

Supplementary Data

Talbe S1

Validation results of each dataset and ranking information of drugs to be tested

Dataset	Cell Lines	Drugs	Actual Effect	Predictive Accuracy	Relative Ranking	Relative Ranking(%)
GSE129221	PC9	Gefitinib	Resistance	Yes	41/118	34.75
GSE129221	PC9	Apatinib	Sensitive	No	Haven't Seen	NA
GSE200029	T47D	Tamoxifen	Resistance	Yes	6/142	4.23
GSE200029	T47D	Erdatinib	Sensitive	Yes	41/142	28.87
GSE268699	MCF7	Palbociclib	Resistance	Yes	47/56	83.93
GSE268699	MCF7	Fulvestrant	Resistance	Yes	2/162	1.23
GSE268699	T47D	Palbociclib	Resistance	No	42/71	59.15
GSE268699	T47D	Fulvestrant	Resistance	No	Haven't Seen	NA
GSE62504	HCC827-BR1	Afatinib	Resistance	Yes	4/130	3.08
GSE62504	HCC827-BR1	Dasatinib	Sensitive	Yes	4/130	3.08
GSE62504	HCC827-BR2	Afatinib	Resistance	Yes	6/130	4.62
GSE62504	HCC827-BR2	Dasatinib	Sensitive	No	59/130	45.38

Table S2

List of predictive drugs that are effective in the CDK4/6 inhibitor dataset after drug target mapping

MCF7_GSE222367	T47D_GSE222367	PDX_GSE229235	MCF7_Lab
DASATINIB	DASATINIB	DASATINIB	TOZASERTIB
CEDIRANIB	ISOLIQURITIGENIN	TAMOXIFEN	NILOTINIB
TOZASERTIB	SUNITINIB	VANDETANIB	CERITINIB
VANDETANIB	SORAFENIB	ENTRECTINIB	PONATINIB
DUVELISIB	DIETHYLSTILBESTROL	CEDIRANIB	GEFITINIB
NILOTINIB	IMATINIB	ERLOTINIB	ERLOTINIB
CERITINIB	MITOXANTRONE	PONATINIB	SORAFENIB
BOSUTINIB	PAZOPANIB	PAZOPANIB	CABOZANTINIB
IBRUTINIB	NILOTINIB	SORAFENIB	OSIMERTINIB
TIRBANIBULIN	CELECOXIB	PALBOCICLIB	AFATINIB
PAZOPANIB	DAUNORUBICIN	BOSUTINIB	CRIZOTINIB
SUNITINIB	DOXORUBICIN	TOZASERTIB	LAPATINIB
SORAFENIB	SELINEXOR	NILOTINIB	NERATINIB
DIETHYLSTILBESTROL	ETHINYL ESTRADIOL	IDELALISIB	MIDOSTAURIN
ISOLIQURITIGENIN	PACLITAXEL	ABEMACICLIB	VENETOCLAX
MITOXANTRONE	MASOPROCOL	GEFITINIB	QUIZARTINIB
PACLITAXEL	QUIZARTINIB	ISOLIQURITIGENIN	DIETHYLSTILBESTROL
IMATINIB	BOSUTINIB	CABOZANTINIB	PAZOPANIB
ALECTINIB	PONATINIB	QUIZARTINIB	ERDAFITINIB
ETHINYL ESTRADIOL	EPIRUBICIN	DINACICLIB	TOFACITINIB
BELINOSTAT	BELINOSTAT	ALVOCIDIB	NINTEDANIB
DOXORUBICIN	BEXAROTENE	OSIMERTINIB	LORLATINIB
QUIZARTINIB	AMSACRINE	PACLITAXEL	MEDROXYPROGESTERONE ACETATE
PHENTOLAMINE	SIROLIMUS	FULVESTRANT	INFIGRATINIB
CRIZOTINIB	IDELALISIB	TOFACITINIB	FUTIBATINIB
INDIRUBIN	VINBLASTINE	AFATINIB	AMSACRINE
VINBLASTINE	VINCRIStINE	RALOXIFENE HYDROCHLORIDE	DAUNORUBICIN
VINBLASTINE SULFATE	CERITINIB	RIBOCICLIB	MASOPROCOL
DOCETAXEL	REGORAFENIB	RUXOLITINIB	RUXOLITINIB
VINCRIStINE	PEXIDARTINIB	FILGOTINIB	UPADACITINIB
VINORELBINE	TRETINOIN	ALPELISIB	BARICITINIB
EMBELIN	VINBLASTINE SULFATE	MITOXANTRONE	FILGOTINIB
DINACICLIB	DOCETAXEL	DOXORUBICIN	PLERIXAFOR
LORLATINIB	VINORELBINE	DUVELISIB	ENZALUTAMIDE
	TIRBANIBULIN	LAPATINIB	SIROLIMUS
	TRANLYCYPROMINE HYDROCHLORIDE	CISPLATIN	LEFLUNOMIDE
	CROCIN	CERITINIB	THIOTEPA
	IDARUBICIN	BORTEZOMIB	DINACICLIB
	ALITRETINOIN	BELINOSTAT	PHENTOLAMINE
	THIOGUANINE	BARICITINIB	PEXIDARTINIB
	AMINOGLUTETHIMIDE	ALECTINIB	FLUTAMIDE
	EVEROLIMUS	IBRUTINIB	CHLOROPYRAMINE

