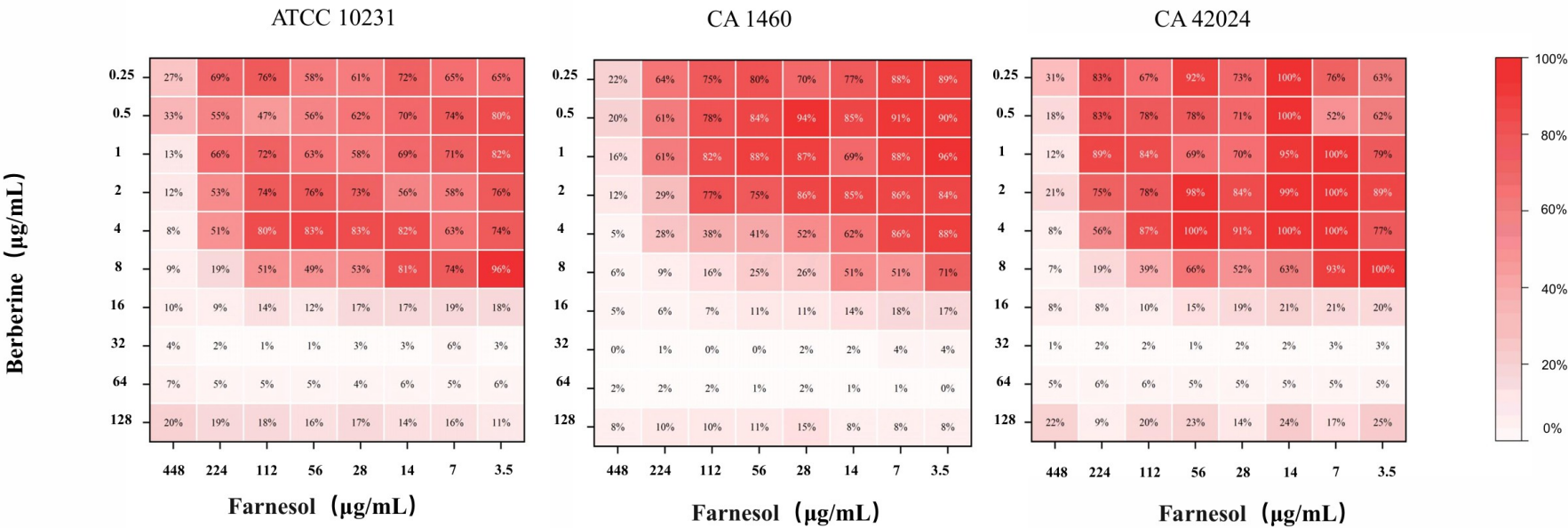


Supplementary Information

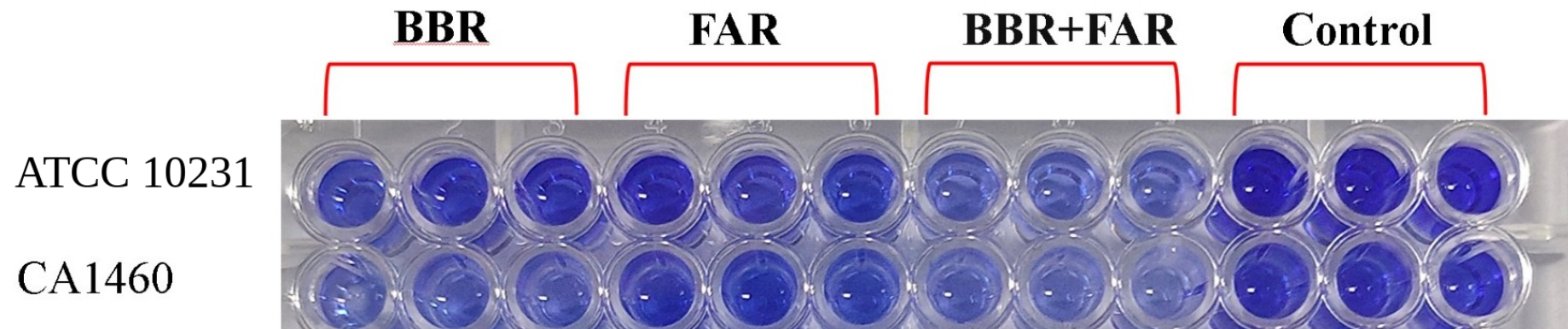
The Combination of Farnesol and Berberine Effectively Inhibits *Candida albicans* Growth and Biofilm Formation

Daiyan Tang et al.

