways                                  | 1.03E-06 | Cyclin D3, JAK1, RPS6, DHFR, NMI, eIF4E, CDC25A, Apo-2L(TNFSF10), IFN-alpha/beta receptor, p21, IFNAR1, I-kB, PI3K reg class IA (p85), GSK3 beta, NF-kB2 (p100), Rb protein, IFN-alpha, p19, CREB1, p130, MEK1/2, RSAD2, b-Myb, NF-kB, AKT(PKB), PDK (PDPK1), p107, p27KIP1, RelA (p65 NF-kB subunit), NF-kB2 (p52), TRAF2, E2F1, IFNAR2, p90RSK1, eIF4G1/3, PCNA, GBP1, Cyclin E, eIF4A, FOXO3A, p15, MNK2(GPRK7), Cyclin A |
| 12 | E-cadherin signaling and its regulation in gastric cancer   | 1.11E-06 | DNMT3B, FGFR2, FGF1, Alpha-actinin, Dsh, Actin, Ubiquitin, GSK3 beta, SIP1 (ZFHX1B), HGF, RhoA, Formin, IQGAP1, WNT, SLUG, SNAIL1, Plakoglobin, HAKAI, HGF receptor (Met), p120-catenin, BMP2, Frizzled  |
| 13 | Signal transduction_Angiotensin II signaling via Beta-arrestin  | 1.18E-06 | eIF4E, 14-3-3, Angiotensin II, Beta-arrestin2, MLCP (reg), STAR, GSK3 beta, Itch, TRPV4, DGK, JNK3(MAPK10), AKT(PKB), MYLK1, p27KIP1, Clathrin heavy chain, MLCK, Casein kinase II, beta chain (Phosvitin), RhoA, CACNA1C, PP2A catalytic, Casein kinase II, alpha' chain (CSNK2A2), p90Rsk, ROCK, TRPC3, MRLC, Beta-adaptin 2, Clathrin, SSH1L, Cofilin, p23 co-chaperone   |
| 14 | Role of activation of WNT signaling in the progression of lung cancer                                 | 1.32E-06 | FZD6, Oct-3/4, SFRP2, Krm1, APC protein, Lef-1, DVL-1, TCF7L2 (TCF4), VEGF-A, p21, Dsh, WIF1, GSK3 beta, Survivin, DKK3, Axin2, SKP2, Axin, CD147, iNOS, Tcf(Lef),   |

|    |   |          |   |
|----|---|----------|---|
|    |   |          | WNT3, ARD1, JNK1(MAPK8), SFRP5, WNT1, SFRP4, WNT2B, LKB1, WNT, WNT10B, WNT2, LRP6, SUZ12, HOXB9, p38 MAPK, Frizzled   |
| 15 | c-Myc in multiple myeloma   | 1.41E-06 | GRP78, eIF4E, YB-1, VEGF-A, HDAC6, p21, IL-6, hnRNP A1, HIF1A, IRF4, CD33, p38 MAPK, PTBP1  |
| 16 | Development_Hedgehog signaling  | 1.75E-06 | GAS1, SPOP, CDK11, KIF27, Smoothened, Beta-arrestin2, Ubiquitin, CDON, GSK3 beta, Itch, Skp2/TrCP/FBXW, DHH, HSP90, SUFU, PTCH1, MLK2(MAP3K10), STK36, GLI-3R, SHH, DYRK2, GLI-3, Casein kinase I, HIP, GLI-1, CDC37, PKA-cat (cAMP-dependent)  |
| 17 | Defective macrophage-mediated bacterial phagocytosis in COPD            | 2.23E-06 | MSR1, FCGR3A, HDAC6, C6orf134, CDC42, MANR, AKT(PKB), LRP1, Tubulin (in microtubules), SR-BI, Sirtuin2, RhoB, CD36, CR1, Tubulin alpha, C1qRp, NRF2   |
| 18 | Immune response_IFN-alpha/beta signaling via MAPKs                      | 2.7E-06  | PML, IP10, JAK1, TCF7L2 (TCF4), Apo-2L(TNFSF10), IFN-alpha/beta receptor, p21, IFNAR1, VAV-1, PL scramblase 1, IKK-epsilon, Ubiquitin, TAP1 (PSF1), MAPKAPK2, IFN-alpha, MEK6(MAP2K6), Axin2, p130, RSAD2, AKT(PKB), p27KIP1, HIP-2, Lck, CD45, MEK3(MAP2K3), IFNAR2, JNK1(MAPK8), MAPKAPK3, AP-1, Filamin B (TABP), FOXO3A, FasR(CD95), TRIM6, JNK(MAPK8-10), p38 MAPK   |
| 19 | DNA damage_ATM/ATR regulation of G2/M checkpoint: cytoplasmic signaling | 3.46E-06 | p38alpha (MAPK14), PP1-cat, 14-3-3, PP2A regulatory, CDC25A, MLCP (reg), TAO2, MAPKAPK2, MEK6(MAP2K6), GADD45 alpha, PLK1, Chk2, Histone H3, CDC25C, MEK3(MAP2K3), CDC25B, Nucleolysin TIAR, MARKK, PP2A catalytic, UBE2C, ATM, FOXO3A, Aurora-B, p38gamma (MAPK12), p38 MAPK, DCK, JIK   |
| 20 | Signal transduction_AKT signaling                                       | 3.53E-06 | RHEB2, Cyclin D3, GAB1, RPS6, p21, I-kB, Bax, PI3K reg class IA, GSK3 alpha/beta, NF-kB, AKT(PKB), HSP90, PDK (PDPK1), p27KIP1, Cyclin D, PP2A catalytic, Caspase-9, Hamartin, GYS1, PCNA, PTEN, FOXO3A, HGF receptor (Met), Bim  |
| 21 | Chemotaxis_Lysophosphatidic acid signaling via GPCRs                    | 3.66E-06 | c-Fos, LARG, ROCK1, PRK1, PKC-zeta, G-protein alpha-q/11, p21, IP3 receptor, YAP1 (YAp65), MLCP (reg), LPAR4, PI3K reg class IA (p85), Bax, GSK3 beta, PLC-beta, DIA1, LPAR6, CREB1, MEK1/2, CDC42, Actin cytoskeletal, TAZ, IL13RA2, AKT(PKB), PDK (PDPK1), RhoA, G-protein alpha-12 family, LPAR1, Tcf(Lef), G-protein alpha-i family, F-Actin cytoskeleton, MKL2, Caspase-9, CD36, G-protein gamma 12, p130CAS, ROCK, PRKD1, AP-1, Caspase-7, PAK, PDZ-RhoGEF, PKC, FasR(CD95), FAK1, SIVA1, Rho GTPase, JNK(MAPK8-10), MKL1, ADAM17, p38 MAPK, Cofilin, PREX1 |
| 22 | Transport_Clathrin-coated vesicle cycle                                 | 3.87E-06 | VTI1A, Myosin I, Rab-8, GCC2, VTI1B, PI3K cat class III (Vps34), DAB2, Actin, YKT6, RAB9P40, RABGEF1, Rab-7, Syntaxin 5, TIP47, GDI2, Actin cytoskeletal, EEA1, Clathrin heavy chain, VAMP8, VAMP7, PIP5KIII, SAR1A, SNX9, VAMP4, Syntaxin 8, Syntaxin 7, GS15, SAR1, Endophilin B1,  |

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|----|---|----------|--|
|    |   |          | RILP (Rab interacting lysosomal protein), Rab-9, Rab11-FIP2, PREB, Clathrin  |
| 23 | Transcription_HIF-1 targets   | 4.07E-06 | PDK1, NIX, PDGF-B, EG-VEGF, PLGF, Oct-3/4, VEGF-A, Cyclin G2, 5'-NTD, ENO1, p21, PGK1, MDR1, ID2, FECH, F263, HXK2, WT1, ALDOC, Mcl-1, Epo, SDF-1, CXCR4, LRP1, PKM2, ARNT, DEC2, iNOS, ROR-alpha, CITED2, HIF1A, HIF-1, GPI, Endoglin, FGF2, IBP1, NANOG, ALDOA, SOX2, CX3CR1, ABCG2, HGF receptor (Met)                |
| 24 | DNA damage_p53 activation by DNA damage                             | 4.71E-06 | P53AIP1, p38alpha (MAPK14), PML, 14-3-3, PP2A regulatory, p21, Bax, TTC5 (Strap), PP2A structural, MEK6(MAP2K6), GADD45 alpha, PUMA, RFWD3, PLK3 (CNK), Chk2, RelA (p65 NF-kB subunit), SMG1, E2F1, DAXX, AATF (Che-1), MARKK, PP2A catalytic, DYRK2, ELAVL1 (HuR), DDB2, USP7, ATM, JNK(MAPK8-10), p38 MAPK, PP2C gamma |
| 25 | Development_Muscle progenitor cell migration in hypaxial myogenesis | 5.02E-06 | GAB1, E2A, MEF2C, FGF8, SPRY1, FGFR1, MYOG, FGF4, PAX3, RBP-J kappa (CBF1), SDF-1, CXCR4, HGF, G-protein alpha-i family, SOS, HES1, SHP-2, MYOD/E47, SNAIL1, LBX1, HGF receptor (Met), ADAM17, MYOD  |
| 26 | Cell cycle_The metaphase checkpoint                                 | 5.59E-06 | CDC20, CENP-C, Aurora-C, CENP-F, MAD1 (mitotic checkpoint), Dynein 1, cytoplasmic, heavy chain, Survivin, PLK1, HP1 gamma, NSL1, CENP-B, CENP-H, INCENP, SPBC25, BUB3, Rod, CDCA1, Aurora-B, HP1 alpha, Zwilch, AF15q14  |
| 27 | Development_TGF-beta receptor signaling                             | 5.62E-06 | Sno-N, eIF4E, GADD45 beta, FKBP12, p21, SMAD2, MEK6(MAP2K6), MEK2(MAP2K2), TSC-22, NF-kB, YY1, TAK1(MAP3K7), MEKK4(MAP3K4), Importin (karyopherin)-beta, SMURF1, TGF-beta receptor type II, Ski, SMURF2, MEK3(MAP2K3), SOS, SARA, NFKBIA, TAB1, p15, FAST-1/2, Caveolin-1, p38 MAPK                                      |
| 28 | Cell adhesion_Tight junctions                                       | 6.08E-06 | Rich1, JAM2, MUPP1, EPB41, F-Actin, ARP3, ACTR3, PKC-zeta, JAM1, Actin, APXL, Myosin VIIA, CDC42, Actin cytoskeletal, Tubulin (in microtubules), RhoA, PARD3, Myosin II, ROCK, Actomyosin, PDZ-RhoGEF, Tubulin alpha, PKC-lambda/iota, MRLC  |
| 29 | Proteolysis_Role of Parkin in the Ubiquitin-Proteasomal Pathway     | 6.64E-06 | FBXW7, UBCH7, Parkin, UBCH8, Caspase-8, SIAH1, HSP70, Tubulin beta, Alpha-synuclein, GPR37, Septin 5 (CDC-REL1), UBE1, Tubulin alpha, Cyclin E, UBC7, Synphilin 1  |
| 30 | Development_PIP3 signaling in cardiac myocytes                      | 7.11E-06 | RHEB2, GAB1, RPS6, 14-3-3, PKC-zeta, PI3K reg class IA, Insulin receptor, GSK3 alpha/beta, CREB1, CDC42, AKT(PKB), PDK (PDPK1), HGF, G-protein alpha-12 family, PARD3, Cyclin D, SOS, Hamartin, p90Rsk, GYS1, PTEN, FOXO3A, IGF-1, HGF receptor (Met), PI3K reg class IB (p101)  |
| 31 | Development_Thrombopoietin signaling via ERK1/2 and PI3K            | 7.94E-06 | PDK1, Cyclin D3, c-Fos, GAB1, PP1-cat, Glycoprotein VI, PKC-zeta, CrkL, VEGF-A, GATA-1, p21, Thrombopoietin, USF1, PI3K reg class IA (p85), GSK3 beta, CREB1, MEK1/2, AKT(PKB), PDK (PDPK1), TAL1, p27KIP1, RelA (p65 NF-kB)   |



