Table SI. Antibodies used for immunohistochemistry staining, immunofluorescence staining and western blotting.

Antibody	Cat. no.	Manufacturer	Host	Description	Specificity	Molecular weight, kDa	Dilution
EGF	AF5148	Affinity Biosciences	Rabbit	Polyclonal	Human, mouse, rat	134	1:1,000
p-EGFR	AP3048	Affinity Biosciences	Rabbit	Polyclonal to p-EGFR (Tyr1173; Tyr1197)	Human, mouse, rat	175	1:500
EGFR	18986-1-AP	Proteintech Group, Inc.	Rabbit	Polyclonal	Human, mouse, rat	100	1:2,000
HDAC1	10197-1-AP	Proteintech Group, Inc.	Rabbit	Polyclonal	Human, mouse, rat	65	1:5,000
Wnt5	55184-1-AP	Proteintech Group, Inc.	Rabbit	Wnt5A/B polyclonal	Human, mouse, rat	55	1:2,000
β-catenin	51067-2-AP	Proteintech Group, Inc.	Rabbit	Polyclonal	Human, mouse, rat	100	1:20,000
VEGFA	66828-1-Ig	Proteintech Group, Inc.	Mouse	Monoclonal	Human, goat, rat	50	1:2,000
Osterix	AF7080	Affinity Biosciences	Rabbit	Polyclonal antibody to p-osterix (Thr319)	Human, mouse, rat	72	1:1,000
RANKL	23408-1-AP	Proteintech Group, Inc.	Rabbit	Polyclonal	Human, mouse, rat	35	1:2,000
OPG	A2100	Abclonal	Rabbit	TNFRSF11B polyclonal (A2100)	Human, mouse, rat	48	1:1,000
PPARG	16643-1-AP	Proteintech Group, Inc.	Rabbit	Polyclonal	Human, mouse, rat	55	1:2,000
RUNX2	20700-1-AP	Proteintech Group, Inc.	Rabbit	Polyclonal	Human, mouse, rat	50	1:400
β-actin	4970S	Cell Signaling Technology, Inc.	Rabbit	β-actin (13E5) monoclonal	Human, mouse, rat	43	1:1,000

p-, phosphorylated; HDAC1, histone deacetylase 1; VEGFA, vascular endothelial growth factor A; RANKL, receptor activator of nuclear factor κB ligand; OPG, osteoprotegerin; TNFRSF11B, tumor necrosis factor receptor superfamily member 11B.

Table SII. Topological features and the shortest path of 31 hub genes.

Category	Gene	Betweenness	Closeness	Degree	Shortest path
Osteoking	ACTB	0.04758777	0.40276498	62	3
Osteoking	AKT1	0.05880362	0.41559677	83	1
Osteoking	ALB	0.04667600	0.38672566	57	2
Osteoking	APP	0.03154047	0.36462244	36	2
Osteoking	BCL2	0.01734211	0.39000446	57	2
Osteoking	CASP3	0.02330316	0.39000446	53	2
Osteoking	CTNNB1	0.03972399	0.40879326	70	1
Osteoking	EGFR	0.07294506	0.42222222	91	1
Osteoking	EP300	0.02515720	0.39087657	66	1
Osteoking	ESR1	0.02657032	0.39529625	55	1
Osteoking	HDAC1	0.01392030	0.36815501	50	1
Osteoking	HIF1A	0.02106911	0.38149280	50	1
Osteoking	HSP90AA1	0.04554722	0.39727273	67	1
Osteoking	HSP90AB1	0.01996381	0.38485249	57	1
Osteoking	IL6	0.03492997	0.39981702	81	1
Osteoking	INS	0.07608408	0.40332257	70	1
Osteoking	MMP9	0.01649008	0.37704918	46	1
Osteoking	NFKB1	0.01320533	0.39052726	58	1
Osteoking	PPARA	0.02769421	0.37318531	36	1
Osteoking	PPARG	0.02732179	0.37868284	48	1

Osteoking	PRKACA	0.08201840	0.38519171	60	2
Osteoking	PTGS2	0.02867325	0.36661074	45	1
Osteoking	SRC	0.03423883	0.40073361	67	1
Osteoking	TLR4	0.02216274	0.38182612	57	2
Osteoking	TNF	0.02616954	0.39601269	75	2
Fracture	CCL2	0.00759514	0.36784512	40	3
Fracture	CXCL8	0.02035887	0.37286689	45	1
Fracture	FOS	0.01385213	0.38066202	43	1
Fracture	IL1B	0.03902061	0.40295067	69	1
Fracture	MYC	0.02743597	0.39745339	71	1
Fracture	STAT1	0.05608088	0.38400703	88	1

Table SIII. Pathway enrichment analysis results of 23 key network targets.

