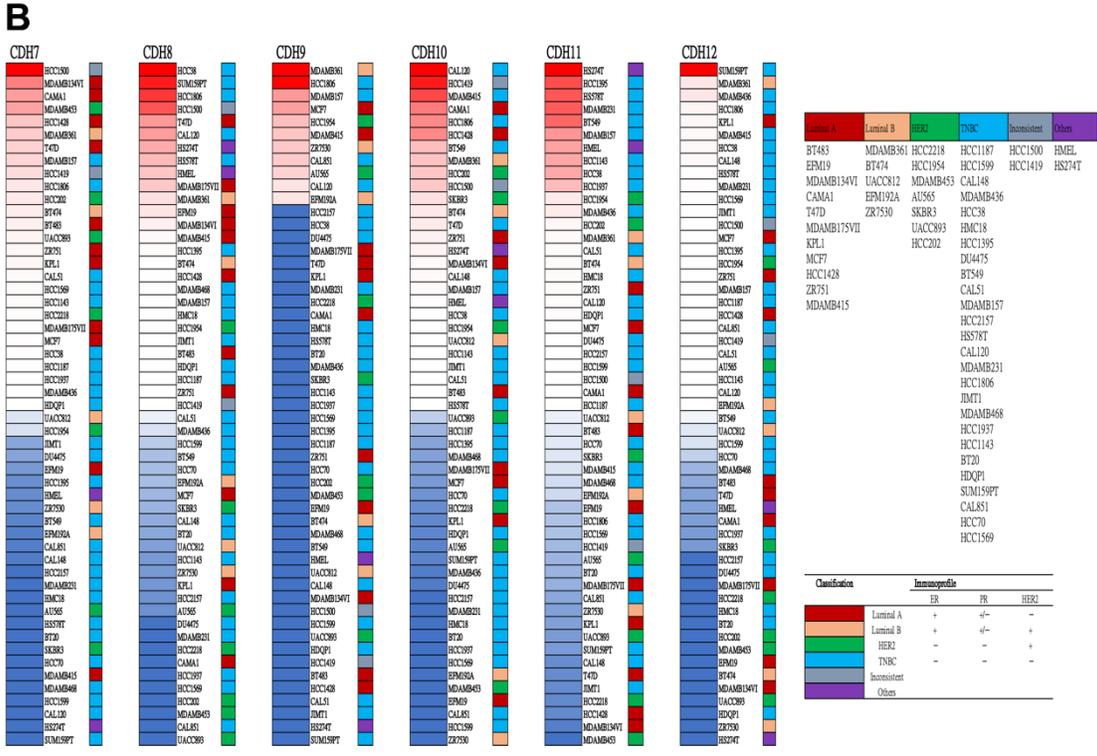
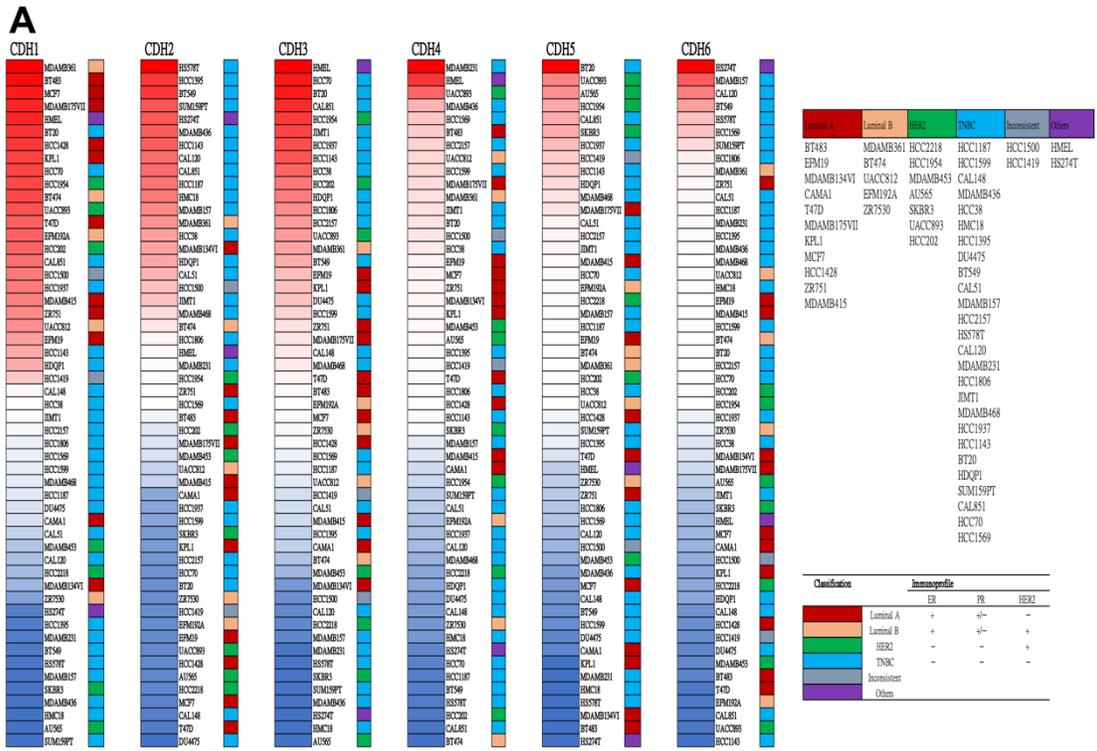
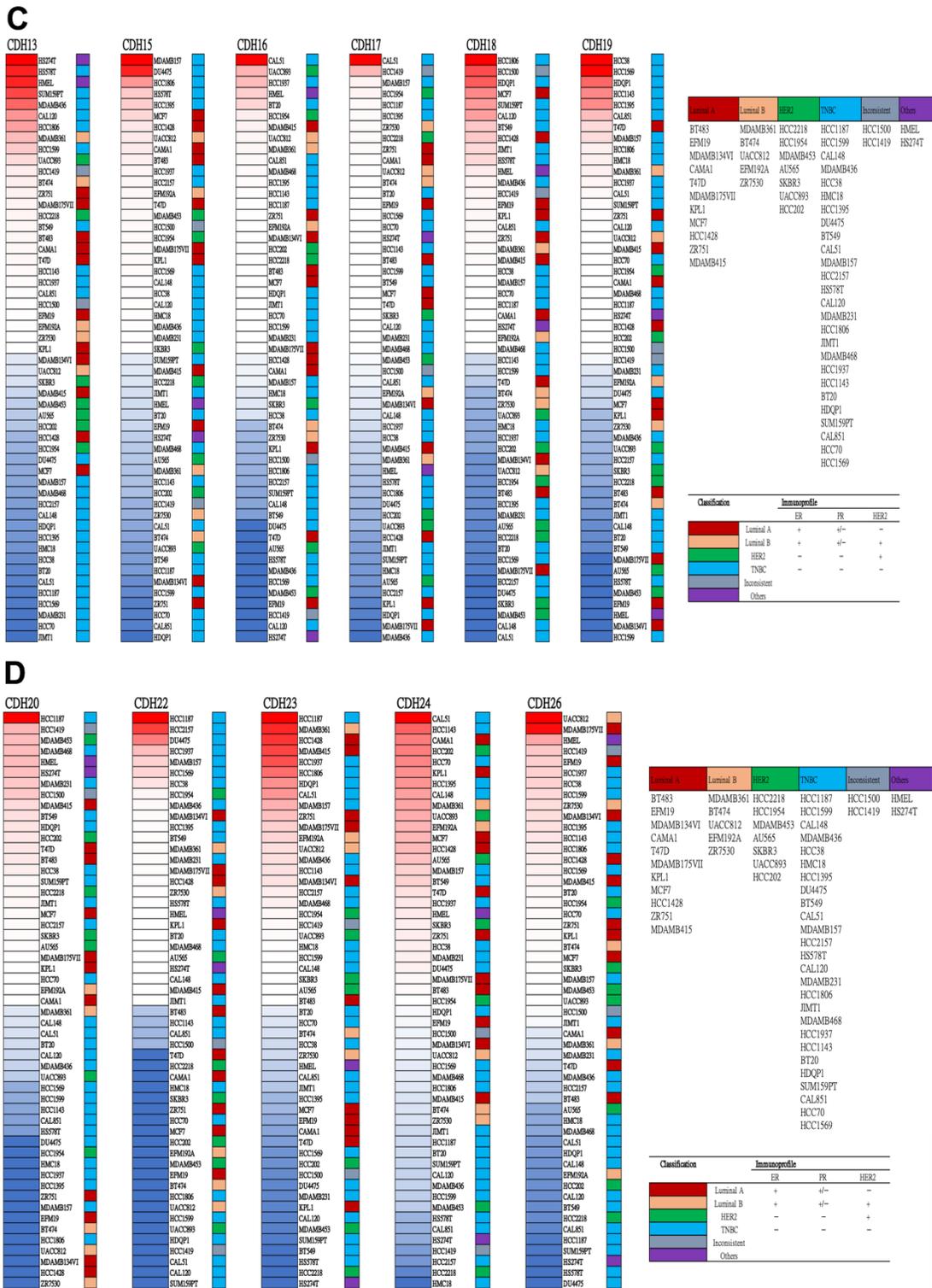
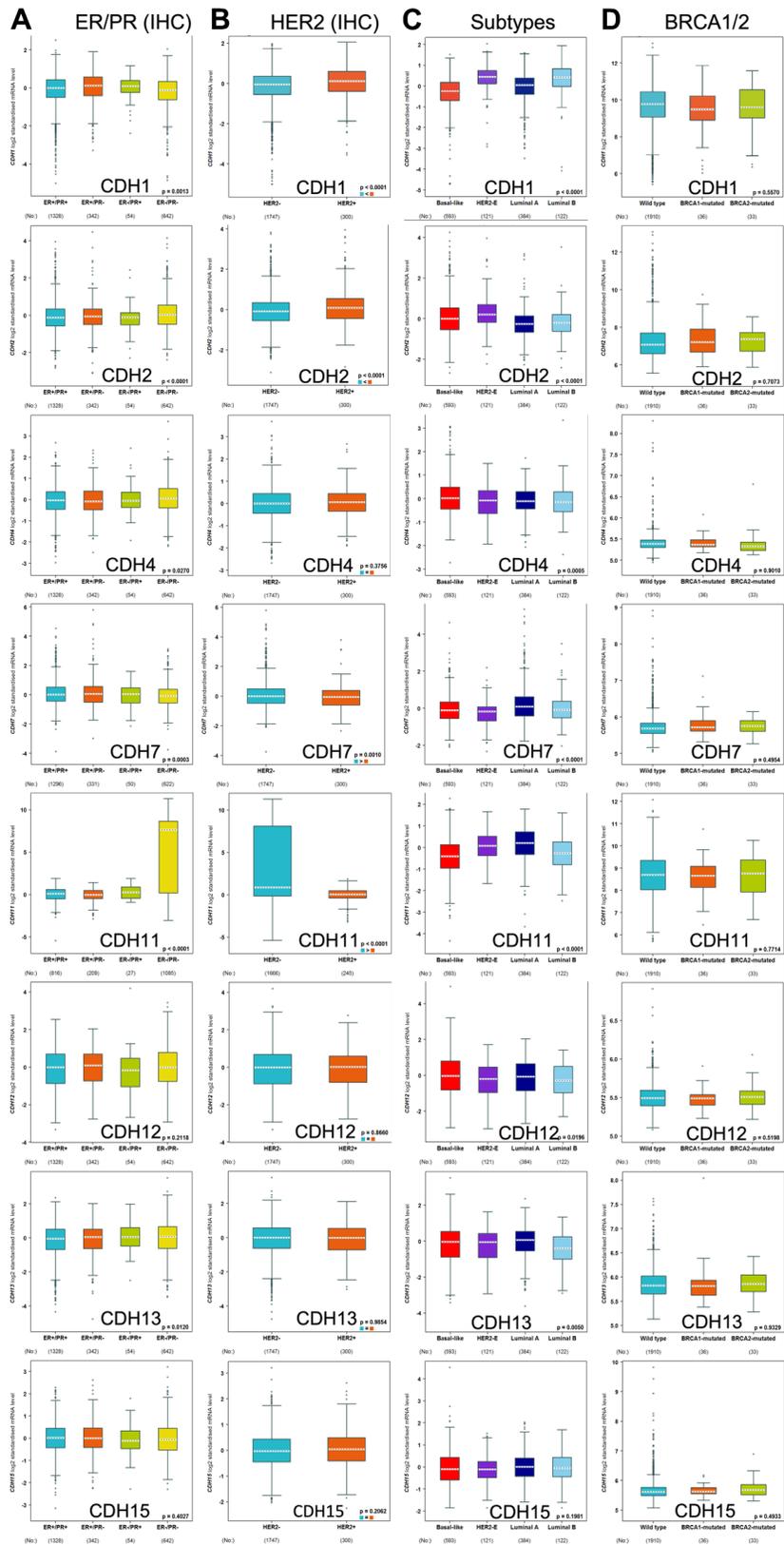