|    |   |          |   |
|----|---|----------|---|
|    |   |          | subunit), ITGA2B, c-Cbl, HIF1A, DNA-PK, SOS1, AML1 (RUNX1), SHP-2, FOXO3A, FLI1, p38 MAPK   |
| 32 | Signal transduction_Angiotensin II/AGTR1 signaling via Notch, Beta-catenin and NF-kB pathways             | 8.45E-06 | HES5, CCL2, TCF7L2 (TCF4), ROCK1, VEGF-A, TRPC6, Angiotensin II, Fibronectin, YAP1 (YAp65), I-kB, GSK3 beta, NF-kB2 (p100), Axin2, IL-6, NF-kB, AKT(PKB), RBP-J kappa (CBF1), PDK (PDPK1), TAK1(MAP3K7), RhoA, HEY1, RelA (p65 NF-kB subunit), NF-kB2 (p52), p90RSK1, PRKD1, PKC, HES1, WISP1, Connexin 43, HEY2, Angiotensinogen, SNAIL1, ADAM17, p38 MAPK, PKA-cat (cAMP-dependent) |
| 33 | Development_Role of growth factors in the maintenance of embryonic stem cell pluripotency                 | 8.95E-06 | FGFR2, c-Fos, GAB1, Oct-3/4, ROCK1, SMAD2, FGFR1, PI3K reg class IA (p85), GSK3 beta, PI3K reg class IA, IGF-2, MEK2(MAP2K2), AKT(PKB), PDK (PDPK1), Activin A, TGF-beta receptor type II, Myosin II, FGF2, SOS, Caspase-9, NANOG, ROCK, SOX2, SHP-2, ActRIIB, IGF-1, Bim   |
| 34 | Development_Role of HDAC and calcium/calmodulin-dependent kinase (CaMK) in control of skeletal myogenesis | 8.95E-06 | p38alpha (MAPK14), HDAC9, ERK5 (MAPK7), Calcineurin A (catalytic), RHEB2, NF-AT1(NFATC2), MEF2C, 14-3-3, HDAC4, p21, CaMK IV, MYOG, PI3K reg class IA, IGF-2, MEK6(MAP2K6), AKT(PKB), PDK (PDPK1), CACNA1C, MEF2, HDAC5, NCOA2 (GRIP1/TIF2), CARM1, Calmodulin, MAP3K3, IGF-1, Calcineurin B (regulatory), MYOD   |
| 35 | Development_YAP/TAZ-mediated co-regulation of transcription   | 9.73E-06 | TEF-5, PML, TBX5, Oct-3/4, Lef-1, TEF-1, ID3, ID1, VEGF-A, SMAD2, YAP1 (YAp65), ID2, Survivin, Neurotractin, SIP1 (ZFHX1B), PAX3, TAZ, Catalase, PUMA, HIF1A, FOXM1, ErbB4(ICD), NANOG, TEF-4, TEF-3, SOX2, SLUG, SNAIL1  |
| 36 | Development_Negative regulation of WNT/Beta-catenin signaling at the receptor level                       | 1.02E-05 | Sclerostin, AP complex 2 medium (mu) chain, DAB2, WIF1, CDON, Krm, Syndecans, Casein kinase II, GSK3 alpha/beta, SFRP, Axin, LRP1, SMURF1, Tcf(Lef), APCDD1, PEDF (serpinF1), LRP4, ZNRF3, WNT, LRP6, Clathrin, Glypican-6, AAK1, Frizzled  |
| 37 | Development_Regulation of cytoskeleton proteins in oligodendrocyte differentiation and myelination        | 1.04E-05 | CNTN1 (F3), CDK5R1 (p35), HDAC6, KLHL2, PDGF-R-alpha, Gelsolin, VAV-1, MLCP (reg), TPPP (p24), ERMN, CDC42, Actin cytoskeletal, Fyn, PDGF receptor, Tubulin (in microtubules), Tubulin beta, RhoA, p190RhoGAP, Myosin II, Tubulin alpha, MAP6, MAP4, PTPR-alpha, MRLC, FAK1, MAG, CDK5R2 (p39), MELC, Cofilin   |
| 38 | Cell cycle_Start of DNA replication in early S phase  | 1.1E-05  | ORC2L, MCM5, RPA3, MCM10, ORC6L, ORC4L, MCM2, CDC45L, CDC7, ORC1L, MCM4, E2F1, PP2A catalytic, Geminin, CDC18L (CDC6), Cyclin E, HP1 alpha, DRF1, Histone H1  |
| 39 | Muscle contraction_GPCRs in the regulation of smooth muscle tone  | 1.19E-05 | TRPC5, TRPC4, LARG, TRPC6, G-protein alpha-q/11, Angiotensin II, IP3 receptor, MLCP (reg), Prostacyclin receptor, PLC-beta, MLCK, RhoA, GEFT, G-protein alpha-12 family, Adenosine A2b receptor, ACM2, G-protein alpha-i family, CACNA1C, AVP extracellular region, Myosin II, OT, TBXA2R, MyHC, ACM3, Histamine H1 receptor, ROCK, PDZ-RhoGEF, G-protein alpha-s, Calmodulin, TRPC3, |

|    |   |          |   |
|----|---|----------|---|
|    |   |          | Alpha-1A adrenergic receptor, MRLC, Telokin, TRPC7, G-protein alpha-q, MELC, PKA-cat (cAMP-dependent)   |
| 40 | Transcription_Role of heterochromatin protein 1 (HP1) family in transcriptional silencing | 1.24E-05 | HDAC9, HDAC4, CDC25A, HP1, MYOG, MBD2, Rb protein, HDAC2, Mi-2 alpha, HP1 gamma, Mi-2, SETDB1, MeCP2, Histone H3, E2F1, MEF2, HDAC5, HP1 beta, Cyclin E, HP1 alpha, Histone H4, MYOD  |
| 41 | Stem cells_Pancreatic cancer stem cells in tumor metastasis                               | 1.24E-05 | LARG, VAV-1, IP3 receptor, G-protein alpha-13, MLCP (reg), CDC42, Fyn, SDF-1, MLCK, CXCR4, RhoA, G-protein alpha-i family, F-Actin cytoskeleton, Myosin II, MyHC, ROCK, PDZ-RhoGEF, Calmodulin, MRLC, FAK1, MELC, PI3K reg class IB (p101)  |
| 42 | Oxidative stress_ROS-induced cellular signaling   | 1.26E-05 | Casein kinase II, alpha chains, p38alpha (MAPK14), HES5, VEGF-A, TXNIP (VDUP1), p21, Bak, FASN, Bax, GSK3 beta, FTL, FTH1, IL-6, GADD45 alpha, NF-kB, AKT(PKB), Catalase, PUMA, Thioredoxin, PLK3 (CNK), Chk2, RelA (p65 NF-kB subunit), iNOS, IRP1, HIF1A, Pin1, Glutaredoxin 1, JNK1(MAPK8), NFKBIA, HSPA1A, ELAVL1 (HuR), PRKD1, PKC, LKB1, PTEN, HES1, ATM, DLC1 (Dynein LC8a), JNK(MAPK8-10), SAE2, NRF2, ADAM17, p38 MAPK, APEX, NALP3            |
| 43 | Neurophysiological process_Dynein-dynactin motor complex in axonal transport in neurons   | 1.4E-05  | DCTN1(p150Glued), Importin (karyopherin)-alpha, HDAC6, Vimentin, Ubiquitin, Centractins, DYNLL, Rab-7, Dynein 1, cytoplasmic, heavy chain, Alpha-centractin, DYNLT, HAP40, JNK3(MAPK10), PRNP, AKT(PKB), Snapin, MAPRPE1(EB1), Tubulin (in microtubules), Importin (karyopherin)-beta, Dynein 1, cytoplasmic, light chains, BPAG1, RILP (Rab interacting lysosomal protein), Kinesin heavy chain, Kinesin light chain, Carboxypeptidase H, BDNF, SPTBN2 |
| 44 | NRF2 regulation of oxidative stress response  | 1.4E-05  | Casein kinase II, alpha chains, CRM1, BACH1, SMRT, Ubiquitin, GSK3 beta, UGT1A1, SOD1, PI3K reg class IA, MafK, Actin cytoskeletal, Fyn, AKT(PKB), GSTA3, MafF, PDK (PDPK1), Casein kinase II, beta chain (Phosvitin), Thioredoxin, eIF2AK3, GCL reg, ENC1, PRDX1, JNK1(MAPK8), PKC, GCL cat, TXNRD1, NRF2  |
| 45 | Anti-apoptotic action of Gastrin in pancreatic cancer                                     | 1.44E-05 | p38alpha (MAPK14), Apaf-1, LARG, PI3K reg class IA (p85), Bax, MEK6(MAP2K6), AKT(PKB), PDK (PDPK1), PPAR-gamma, MEKK4(MAP3K4), RhoA, RelA (p65 NF-kB subunit), CCKBR, MEK3(MAP2K3), Caspase-9, NFKBIA, Annexin II, FOXO3A, FAK1, G-protein alpha-q  |
| 46 | Cytoskeleton remodeling_Neurofilaments  | 1.45E-05 | NEFL, CDK5R1 (p35), GFAP, DCTN1(p150Glued), Vimentin, Tubulin gamma 1, Actin cytoskeletal, Peripherin, Tubulin (in microtubules), Plectin 1, Tubulin beta, Tubulin gamma, MUNC18, BPAG1, Tubulin alpha, Kinesin heavy chain   |
| 47 | Inhibition of Ephrin receptors in colorectal cancer                                       | 1.54E-05 | c-Rel (NF-kB subunit), TCF7L2 (TCF4), Ephrin-A receptor 3, CDC42, Ephrin-B1, RhoA, Ephrin-A receptor 1, Ephrin-A receptors, Ephrin-B receptor 3, Ephrin-B receptor 1, ROCK,   |

|    |   |          |   |
|----|---|----------|---|
|    |   |          | Ephrin-B, WNT, Ephrin-B receptor 2, FAK1, Ephrin-A, Ephrin-B receptors, Frizzled  |
| 48 | Immune response_Fc epsilon RI pathway: Lyn-mediated cytokine production | 1.62E-05 | ERK5 (MAPK7), Calcineurin A (catalytic), c-Fos, NF-AT1(NFATC2), CCL2, MEF2C, BFL1, GATA-1, TSLP, VAV-1, IP3 receptor, Fc epsilon RI alpha, MEK6(MAP2K6), IL-13, IL-6, MEK1/2, CDC42, NF-kB, TAK1(MAP3K7), NF-AT2(NFATC1), IL-2, CCL1, MIST, IL-5, MEK3(MAP2K3), Fer, SOS, Fc epsilon RI beta, Btk, NFKBIA, NF-AT, AP-1, Calmodulin, PKC, IL-33, JNK(MAPK8-10), Bcl-10, p38 MAPK |
| 49 | Canonical WNT signaling pathway in colorectal cancer                    | 1.68E-05 | Galectin-3, SFRP2, APC protein, Lef-1, DVL-1, TCF7L2 (TCF4), VEGF-A, Axin1, p21, Dsh, WIF1, PI3K reg class IA (p85), GSK3 beta, Survivin, Axin2, CAS-L, Axin, iNOS, ENC1, Leptin receptor, SFRP5, WNT1, SFRP4, Mucin 2, WNT, SLUG, WNT2, LRP6, HGF receptor (Met), Frizzled, WNT6   |
| 50 | Proteolysis_Putative ubiquitin pathway                                  | 1.94E-05 | FBXW7, UBCH7, Parkin, UBCH8, Ubiquitin, UBCH6, SKP2, UEV1A, HSP70, GPR37, Septin 5 (CDC-REL1), UBE1, MJD (ataxin-3), RING-box protein 1, Synphilin 1  |