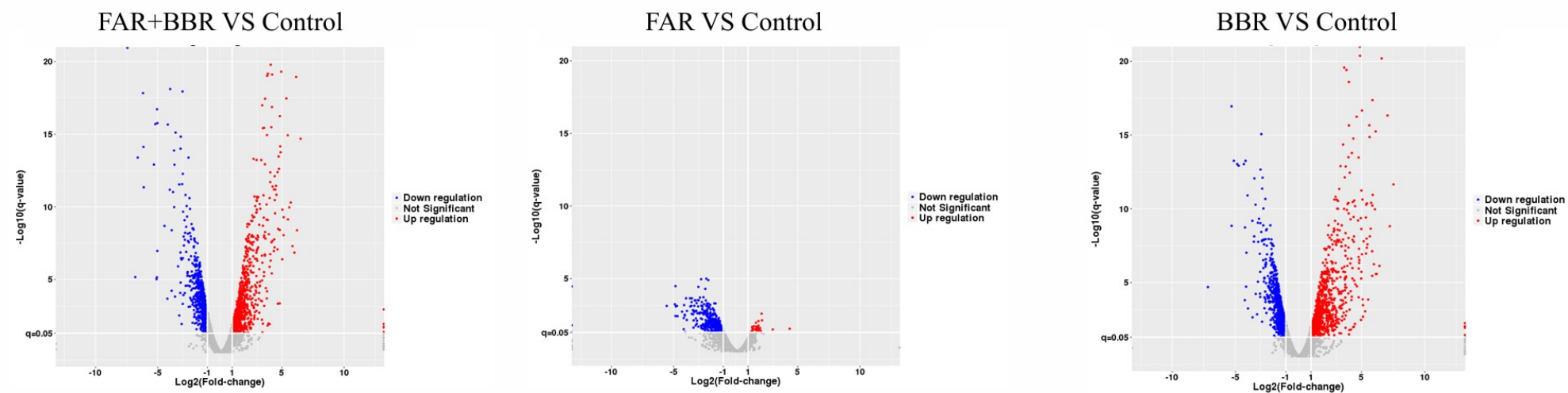
Supplementary Figures



Supplementary Figure S1. Checkerboard assay heatmaps showing the growth rates of *C. albicans* ATCC 10231, CA1460, and CA42024 following combined treatment with farnesol (FAR) and berberine (BBR). Values in each cell indicate the growth rate (%) at the corresponding FAR and BBR concentrations; lighter colors indicate lower growth rates and stronger inhibitory effects.

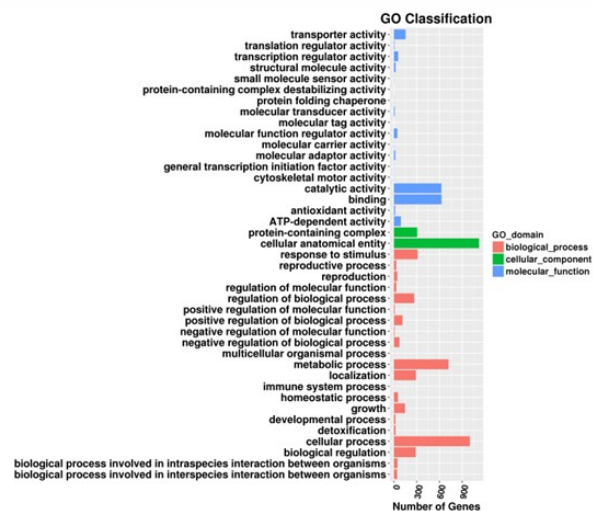


Supplementary Figure S2. Representative crystal violet staining of *C. albicans* biofilms after treatment with BBR, FAR, FAR+BBR, or control conditions. Mature biofilms were stained with crystal violet to visualize attached biofilm biomass after drug treatment.