SUPPLEMENTARY FIGURES

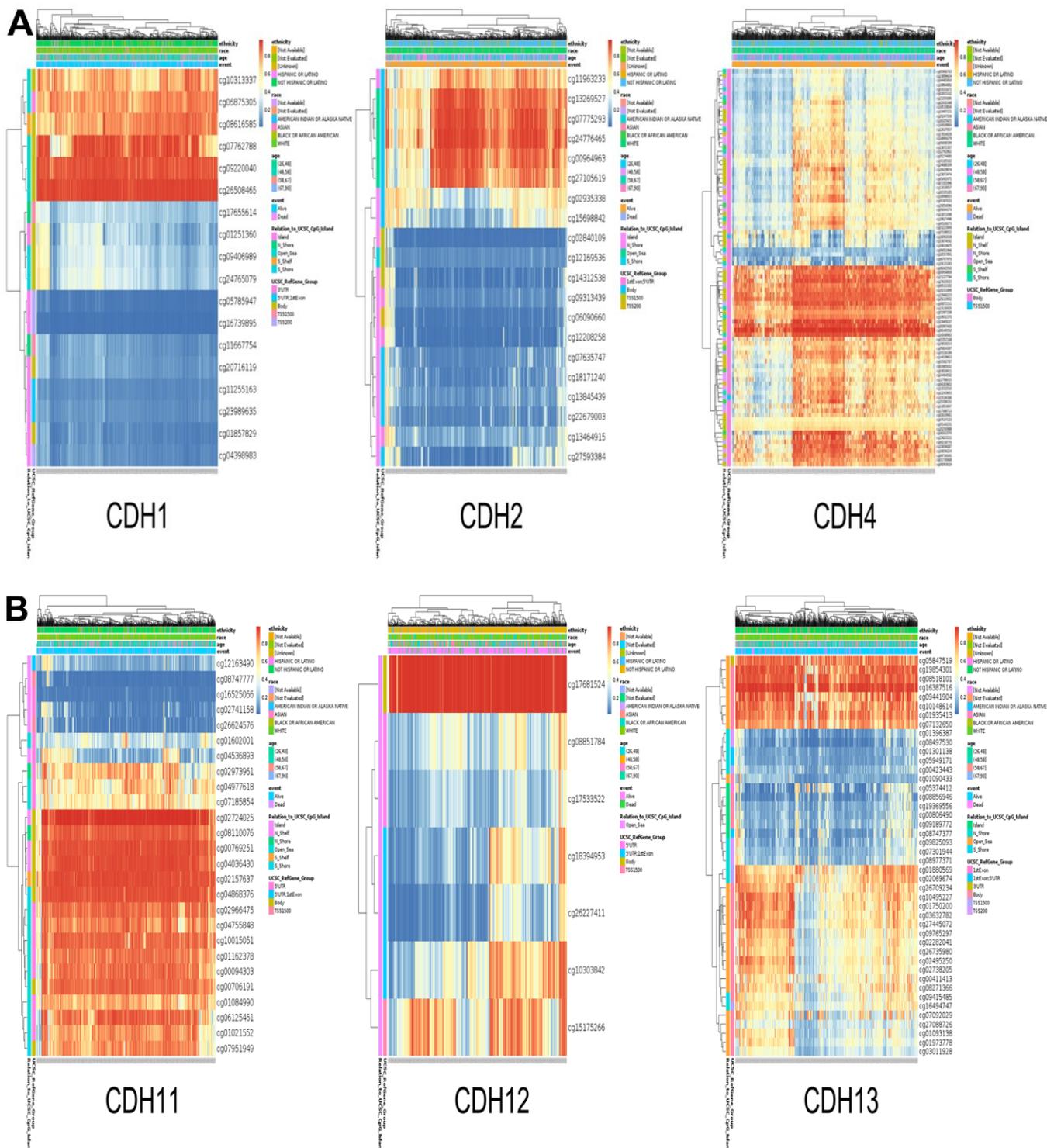




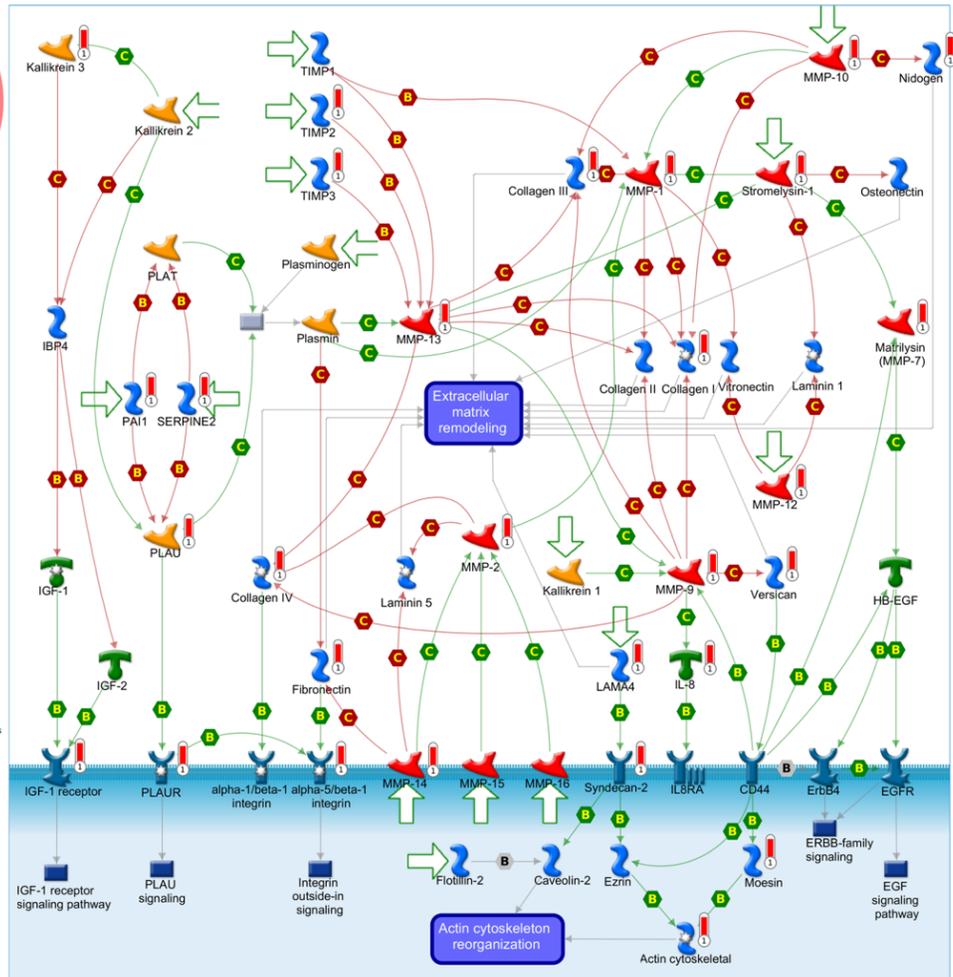
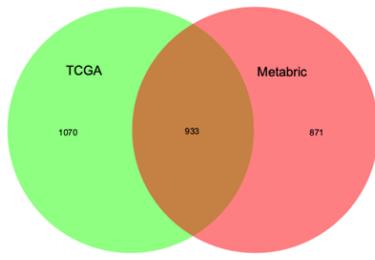
Supplementary Figure 1. (A–D) Molecular subtypes of breast cancer cell lines with expressions of CDH family. Colored columns on the right side displayed the molecular subtypes of each cell line. “Inconsistent” denoted cell lines that are inconsistently annotated regarding the status of markers. “Others” included two cell lines that were not breast cancers (HMEL, engineered breast; HS274T, breast fibroblast). TNBC, triple negative breast cancer.



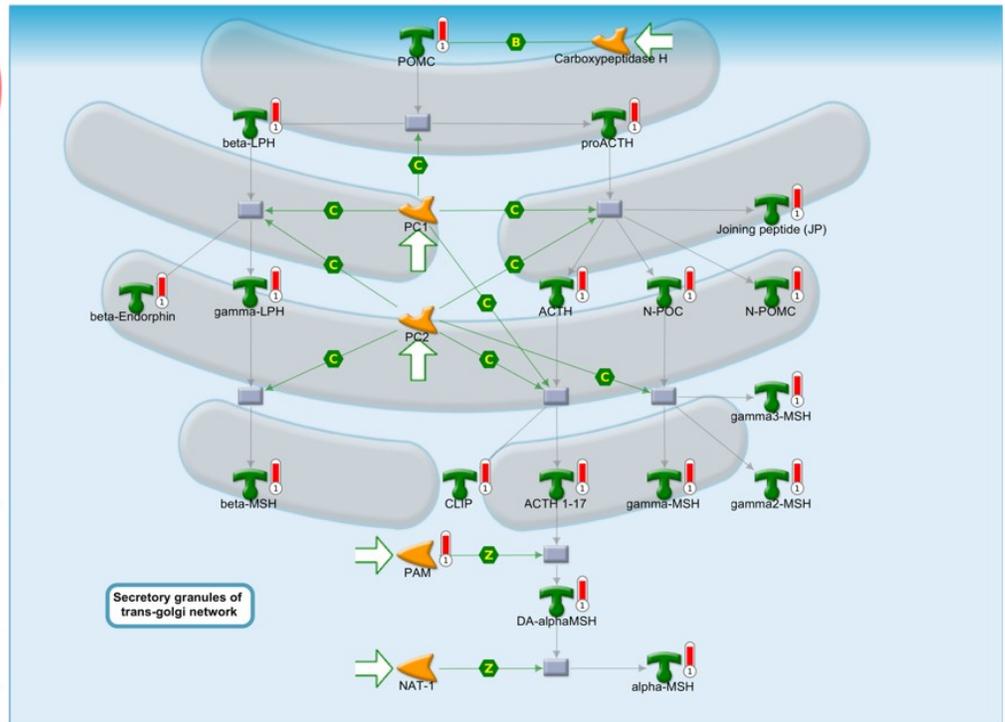
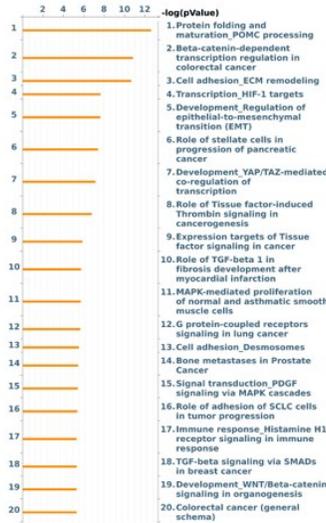
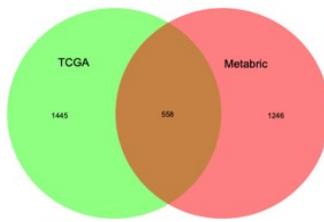
Supplementary Figure 2. Clinical indicators for treatment and subtypes of breast invasive carcinoma patients with cadherin 1 (CDH1)/2/4/7/11/12/13/15 expressions. (A) Estrogen receptor (ER)/progesterone (PR) expression with *CDH* family genes co-expression. (B) Human epidermal growth factor receptor-2 (HER2) expression with *CDH* family genes co-expression. (C) Subtypes of breast invasive carcinoma with *CDH* family genes co-expression. (D) Breast cancer gene-1 (*BRCA1*)/*BRCA2* mutations type with *CDH* family genes co-expression.