**Table S5.** Pathway analysis of LAGE2B-coexpressed genes from public breast cancer databases using the MetaCore database (p<0.01 set as the cutoff value)

| # | Maps   | pValue   | Network Objects from Active Data  |
|---|--|----------|---|
| 1 | Immune response_IFN-alpha/beta signaling via PI3K and NF-kB pathways | 3.69E-09 | PI3K cat class IA, RelA (p65 NF-kB subunit), Cyclin D3, Tyk2, TRAF2, IRS-1, PDCD4, E2F1, RPS6, DHFR, NMI, eIF4E, ERK1/2, IFNAR2, eIF4B, CDC25A, p90RSK1, eIF4G1/3, IFN-alpha/beta receptor, NIK(MAP3K14), IFNAR1, PKC-epsilon, PCNA, 4E-BP1, I-kB, p70 S6 kinases, GSK3 beta, CDK4, IFN-alpha, p19, eIF4A, CREB1, p130, MEK1/2, Cyclin A, b-Myb, NF-kB, p107, p27KIP1, IL-12 beta |
| 2 | Development_PIP3 signaling in cardiac myocytes                       | 1.33E-08 | HGF, G-protein alpha-12 family, PI3K cat class IA, PARD3, RHEB2, GAB1, IRS-1, RPS6, Cyclin D, 14-3-3, PKC-zeta, PTP-1B, SOS, Hamartin, p90Rsk, BAD, 4E-BP1, PI3K reg class IA, PTEN, Insulin receptor, GSK3 alpha/beta, CREB1, IGF-1 receptor, G-protein beta/gamma, HGF receptor (Met)   |
| 3 | Signal transduction_AKT signaling                                    | 4.43E-08 | PI3K cat class IA, RHEB2, Cyclin D3, GAB1, IRS-1, RPS6, Cyclin D, PP2A catalytic, Hamartin, BAD, PCNA, 4E-BP1, I-kB, Bax, PI3K reg class IA, PTEN, MDM2, GSK3 alpha/beta, IGF-1 receptor, NF-kB, HGF receptor (Met), p27KIP1, Bim   |
| 4 | Apoptosis and survival_Role of PKR in stress-induced apoptosis       | 6.07E-08 | TRAF3, Tyk2, ATF-3, TRAF2, eIF4E, ERK1/2, ATF-4, PP2A regulatory, PP2A catalytic, IFN-alpha/beta receptor, NFKBIA, PACT, 4E-BP1, I-kB, TARBP2, IFN-alpha, IKK-beta, NFAT-90, PPP2R5A, NFKBIB, IRF3, NF-kB, MSK2, TAB2, NF-kB p50/p65, TLR3  |
| 5 | DNA damage_ATM/ATR regulation of G1/S checkpoint                     | 7.8E-08  | Chk2, hnRNP K, SMG1, FBXW7, ERK1/2, Histone H2AX, PP2A regulatory, CDC25A, PP2A catalytic, BTG2, PER3, PCNA, p70  |

|    |  |          |  |
|----|--|----------|--|
|    |  |          | S6 kinases, CDK4, PP2A structural, ATM, MEK2(MAP2K2), MDM2, c-Abl, Cyclin A, Cyclin D1, FBXO31, p27KIP1  |
| 6  | Immune response_IL-11 signaling pathway via MEK/ERK and PI3K/AKT cascades      | 8.21E-08 | gp130, RelA (p65 NF-kB subunit), ICAM1, IL-8, RPS6, ATF-1, ERK1/2, Leukocyte elastase, SOS, IL-11 receptor, p90Rsk, NFKBIA, YAP1 (YAp65), IL11RA, I-kB, p70 S6 kinases, PI3K cat class IA (p110-alpha), GSK3 beta, sIL11-RA, NFKBIB, CREB1, IL-6, MEK1/2, Fyn, Cyclin D1, SNAIL1, SFK, p27KIP1, IL-12 beta, IL-2   |
| 7  | Development_Positive regulation of WNT/Beta-catenin signaling in the cytoplasm | 1.78E-07 | GSKIP, TBL1X, TGF-beta 1, IRS-1, RIPK4, APC protein, Alpha-1 catenin, 14-3-3, PKA-reg type II (cAMP-dependent), PP2A catalytic, RNF220, ZBED3, Beta-arrestin2, YAP1 (YAp65), PPP2R2A, Trabid, Tankyrases, USP9X, USP25, WNT, Insulin receptor, USP7, Joubertin, GSK3 alpha/beta, PP2C alpha, IGF-1 receptor, TBLR1, ERK2 (MAPK1), NKD2, Axin, MITF, SET7 |
| 8  | Activation of TNF-alpha-dependent pro-tumoral effect in colorectal cancer      | 2.03E-07 | RelA (p65 NF-kB subunit), IP10, NF-kB1 (p50), ICAM1, CCL2, MADD, TRAF2, IL-8, ERK1/2, ALDR, TRADD, SOS, NIK(MAP3K14), I-kB, GRO-1, NF-kB p65/c-Rel, TRAF1, IKK-beta, IL-6, MEK1/2, NF-kB, NF-kB p50/p65, p38 MAPK, Axin  |
| 9  | Development_Delta- and kappa-type opioid receptors signaling via beta-arrestin | 3.04E-07 | Metenkefalin, GRK6, G-protein alpha-i family, GRK3, Kappa-type opioid receptor, Beta-arrestin2, Dynamin-1, PKC, GRK5, CREB1, G-protein beta/gamma, Clathrin, Leu-enkephalin, p27KIP1, Histone H4   |
| 10 | IGF family signaling in colorectal cancer                                      | 3.2E-07  | RelA (p65 NF-kB subunit), IRS-1, IL-8, E2F1, eIF4E, ERK1/2, Clusterin, SOS, IGF-2 receptor, Rad51, GIPC, 4E-BP1, I-kB, PI3K cat class IA (p110-alpha), ZNF143, GSK3 beta, PTEN, c-Myb, GSK3 alpha/beta, IGF-1 receptor, MEK1/2, Cyclin D1, NF-kB, ERK2 (MAPK1), ERK1 (MAPK3), IBP, MAT2A   |
| 11 | Skeletal muscle atrophy in COPD  | 3.8E-07  | ALK-4, KCRM, RelA (p65 NF-kB subunit), iNOS, RHEB2, MLC1F, ERK1/2, 14-3-3, MuRF1, eIF3S5, beta-MHC, SMAD2, MyHC, NEDD4, NFKBIA, MYOG, Myosin-IIA, 4E-BP1, I-kB, GSK3 beta, MLC2, Beta TnTF, ERK2 (MAPK1), NF-kB p50/p65, p38 MAPK, MYOD  |
| 12 | Transport_Clathrin-coated vesicle cycle  | 3.92E-07 | VTI1A, AP180, VAMP8, Myosin I, Rabaptin-5, HIP1, Rab11-FIP1, GOS-28, SAR1A, VTI1B, SNX9, PI3K cat class III (Vps34), VAMP4, Actin, YKT6, GS15, Rabenosyn-5, Rab-5A, RABGEF1, Myosin VI, SAR1, Rab-11A, RILP (Rab interacting lysosomal protein), Epsin 1, Syntaxin 5, Rab11-FIP2, PREB, EEA1, Clathrin, Clathrin heavy chain                             |
| 13 | Neurogenesis_NGF/ TrkA MAPK-mediated signaling                                 | 4.58E-07 | GAB2, MATK, Efs/Sin, RIN, NF-kB1 (p50), SAC, MEK3(MAP2K3), ERK1/2, HB-EGF, PKC-zeta, CrkL, EGR1, SGK1, PP2A regulatory, PKA-reg (cAMP-dependent), SOS, PP2A catalytic, FRS2, C3G, PKC-epsilon, SH2B, p90Rsk, TY3H, NGF, MAPKAPK2, Calmodulin, MAGI-2, KIDINS220, CREB1, MEK1/2, SUR-8, Cyclin D1, RASGRF1, SP1, RGS2, p107, RIT, p38 MAPK, KCTD11        |
| 14 | Immune response_IL-33 signaling pathway  | 5.79E-07 | PI3K cat class IA, RelA (p65 NF-kB subunit), ICAM1, CCL2, IL-8, Histone H2B, MEK3(MAP2K3), ERK1/2, ST2L, NIK(MAP3K14), Ubiquitin, I-kB, GRO-1, PI3K reg class IA,  |