SORAFENIB TOSYLATE	ACALABRUTINIB	IDARUBICIN
AMRUBICIN	NERATINIB	BEXAROTENE
MELPHALAN	INDIRUBIN	GILTERITINIB
ENASIDENIB	ADAGRASIB	ALVOCIDIB
PHENTOLAMINE	ASCIMINIB	APALUTAMIDE
CAMPTOTHECIN	ROCILETINIB	CAMPTOTHECIN
	DACOMITINIB	VEMURAFENIB
	AFATINIB DIMALEATE	
	CRIZOTINIB	
	ULIPRISTAL ACETATE	
	SELINEXOR	
	IXAZOMIB	
	VENETOCLAX	
	AXITINIB	
	DABRAFENIB	
	COPANLISIB	
	TRILACICLIB	
	LORLATINIB	
	INFIGRATINIB	
	UPADACITINIB	
	BICALUTAMIDE	
	CARFILZOMIB	
	MASOPROCOL	
	ENZALUTAMIDE	
	NILUTAMIDE	
	ZANUBRUTINIB	
	CELECOXIB	
	APALUTAMIDE	
	ENASIDENIB	
	VINBLASTINE	
	VINCRIStINE	
	ENTINOSTAT	
	GILTERITINIB	
	METHOTREXATE	
	VORINOSTAT	
	PLERIXAFOR	
	VINBLASTINE SULFATE	
	DOCETAXEL	
	VINORELBINE	
	TIRBANIBULIN	
	SIROLIMUS	
	PHENTOLAMINE	
	PANOBINOSTAT	
	EMBELIN	
	FLUPIRTINE MALEATE	
	THIOGUANINE	
	MELPHALAN	
	MYCOPHENOLIC ACID	
	AMSACRINE	

THIOTEPA
PEMETREXED

Table S3

Details of Sorafenib Matching Results

Gene	Target Importance	Standard Value(nM)	Log ₂ FC	Effective Type
BLK	2.37	794.33	-6.15	Suppress
EPHA2	7.32	794.33	-3.56	Suppress
LYN	13.20	398.11	-4.80	Suppress
FGFR3	7.50	1258.93	1.20	Suppress
FLT3	5.41	2	2.75	Suppress
MAOA	4.63	8258.3	-5.21	Suppress
KIT	19.18	11	-1.62	Suppress

Table S4

Summary of the binding energy and hydrogen bond details regarding the stable binding mode of Sorafenib with the two targets