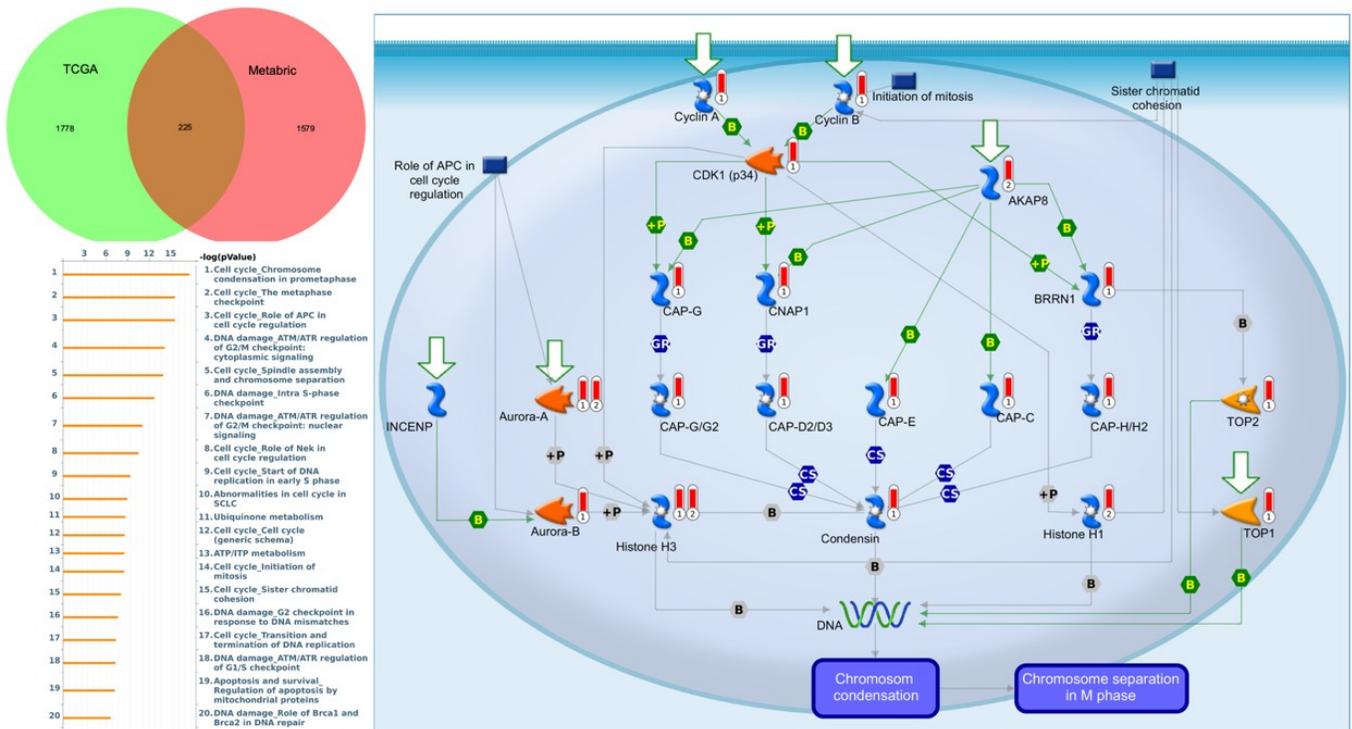
Supplementary Figure 3. Heatmap of DNA methylation expression levels of *CDH1/2/4/11/12/13* in breast cancer by the MethSurv platform. Blue bars indicated low expressions, while red bars indicated high expressions. Different colored boxes indicated different ethnicities, races, ages, events, relation to UCSC CpG island and UCSC RefGene Groups. DNA methylation status was represented as β -values (ranging from 0 to 1). (A) Among *CDH1*, cg26508465 and cg09220040 showed the highest levels of DNA methylation; cg24776465 showed the highest level among *CDH2*; cg6140152 showed the highest level among *CDH4*; (B) cg02724025 showed the highest level among *CDH11*; cg17681524 showed the highest level among *CDH12*; cg16387516 showed the highest level among *CDH13*.



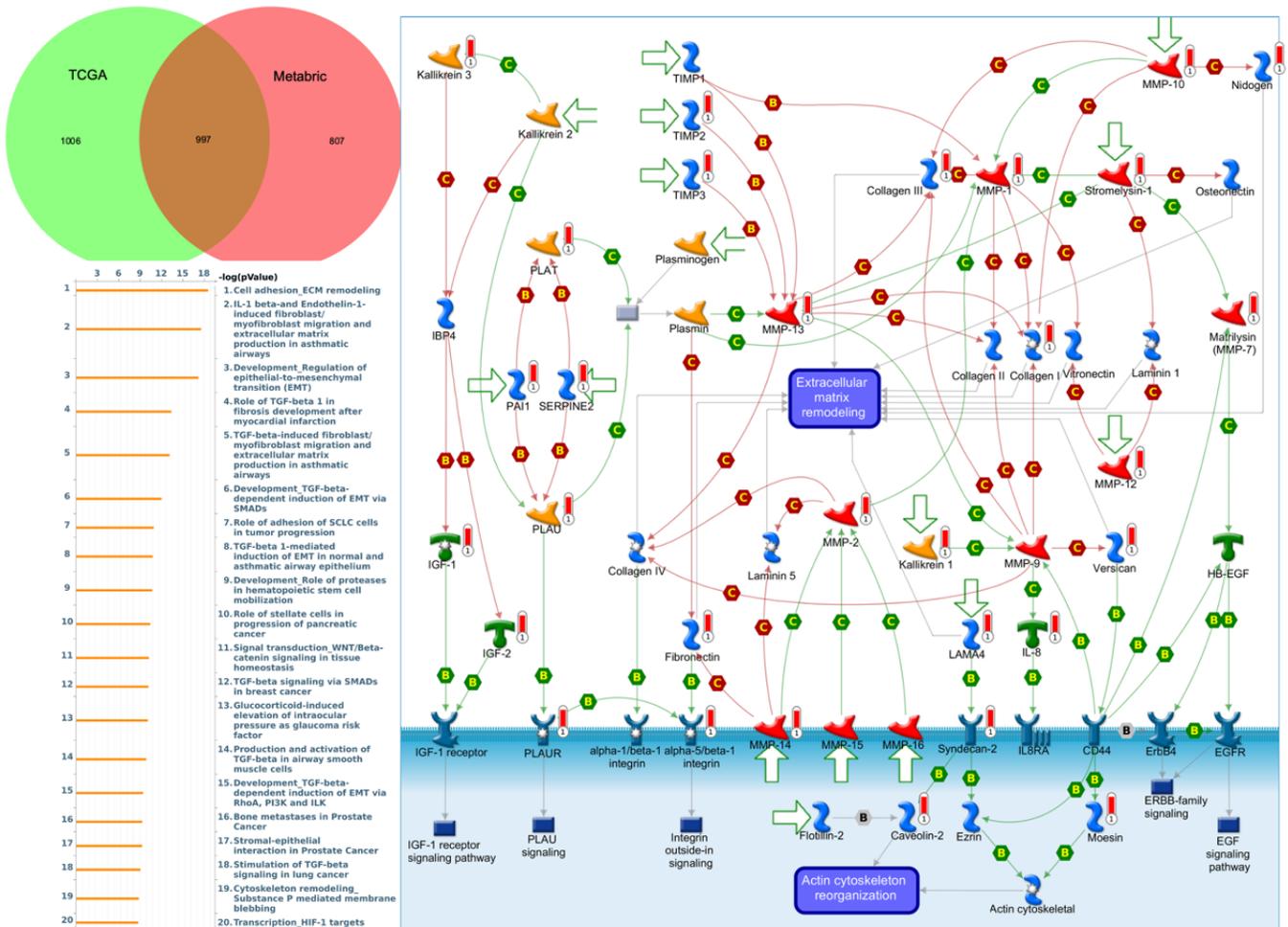
Supplementary Figure 4. MetaCore enrichment pathway analysis of genes co-expressed with cadherin 2 (*CDH2*). Top 10% of expression gene lists from both Metabric (1804 genes) and TCGA (2003 genes) were extracted. Overlapped (933) genes were integrated to implement pathway analysis, which formed a pathway list ordered by the $-\log p$ -value. “Cell adhesion_ECM remodeling” was at the top of the pathway list when performing the “biological process” analysis. The figure demonstrates the interactions between genes and proteins. Symbols represent proteins. Arrows depict protein interactions (green, activation; red, inhibition). Thermometer-like histograms indicate microarray gene expression (blue, down-regulation; red, up-regulation).



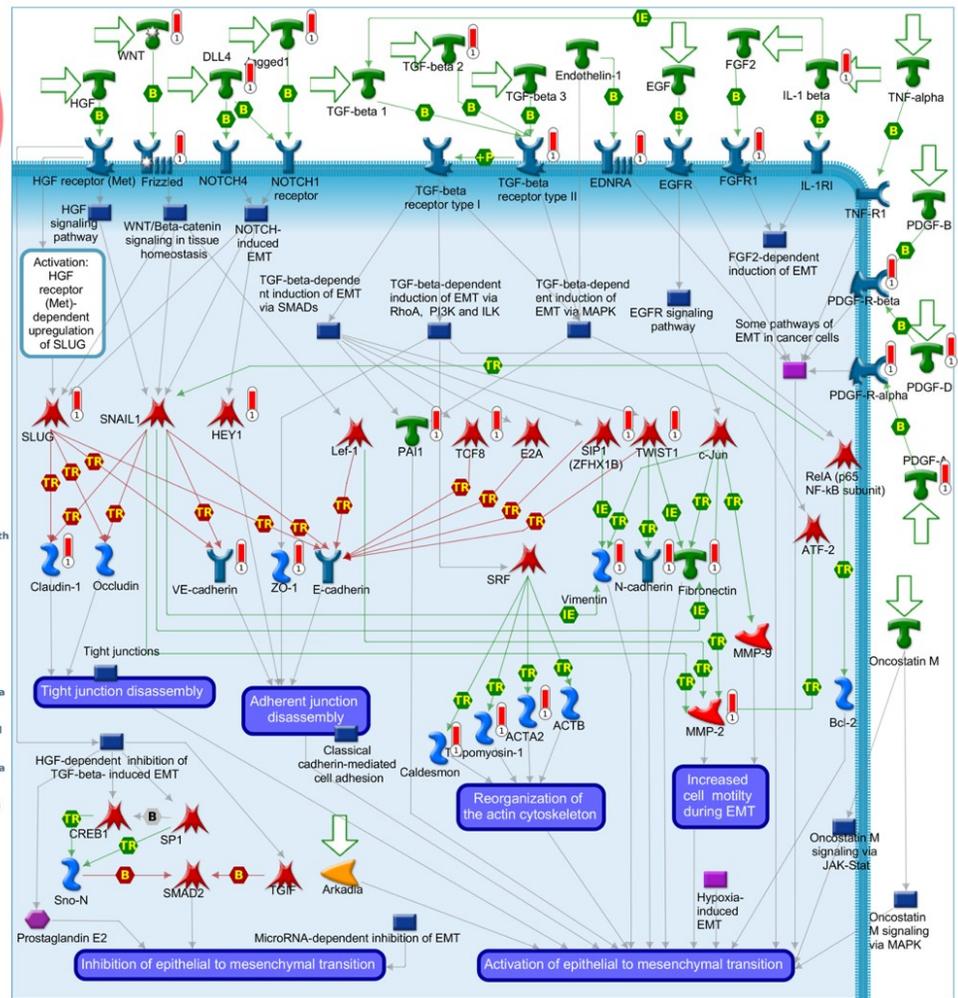
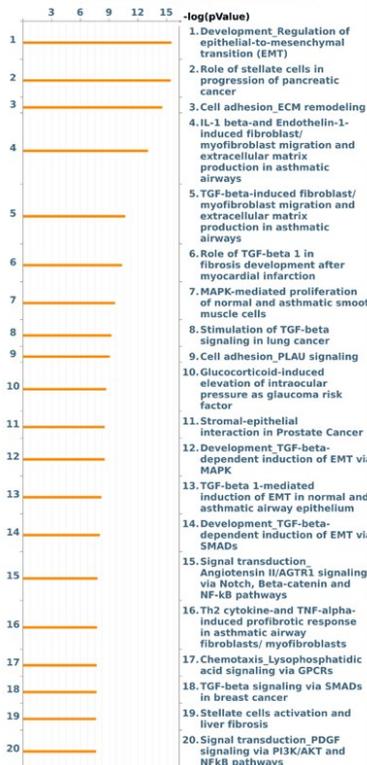
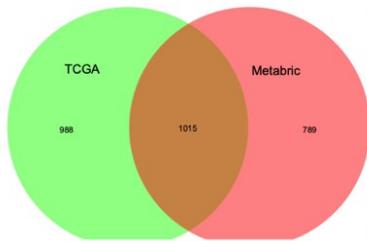
Supplementary Figure 5. MetaCore enrichment pathway analysis of genes co-expressed with cadherin 4 (*CDH4*). Top 10% of expression gene lists from both Metabric (1804 genes) and TCGA (2003 genes) were extracted. Overlapped (558) genes were integrated to implement pathway analysis, which formed a pathway list ordered by the $-\log p$ -value. “Protein folding and maturation_POMC processing” was at the top of the pathway list when performing the “biological process” analysis. The figure demonstrates the interactions between genes and proteins. Symbols represent proteins. Arrows depict protein interactions (green, activation; red, inhibition). Thermometer-like histograms indicate microarray gene expression (blue, down-regulation; red, up-regulation).



Supplementary Figure 6. MetaCore enrichment pathway analysis of genes co-expressed with cadherin 7 (*CDH7*). Top 10% of expression gene lists from both Metabric (1804 genes) and TCGA (2003 genes) were extracted. Overlapped (225) genes were integrated to implement pathway analysis, which formed a pathway list ordered by the $-\log p$ -value. “Cell cycle_Chromosome condensation in prometaphase” was at the top of the pathway list when performing the “biological process” analysis. The figure demonstrates the interactions between genes and proteins. Symbols represent proteins. Arrows depict protein interactions (green, activation; red, inhibition). Thermometer-like histograms indicate microarray gene expression (blue, down-regulation; red, up-regulation).



