# Supplement

## II. : Mapped predicted genes in cancer pathways

We performed pathway enrichment analysis on the predicted UR and DR genes in the biological test data of the BRCA and UCEC datasets. In the Figure, we report 13 important pathways related to the progress of various cancer datasets, all of which are sourced from the predicted UR and DR genes of BRCA and UCEC. We will discuss a few genes mapped to these pathways in the following paragraphs.

BRCA Datasets: In general, BRCA gene mutations can affect multiple signaling pathways and physiological pro cesses, including but not limited to DNA repair, cell cycle regulation, apoptosis, transcription regulation, protein stability, and signal transduction. WP OXIDATIVE STRESS RESPONSE: This pathway involves the organism's response and regulation to oxidative stress. The production of oxygen free radicals and other reactive substances can cause DNA damage, accumulation of oxidized proteins and lipids, and lead to various diseases, including cancer. In the process of cancer initiation and progression, the level of oxidative stress in the body is often affected, resulting in physiological effects such as DNA damage and abnormal cell cycle, thereby promoting the growth and metastasis of tumor cells. For example, the FOS gene encodes a transcription factor protein, the c-Fos precursor protein, which plays an important role in multiple biological processes such as cell proliferation, differentiation, apoptosis, and inflammation. Abnormal expression of this gene is related to the occur rence and development of breast cancer.

UCEC Datasets: Studies have shown that the molecular composition associated with the tumor microenvironment in endometrial cancer tissue includes genes related to neurodevelopment and angiogenesis, as well as extracellular matrix proteins related to the interaction between tumor cells and the matrix (including components in NABA CORE MATRISOME). For example, HGF encodes a promoter, which is an important factor that promotes cell proliferation and migration and is closely related to the occurrence and development of UCEC cancer. IGFBP6 encodes an extracel lular matrix protein that can inhibit apoptosis and promote cell proliferation, and has been shown to be upregulated in UCEC cell lines.

| Cancer | Pathways | Mapped predicted genes |
|---|---|---|
| UCEC_UP | KEGG_SYSTEMIC_LUPUS_ERYTHEMATOSUS | HLA-DQB1,FCGR3B,C1QC,C2 |
| | REACTOME_TRANSCRIPTIONAL_REGULATION_OF_GRANULOPOIESIS | SPI1 |
| | REACTOME_ANTIMICROBIAL_PEPTIDES | BPIFA1,S100A7,SLC11A1,BPIFB4,BPIFB2, PRSS3,RNASE7,BPIFB6,LCN2 |
| | REACTOME_TRANSCRIPTIONAL_REGULATION_BY_SMALL_RNAS | POLR2I,NUP210 |
| UCEC_DOWN | NABA_MATRISOME | HGF,SERPINF1,CD109,CCL26,FGF7,CCL15,COL6A3,VTN,MMP28,WNT2B, WNT9B,NRG2,IGFBP5,IGFBP6,CLEC14A,GAS6,SEMA3G,FREM1,FGF16, SULF2,NGF,CHRDL1,NID1,ADAMTSL1,LAMA4,EMILIN1,TIMP2,CCBE1, TLL1,EGFL7,ANGPTL7,LGI1 |
| | KEGG_NEUROACTIVE_LIGAND_RECEPTOR_INTERACTION | TSHB,ADRA1A,ADRB3,HTR1B,FSHR,GABBR1,AVPR1A,AVPR2,PTGER3, PTH1R,TACR1,NMBR,NPY1R,GRID1,GRIN2A,S1PR3,EDNRA,P2RX1,LPAR6 |
| | NABA_CORE_MATRISOME | CRIM1,HMCN2,COL6A3,FBLN5,VTN,LGI4,IGFBP5,IGFBP6,PRELP,LGI3,PODN, GAS6,COL21A1,NID1,IMPG2,LAMA4,KERA,EMILIN1,LGI2,LGI1 |
| BRCA_UP | NABA_MATRISOME | REG4, HPSE2, S100A2, S100A8, S100A12, SERPINB5, MMP9, CCL11, CCL19, CLEC10A, CCL24, MMP26, COL2A1, AMBP, PAPPA2, COL4A6, COL9A1, COL11A2, ITLN1, BCAN, EGFL6, S100A7A, SCUBE2, SLIT1, IL1A, MUC7, FBN3, ADAM18, CST11, GDF1, NELL1, BMP7 |
| | NABA_MATRISOME_ASSOCIATED | REG4,HPSE2,S100A2,S100A8,S100A12,SERPINB5,MMP9,CCL11,CCL19,CLEC10A, CCL24,MMP26,AMBP,ITLN1,MUC13,S100A7A,SCUBE2,IFNE,IL1A,MUC7,IFNK, BRINP3,ADAM18,IL17C,CST11,GDF1,BMP7,ADAMDEC1 |
| | KEGG_METABOLISM_OF_XENOBIOTICS_BY_CYTOCHROME_P450 | UGT2B4,UGT2B28,UGT1A10,CYP2B6,CYP2F1,GSTA1,GSTM5,UGT2A3 |
| BRCA_DOWN | KEGG_FOCAL_ADHESION | COMP,COL6A6,ACTN3,CAV3,ITGA7,THBS4,IGF1,PAK3,MAPK10,VEGFD,TNXB |
| | NABA_CORE_MATRISOME | DPT,GLDN,FMOD,COMP,COL6A6,MMRN1,THBS4,ADIPOQ,PCOLCE2,TNXB |
| | WP_OXIDATIVE_STRESS_RESPONSE | MAOA,FOS,MAPK10,SOD3 |