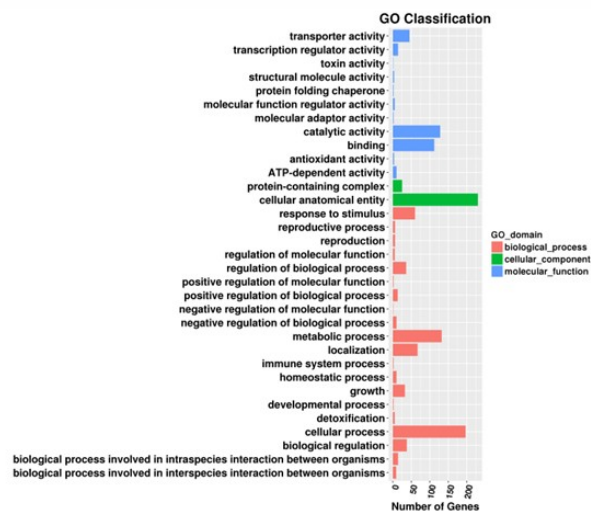


Supplementary Figure S3. Volcano plots showing differentially expressed genes (DEGs) in the FAR+BBR vs. Control, FAR vs. Control, and BBR vs. Control comparisons. Red and blue points indicate significantly upregulated and downregulated genes, respectively, whereas gray points indicate genes without significant differential expression.

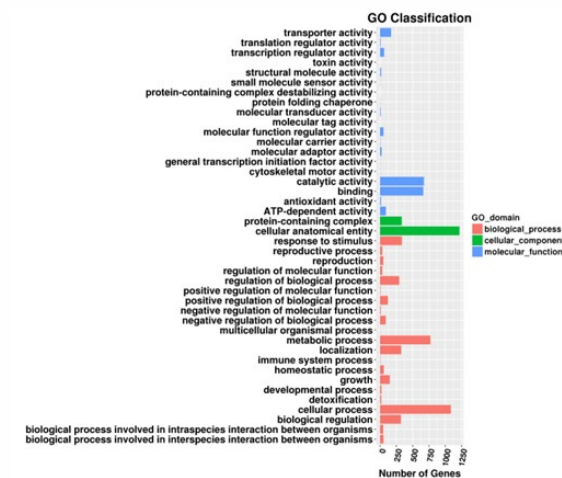
FAR+BBR VS Control



FAR VS Control

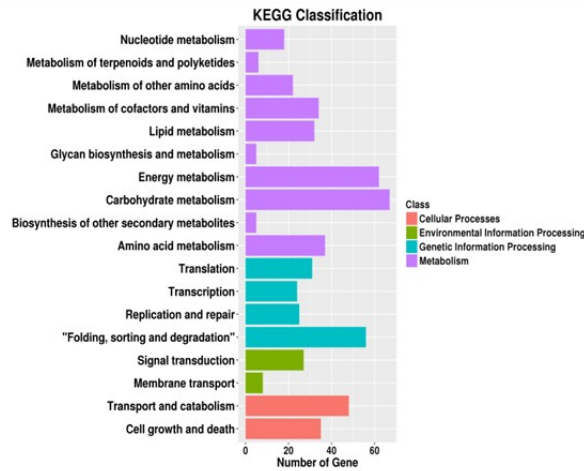


BBR VS Control

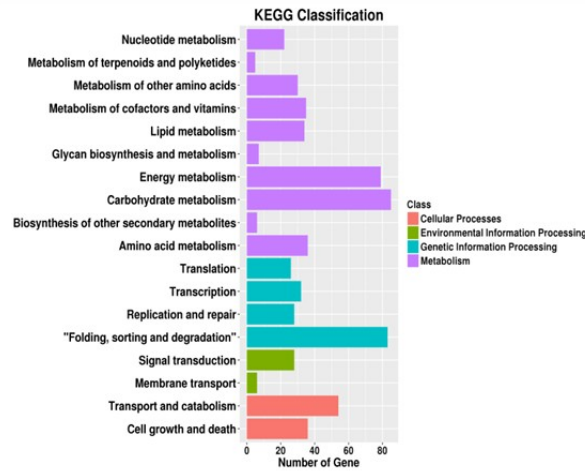


Supplementary Figure S4. Gene Ontology (GO) functional classification of DEGs in the FAR+BBR vs. Control, FAR vs. Control, and BBR vs. Control comparisons. The classified GO terms were grouped into biological process, cellular component, and molecular function categories.