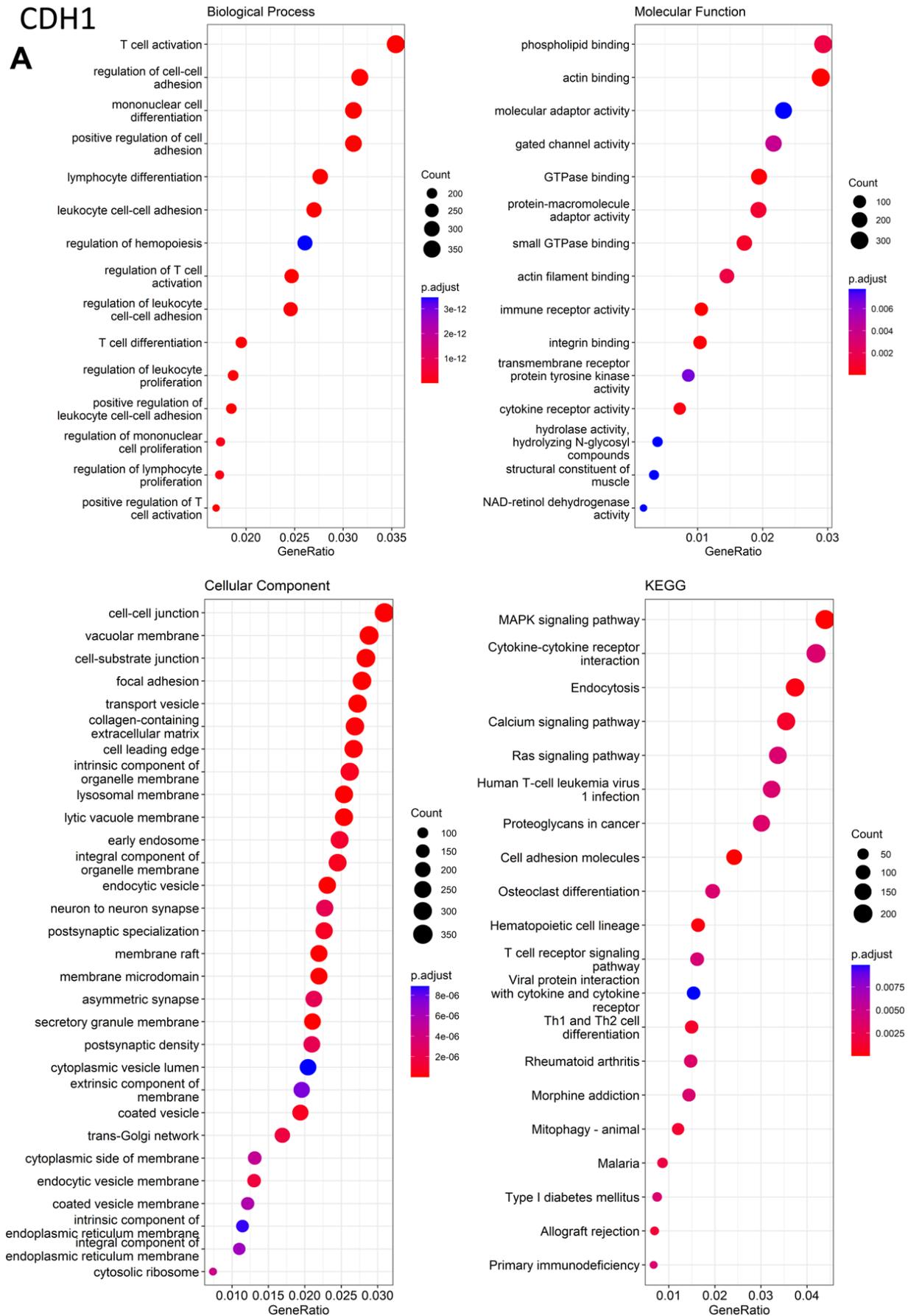
Supplementary Figure 7. MetaCore enrichment pathway analysis of genes co-expressed with cadherin 11 (*CDH11*). Top 10% of expression gene lists from both Metabric (1804 genes) and TCGA (2003 genes) were extracted. Overlapped (997) genes were integrated to implement pathway analysis, which formed a pathway list ordered by the $-\log p$ -value. “Cell adhesion_ECM remodeling” was at the top of the pathway list when performing the “biological process” analysis. The figure demonstrates the interactions between genes and proteins. Symbols represent proteins. Arrows depict protein interactions (green, activation; red, inhibition). Thermometer-like histograms indicate microarray gene expression (blue, down-regulation; red, up-regulation).

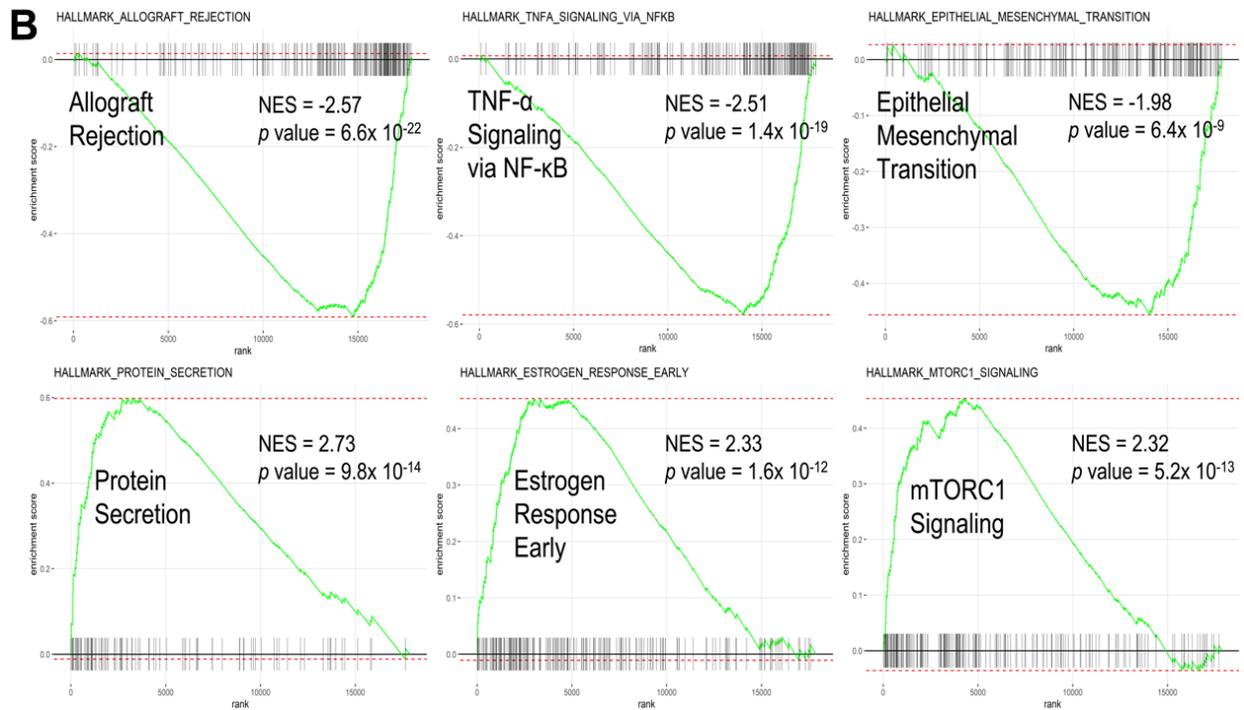


Supplementary Figure 8. MetaCore enrichment pathway analysis of genes co-expressed with cadherin 13 (*CDH13*). Top 10% of expression gene lists from both Metabric (1804 genes) and TCGA (2003 genes) were extracted. Overlapped (1015) genes were integrated to implement pathway analysis, which formed a pathway list ordered by the $-\log p$ -value. “Development_Regulation of epithelial-to-mesenchymal transition (EMT)” was at the top of the pathway list when performing the “biological process” analysis. The figure demonstrates the interactions between genes and proteins. Symbols represent proteins. Arrows depict protein interactions (green, activation; red, inhibition). Thermometer-like histograms indicate microarray gene expression (blue, down-regulation; red, up-regulation).