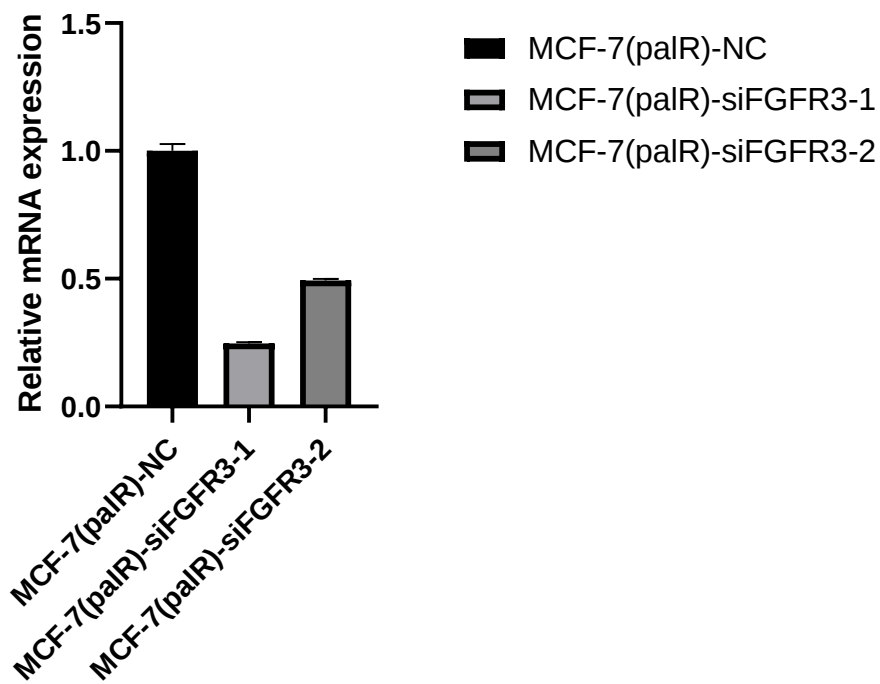
Mode Number	Target Name	Binding Energy (kcal/mol)	Amino Acid Residue	H-bonding Distance
1	FGFR3	-8.646	Arginine-570	2 Å 4.3 Å
			Lysine-560	3 Å 3.4 Å
12	FLT3	-8.383	Cysteine-694	2.1 Å 2.6 Å
			Phenylalanine-830	2.7 Å

Table S5

Primer and siRNA sequences.

Primers	Sequences
GAPDH-homo(Sequences-F)	GGAGCGAGATCCCTCCAAAAT
GAPDH-homo(Sequences-R)	GGCTGTTGTCATACTTCTCATGG
FGFR3-homo(Sequences-F)	AGGATGCCTGCATACACACTGC
FGFR3-homo(Sequences-R)	ACACCCTACGTTACCGTGCTCAAG
FLT3-homo(Sequences-F)	AGTCAGAAGGGACTGGCTCC
FLT3-homo(Sequences-R)	GAGTGCTGCTTAGCAGATTACC
Sequences for siRNAs	
si-FGFR3#1(Sequences-F)	CCACCGACAAGGAGCUAGATT
si-FGFR3#1(Sequences-R)	UCUAGCUCCUUGUCGGUGGTT
si-FGFR3#2(Sequences-F)	CGCGUACUGUGCCACUUCATT
si-FGFR3#2(Sequences-R)	UGAAGUGGCACAGUACGCGTT