|    |   |          |  |
|----|---|----------|--|
|    |   |          | ATF-2, GM-CSF, IL-33, IKK-beta, IRAK1, eNOS, IL-6, MEK1/2, NF-kB, TAB2, NF-kB p50/p65, Histone H2A   |
| 15 | Immune response_IL-2 signaling via ERK, PI3K, and PLC-gamma                               | 8.04E-07 | GAB2, PI3K cat class IA, Lck, Cyclin D3, c-Cbl, IRS-1, E2F1, RPS6, ERK1/2, CrkL, SOS1, JAK3, 4E-BP1, p70 S6 kinases, Sirtuin1, PKC-theta, CDK4, c-Myb, MEK1/2, Cyclin A, Fyn, PYGM, NF-kB, ERK2 (MAPK1), ALPHA-PIX, p70 S6 kinase2, p27KIP1, ERK1 (MAPK3), Bim, IL-2   |
| 16 | Apoptosis and survival_APRIL and BAFF signaling   | 8.26E-07 | RelA (p65 NF-kB subunit), Calcineurin A (catalytic), TRAF3, NF-kB1 (p50), NF-AT1(NFATC2), TRAF2, BAFF-R, MIP-1-beta, BFL1, NIK(MAP3K14), CD21, TRAF5, NF-kB p50/p50, I-kB, IKK-beta, BCMA(TNFRSF17), TACI(TNFRSF13B), Cyclophilin B, CD23, NF-kB p50/p65   |
| 17 | Oxidative stress_ROS-induced cellular signaling   | 1.05E-06 | NOTCH1 (NICD), Thioredoxin, PLK3 (CNK), Chk2, ACACA, RelA (p65 NF-kB subunit), iNOS, IL-8, ERK1/2, EGR1, PKA-reg (cAMP-dependent), Pin1, NIK(MAP3K14), Bak, Cytochrome c, E2I, NFKBIA, HSPA1A, Bax, Sirtuin1, GSK3 beta, GPX1, PKC, LKB1, PTEN, FTH1, ATM, IKK-beta, DLC1 (Dynein LC8a), MDM2, c-Abl, IL-6, Cyclin D1, NF-kB, SP1, NF-kB p50/p65, PUMA, ADAM17, p38 MAPK |
| 18 | Development_Notch Signaling Pathway   | 1.25E-06 | NOTCH1 (NICD), NOTCH1 receptor, Histone H3, c-Rel (NF-kB subunit), FBXW7, MAML1, GCN5, Jagged2, TLE, NFKBIA, Ubiquitin, p63, p73, HDAC2, Radical fringe, NOTCH1 precursor, HEY2, NOTCH1 (NEXT), ADAM17, Histone H4, MYOD   |
| 19 | DNA damage_p53 activation by DNA damage   | 1.29E-06 | PLK3 (CNK), Chk2, RelA (p65 NF-kB subunit), PML, SMG1, E2F1, DAXX, 14-3-3, PP2A regulatory, MARKK, PP2A catalytic, 14-3-3 theta, Tip60, Bax, Sirtuin1, TTC5 (Strap), PP2A structural, USP7, ATM, MDM2, c-Abl, PI3G, FBXO31, PUMA, p38 MAPK, PP2C gamma   |
| 20 | PDE4 regulation of cyto/chemokine expression in inflammatory skin diseases                | 1.48E-06 | RelA (p65 NF-kB subunit), iNOS, IP10, NF-kB1 (p50), NF-AT1(NFATC2), CCL2, IL-8, G-protein alpha-i family, ERK1/2, 14-3-3, PKA-reg (cAMP-dependent), NFKBIA, NF-kB p50/p50, G-protein alpha-i1, MAPKAPK2, Adenylate cyclase, CREB1, IL-6, MEK1/2, NF-kB p50/p65, p38 MAPK, IL-12 beta, IL-2   |
| 21 | Development_MAG-dependent inhibition of neurite outgrowth                                 | 1.52E-06 | NGFR(TNFRSF16), TrkC, Destrin, Myosin II, NT-4/5, Reticulon 4, MyHC, RhoGDI alpha, MLCP (reg), NGF, NGFR (ICD), RTN4R, NGFR (CTF), MRLC, RASGRF1, p200RhoGAP, MELC, ADAM17, BDNF   |
| 22 | Signal transduction_Angiotensin II signaling via Beta-arrestin                            | 1.57E-06 | GRAF2, GRK6, eIF4E, ERK1/2, 14-3-3, CACNA1C, PP2A catalytic, p90Rsk, Beta-arrestin2, BAD, MLCP (reg), p70 S6 kinases, GSK3 beta, AP-2 alpha subunits, GRK5, MRLC, Beta-adaptin 2, TRPV4, DGK, Clathrin, MYLK1, p27KIP1, Clathrin heavy chain, SSH1L, MLCK  |
| 23 | IL-17 and IL-17F-induced inflammatory signaling in normal and asthmatic airway epithelium | 1.59E-06 | IP10, ICAM1, IL-8, ERK1/2, ENA-78, p90Rsk, I-kB, GRO-1, GCP2, GM-CSF, MEK2(MAP2K2), CREB1, IL-6, NF-kB p50/p65, G-CSF, p38 MAPK  |

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| 24 | Development_BMP signaling in cardiac myogenesis  | 1.61E-06 | BMP5, BMP receptor 2, MEK3(MAP2K3), BMP7, beta-MHC, CSX (Nkx2.5), BNP, alpha-MHC, ID2, ACTA1, MLC2, BMP6, ATF-2, BMPR1A, Cyclin D1, p38 MAPK, N-Myc, BMP2   |
| 25 | Immune response_Histamine H1 receptor signaling in immune response                               | 1.74E-06 | RelA (p65 NF-kB subunit), Calcineurin A (catalytic), iNOS, ICAM1, MMP-1, IL-8, G-protein alpha-q/11, NFKBIA, I-kB, Calmodulin, PLC-beta, cPLA2, GM-CSF, IKK-beta, MEK2(MAP2K2), eNOS, IL-6, G-protein beta/gamma, ERK2 (MAPK1), NF-kB p50/p65, p38 MAPK, ERK1 (MAPK3)   |
| 26 | Development_Hedgehog signaling   | 1.74E-06 | Cul3/SPOP/Rbx1 E3 ligase, SPOP, Sin3A, PTCH1, MLK2(MAP3K10), STK36, GLI-3R, KIF27, Beta-arrestin2, GLI-2, Ubiquitin, CDON, BOC, GSK3 beta, GLI-3, Casein kinase I, Skp2/TrCP/FBXW, DHH, GLI-1, CDC37, Cullin 3, NUMB  |
| 27 | Putative role of Estrogen receptor and Androgen receptor signaling in progression of lung cancer | 2.32E-06 | CYP1B1, RHEB2, G-protein alpha-i family, ERK1/2, 14-3-3, SOS, Cytochrome c, ESR2 (nuclear), NCOA2 (GRIP1/TIF2), ESR2 (mitochondrial), ESR2 (membrane), Kallikrein 3 (PSA), BAD, Androgen receptor, ID2, Bax, MAPKAPK2, MEK2(MAP2K2), CYP19, CREB1, Cyclin D1, NCOA1 (SRC1), ERK2 (MAPK1), p38 MAPK, ERK1 (MAPK3)  |
| 28 | Transport_RAN regulation pathway   | 3.49E-06 | Importin (karyopherin)-beta, CRM1, SUMO-1, RanBP1, NUP153, Importin (karyopherin)-alpha, RCC1, RanGAP1, NUP62, RanBP2, E2I, NUP58   |
| 29 | Apoptosis and survival_Anti-apoptotic TNFs/NF-kB/Bcl-2 pathway                                   | 3.68E-06 | NGFR(TNFRSF16), RelA (p65 NF-kB subunit), TRAF3, RANKL(TNFSF11), TRAF2, PKC-zeta, BFL1, TRADD, NIK(MAP3K14), TRAF5, FN14(TNFRSF12A), RANK(TNFRSF11A), NGF, I-kB, IKK-beta, BCMA(TNFRSF17), TACI(TNFRSF13B), IRAK1/2, NF-kB, CD40L(TNFSF5)   |
| 30 | Development_Negative regulation of WNT/Beta-catenin signaling in the cytoplasm                   | 4.4E-06  | Prickle-1, NOTCH1 receptor, c-Cbl, CXXC4, E2F1, RIPK4, APC protein, Alpha-1 catenin, FAF1, Casein kinase I epsilon, PP2A catalytic, PI3K cat class III (Vps34), SENP2, RNF185, Casein kinase I alpha, YAP1/TAZ, YAP1 (YAp65), G-protein alpha-13, WWP1, LATS1, STK4, WNT, GSK3 alpha/beta, G-protein beta/gamma, WDR26, Skp2/TrCP/FBXW, TAZ, Cyclin D1, NKD2, DACT3, Axin |
| 31 | Development_Thrombopoietin signaling via ERK1/2 and PI3K   | 4.43E-06 | GAB2, PI3K cat class IA, RelA (p65 NF-kB subunit), Cyclin D3, GAB1, ITGA2B, c-Cbl, NF-kB p50/c-Rel, DNA-PK, ERK1/2, PKC-zeta, CrkL, EGR1, PDHA (somatic), SOS1, Thrombopoietin, C3G, 4E-BP1, NF-E2 (45 kDa), GSK3 beta, CREB1, MEK1/2, SP1, FLI1, TAL1, p27KIP1, p38 MAPK   |
| 32 | Immune response_IL-17 signaling pathways   | 4.88E-06 | PI3K cat class IA, CCL20, iNOS, ICAM1, CCL2, RANKL(TNFSF11), MMP-1, IL-8, MEK3(MAP2K3), ERK1/2, ENA-78, NIK(MAP3K14), I-kB, GSK3 beta, GRO-1, PI3K reg class IA, GCP2, GM-CSF, IKK-beta, MEK2(MAP2K2), IL-6, NF-kB, SP1, G-CSF, p38 MAPK  |
| 33 | CHDI_Correlations from Replication data_Causal network (positive correlations)                   | 5.62E-06 | PI3K cat class IA, IL-1 alpha, Calcineurin A (catalytic), Lck, NF-AT1(NFATC2), ICAM1, HIP1, MEK3(MAP2K3), PSMC2, CD28, MSK1/2 (RPS6KA5/4), MEF2, NIK(MAP3K14), LAT, RhoGDI alpha, I-kB, PKC-theta, Calmodulin, ZAP70, NR2,  |

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|    |   |          | IKK-beta, CREB1, G-protein beta/gamma, PSD-95, IRAK1/2, CD83, NF-kB, HSP70, p38 MAPK, MEKK4(MAP3K4)   |
| 34 | Transcription_Epigenetic regulation of gene expression    | 6.05E-06 | SMYD2, GASC1, Histone H3, UTX, Histone H2B, GCN5, PRMT1, HDAC6, Sirtuin6, DOT1, RBB2, HBOA, Tip60, MLL1 (HRX), CARM1, Sirtuin1, DNMT3L, HDAC2, MYST1, MORF, Histone H2A, AOF1, Histone H4, SET7   |
| 35 | PI3K signaling in gastric cancer                          | 6.19E-06 | HGF, PI3K cat class IA, RelA (p65 NF-kB subunit), IRS-1, CCKBR, IL-8, ErbB3, CBL-B, G-protein alpha-q/11, MDR1, BAD, I-kB, PI3K cat class IA (p110-alpha), GSK3 beta, PI3K reg class IA, PTEN, Cyr61, Cyclin D1, PRNP, NF-kB p50/p65, HGF receptor (Met), BMP2  |
| 36 | Role of tumor-infiltrating B cells in anti-tumor immunity | 6.28E-06 | G3P2, IP10, CD20, MAGEC1, GAS11, T-bet, DHFR, G-protein alpha-i family, MAGE-1 antigen, CXCR5, POLR2B, IFN-alpha/beta receptor, IL4RA, IRF4, CD19, JAK3, Btk, ADAM-TS9, MAGE-3, ATF-2, IFN-alpha, GAGE2, KTN1, G-protein beta/gamma, NXF2, MAGEB2, NF-kB, CT47A, MAGEC2, CD23, IL-12 beta, IL-2, CD40L(TNFSF5)  |
| 37 | ERBB family and HGF signaling in gastric cancer           | 7.47E-06 | HGF, PI3K cat class IA, IL-8, MEK3(MAP2K3), ERK1/2, ErbB3, HB-EGF, EGR1, ErbB4, SOS, BAD, Amphiregulin, GSK3 beta, PI3K reg class IA, MEK1/2, Cyclin D1, TGF-alpha, ERK2 (MAPK1), SP1, HGF receptor (Met), p27KIP1, p38 MAPK, ERK1 (MAPK3)  |
| 38 | NF-AT signaling in cardiac hypertrophy                    | 7.79E-06 | gp130, PI3K cat class IA, Calcineurin A (catalytic), GAB1, IRS-1, G-protein alpha-i family, ADSSL1, MYBPC3, HDAC5, G-protein alpha-q/11, beta-MHC, PKC-epsilon, CSX (Nkx2.5), Troponin I, cardiac, alpha-MHC, MEF2D, GSK3 beta, Calmodulin, PI3K reg class IA, LIF, IL-6, IGF-1 receptor, G-protein beta/gamma, Beta-1 adrenergic receptor, Troponin T, cardiac, LIF receptor |
| 39 | Aberrant production of IL-2 and IL-17 in SLE T cells      | 8.68E-06 | NOTCH1 (NICD), TGF-beta 1, RelA (p65 NF-kB subunit), Lck, NF-AT1(NFATC2), Fc epsilon RI gamma, ROR-gamma, ERK1/2, PP2A cat (beta), PKA-reg (cAMP-dependent), SOS, LAT, I-kB, Calmodulin, ZAP70, NOTCH1 precursor, CREB1, IL-6, MEK1/2, CD3 epsilon, SP1, NF-kB p50/p65, p70 S6 kinase2, IL-2  |
| 40 | Signal transduction_PKA signaling                         | 9.17E-06 | G-protein alpha-12 family, PDE3B, G-protein alpha-i family, PHK gamma, KDELR, PP2A regulatory, PKA-reg type II (cAMP-dependent), PKA-reg (cAMP-dependent), p90RSK1, PDE3A, Troponin I, cardiac, AKAP8, NFKBIA, G-protein alpha-13, BAD, Androgen receptor, Adenylate cyclase, GSK3 alpha/beta, NFKBIB, CREB1, GABA-A receptor beta-2 subunit, PKI                             |
| 41 | Immune response_BAFF-induced signaling                    | 9.17E-06 | RHEB2, TRAF2, RPS6, BAFF-R, MEK3(MAP2K3), eIF4E, ERK1/2, TRIM2, PI3K cat class IA (p110-delta), BAD, Ubiquitin, 4E-BP1, MAPKAPK2, GSK3 alpha/beta, BCMA(TNFRSF17), CREB1, MEK1/2, TACI(TNFRSF13B), ERK2 (MAPK1), p38 MAPK, ERK1 (MAPK3), Bim  |