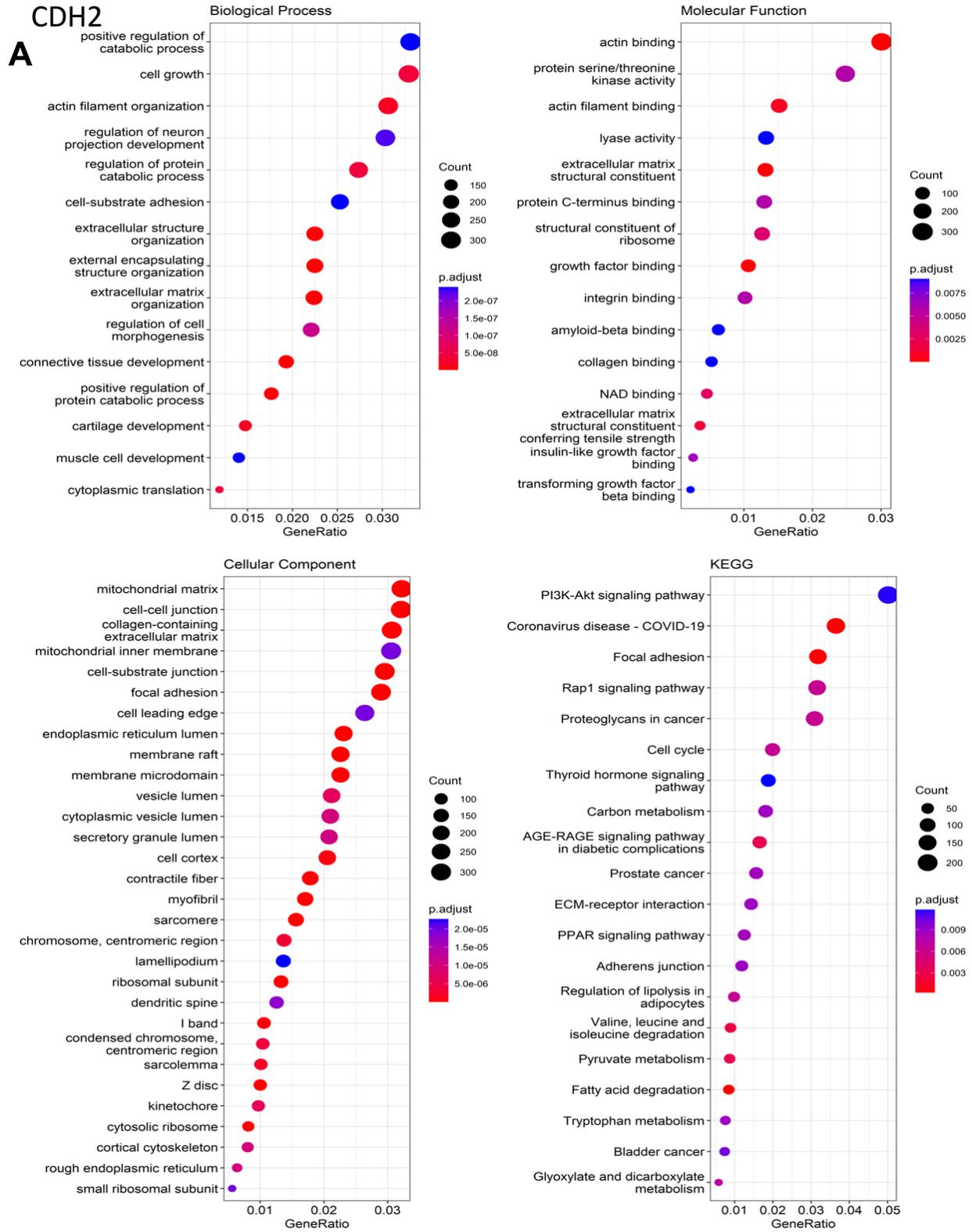
CDH1

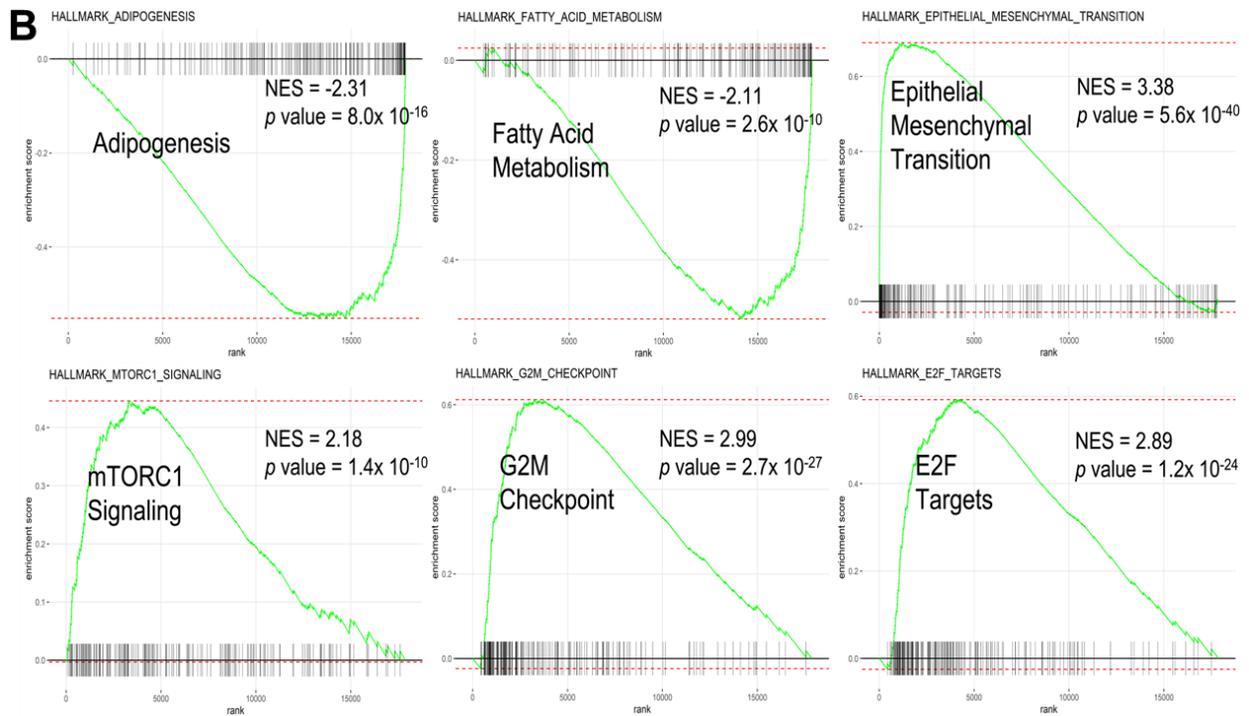
A



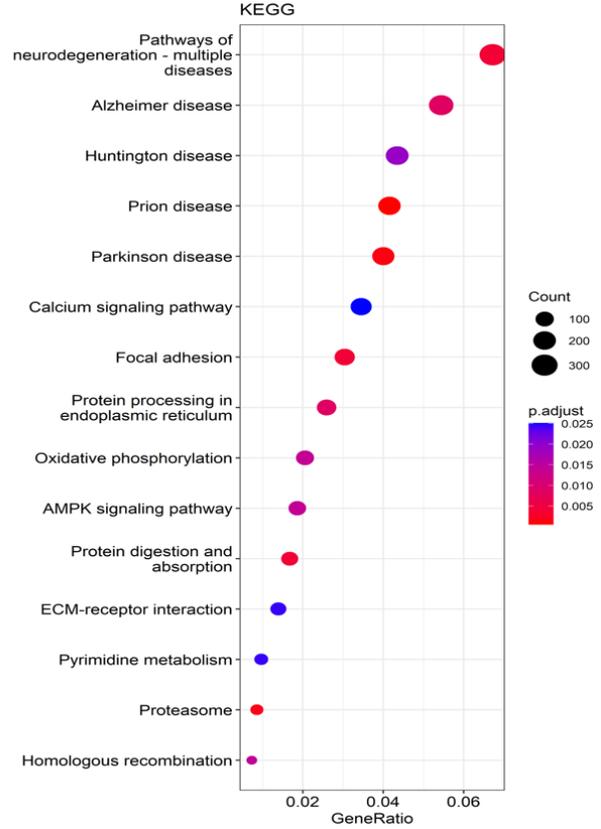
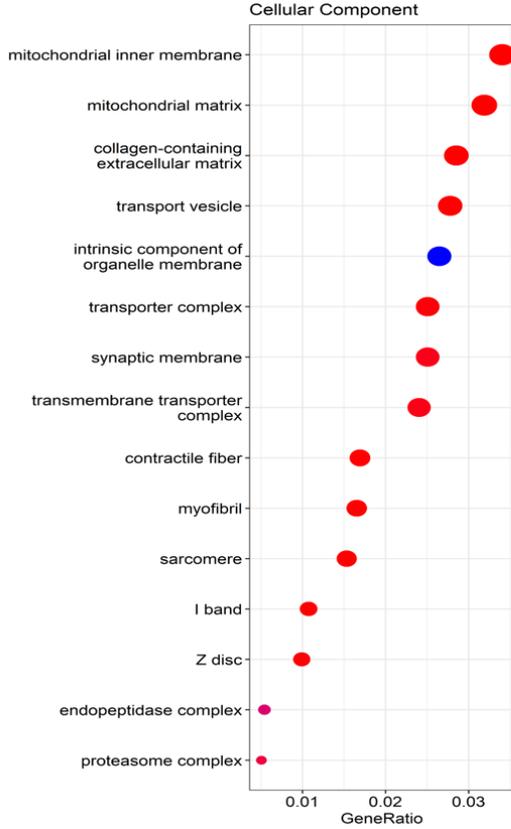
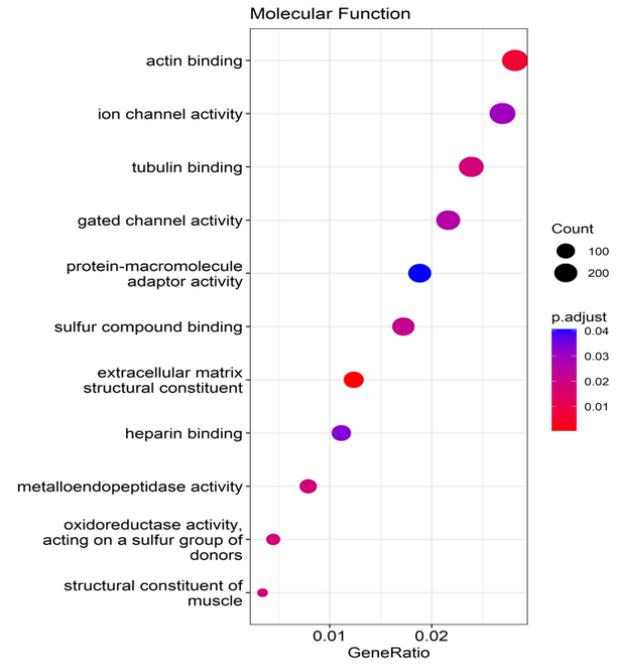
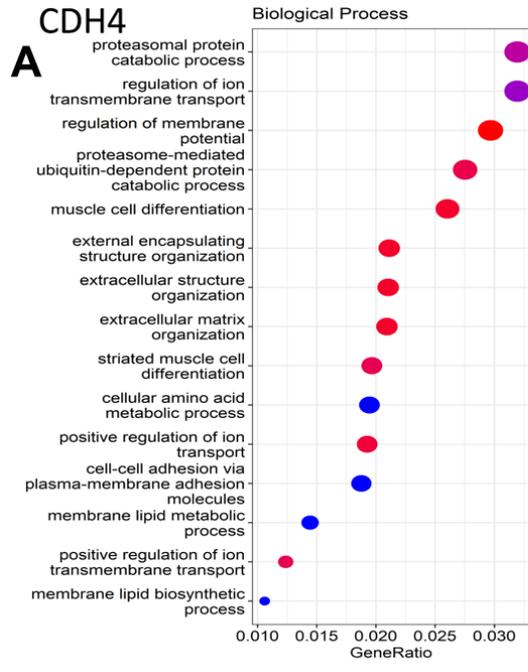


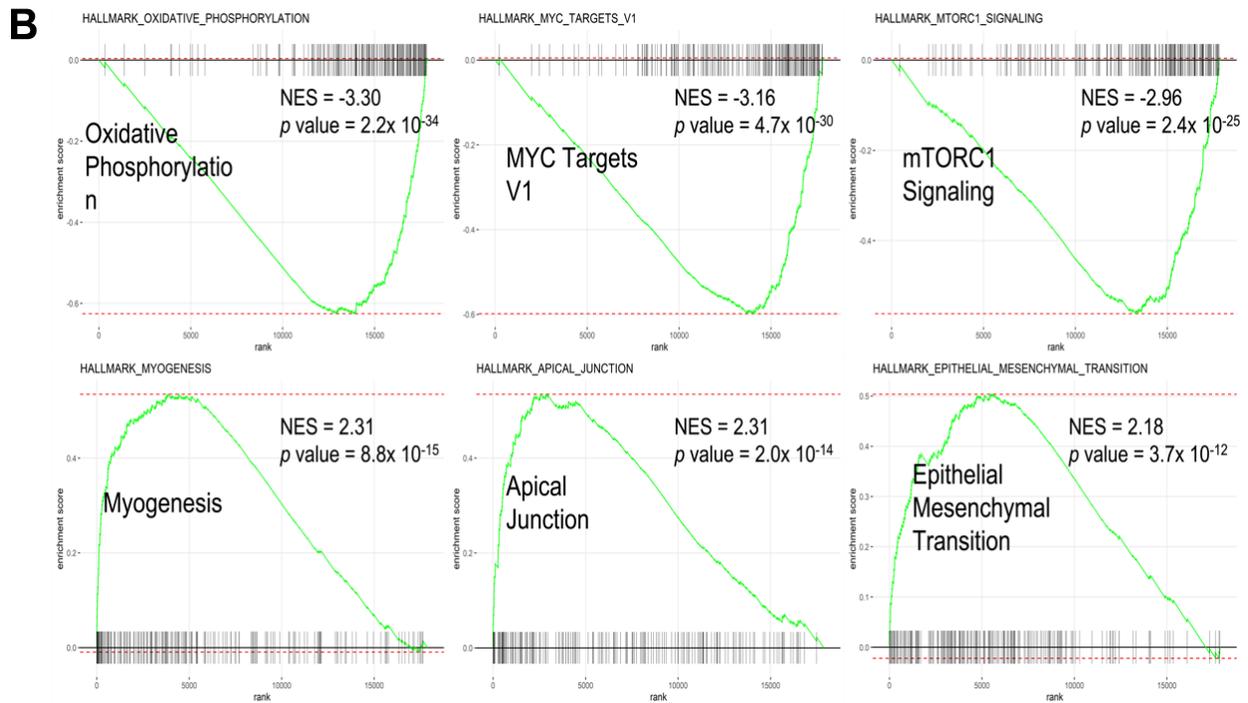
Supplementary Figure 9. (A, B) Gene Ontology (GO) analysis and Gene Set Enrichment Analysis (GSEA) based on genes co-expressed with *CDH1*. **(A)** Dot plots display biological processes, cellular components, molecular functions, and KEGG. The dot size is determined by the count of enriched genes in the pathway, and the color of the dots represents the significance of enrichment pathway. “clusterProfiler” package in R/Bioconductor was used to perform the GO analyses of dot plots. **(B)** Hallmark signaling pathway analysis of *CDH1* in breast cancer. Results of the analysis showed significant values of gene classes in the Hallmark database. Statistical significance was presented by p value, and the normalized enrichment score (NES) reflected the rank of gene classes.