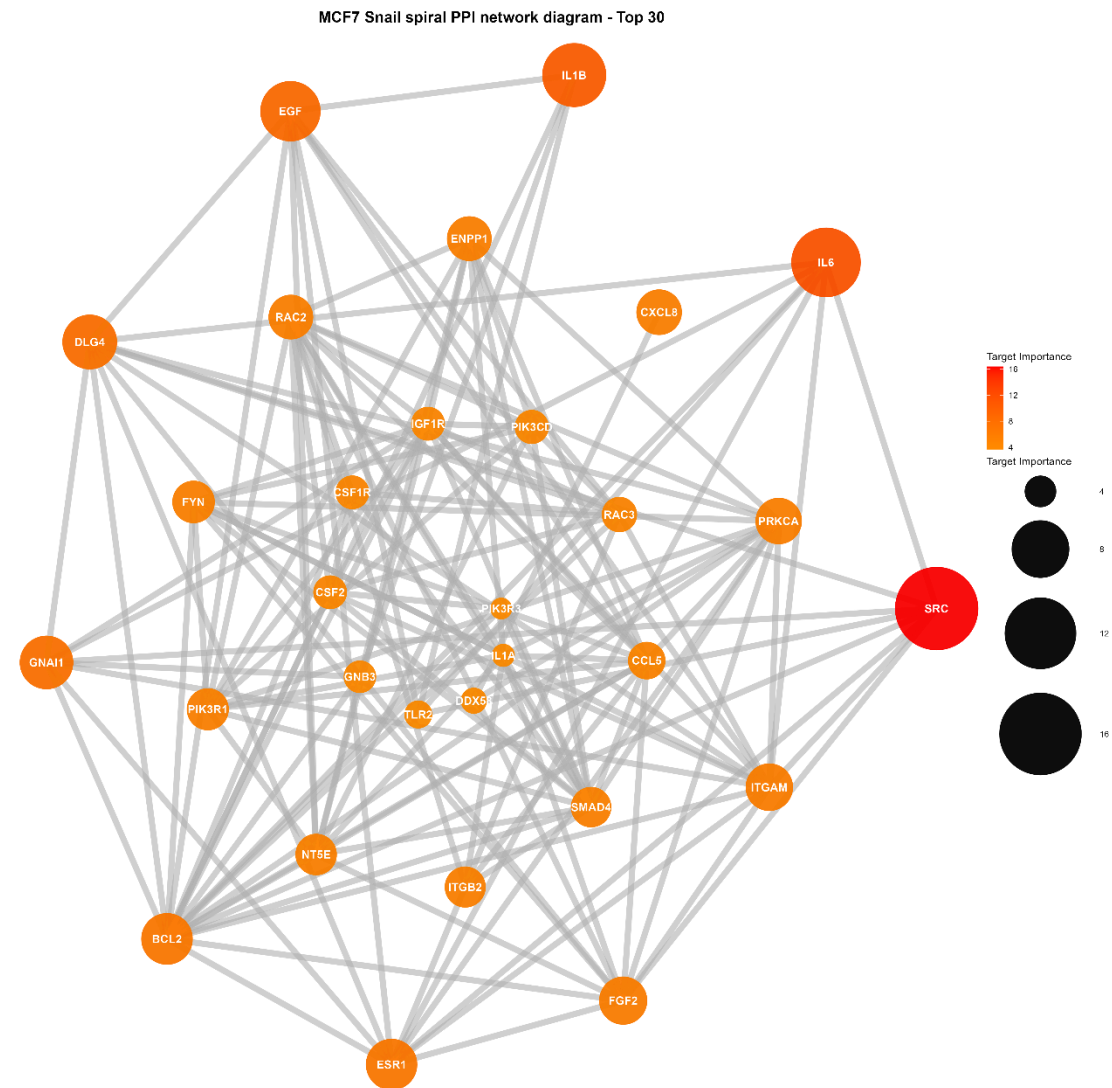
MCF7palR siFGFR3 qPCR.



FGFR3 knockdown efficiency in MCF-7(palR) cells.