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| 42 | Cell cycle_Nucleocytoplasmic transport of CDK/Cyclins                                     | 9.43E-06 | CRM1, Cyclin D3, Cyclin D, Importin (karyopherin)-alpha, Karyopherin beta 1, GSK3 beta, CDK4, Cyclin A, Cyclin D1, ERK1 (MAPK3)  |
| 43 | Development_Muscle progenitor cell migration in hypaxial myogenesis                       | 1.06E-05 | NOTCH1 (NICD), HGF, NOTCH1 receptor, GAB1, E2A, G-protein alpha-i family, MAML1, ERK1/2, SOS, FRS2, FGFR1, MYOG, G-protein beta/gamma, MYOD/E47, SNAIL1, NOTCH1 (NEXT), HGF receptor (Met), ADAM17, MYOD   |
| 44 | Development_Negative regulation of WNT/Beta-catenin signaling in the nucleus              | 1.06E-05 | KDM2, TBL1X, TRRAP, Calcineurin A (catalytic), c-Cbl, HBP1, Oct-3/4, CDX2, E2F1, APC protein, SOX17, Alpha-1 catenin, 14-3-3, Casein kinase I epsilon, TRIM33, GLI-3R, CHD8, TLE, SENP2, NF-AT5, GSK3 beta, HDAC2, WNT, eNOS, HIC1, CtBP, TBLR1, TAB2, HIC5, PPAR-gamma, Axin, Histone H1                      |
| 45 | Cell cycle_Regulation of G1/S transition (part 1)   | 1.23E-05 | PLK3 (CNK), Chk2, TGF-beta 1, Cyclin D3, Cyclin D, PP2A regulatory, CDC25A, PP2A catalytic, SMAD2, Ubiquitin, GSK3 beta, CDK4, Cyclin A, Skp2/TrCP/FBXW, Cyclin D1, RING-box protein 1, SP1, p27KIP1   |
| 46 | TNF-alpha-induced inflammatory signaling in normal and asthmatic airway epithelium        | 1.23E-05 | CCL17, IP10, ICAM1, CCL2, IL-8, ERK1/2, PP2A catalytic, TSLP, NFKBIA, FN14(TNFRSF12A), I-kB, GRO-1, GM-CSF, IKK-beta, IL-6, NF-kB, NF-kB p50/p65, p38 MAPK   |
| 47 | Immune response_IL-1 signaling pathway  | 1.34E-05 | JAM2, PI3K cat class IA, IL-1 alpha, RelA (p65 NF-kB subunit), iNOS, NF-kB1 (p105), IP10, NF-kB1 (p50), ICAM1, CCL2, RANKL(TNFSF11), MMP-1, IL-8, MEK3(MAP2K3), ERK1/2, PKC-zeta, EGR1, NIK(MAP3K14), I-kB, MAPKAPK2, GRO-1, GM-CSF, IRAK1, IL-6, MEK1/2, Collagen II, NF-kB, NF-kB p50/p65, MYLK1, PPAR-gamma |
| 48 | Signal transduction_Adenosine A2A receptor signaling pathway                              | 1.34E-05 | RelA (p65 NF-kB subunit), Kif2a, NF-kB1 (p50), DNA-PK, ERK1/2, PKA-reg (cAMP-dependent), SOS, Kir6.2, SK4/IK1, I-kB, GSK3 beta, Adenylate cyclase, ATM, eNOS, CREB1, MEK1/2, SFK, p38 MAPK, IL-12 beta, Adenosine A2a receptor, Dopamine D2 receptor, IL-2   |
| 49 | Interleukins-induced inflammatory response in asthmatic airway fibroblasts                | 1.42E-05 | GRO-2, IL-1 alpha, RelA (p65 NF-kB subunit), ICAM1, CCL2, IL-8, ERK1/2, NGF, GRO-1, GM-CSF, IL-33, IL-6, MEK1/2, NF-kB, NF-kB p50/p65, G-CSF, p38 MAPK   |
| 50 | Th2 cytokine- and TNF-alpha-induced inflammatory response in asthmatic airway fibroblasts | 1.42E-05 | TGF-beta 1, RelA (p65 NF-kB subunit), ICAM1, CCL2, IL-8, IL-4R type II, ERK1/2, Eotaxin-3, IL4RA, IL13RA1, GM-CSF, IL-6, NF-kB, NF-kB p50/p65, ITGA5, G-CSF, CD40L(TNFSF5)   |

**Table S6.** Pathway analysis of LAGE3-coexpressed genes from public breast cancer databases using the MetaCore database (p<0.01 set as the cutoff value)

| # | Maps  | pValue   | Network Objects from Active Data  |
|---|---|----------|---|
| 1 | DNA damage_ATM/ATR regulation of G2/M checkpoint: cytoplasmic signaling | 2.52E-13 | p38alpha (MAPK14), BORA, PP1-cat, 14-3-3, PP2A regulatory, CDC25A, Nek11, CDK1 (p34), MLCP (reg), Chk1, MAPKAPK2, MEK6(MAP2K6), B56G, Cyclin B1, PLK1, MLCP (cat), Chk2, Brca1, Histone H3, CDC25C, beta-TrCP, MEK3(MAP2K3), CDC25B, JAB1, MARKK, PP2A catalytic, |



|   |  |          |   |
|---|--|----------|---|
|   |  |          | ATR, Aurora-A, MEK4(MAP2K4), UBE2C, MEKK1(MAP3K1), FOXO3A, c-Abl, Aurora-B, JNK2(MAPK9), Brca1/Bard1, p38 MAPK, DCK   |
| 2 | Transcription_Negative regulation of HIF1A function                            | 6.02E-13 | FHL3, p14ARF, Casein kinase I delta, VHL, COMMD1 (MURR1), FBXW7, SART1, VCP, SKP1, UBXD7, Ubiquitin, GSK3 beta, EGLN2, MCM7, Elongin B, EAF2, HSP40, MCM2, HSP90, Calpain 1(mu), HSP70, HSPA4, SAT2, EGLN1, PLK3 (CNK), MCM3, DEC2, HSC70, PRDX2, CITED2, HIF1A, ARD1, PSMA7, Sirtuin2, HSP90 beta, AML1 (RUNX1), FHL1 (SLIM1), Cul2/Rbx1 E3 ligase, PTEN, Sirtuin7, SSAT, Elongin C, HIF-prolyl hydroxylase, PRDX4, CHIP, RUVBL2   |
| 3 | Development_Negative regulation of WNT/Beta-catenin signaling in the nucleus   | 1.82E-12 | ZNF703, TBL1X, Casein kinase I delta, Calcineurin A (catalytic), BACH1, HBP1, Oct-3/4, VHL, PGAM5, Alpha-1 catenin, TCF7L2 (TCF4), 14-3-3, Jade-1, Casein kinase I epsilon, Beta-catenin, PAX7, BCL9/B9L, PC1-CTT, TLE, Dsh, Menin, NF-AT5, GSK3 beta, HDAC2, ICAT, HIC1, LATS2, P15RS, CtBP, TBLR1, TAB2, PJA2, PPAR-gamma, Axin, TAK1(MAP3K7), SOX9, TRRAP, Tcf(Lef), CDX2, TRIM33, GLI-3R, CHD8, SENP2, Kaiso, SOX2, WNT, FOXO3A, GPX4, CHIBBY, HDAC1, Plakoglobin, RUVBL2, Frizzled, Histone H1   |
| 4 | Development_Negative regulation of WNT/Beta-catenin signaling in the cytoplasm | 1.93E-12 | Casein kinase I delta, VHL, PP1-cat, RIPK4, Presenilin 1, Alpha-1 catenin, Laforin, FAF1, Casein kinase I epsilon, Beta-catenin, CYLD, PI3K cat class III (Vps34), DAB2, Dsh, Rac1, G-protein alpha-13, STK4, Itch, GSK3 alpha/beta, Ankyrin-G, LATS2, G-protein beta/gamma, WDR26, Skp2/TrCP/FBXW, TAZ, Axin, KLHL12, HECTD1, Prickle-1, HIPK2, Tcf(Lef), beta-TrCP, PP2A catalytic, PR72, SENP2, RNF185, YAP1/TAZ, MAP1LC3A, ELAVL1 (HuR), PEG3, Cul2/Rbx1 E3 ligase, Malin, PKC-alpha, Porf-2, WNT, Beclin 1, NEDD4L, Cyclin D1, NKD2, DACT3, Frizzled |
| 5 | Transcription_HIF-1 targets  | 3.81E-12 | PDK1, NIX, TGF-beta 1, PDGF-B, EG-VEGF, PLGF, Oct-3/4, P4HA2, PFKL, REDD1, ENO1, Carbonic anhydrase IX, PGK1, Stanniocalcin 2, NIP3, MDR1, AK3, ID2, FECH, Adipophilin, F263, HXK2, PLAUR (uPAR), DEC1 (Stra13), Mcl-1, Epo, SDF-1, CXCR4, LRP1, PKM2, G3P2, TGF-beta 2, DEC2, Lysyl oxidase, ROR-alpha, Adrenomedullin, CITED2, HIF1A, GPI, Endoglin, FGF2, Angiopoietin 2, MGF, GLUT1, Carbonic anhydrase XII, ALDOA, SOX2, TGF-beta 3, CX3CR1, LOXL2, TGM2, Galectin-1, MCT4, ABCG2, HGF receptor (Met), Leptin  |
| 6 | Development_Positive regulation of WNT/Beta-catenin signaling in the cytoplasm | 3.83E-12 | TBL1X, Bcl-9, TGF-beta 1, BIG1, IRS-2, IRS-1, UBE2B, PP1-cat, RIPK4, Alpha-1 catenin, 14-3-3, Beta-catenin, TGIF, Dsh, USP47, Rac1, Beta-arrestin2, CDK1 (p34), PPP2R2A, USP25, PR130, GSK3 alpha/beta, IGF-1 receptor, TBLR1, AKT(PKB), Axin, GSKIP, HECTD1, ITGB1, HIPK2, Tcf(Lef), 14-3-3 zeta/delta, TGT, PKA-reg type II (cAMP-dependent), PP2A catalytic, RNF220, ILK, Tankyrases, BIG2, USP9X, WNT, Jouberin, FAK1, PP2C alpha, JNK(MAPK8-10), SMAD3, NKD2, Frizzled   |