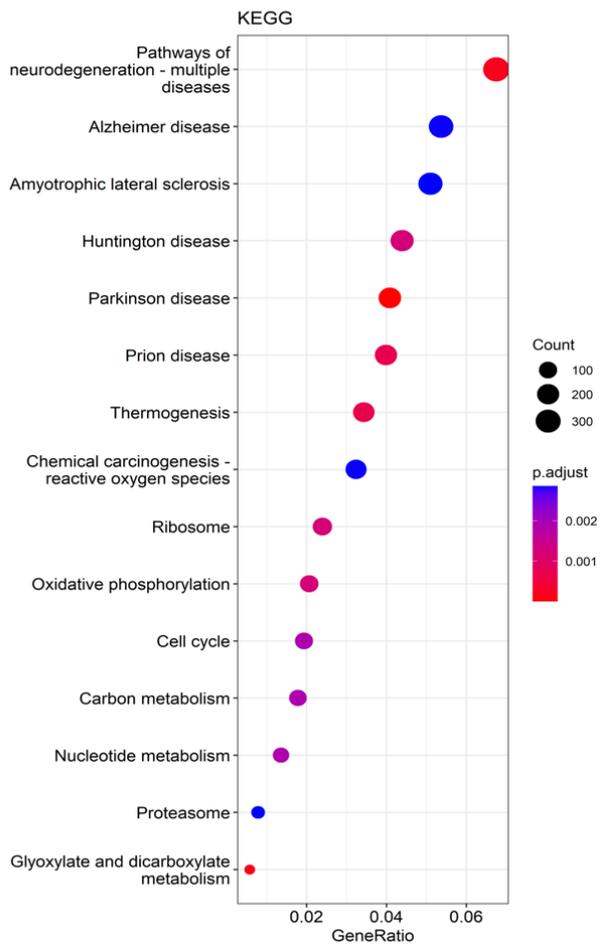
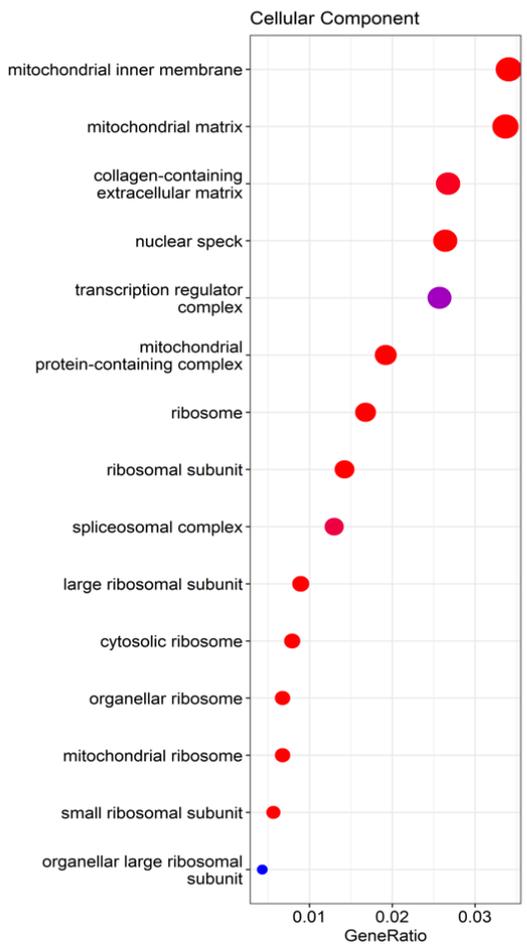
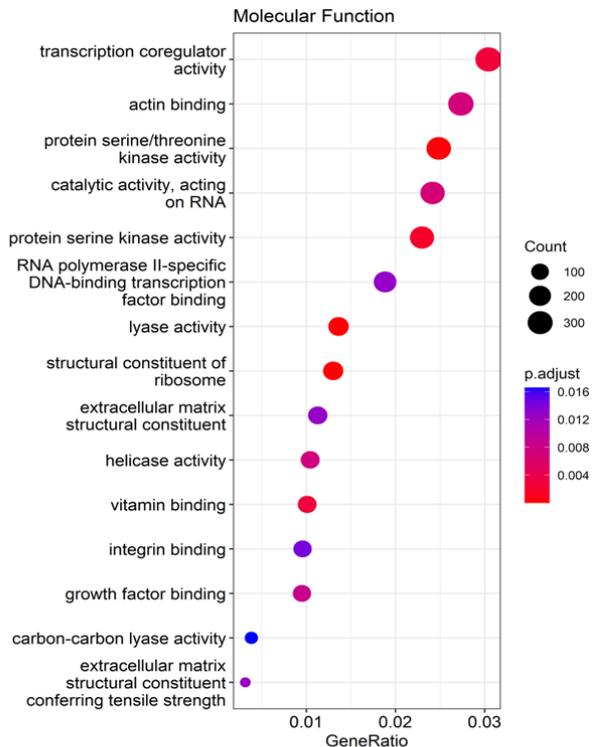
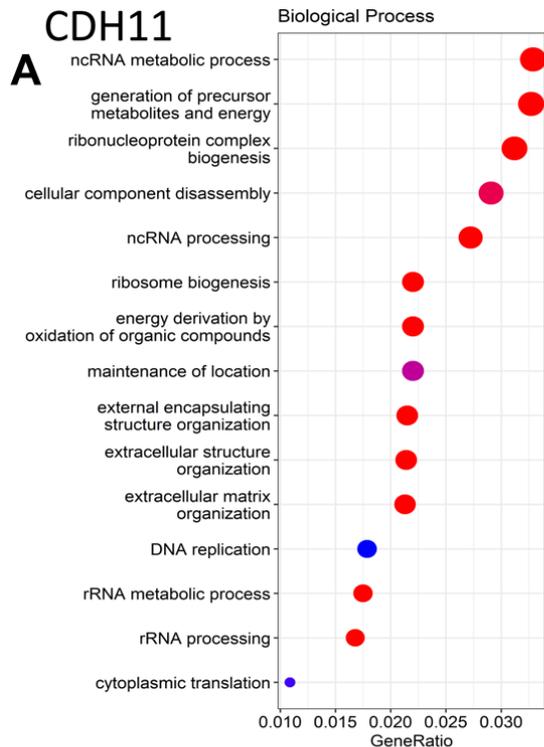


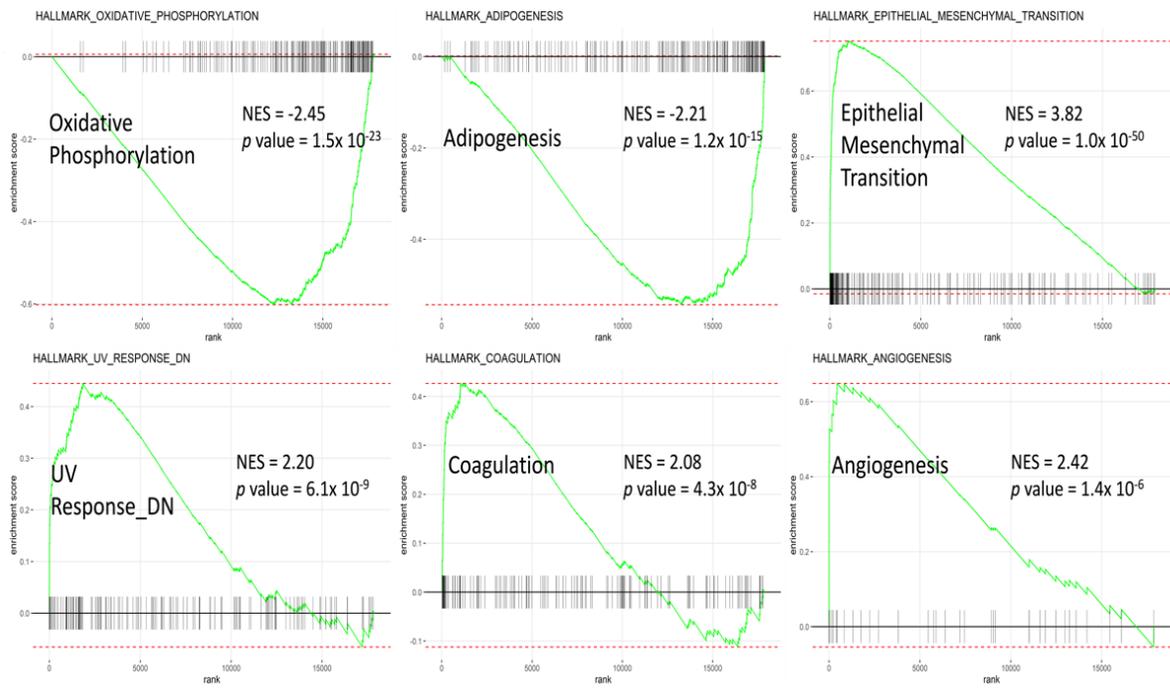
Supplementary Figure 10. (A, B) Gene Ontology (GO) analysis and Gene Set Enrichment Analysis (GSEA) based on genes co-expressed with *CDH2*. **(A)** Dot plots display biological processes, cellular components, molecular functions, and KEGG. The dot size is determined by the count of enriched genes in the pathway, and the color of the dots represents the significance of enrichment pathway. “clusterProfiler” package in R/Bioconductor was used to perform the GO analyses of dot plots. **(B)** Hallmark signaling pathway analysis of *CDH2* in breast cancer. Results of the analysis showed significant values of gene classes in the Hallmark database. Statistical significance was presented by p value, and the normalized enrichment score (NES) reflected the rank of gene classes.





Supplementary Figure 11. (A, B) Gene Ontology (GO) analysis and Gene Set Enrichment Analysis (GSEA) based on genes co-expressed with *CDH4*. (A) Dot plots display biological processes, cellular components, molecular functions, and KEGG. The dot size is determined by the count of enriched genes in the pathway, and the color of the dots represents the significance of enrichment pathway. “clusterProfiler” package in R/Bioconductor was used to perform the GO analyses of dot plots. (B) Hallmark signaling pathway analysis of *CDH4* in breast cancer. Results of the analysis showed significant values of gene classes in the Hallmark database. Statistical significance was presented by p value, and the normalized enrichment score (NES) reflected the rank of gene classes.