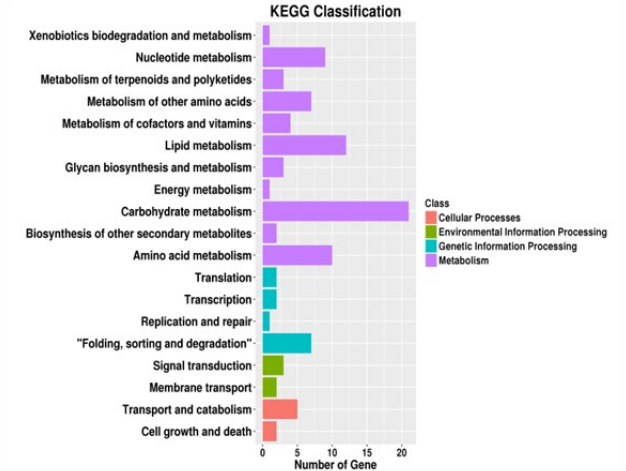
FAR+BBR VS Control



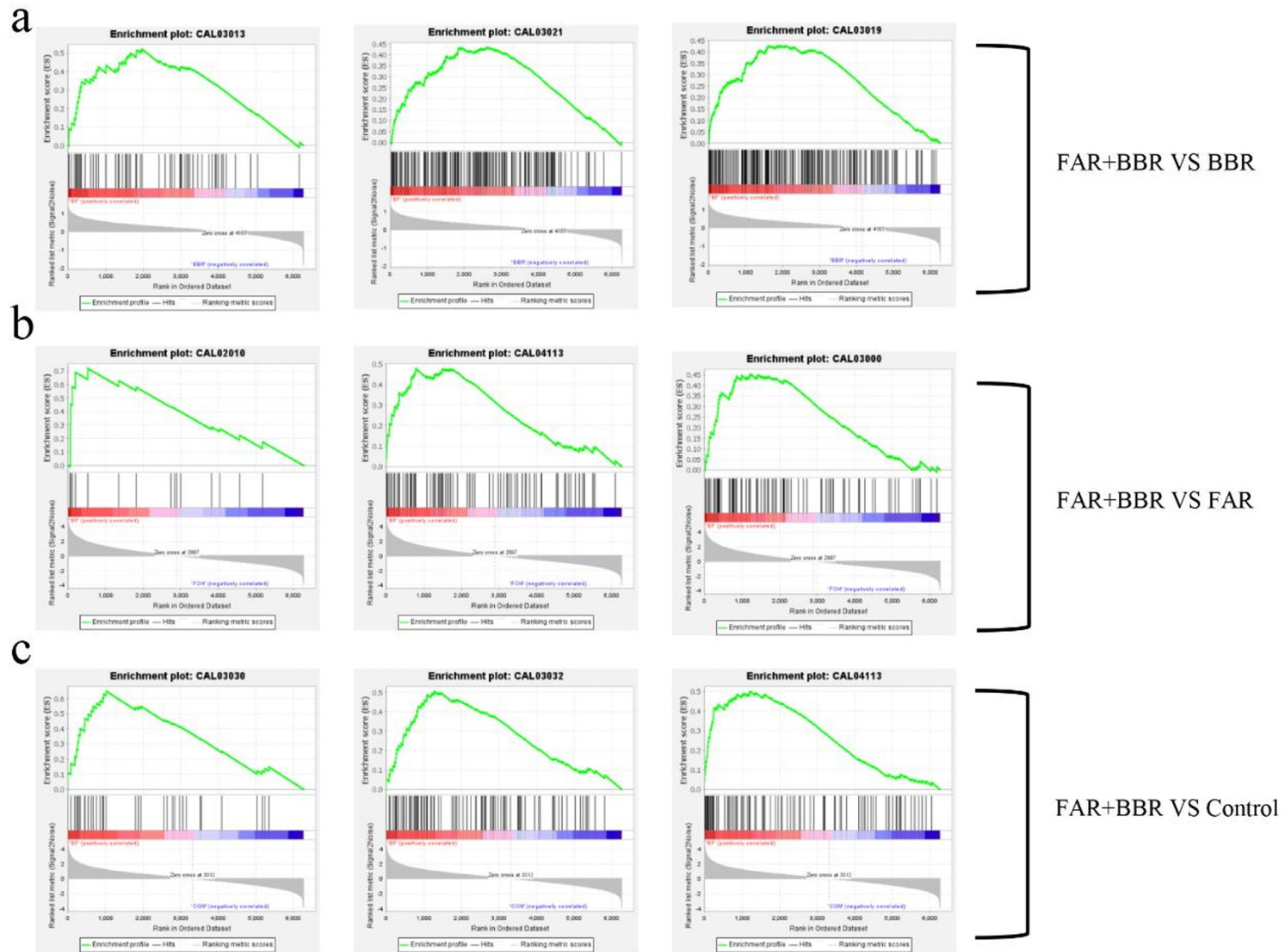
FAR VS Control



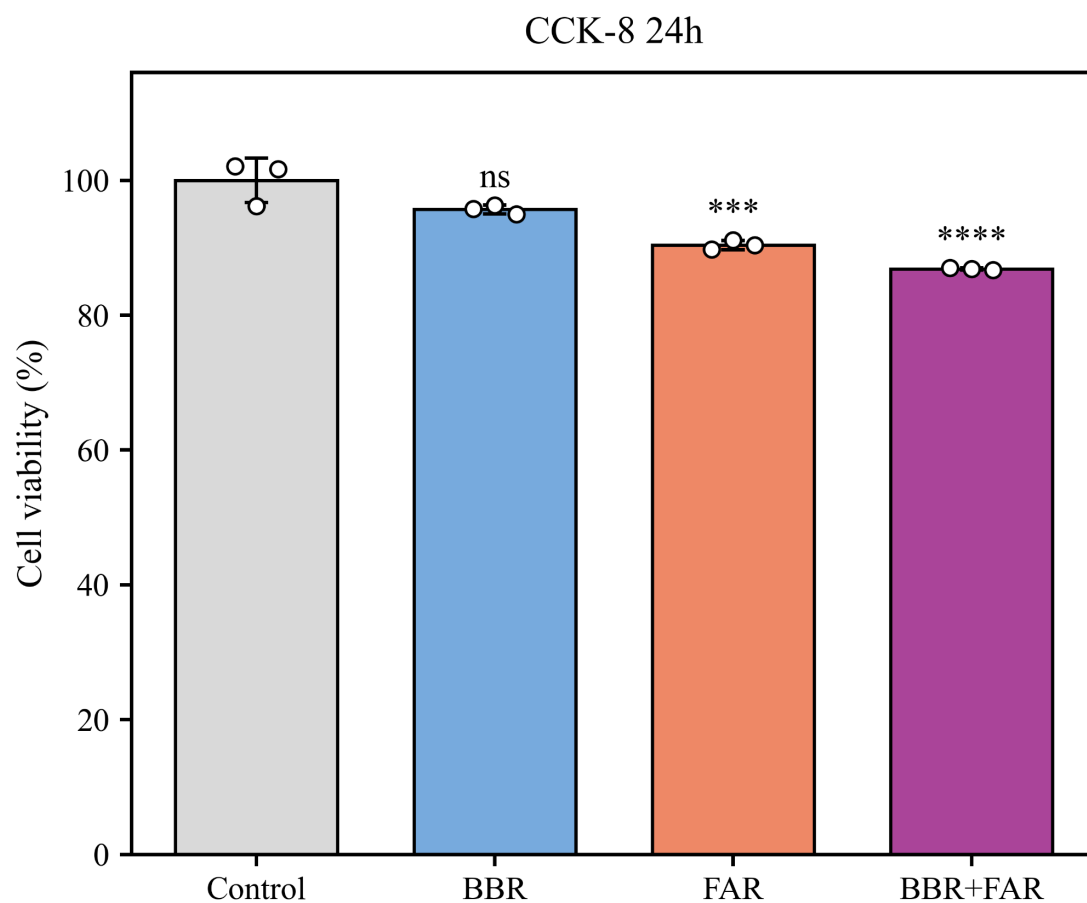
BBR VS Control



Supplementary Figure S5. Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway classification of DEGs in the FAR+BBR vs. Control, FAR vs. Control, and BBR vs. Control comparisons. The analysis summarizes the distribution of DEGs across major functional pathway classes, including metabolism, genetic information processing, environmental information processing, and cellular processes.



Supplementary Figure S6. Gene set enrichment analysis (GSEA) plots for selected pathways in the FAR+BBR vs. BBR (a), FAR+BBR vs. FAR (b), and FAR+BBR vs. Control (c) comparisons. Each plot shows the running enrichment score, the positions of pathway genes in the ranked list, and the ranked-list metric.