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| 7  | Chemotaxis_Lysophosphatidic acid signaling via GPCRs  | 7.37E-12 | c-Fos, alpha-6/beta-1 integrin, PI3K cat class IA (p110-beta), H-Ras, LARG, ROCK1, PRK1, PKC-zeta, Beta-catenin, EGR1, HDAC7, G-protein alpha-q/11, PKC-epsilon, TRIP6, Rac1, IP3 receptor, LPAR2, MLCP (reg), LPAR4, PI3K reg class IA (p85), Bax, GSK3 beta, PLC-beta, FKHR, DIA1, LPAR6, Caspase-3, CREB1, MEK1/2, G-protein beta/gamma, CDC42, Actin cytoskeletal, N-CoR, TAZ, MSK1, AKT(PKB), PDK (PDPK1), c-Src, Tiam1, cPKC (conventional), G-protein alpha-12 family, PLC-eta 1, LPAR1, Tcf(Lef), G-protein alpha-i family, F-Actin cytoskeleton, MEK4(MAP2K4), 4E-BP1, p130CAS, ROCK, PRKD1, Caspase-7, PAK, p70 S6 kinase1, PKC, Vinculin, PLC-delta 1, Bcl-2, FasR(CD95), FAK1, SIVA1, Rho GTPase, JNK(MAPK8-10), MKL1, PLC-beta3, ADAM17, p38 MAPK, Elk-1, PREX1 |
| 8  | Immune response_IFN-alpha/beta signaling via MAPKs    | 6E-11    | PML, IP10, ISG15, Tyk2, TCF7L2 (TCF4), Beta-catenin, PRMT1, ZNF145, PIAS1, Apo-2L(TNFSF10), IFN-alpha/beta receptor, IFNAR1, IFN-beta, Rac1, Ubiquitin, TAP1 (PSF1), MAPKAPK2, PKC-theta, MEK6(MAP2K6), Axin2, p130, MSK1, AKT(PKB), p27KIP1, FZD7, HIP-2, Lck, CD45, PKR, MEK3(MAP2K3), IFNAR2, IRF9, MEK4(MAP2K4), Ku80, MAPKAPK3, MEKK1(MAP3K1), Filamin B (TAPB), FOXO3A, FasR(CD95), IRF7, Cyclin D1, JNK(MAPK8-10), HDAC1, SMAD3, p38 MAPK   |
| 9  | Transport_Clathrin-coated vesicle cycle               | 7.6E-11  | NSF, VTI1A, AP180, Myosin I, Rabaptin-5, Rab-8, Eps15, VTI1B, PI3K cat class III (Vps34), DAB2, Dynamin-2, Actin, YKT6, RABGEF1, Syntaxin 5, Syntaxin 12, VPS45A, BIN1 (Amphiphysin II), TIP47, Actin cytoskeletal, EEA1, RABGDIA, Clathrin heavy chain, VAMP2, Syntaxin 6, Rab-4, PI3K reg class III (p150), VAMP8, HIP1, PIP5KIII, GOS-28, SAR1A, VAMP4, ARF1, Syntaxin 7, Rab-5A, SAR1, Rab-11A, Endophilin B1, Rab-9, Rab11-FIP2, Clathrin, Myosin Vb, Rip11   |
| 10 | Oxidative stress_ROS-induced cellular signaling       | 7.81E-11 | p38alpha (MAPK14), SREBP1 (nuclear), EGR1, PKA-reg (cAMP-dependent), TXNIP (VDUP1), Bak, Cytochrome c, FASN, E2I, Carbonic anhydrase IX, Bax, GSK3 beta, FTL, FTH1, IRP2, GRP75, NF-kB, AKT(PKB), NF-kB p50/p65, Cyclin B1, c-Src, Thioredoxin, PLK3 (CNK), Chk2, ACACA, RelA (p65 NF-kB subunit), KEAP1, Cul3/KEAP1/Rbx1 E3 ligase, Adrenomedullin, IRP1, HIF1A, SRX1, AMPK alpha subunit, Pin1, p300, HSPA1A, ELAVL1 (HuR), HSF1, PRKD1, p70 S6 kinase1, GPX1, PKC, PTEN, MEKK1(MAP3K1), HES1, HSP27, IKK-beta, DLC1 (Dynein LC8a), c-Abl, Cyclin D1, JNK(MAPK8-10), HIF-prolyl hydroxylase, HDAC1, SP1, NRF2, ADAM17, p38 MAPK, APEX, NALP3   |
| 11 | Cell cycle_Spindle assembly and chromosome separation | 1.89E-10 | Cyclin B, Separase, Nek2A, CDC20, MAD2a, Importin (karyopherin)-alpha, RCC1, Kid, CSE1L, CDK1 (p34), Ubiquitin, Dynein 1, cytoplasmic, heavy chain, TPX2, Ran, Tubulin (in microtubules), Importin (karyopherin)-beta, NUMA1, ZW10, Dynein 1, cytoplasmic, light chains, Aurora-   |

|    |  |          |   |
|----|--|----------|---|
|    |  |          | A, Securin, Tubulin alpha, KNSL1, Aurora-B, HEC, Dynein 1, cytoplasmic, intermediate chains   |
| 12 | Translation_Regulation of EIF4F activity               | 2E-10    | TGF-beta 1, RHEB2, IRS-1, H-Ras, eIF4E, PKC-zeta, Rac1, PI3K reg class IA, IGBP1, eIF4G2, MEK6(MAP2K6), MEK2(MAP2K2), CDC42, MSK1, AKT(PKB), PDK (PDPK1), TAK1(MAP3K7), MEK1(MAP2K1), Tiam1, PI3K cat class IA, TGF-beta receptor type II, MEK3(MAP2K3), eIF4B, SOS, PP2A catalytic, eIF4G1/3, PAK1, Hamartin, MEK4(MAP2K4), 4E-BP1, p70 S6 kinase1, MEKK1(MAP3K1), eIF4A, TAB1, p70 S6 kinase2, p38 MAPK |
| 13 | DNA damage_ATM/ATR regulation of G1/S checkpoint       | 4.35E-10 | p38alpha (MAPK14), NFBD1, FBXW7, PP2A regulatory, CDC25A, PER3, p70 S6 kinases, Chk1, CDK4, PP2A structural, MEK2(MAP2K2), B56G, FBXO31, p27KIP1, Chk2, Brca1, SMG1, beta-TrCP, Histone H2AX, PP2A catalytic, BTG2, ATR, CDK2, ELAVL1 (HuR), PCNA, Cyclin E, FOXO3A, c-Abl, Cyclin A, Cyclin D1, Brca1/Bard1  |
| 14 | Epithelial cell anoikis in COPD                        | 6.42E-10 | IRS-2, IRS-1, H-Ras, Alpha-actinin, alpha-6/beta-4 integrin, Bak, BAD, Talin, Bax, PI3K reg class IA, MEK6(MAP2K6), MMP-12, MEK1/2, Actin cytoskeletal, AKT(PKB), PDK (PDPK1), alpha-3/beta-1 integrin, PI3K cat class IA, MMP-1, ASK1 (MAP3K5), MEK3(MAP2K3), BPAG1, SOS, Beta-parvin, MKK7 (MAP2K7), ILK, MEK4(MAP2K4), Vinculin, Bcl-2, FAK1, Alpha-parvin, JNK(MAPK8-10), p38 MAPK, Bim               |
| 15 | Development_Differentiation of white adipocytes        | 1.14E-09 | p38alpha (MAPK14), SREBP1 (nuclear), BMP receptor 2, BMP4, H-Ras, FOXC2, HDAC3, SREBP1 precursor, UCP1, HIVEP2, FTase-alpha, MEK2(MAP2K2), CREB1, MEK1/2, PPARGC1 (PGC1-alpha), p107, PPAR-gamma, TAK1(MAP3K7), MEK1(MAP2K1), C/EBPbeta, SOS, p90RSK1, LIPS, p300, RIP140, PSAT, TAB1, BMPR1A, SMAD1, Leptin, BMP2, LPL, Perilipin, C/EBPalpha, C/EBPdelta  |
| 16 | Anti-apoptotic action of Gastrin in pancreatic cancer  | 1.8E-09  | p38alpha (MAPK14), Apaf-1, IRS-1, LARG, Cytochrome c, BAD, PI3K reg class IA (p85), Bax, FKHR, Caspase-3, MEK6(MAP2K6), AKT(PKB), Gastrin 17, PDK (PDPK1), Progastrin, c-Src, PPAR-gamma, MEKK4(MAP3K4), PI3K cat class IA, RelA (p65 NF-kB subunit), MEK3(MAP2K3), Annexin II, Bcl-2, FOXO3A, FAK1, G-protein alpha-q  |
| 17 | Signal transduction_CXCR4 signaling via MAPKs cascades | 2.96E-09 | PDGF-B, c-Fos, IRS-1, EGR1, p90RSK2(RPS6KA3), G-protein alpha-i2, Rac1, Beta-arrestin2, G-protein alpha-13, BAD, Ubiquitin, N-Ras, CREB1, MEK1/2, G-protein beta/gamma, c-Src, SDF-1, CXCR4, MEK1(MAP2K1), RelA (p65 NF-kB subunit), NF-kB1 (p50), K-RAS, G-protein alpha-i family, ROCK, PAK, MEKK1(MAP3K1), CD3, CD3 zeta, ACKR3, JNK(MAPK8-10), SMAD3, p38 MAPK, Elk-1, PREX1                          |
| 18 | Signal transduction_IGF-1 receptor signaling pathway   | 3.8E-09  | SREBP1 (nuclear), GAB1, IRS-2, IRS-1, H-Ras, eIF4E, PKC-zeta, FASN, BAD, Androgen receptor, I-kB, PI3K reg class IA (p85), GSK3 beta, FKHR, IGF-2, IGF-1 receptor, MEK1/2, AKT(PKB), PDK (PDPK1), PI3K cat class IA, RelA (p65 NF-kB subunit), ASK1 (MAP3K5), 14-3-3 zeta/delta, Cyclin D, SOS, MKK7  |