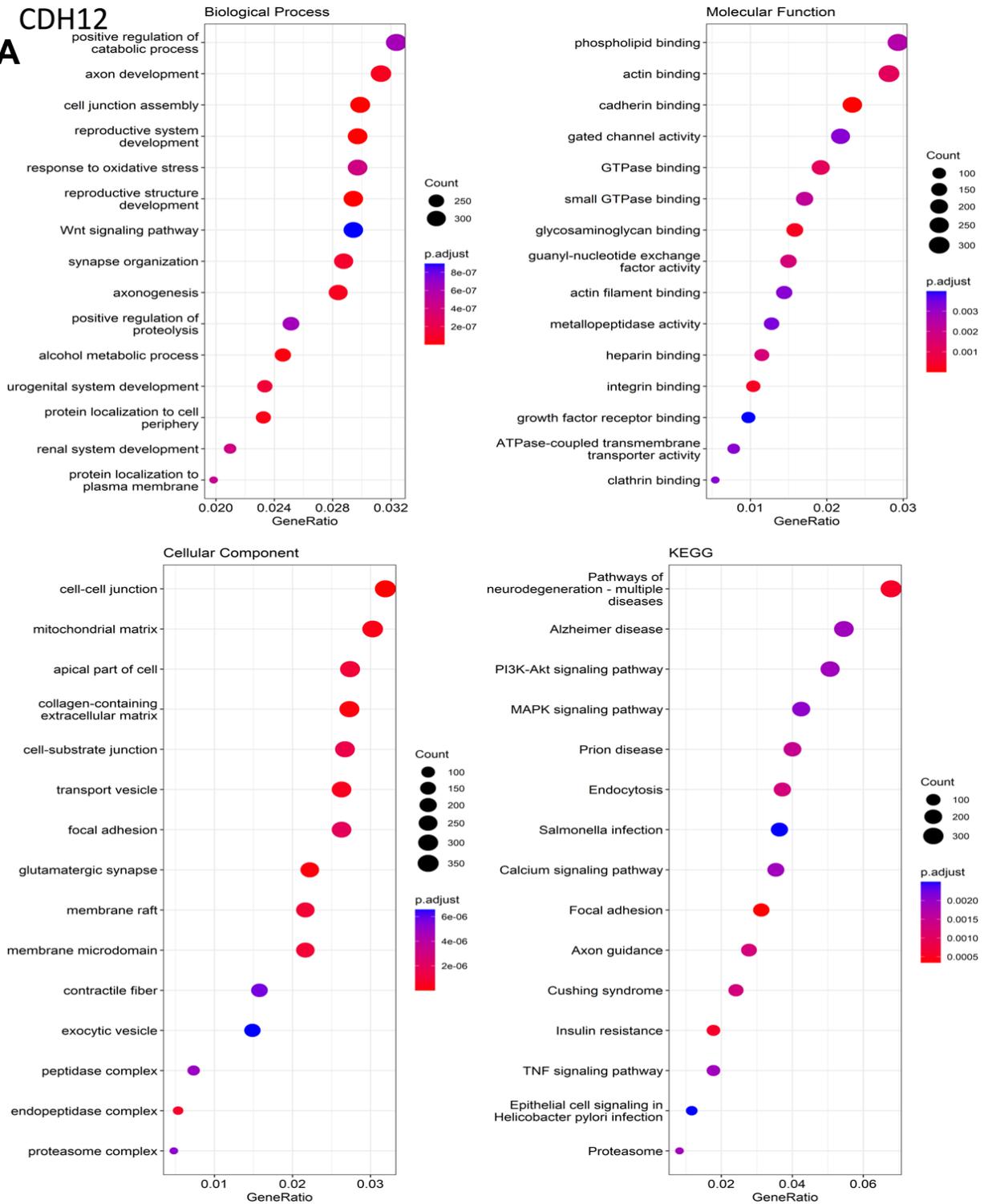


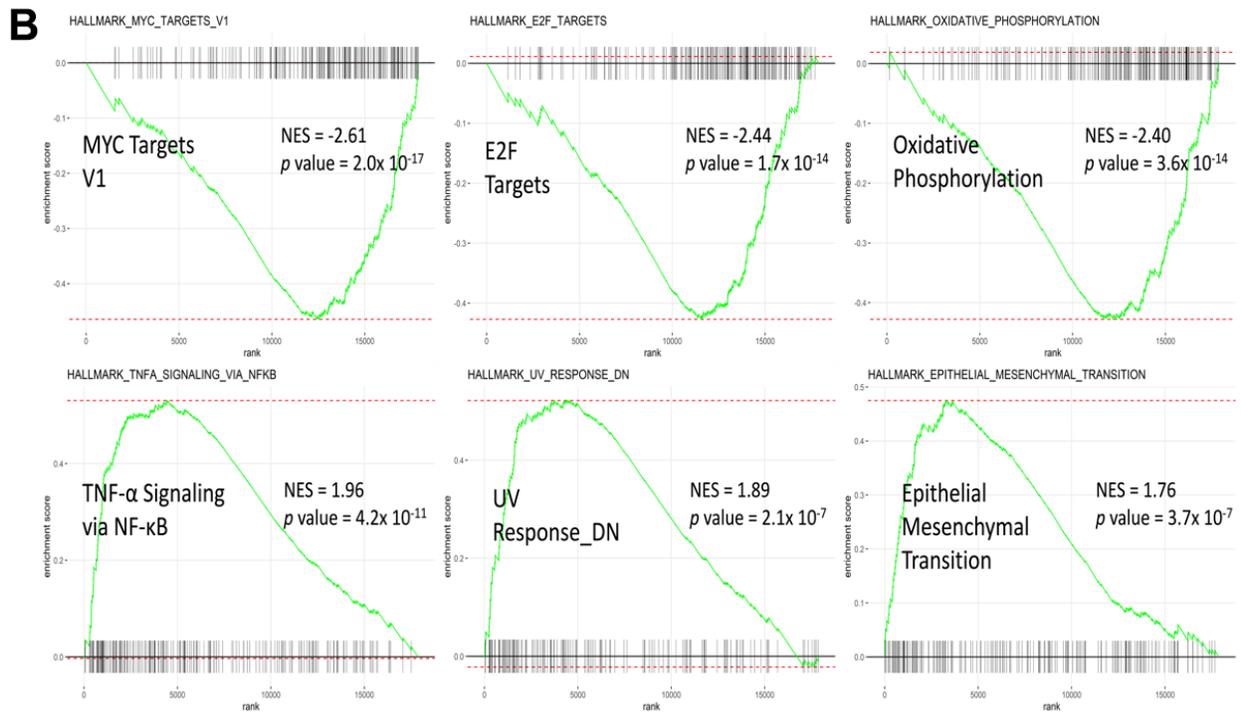
B

Supplementary Figure 12. (A, B) Gene Ontology (GO) analysis and Gene Set Enrichment Analysis (GSEA) based on genes co-expressed with *CDH11*. **(A)** Dot plots display biological processes, cellular components, molecular functions, and KEGG. The dot size is determined by the count of enriched genes in the pathway, and the color of the dots represents the significance of enrichment pathway. “clusterProfiler” package in R/Bioconductor was used to perform the GO analyses of dot plots. **(B)** Hallmark signaling pathway analysis of *CDH11* in breast cancer. Results of the analysis showed significant values of gene classes in the Hallmark database. Statistical significance was presented by p value, and the normalized enrichment score (NES) reflected the rank of gene classes.

CDH12

A

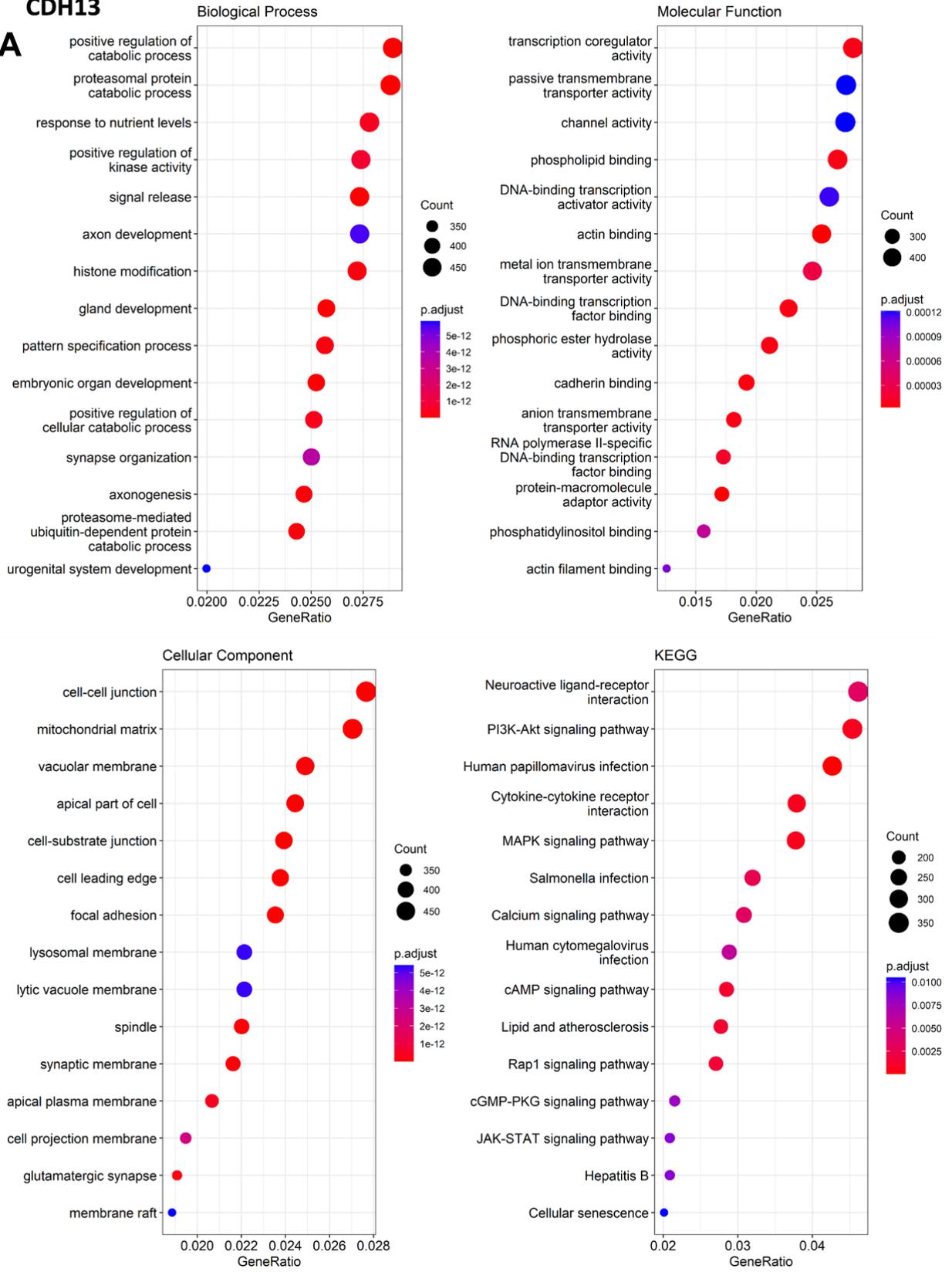


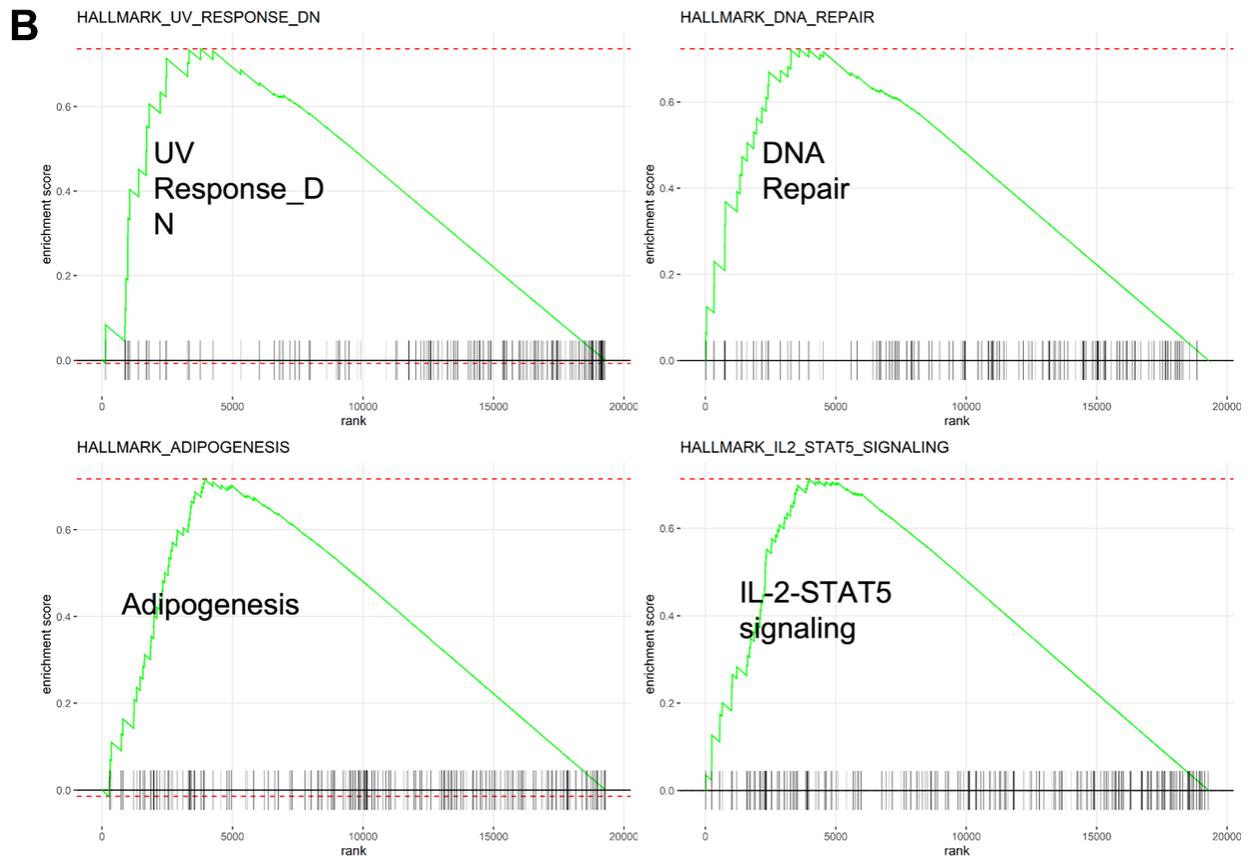


Supplementary Figure 13. (A, B) Gene Ontology (GO) analysis and Gene Set Enrichment Analysis (GSEA) based on genes co-expressed with *CDH12*. **(A)** Dot plots display biological processes, cellular components, molecular functions, and KEGG. The dot size is determined by the count of enriched genes in the pathway, and the color of the dots represents the significance of enrichment pathway. “clusterProfiler” package in R/Bioconductor was used to perform the GO analyses of dot plots. **(B)** Hallmark signaling pathway analysis of *CDH12* in breast cancer. Results of the analysis showed significant values of gene classes in the Hallmark database. Statistical significance was presented by p value, and the normalized enrichment score (NES) reflected the rank of gene classes.