Supplementary Figure S7. Cell viability of HEK293 cells treated with berberine (BBR), farnesol (FAR), or their combination for 24 h, assessed by CCK-8 assay. Data are presented as mean $\pm$ SD. Statistical significance was determined using one-way ANOVA followed by Tukey's multiple comparisons test. ns, not significant; $p < 0.05$; $p < 0.01$; $p < 0.001$; $p < 0.0001$.

Supplementary Table S1. Primer sequences used for qPCR and RT-qPCR analyses.

Gene	Primer sequence (5'-3')	Length (bp)	Product size (bp)	Function
CEK2-F	CTACTGGCCCCACTCAAAC	20	91	MAPK-family kinase related to signal transduction.
CEK2-R	ATGCCATAAGCACCTCTCC	20		
MKC1-F	GGCTGATGTGTTCATCGTG	20	122	MAPK involved in cell wall integrity and stress response.
MKC1-R	CAGCATTTCGTCGGGGTTC	20		
CEK1-F	TGGCAGAAATGTTGAGTGGT	20	245	MAPK involved in signaling related to morphogenesis and biofilm regulation.
CEK1-R	AATATTTGCTACCGCCAGT	21		
HOG1-F	CGACTTGTTGCTGTGGGTT	20	243	MAPK involved in osmotic and environmental stress responses.
HOG1-R	ATAGCCTCCGGTTCAACGTG	20		
CDR1-F	CCATGACTCCTGCTACCGTG	20	92	ABC transporter involved in drug efflux and multidrug resistance.