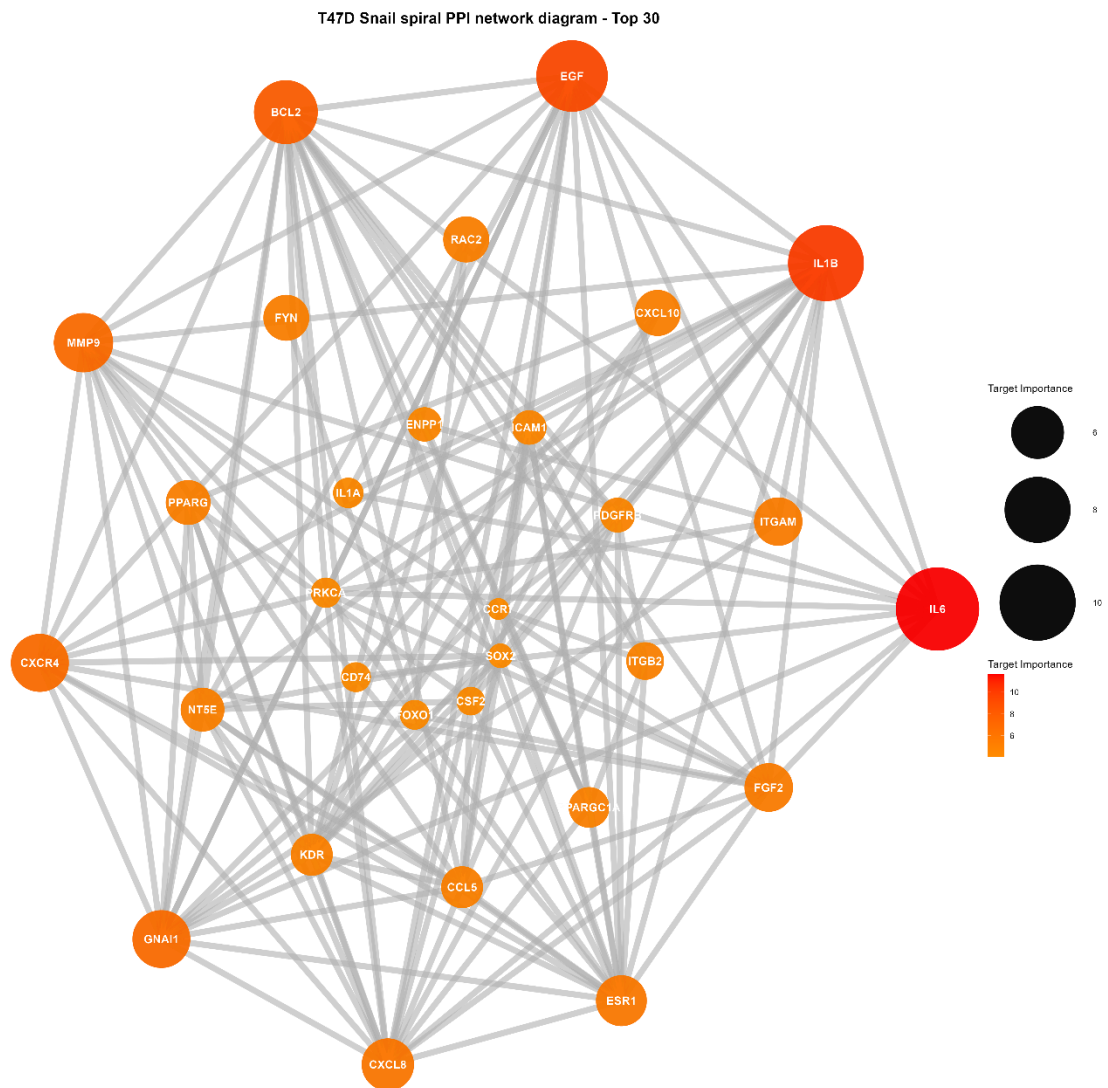
Quantitative PCR analysis of FGFR3 mRNA expression following siRNA-mediated knockdown in MCF-7(palR) cells. Compared to negative control (NC), siFGFR3-1 reduced FGFR3 expression by approximately 75%, while siFGFR3-2 achieved ~51% knockdown. Data are presented as mean $\pm$ SEM (n = 3). GAPDH was used as the internal reference for normalization.

Supplementary figure S2. **Snail spiral PPI network diagram of MCF7 cell line(GSE222367).**