Term	Count	%	P-value	Genes
Lipid and atherosclerosis	12	56.52174	$2.32x10^{-14}$	HSP90AA1, CXCL8, HSP90AB1, SRC, FOS, TNF, MMP9, NFKB1, IL6, IL1B, AKT1, PPARG
IL-17 signaling pathway	10	43.47826	6.77x10^-13	IL6, HSP90AA1, CXCL8, HSP90AB1, IL1B, FOS, PTGS2, TNF, MMP9, NFKB1
Toll-like receptor signaling pathway	9	39.13043	1.33x10^-10	IL6, CXCL8, STAT1, IL1B, AKT1, FOS, TNF, TLR4, NFKB1
Fluid shear stress and atherosclerosis	9	39.13043	$1.02x10^{-9}$	HSP90AA1, HSP90AB1, SRC, IL1B, AKT1, FOS, TNF, MMP9, NFKB1
Wnt signaling pathway	13	43.47826	$1.08x10^{-9}$	HSP90AA1, HSP90AB1, SRC, MYC, AKT1, FOS, PPARA, ESR1, EGFR, NFKB1
C-type lectin receptor signaling pathway	8	34.78261	$4.58x10^{-9}$	IL6, STAT1, SRC, IL1B, AKT1, PTGS2, TNF, NFKB1
Th17 cell differentiation	8	34.78261	$5.98x10^{-9}$	IL6, HSP90AA1, HSP90AB1, STAT1, IL1B, FOS, HIF1A, NFKB1
HIF-1 signaling pathway	8	34.78261	$6.38x10^{-9}$	IL6, EP300, AKT1, HIF1A, TLR4, EGFR, NFKB1, INS
TNF signaling pathway	8	34.78261	$8.74x10^{-9}$	IL6, IL1B, AKT1, FOS, PTGS2, TNF, MMP9, NFKB1
NOD-like receptor signaling pathway	9	39.13043	$1.03x10^{-8}$	IL6, HSP90AA1, CXCL8, HSP90AB1, STAT1, IL1B, TNF, TLR4, NFKB1
Thyroid hormone signaling pathway	8	34.78261	$1.33x10^{-8}$	STAT1, HDAC1, SRC, MYC, EP300, AKT1, HIF1A, ESR1
Prolactin signaling pathway	7	30.43478	$1.59x10^{-8}$	STAT1, SRC, AKT1, FOS, ESR1, NFKB1, INS
Estrogen signaling pathway	8	34.78261	$3.15x10^{-8}$	HSP90AA1, HSP90AB1, SRC, AKT1, FOS, ESR1, MMP9, EGFR
Osteoclast differentiation	7	30.43478	8.2x10^-7	STAT1, IL1B, AKT1, PPARG, FOS, TNF, NFKB1
PI3K-Akt signaling pathway	9	39.13043	$1.65x10^{-6}$	IL6, HSP90AA1, HSP90AB1, MYC, AKT1, TLR4, EGFR, NFKB1, INS
NF-kappa B signaling pathway	6	26.08696	$4.35x10^{-6}$	CXCL8, IL1B, PTGS2, TNF, TLR4, NFKB1
MAPK signaling pathway	8	34.78261	$5.29x10^{-6}$	IL1B, MYC, AKT1, FOS, TNF, EGFR, NFKB1, INS
Relaxin signaling pathway	6	26.08696	$6.58x10^{-6}$	SRC, AKT1, FOS, MMP9, EGFR, NFKB1

Necroptosis	6	26.08696	$1.52x10^{-5}$	HSP90AA1, HSP90AB1, STAT1, IL1B, TNF, TLR4
JAK-STAT signaling pathway	4	26.08696	$4.17x10^{-5}$	AKT1, INS, NFKB1, PPARG
Adipocytokine signaling pathway	4	17.39130	$5.13x10^{-5}$	AKT1, PPARA, TNF, NFKB1
EGFR tyrosine kinase inhibitor resistance	4	17.39130	$6.86x10^{-4}$	IL6, SRC, AKT1, EGFR
ErbB signaling pathway	4	17.39130	$1.018x10^{-3}$	SRC, MYC, AKT1, EGFR
Notch signaling pathway	4	21.73913	$1.259x10^{-3}$	HDAC1, SRC, AKT1, NFKB1
TGF-beta signaling pathway	4	17.39130	$1.268x10^{-3}$	HDAC1, MYC, EP300, TNF
Regulation of lipolysis in adipocytes	3	13.04348	$2.505x10^{-3}$	AKT1, PTGS2, INS
mTOR signaling pathway	7	6.603774	$9.586x10^{-3}$	PIK3CA, PIK3CD, AKT1, IGF1, PIK3CB, TNF, INS
VEGF signaling pathway	3	13.04348	$9.817x10^{-3}$	SRC, AKT1, PTGS2
PPAR signaling pathway	5	4.716981	$1.12x10^{-2}$	CPT1A, ACOX1, LPL, PPARG, PPARA
Cytosolic DNA-sensing pathway	3	13.04348	$1.553x10^{-2}$	IL6, IL1B, NFKB1
Adherens junction	3	13.04348	$2.329x10^{-2}$	SRC, EP300, EGFR
AMPK signaling pathway	3	13.04348	$3.787x10^{-2}$	AKT1, PPARG, INS