CDR1-R	CCATCGAGACCAACCAACA	20		
CDR2-F	TGCTGAACCGACAGACTCAG	20	188	ABC transporter involved in drug efflux and multidrug resistance.
CDR2-R	GACCAGCCAATACCCACAA	20		
NAD5-F	TCATGGGTGCAGGTTCACTT	20	150	Complex I subunit involved in mitochondrial electron transport.
NAD5-R	AACCAGTAAGGCCAGGGATG	20		
NAD2-F	ATCACCTTGCGTCGAATGTT	20	209	Complex I subunit involved in NADH-linked respiration.
NAD2-R	ATTGGTGCGTTACCTGGAGT	20		
ATP6-F	TGGAGGTCATTCTTCCCTCT	21	187	ATP synthase subunit involved in ATP production.
ATP6-R	GGCAAAGAAACCTCATCCAT	20		
COX2-F	GAGCCTGGTGCTTTACGTCT	20	232	Complex IV subunit involved in terminal electron transfer.
COX2-R	TACCGTGGTTAACCCACAT	20		
ACT1-F	TCTGTCGGCAGTGGTTTCAA	20	120	Cytoskeletal actin used as an internal control.
ACT1-R	GCCTTGACAAGTACACGTAG	21		

Abbreviations: FAR, farnesol; BBR, berberine; DEG, differentially expressed gene; GO, Gene Ontology; KEGG, Kyoto Encyclopedia of Genes and Genomes; CV, crystal violet.