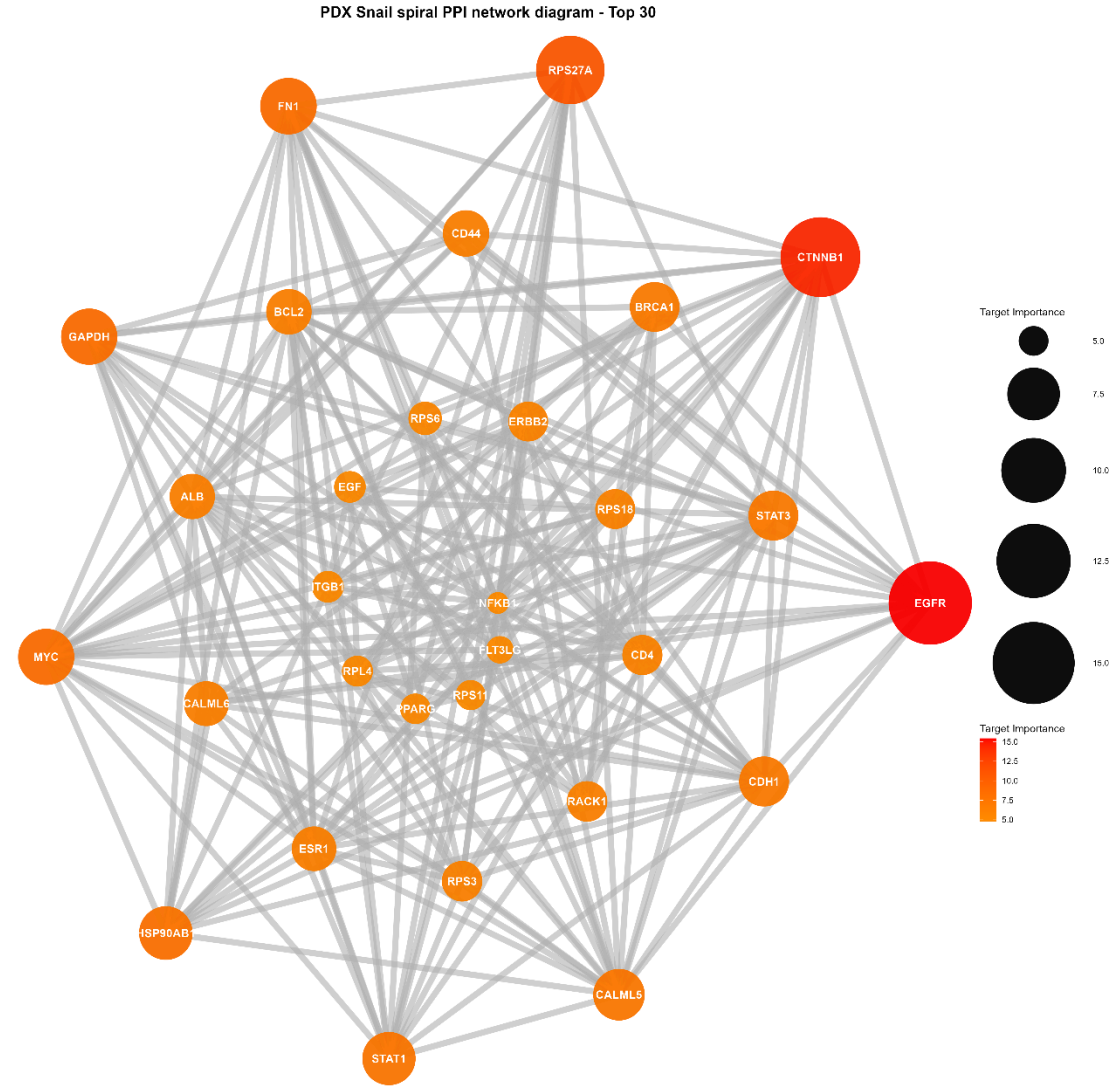
This figure illustrates the top 30 high-importance protein targets in the MCF7 cell line based on network topology-weighted scoring. Each node represents a protein, with node size proportional to its importance score derived from integrated topological features. The layout follows a snail spiral path from outermost (most important) to innermost targets. Edges indicate high-confidence protein-protein interactions (PPIs), and the network is constructed from curated interaction databases.

Supplementary figure S3. **Snail spiral PPI network diagram of T47D cell line(GSE222367).**



Displayed here are the top 30 protein targets prioritized by importance score in the T47D breast cancer cell line. The spiral layout arranges targets from most to least important in an outward-to-inward manner. The size of each node encodes the computed importance value, while connections denote high-confidence PPIs among the selected proteins. This visualization highlights critical nodes potentially involved in CDK4/6 resistance mechanisms.