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|    |  |          | (MAP2K7), MEK4(MAP2K4), 4E-BP1, 14-3-3 beta/alpha, p70 S6 kinase1, SHP-2, Bcl-2, FOXO3A, FAK1, MNK2(GPRK7), Bim  |
| 19 | Cell cycle_Regulation of G1/S transition (part 1)                    | 4.42E-09 | TGF-beta 1, Cyclin D3, PP2A regulatory, CDC25A, Cyclin D2, Ubiquitin, GSK3 beta, CDK4, Skp2/TrCP/FBXW, p16INK4, p27KIP1, PLK3 (CNK), TGF-beta 2, Chk2, Brca1, TGF-beta receptor type II, beta-TrCP, Cyclin D, PP2A catalytic, CDK2, p70 S6 kinase1, Cyclin E, Cyclin A, Cyclin D1, RING-box protein 1, SMAD3, SP1  |
| 20 | Cell cycle_The metaphase checkpoint                                  | 4.9E-09  | Nek2A, CDC20, MAD2a, MAD2b, PMF1, CENP-C, CENP-E, BUB1, CENP-F, Dynein 1, cytoplasmic, heavy chain, Survivin, PLK1, HP1 gamma, MIS12, HZWint-1, ZW10, CENP-A, CENP-H, INCENP, SPBC25, Aurora-A, CDCA1, Aurora-B, HEC, HP1 alpha, AF15q14   |
| 21 | G-protein signaling_Ras family GTPases in kinase cascades            | 5E-09    | p38alpha (MAPK14), c-Fos, H-Ras, Rac1, p38beta (MAPK11), N-Ras, MEK2(MAP2K2), CDC42, MEKK4(MAP3K4), MEK1(MAP2K1), B-Raf, K-RAS, C/EBPbeta, MEK3(MAP2K3), PAK1, MEK4(MAP2K4), MEKK1(MAP3K1), JNK(MAPK8-10), R-Ras, p38 MAPK, Elk-1  |
| 22 | Immune response_IFN-alpha/beta signaling via PI3K and NF-kB pathways | 7.18E-09 | Cyclin D3, ISG15, IRS-2, Tyk2, IRS-1, NMI, eIF4E, CDC25A, Apo-2L(TNFSF10), IFN-alpha/beta receptor, IFNAR1, PKC-epsilon, IFN-beta, CDK1 (p34), I-kB, p70 S6 kinases, PI3K reg class IA (p85), GSK3 beta, CDK4, EMSY, p19, CREB1, p130, MEK1/2, b-Myb, NF-kB, AKT(PKB), PDK (PDPK1), p16INK4, p107, p27KIP1, IFI17, PI3K cat class IA, RelA (p65 NF-kB subunit), I-TAC, IFNAR2, eIF4B, p90RSK1, eIF4G1/3, CDK2, PCNA, 4E-BP1, GBP1, PKC-alpha, Cyclin E, eIF4A, FOXO3A, IRF7, MNK2(GPRK7), Cyclin A   |
| 23 | Immune response_B cell antigen receptor (BCR) pathway                | 7.54E-09 | STIM1, Calcineurin A (catalytic), NCK1, c-Fos, c-Rel (NF-kB subunit), H-Ras, NF-kB p50/c-Rel, EGR1, BCAP, Fibronectin, CD19, Rac1, IP3 receptor, BAD, Cyclin D2, PI3K reg class IA (p85), ORAI1, GSK3 beta, CD79A, CDK4, FKHR, N-Ras, MEK6(MAP2K6), MEK2(MAP2K2), GSK3 alpha/beta, MEK1/2, CDC42, Actin cytoskeletal, NF-kB, AKT(PKB), NF-kB p50/p65, PDK (PDPK1), TAK1(MAP3K7), NF-AT2(NFATC1), MEKK4(MAP3K4), MEK1(MAP2K1), RelA (p65 NF-kB subunit), B-Raf, NF-kB1 (p50), K-RAS, PIP5KIII, MEK3(MAP2K3), CIN85, PP2A catalytic, SOS1, PIP5KI, p70 S6 kinase1, Calmodulin, CalDAG-GEFIII, CKLFSF7, MEKK1(MAP3K1), IKK-beta, PLC-gamma, Bcl-10, p38 MAPK, Elk-1 |
| 24 | Neurogenesis_NGF/ TrkA MAPK-mediated signaling                       | 8.78E-09 | ERK5 (MAPK7), CDK5, c-Fos, APS, Fra-1, H-Ras, MEF2C, PKC-zeta, CrkL, EGR1, PP2A regulatory, PKA-reg (cAMP-dependent), DNAJA3 (TID1), VGF, PKC-epsilon, IP3 receptor, TY3H, MAPKAPK2, PLC-gamma 1, N-Ras, MEK6(MAP2K6), MAP2K5 (MEK5), KIDINS220, CREB1, MEK1/2, PLAUR (uPAR), MSK1, RUSC1 (NESCA), p107, c-Src, KCTD11, GAB2, B-Raf, NF-kB1 (p50), K-RAS, MEK3(MAP2K3), SOS, PP2A catalytic, C3G, SH2B, p90Rsk, p130CAS, Calmodulin, PKC-  |

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|    |   |          | lambda/iota, SHP-2, SUR-8, Cyclin D1, SORBS1, SP1, JMJD3, SHB, p38 MAPK, Elk-1, FosB   |
| 25 | Development_Positive regulation of WNT/Beta-catenin signaling in the nucleus          | 8.89E-09 | SMYD2, TBL1X, Alpha-1 catenin, TCF7L2 (TCF4), FOXP1, USP5, Jade-1, Beta-catenin, BCL9/B9L, VCP, TLE, Dsh, UBR5, GSK3 beta, HDAC2, WIP1, RUNX, FOXK2, ICAT, TBLR1, SOX9, SOX11, Tcf(Lef), PIAS4, beta-TrCP, FOXM1, SHH, Pin1, p300, NCOA2 (GRIP1/TIF2), FAM53B, Kindlin-2, CARF, WNT, FOXO3A, HMGB2, HDAC1, APPL, RUVBL2, Frizzled  |
| 26 | Transcription_Sin3 and NuRD in transcription regulation                               | 9.32E-09 | TR-alpha, RARbeta, SMRT, SAP130, RBBP4 (RbAp48), ARID4A, MBD2, HDAC2, NRSF, Mi-2 alpha, N-CoR, ARID4B, p66beta, PSF, MTA1, Mi-2, Histone H3, Sin3A, RXRA, RAR-beta/RXR-alpha, MTA2, SAP18, RBBP7 (RbAp46), HDAC1, SAP30, NRB54, p66alpha, Histone H4   |
| 27 | Signal transduction_Angiotensin II signaling via Beta-arrestin                        | 9.4E-09  | GRK6, eIF4E, 14-3-3, Beta-arrestin2, BAD, MLCP (reg), Cytohesin2, p70 S6 kinases, GSK3 beta, PLC-gamma 1, Itch, DGK, AKT(PKB), c-Src, p27KIP1, Clathrin heavy chain, MLCK, MLCP (cat), MEK1(MAP2K1), Casein kinase II, beta chain (Phosvitin), GRAF2, ASK1 (MAP3K5), SET, AGTR1, CACNA1C, PP2A catalytic, p90Rsk, MEK4(MAP2K4), ROCK, GRK5, MRLC, Beta-adaptin 2, Clathrin, Beta-arrestin1, p23 co-chaperone   |
| 28 | Cell cycle_Chromosome condensation in prometaphase                                    | 1.09E-08 | TOP1, Cyclin B, CAP-G/G2, CAP-D2/D3, AKAP8, CDK1 (p34), TOP2, BRRN1, Histone H3, CAP-G, INCENP, Aurora-A, CAP-E, CAP-H/H2, Cyclin A, CNAP1, Aurora-B, Histone H1   |
| 29 | Neutrophil resistance to apoptosis in COPD and proresolving impact of lipid mediators | 1.39E-08 | SAA1, TNF-R1 soluble, Apaf-1, FasR(CD95) soluble, gp91-phox, 14-3-3, TRADD, Bak, Cytochrome c, Caspase-8, p47-phox, BAD, Bax, PI3K reg class IA, Calpastatin, Caspase-3, MEK6(MAP2K6), RIPK1, FasL(TNFSF6), AKT(PKB), Calpain 1(mu), TNF-R1, Mcl-1, FPRL1, PI3K cat class IA, Cytochrome b-558, p22-phox, MEK3(MAP2K3), p90RSK1, MAP3K3, tBid, FasR(CD95), p40-phox, Smac/Diablo, p38 MAPK, Bid  |
| 30 | Immune response_IL-3 signaling via JAK/STAT, p38, JNK and NF-kB                       | 1.53E-08 | STAT5A, MHC class II, DHA2, Cyclin D3, c-Fos, Tyk2, Granzyme B, H-Ras, SOCS1, ID1, Fibronectin, SPECC1, Rac1, BAD, Cyclin D2, I-kB, SRP9, Survivin, Cyclin A2, IL3RA, NF-kB, AKT(PKB), NF-kB p50/p65, Cyclin B1, c-Src, Mcl-1, P-selectin, IL-2R alpha chain, PKM2, Ephrin-B1, ITGB1, PI3K cat class IA, C/EBPbeta, MEK3(MAP2K3), RXRA, Bcl-6, MKK7 (MAP2K7), JAK3, MEK4(MAP2K4), IKK-beta, Bcl-2, Oncostatin M, STAT5, Cyclin D1, HDAC1, STAT6, Ephrin-B2, p38 MAPK, BMP2 |
| 31 | Mechanisms of drug resistance in SCLC   | 1.57E-08 | alpha-6/beta-1 integrin, Apaf-1, alpha-V/beta-1 integrin, Cytochrome c, Caspase-8, Fibronectin, Rad51, PKC-epsilon, MDR1, BAD, Bax, GSK3 beta, Survivin, PI3K reg class IA, Caspase-3, IGF-1 receptor, AKT(PKB), Collagen IV, HSP70, PDK (PDPK1), alpha-3/beta-1 integrin, ITGB1, Osteopontin, PI3K cat class IA, RelA (p65 NF-kB subunit), B-Raf, TERC, FGF2, CD9, MGF, HSPA1A, HSF1, p70 S6 kinase1, tBid, Bcl-2, FAK1, TOP2 alpha, Cyclin D1, p70 S6 kinase2, Bid       |

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| 32 | Cytoskeleton remodeling_Regulation of actin cytoskeleton organization by the kinase effectors of Rho GTPases | 1.79E-08 | Spectrin, PRK1, Alpha-actinin, RhoC, Rac1, Talin, MLCP (reg), GIT1, Cdc42 subfamily, MSN (moesin), ERM proteins, ARPC1B, RhoA-related, CDC42, Actin cytoskeletal, MLCK, MLCP (cat), BETA-PIX, RhoJ, F-Actin cytoskeleton, Myosin II, CPI-17, Alpha adducin, PAK1, PIP5KI, MyHC, Rac3, MRCK, ROCK, Actomyosin, PAK, Rac1-related, Vinculin, Rhov, MRLC  |
| 33 | Immune response_Gastrin in inflammatory response   | 2.06E-08 | GRO-2, p38alpha (MAPK14), ERK5 (MAPK7), c-Fos, IRS-1, H-Ras, LARG, MEF2C, G-protein alpha-q/11, PKC-epsilon, IP3 receptor, I-kB, PI3K reg class IA (p85), PLC-gamma 1, MEK6(MAP2K6), MAP2K5 (MEK5), MEK2(MAP2K2), CREB1, PAI2, AKT(PKB), NF-kB p50/p65, Gastrin 17, PDK (PDPK1), c-Src, TAK1(MAP3K7), MEK1(MAP2K1), PI3K cat class IA, SOS, MEF2, MEK4(MAP2K4), ELAVL1 (HuR), MEF2D, MEKK1(MAP3K1), PKC-alpha, IKK-beta, FAK1, G-protein alpha-q, JNK(MAPK8-10), Elk-1   |
| 34 | Apoptosis and survival_BAD phosphorylation   | 2.12E-08 | Calcineurin A (catalytic), IRS-1, H-Ras, 14-3-3, PKA-reg (cAMP-dependent), PP2C, Cytochrome c, CDK1 (p34), BAD, Bax, PI3K reg class IA, PP1-cat alpha, MEK2(MAP2K2), IGF-1 receptor, G-protein beta/gamma, AKT(PKB), PDK (PDPK1), MEK1(MAP2K1), PI3K cat class IA, Adenylate cyclase type I, SOS, PP2A catalytic, p90Rsk, p70 S6 kinase1, G-protein alpha-s, Bcl-2, Beclin 1, p70 S6 kinase2   |
| 35 | Inhibition of apoptosis in gastric cancer  | 2.12E-08 | Gastrin 17-Gly, TGF-beta 1, DR5(TNFRSF10B), Apaf-1, Apo-2L(TNFSF10), Cytochrome c, Caspase-8, BAD, Bax, Caspase-3, NF-kB, AKT(PKB), DR4(TNFRSF10A), Gastrin 17, Progastrin, Mcl-1, TGF-beta receptor type II, PAK1, ROCK, Caspase-7, Gasdermin, tBid, Bcl-2, HtrA2, HGF receptor (Met), Smac/Diablo, Bim, Bid  |
| 36 | Apoptosis and survival_Endoplasmic reticulum stress response pathway   | 2.3E-08  | p38alpha (MAPK14), GRP78, C/EBP zeta, Apaf-1, PP1-cat, ATF-4, S2P, GADD34, ATF-6 alpha (90kDa), Bak, Cytochrome c, I-kB, Bax, PP1-cat alpha, eIF2S1, Calpain 1(mu), NF-kB p50/p65, ATF-6 alpha (50kDa), Derlin-2, eIF2AK3, ASK1 (MAP3K5), MEK3(MAP2K3), S1P, MEK4(MAP2K4), Caspase-7, Caspase-12, tBid, Bcl-2, IP3R1, JNK(MAPK8-10), DNAJC3, Bim, Bid, ERP5  |
| 37 | Development_Positive regulation of STK3/4 (Hippo) pathway and negative regulation of YAP/TAZ function        | 2.71E-08 | Willin, Casein kinase I delta, SCRIB, Cullin 2, INADL, AMPK beta subunit, Alpha-1 catenin, 14-3-3, Casein kinase I epsilon, AMPK gamma subunit, Beta-catenin, PKA-reg (cAMP-dependent), ZO-2, RASSF2, CRB3, STK4, Adenylate cyclase, Itch, RASSF5, LATS2, Actin cytoskeletal, Skp2/TrCP/FBXW, TAZ, LRR-1, AMOTL1 (Jeap), Axin, beta-TrCP, AMPK alpha subunit, EBP50, MARKK, Alpha-catenin, MALS-3, Cul2/Rbx1 E3 ligase, G-protein alpha-s, FasR(CD95), Mol1b, Beta-2 adrenergic receptor, PEZ, Angiomotin (AMOT), LIF receptor |
| 38 | Development_FGFR signaling pathway   | 2.95E-08 | GAB1, H-Ras, Syndecan-4, FGFR1, Rac1, IP3 receptor, Ubiquitin, MAPKAPK2, EPS8, PI3K reg class IA, PLC-gamma 1, MEK6(MAP2K6), MEK2(MAP2K2), CREB1, AKT(PKB),  |

