

Prediction of the Mechanism of Epimedin C Promoting Tunneling Nanotubes Production Based on Network Pharmacology

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Supplementary Materials

Table S1 PPI network for intersection targets of Epimedin C and TNTs.

Color	Number of targets	Name of proteins
Red	5	ACHE,ALB,ANXA5,CDK2,LCN2
Green	4	EGFR,IGF1,MMP2,SRC
Blue	2	BMP2,BMP7

Table S2 GO functional analysis of intersection targets (BP).

Term	FDR	PValue	Count	Genes
Positive regulation of transcription, DNA-templated	0.00713023	1.58E-05	6	BMP2, SRC, CDK2, IGF1, BMP7, EGFR
Negative regulation of apoptotic process	0.024702406	1.09E-04	5	SRC, ANXA5, ALB, IGF1, EGFR
Positive regulation of ERK1 and ERK2 cascade	0.026199537	1.84E-04	4	BMP2, SRC, IGF1, EGFR
Positive regulation of cell migration	0.026199537	2.85E-04	4	BMP2, MMP2, IGF1, EGFR
Epithelial to mesenchymal transition	0.026199537	3.23E-04	3	BMP2, IGF1, BMP7
Positive regulation of vascular smooth muscle cell proliferation	0.026199537	3.48E-04	3	SRC, MMP2, IGF1
Positive regulation of apoptotic process	0.036429211	5.64E-04	4	BMP2, SRC, MMP2, BMP7
Positive regulation of osteoblast differentiation	0.037494949	6.64E-04	3	BMP2, IGF1, BMP7
Skeletal system development	0.102261155	0.002042202	3	BMP2, IGF1, BMP7
Positive regulation of cell proliferation	0.102261155	0.002262415	4	BMP2, CDK2, IGF1, EGFR



Table S3 GO functional analysis of intersection targets (CC)

Term	FDR	ρ Value	Count	Genes
Extracellular space	6.03E-04	7.01E-06	8	ACHE, BMP2, MMP2, ALB, LCN2, IGF1, BMP7, EGFR
Extracellular region	6.17E-04	1.43E-05	8	ACHE, BMP2, MMP2, ANXA5, ALB, LCN2, IGF1, BMP7
Focal adhesion	0.507983005	0.017720337	3	SRC, ANXA5, EGFR
Platelet alpha granule lumen	0.605510547	0.032437564	2	ALB, IGF1
Cell surface	0.605510547	0.038470638	3	ACHE, BMP2, EGFR
Ruffle membrane	0.605510547	0.047835369	2	SRC, EGFR
Perinuclear region of cytoplasm	0.605510547	0.049285742	3	ACHE, SRC, EGFR
Extracellular exosome	0.917846956	0.085381112	4	SRC, ANXA5, ALB, LCN2

Table S4 GO functional analysis of intersection targets (MF).

Term	FDR	ρ Value	Count	Genes
BMP receptor binding	0.002327277	2.61E-05	3	BMP2, SRC, BMP7
Enterobactin binding	0.046890226	0.001053713	2	ALB, LCN2
Growth factor activity	0.098122257	0.003307492	3	BMP2, IGF1, BMP7
Insulin receptor binding	0.258217369	0.012057522	2	SRC, IGF1
Protein kinase activity	0.258217369	0.016507615	3	SRC, CDK2, EGFR
Protein binding	0.258217369	0.017407913	11	ACHE, BMP2, SRC, MMP2, ANXA5, ALB, CDK2, LCN2, IGF1, BMP7, EGFR
Protein serine/threonine/tyrosine Kinase activity	0.277160748	0.02179916	3	SRC, CDK2, EGFR
ATPase binding	0.494145071	0.044417535	2	SRC, EGFR
Kinase binding	0.520570173	0.054489192	2	SRC, EGFR
Protein tyrosine kinase activity	0.520570173	0.058491031	2	SRC, EGFR

Table S5 KEGG pathway enrichment analysis.

Term	FDR	<i>p</i> Value	Count	Genes
Relaxin signaling pathway	0.0803216	0.0075256 28	3	SRC, MMP2, EGFR
FoxO signaling pathway	0.0803216	0.0077532 59	3	CDK2, IGF1, EGFR
Estrogen signaling pathway	0.0803216	0.0084549 05	3	SRC, MMP2, EGFR
Prostate cancer	0.058611684	0.0043187 56	3	CDK2, IGF1, EGFR
GnRH signaling pathway	0.058611684	0.0039767 91	3	SRC, MMP2, EGFR
EGFR tyrosine kinase inhibitor resistance	0.054833845	0.0028859 92	3	SRC, IGF1, EGFR
Pathways in cancer	0.033706662	0.0014192 28	5	BMP2, MMP2, CDK2, IGF1, EGFR
Proteoglycans in cancer	0.032082292	0.0010131 25	4	SRC, MMP2, IGF1, EGFR
Bladder cancer	0.032082292	7.84E-04	3	SRC, MMP2, EGFR
Endocrine resistance	0.010948509	1.15E-04	4	SRC, MMP2, IGF1, EGFR