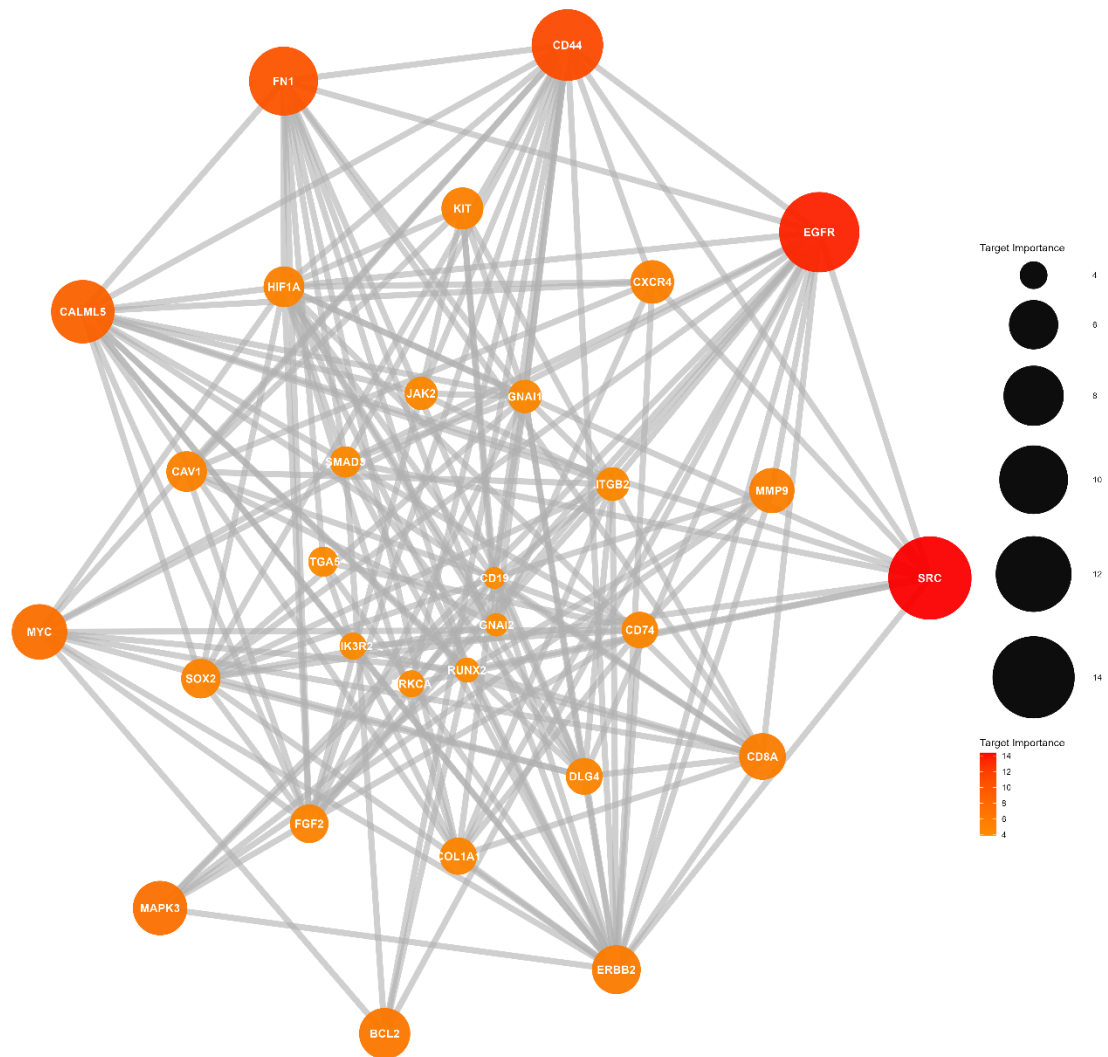
Supplementary figure S4. **Snail spiral PPI network diagram of PDX model(GSE229235).**



The diagram presents the top 30 key protein targets identified in a patient-derived xenograft (PDX) model. Importance scores were calculated based on topological shift metrics and weighted integration. The spiral layout reflects descending target importance, emphasizing the network context of these proteins through known interactions. This visualization supports translational insights into drug targeting in clinically relevant models.

Supplementary figure S5. **Snail spiral PPI network diagram of MCF7 (our lab).**

MCF7 (our lab) Snail spiral PPI network diagram - Top 30



This network highlights the top 30 prioritized protein targets identified in the MCF7 cell line using data generated in our laboratory. Node size correlates with the computed importance score derived from custom-integrated topological parameters. The spiral layout emphasizes the relative ranking of targets, and edge connections represent experimentally supported protein-protein interactions. This network captures target prioritization from our customized computational pipeline.