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|    |   |          | PDK (PDPK1), E3b1(ABI-1), MEK1(MAP2K1), PI3K cat class IA, Syndecan-1, DOCK1, FGF2, SOS, PAK1, MEK4(MAP2K4), MEKK1(MAP3K1), SHP-2, Perlecan, JNK(MAPK8-10), SHB, p38 MAPK, Elk-1, Syndecan-2  |
| 39 | Neurophysiological process_Dynein-dynactin motor complex in axonal transport in neurons | 2.95E-08 | CDK5, NudE, Importin (karyopherin)-alpha, Ubiquitin, DYNLL, ORP1, Dynein 1, cytoplasmic, heavy chain, Tctex-1, MAPRE3(EB3), DYNLT, HAP40, AKT(PKB), Snapin, PAFAH alpha (LIS1), DYI2, NT-3, Tubulin (in microtubules), Importin (karyopherin)-beta, Dynein 1, cytoplasmic, light chains, TrkC, Sortilin, BPAG1, TrkB, JSAP1, Rab-5A, Kinesin heavy chain, Bassoon, Kinesin light chain, Carboxypeptidase H, Dynein 1, cytoplasmic, intermediate chains, BDNF, NUDEL, SPTBN2 |
| 40 | DNA damage_ATM/ATR regulation of G2/M checkpoint: nuclear signaling                     | 3.73E-08 | NFBD1, Cyclin B, Cyclin B2, PALB2, CDK1 (p34), SMAR1, Chk1, Wee1, Cyclin B1, Mcl-1, PLK1, Chk2, Brca1, CDC25C, DNA-PK, Histone H2AX, BTG2, ATR, PCBP-4 (mcg10), CDC14b, ATRIP, CDK2, CDC18L (CDC6), HSF1, 14-3-3 sigma, Ku70, Cyclin A, DNMT1, TTK  |
| 41 | Cytoskeleton remodeling_FAK signaling   | 4.32E-08 | Cyclin D3, H-Ras, VEGFR-2, G-protein alpha-q/11, Fibronectin, FARP2, Rac1, IP3 receptor, Talin, GRP-R, GSK3 beta, PI3K reg class IA, PLC-beta, PLC-gamma 1, RIPK1, MEK2(MAP2K2), CDC42, AKT(PKB), c-Src, MEK1(MAP2K1), PI3K cat class IA, TRAF3, DOCK1, SOS, PAK1, C3G, MKK7 (MAP2K7), p130CAS, Calmodulin, PTEN, GRP(1-27), MEKK1(MAP3K1), FAK1, Elk-1   |
| 42 | Cell cycle_Role of Nek in cell cycle regulation   | 4.49E-08 | Nek2A, IRS-1, MAD2a, RCC1, Nek11, CDK1 (p34), PI3K reg class IA, NEK7, Cyclin B1, TPX2, PDK (PDPK1), Ran, Tubulin (in microtubules), Tubulin beta, Tubulin gamma, PI3K cat class IA, Histone H3, Aurora-A, p70 S6 kinase1, Tubulin alpha, NEK1, HEC, Histone H1   |
| 43 | Cytoskeleton remodeling_Reverse signaling by Ephrin-B                                   | 4.49E-08 | F-Actin, H-Ras, Beta-catenin, GSK3 beta, NCK2, G-protein beta/gamma, Actin cytoskeletal, Tau (MAPT), c-Src, Axin, SDF-1, CXCR4, WaspIP, Tubulin (in microtubules), PINCH, G-protein alpha-i family, SOS, PAK1, ILK, Tubulin alpha, Ephrin-B, FAK1, Ephrin-B receptors   |
| 44 | Signal transduction_Calcium-mediated signaling  | 4.62E-08 | Calcineurin A (catalytic), c-Fos, 14-3-3, CaMK I, EGR1, MUNC13, p47-phox, Rac1, IP3 receptor, BAD, MLCP (reg), I-kB, MEK6(MAP2K6), CREB1, PPARGC1 (PGC1-alpha), NF-kB, AKT(PKB), NF-AT2(NFATC1), MLCP (cat), Tiam1, cPKC (conventional), RelA (p65 NF-kB subunit), ASK1 (MAP3K5), MEK3(MAP2K3), AMPK alpha subunit, Myosin II, MEF2, p300, MEK4(MAP2K4), ROCK, Calmodulin, PKC, MYH11, PKC-alpha, IKK-beta, JNK(MAPK8-10), Bcl-10, NURR1, p38 MAPK, Elk-1                   |
| 45 | Ligand-independent activation of Androgen receptor in Prostate Cancer                   | 4.72E-08 | STAT5A, FGFR2, GAB1, WNT3A, IRS-1, Neuregulin 1, H-Ras, Beta-catenin, PP2A regulatory, STAT5B, FGFR1, Kallikrein 3 (PSA), Prolactin receptor, Androgen receptor, GSK3 beta, PI3K reg class IA, N-Ras, MEK2(MAP2K2), IGF-1 receptor, AKT(PKB), PDK (PDPK1), MEK1(MAP2K1), PI3K cat class IA,   |

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|    |   |          | B-Raf, K-RAS, NCOA3 (pCIP/SRC3), Tcf(Lef), FGF2, SOS, PP2A catalytic, NCOA2 (GRIP1/TIF2), FRS2beta, c-Abl, Cyclin D1, NCOA1 (SRC1), HDAC1, SRD5A1, Frizzled   |
| 46 | Development_Thrombopoietin signaling via ERK1/2 and PI3K                  | 4.72E-08 | PDK1, Cyclin D3, c-Fos, GAB1, IRS-2, BMP4, PP1-cat, H-Ras, NF-kB p50/c-Rel, PKC-zeta, CrkL, EGR1, Thrombopoietin, PI3K reg class IA (p85), GSK3 beta, CREB1, MEK1/2, AKT(PKB), PDK (PDPK1), p27KIP1, GAB2, PI3K cat class IA, RelA (p65 NF-kB subunit), B-Raf, ITGA2B, HIF1A, DNA-PK, PDHA (somatic), SOS1, C3G, AML1 (RUNX1), 4E-BP1, p70 S6 kinase1, SHP-2, FOXO3A, SP1, p38 MAPK, Elk-1  |
| 47 | TGF-beta 1-induced transactivation of membrane receptors signaling in HCC | 4.79E-08 | TGF-beta 1, alpha-6/beta-1 integrin, Beta-catenin, Fibronectin, Actin, Rac1, GSK3 beta, PI3K reg class IA, CDK4, AKT(PKB), PDGF receptor, c-Src, Axin, alpha-3/beta-1 integrin, ITGB1, PI3K cat class IA, TGF-beta receptor type II, DOCK1, TGF-beta, ITGA6, PAK1, CDK2, p130CAS, PTEN, Cyclin E, SLUG, FAK1, c-Abl, Cyclin A, Cyclin D1, PDGF-R-beta   |
| 48 | Development_VEGF signaling via VEGFR2 - generic cascades                  | 5.03E-08 | Calcineurin A (catalytic), NCK1, H-Ras, TCF7L2 (TCF4), ROCK1, eIF4E, Beta-catenin, VEGFR-2, Rac1, IP3 receptor, I-kB, p120GAP, GSK3 beta, MAPKAPK2, PI3K reg class IA, PLC-gamma 1, MEK2(MAP2K2), CREB1, PLAUR (uPAR), CDC42, Actin cytoskeletal, Fyn, MSK1, AKT(PKB), HSP90, NF-kB p50/p65, PDK (PDPK1), c-Src, TSAD, NF-AT2(NFATC1), MLCK, MEK1(MAP2K1), PI3K cat class IA, MEK3(MAP2K3), SOS, PAK1, p90Rsk, Calmodulin, PKC, MEKK1(MAP3K1), Vinculin, PKC-alpha, HSP27, IKK-beta, FAK1, Neurofibromin, SHB, p38 MAPK |
| 49 | Cell cycle_Initiation of mitosis  | 5.28E-08 | Cyclin B2, CDK1 (p34), CDK7, Wee1, Lamin B, AKT(PKB), Cyclin B1, PLK1, Histone H3, CDC25C, CDC25B, MYRL2, FOXM1, p90RSK1, AP-2A, Cyclin H, Nucleolin, Kinase MYT1, KNSL1, Histone H1  |
| 50 | Main pathways of Schwann cells transformation in neurofibromatosis type 1 | 5.37E-08 | PDGF-B, RHEB2, c-Fos, Neuregulin 1, H-Ras, Beta-catenin, IP3 receptor, BAD, PI3K reg class IA (p85), Amphiregulin, GSK3 beta, PLC-gamma 1, N-Ras, IGF-1 receptor, MEK1/2, CDC42, AKT(PKB), PDGF receptor, PDK (PDPK1), SOX9, SDF-1, CXCR4, MEK1(MAP2K1), ITGB1, PI3K cat class IA, K-RAS, HIF1A, S100B, BRD4, ErbB4, PAK1, Myelin basic protein, p70 S6 kinase1, Calmodulin, PTEN, Bcl-2, FAK1, Neurofibromin, Cyclin D1, p38 MAPK, Bim, Elk-1, PDGF-R-beta   |