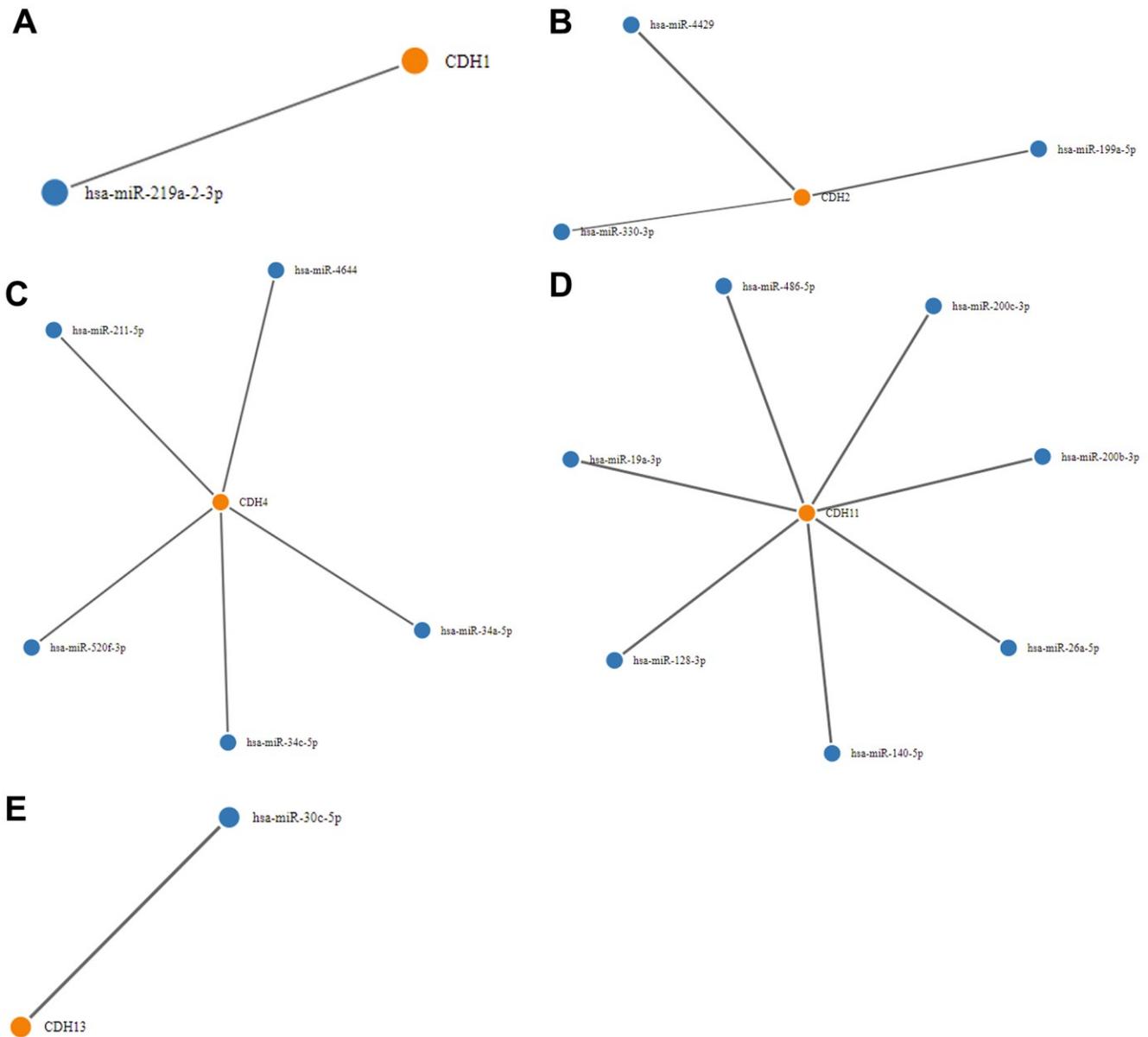
CDH13

A



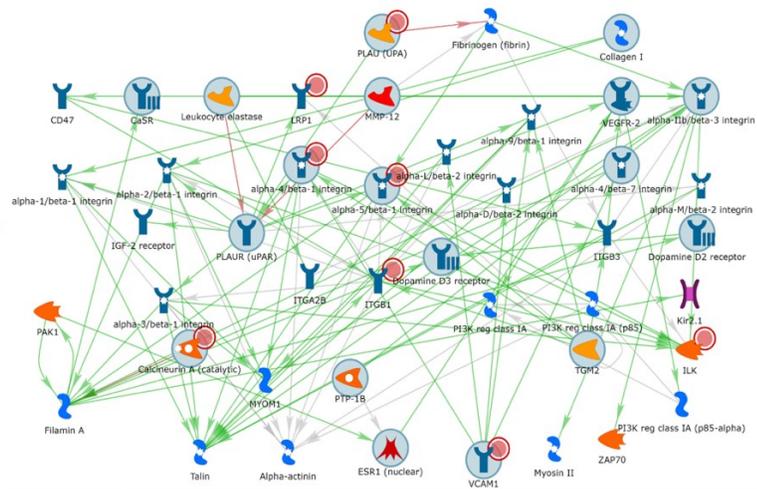
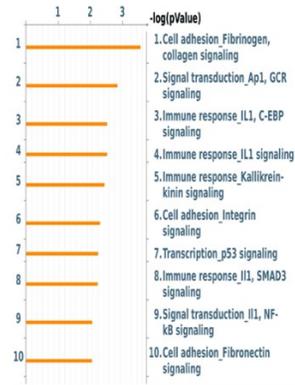


Supplementary Figure 14. (A, B) Gene Ontology (GO) analysis and Gene Set Enrichment Analysis (GSEA) based on genes co-expressed with *CDH13*. **(A)** Dot plots display biological processes, cellular components, molecular functions, and KEGG. The dot size is determined by the count of enriched genes in the pathway, and the color of the dots represents the significance of enrichment pathway. “clusterProfiler” package in R/Bioconductor was used to perform the GO analyses of dot plots. **(B)** Hallmark signaling pathway analysis of *CDH13* in breast cancer. Results of the analysis showed significant values of gene classes in the Hallmark database. Statistical significance was presented by *p* value, and the normalized enrichment score (NES) reflected the rank of gene classes.

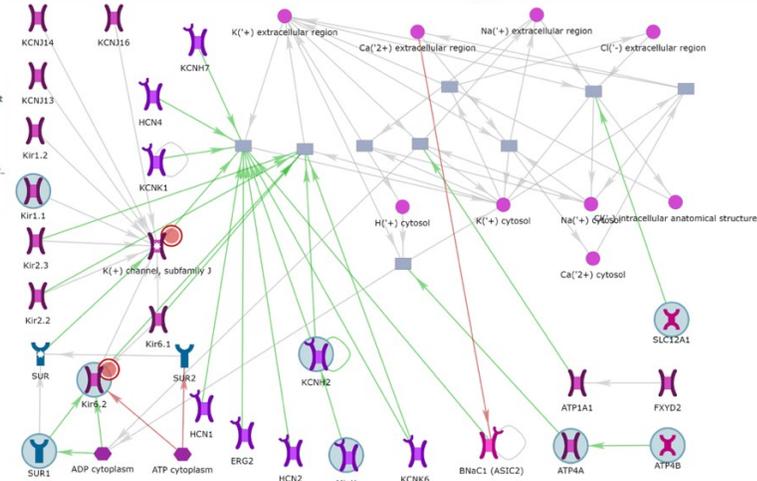
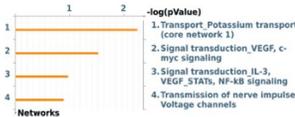


Supplementary Figure 15. Analysis of micro-(mi)RNA networks with *CDH1/2/4/11/13* in breast cancer. (A) *CDH1* demonstrated network interaction with hsa-miR-219a-2-3p in breast cancer development; (B) *CDH2* demonstrated network interaction with hsa-miR-330-3p, has-miR-4429, and hsa-miR-199a-5p; (C) *CDH4* demonstrated network interaction with hsa-miR-4644, hsa-miR-211-5p, hsa-miR-520f-3p, hsa-miR-34e-5p, and hsa-miR-34a-5p; (D) *CDH11* demonstrated network interaction with hsa-miR-486-5p, hsa-miR-200c-3p, hsa-miR-200b-3p, hsa-miR-26a-5p, hsa-miR-140-5p, hsa-miR-128-3p, and hsa-miR-19a-3p; (E) *CDH13* demonstrated network interaction with hsa-miR-30c-5p.

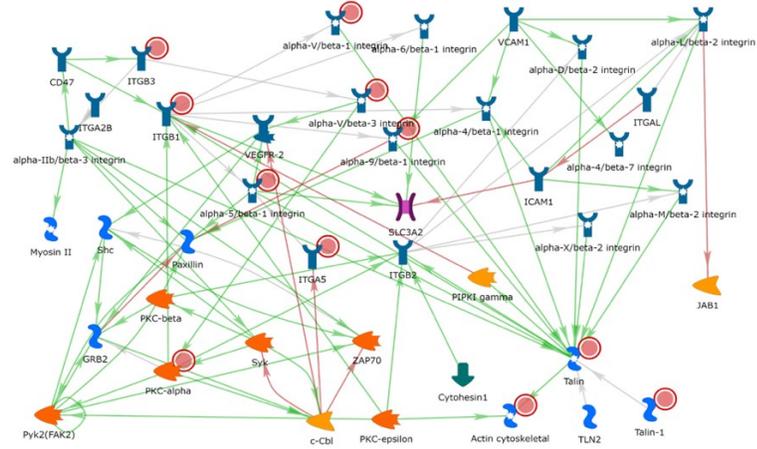
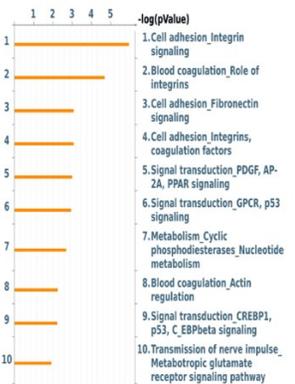
B CDH11



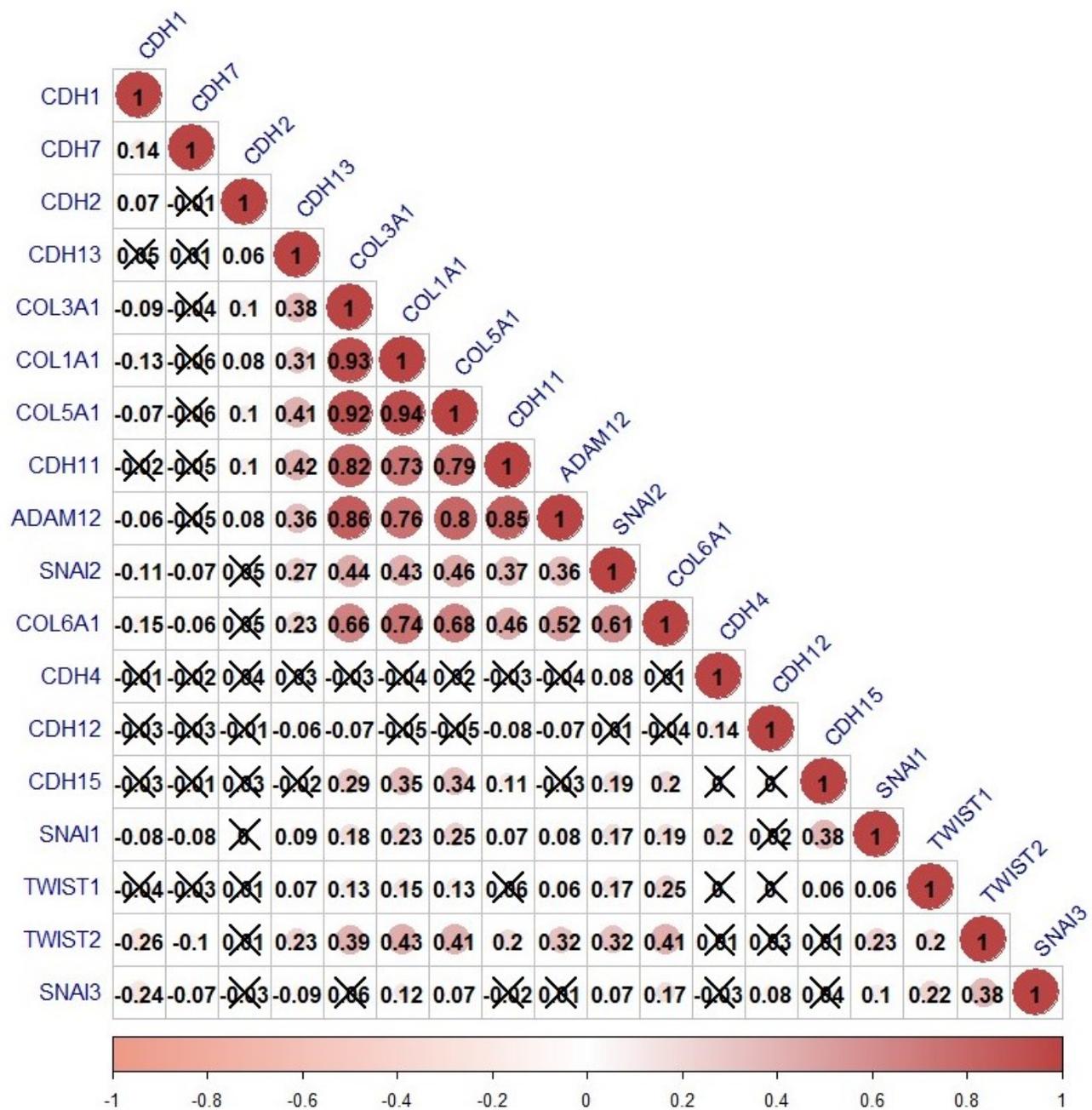
CDH12



CDH13



Supplementary Figure 16. (A, B) Drug target networks analysis of genes co-expressed with cadherin (*CDH*) 1/2/4/11/12/13. Genes co-expressed with *CDH*1/2/4/11/12/13 were integrated to implement drug target networks analysis, which formed a pathway list ordered by the $-\log p$ -value on the left. (A) “Signal transduction_c-myc, CREB1 signaling” was at the top of the drug target of *CDH*1; “Cell adhesion_Fibrinogen, collagen signaling” was at the top of the drug target of *CDH*4; “Metabolism_PPAR, RXR, VDR regulation of metabolism” was at the top of the drug target of *CDH*11; (B) “Cell adhesion_Fibrinogen, collagen signaling” was at the top of the drug target of *CDH*11; “Transport_Potassium transport (core work 1)” was at the top of the drug target of *CDH*12; “Cell adhesion_Integrin signaling” was at the top of the drug target of *CDH*13. The figure demonstrates the interactions between genes and proteins. Symbols represent proteins. Arrows depict protein interactions (green, activation; red, inhibition).



Supplementary Figure 17. Correlations between cadherin (CDH) family and epithelial-mesenchymal transition (EMT)-regulated genes in breast cancer using TCGA dataset. The symmetric correlation matrix was created by the “corrplot” R package. The color represents the degree of pairwise correlation regarding Spearman’s rank correlation coefficient. Darker red and larger dot size mean stronger positive correlation, while orange indicates stronger negative correlation. The cross symbols represent non-significant correlation coefficient values (p value > 0.01).