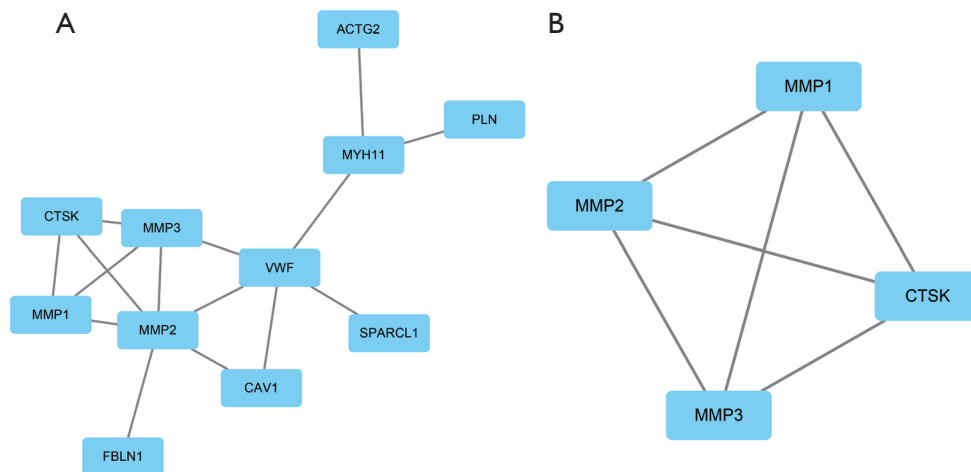


**Figure S1** GO/KEGG pathway enrichment analysis of down-regulated DEGs. (A) Biological process. (B) Cellular component. (C) Molecular function. (D) KEGG pathway enrichment analysis. BP, biological process; CC, cellular component; MF, molecular function; KEGG, Kyoto Encyclopedia of Genes and Genomes; GO, Gene Ontology; DEGs, differentially expressed genes.



**Figure S2** PPI network of down-regulated DEGs constructed via STRING and Cytoscape. (A) PPI network of downregulated DEGs. The blue nodes indicated downregulated genes; the edges represent proteins interaction. (B) Module 1. PPI, protein-protein interaction; DEGs, differentially expressed genes; STRING, Search Tool for the Retrieval of Interacting Genes.

**Table S1** Functional enrichment analysis in upregulated genes. (Top 10)

Category	term	Count	P Value	FDR
GOTERM_BP_DIRECT	cellular protein metabolic process	21	1.37E-26	8.24E-24
GOTERM_BP_DIRECT	post-translational protein modification	19	1.54E-16	2.31E-14
GOTERM_BP_DIRECT	platelet degranulation	16	2.49E-19	7.49E-17
GOTERM_BP_DIRECT	negative regulation of endopeptidase activity	13	1.97E-13	2.37E-11
GOTERM_BP_DIRECT	blood coagulation	12	8.05E-11	6.92E-09
GOTERM_BP_DIRECT	acute-phase response	11	1.30E-16	2.31E-14
GOTERM_BP_DIRECT	receptor-mediated endocytosis	10	6.30E-09	3.79E-07
GOTERM_BP_DIRECT	innate immune response	10	2.83E-04	0.004483
GOTERM_BP_DIRECT	retinoid metabolic process	8	2.84E-09	2.14E-07
GOTERM_BP_DIRECT	neutrophil degranulation	8	0.001623	0.0177
GOTERM_CC_DIRECT	extracellular region	50	8.68E-33	4.17E-31
GOTERM_CC_DIRECT	extracellular exosome	46	7.09E-27	1.70E-25
GOTERM_CC_DIRECT	extracellular space	44	3.60E-27	1.15E-25
GOTERM_CC_DIRECT	blood microparticle	27	7.91E-39	7.60E-37
GOTERM_CC_DIRECT	endoplasmic reticulum lumen	21	1.37E-20	2.64E-19
GOTERM_CC_DIRECT	cell surface	12	7.56E-06	5.19E-05
GOTERM_CC_DIRECT	platelet alpha granule lumen	11	2.37E-14	3.79E-13
GOTERM_CC_DIRECT	intracellular membrane-bounded organelle	10	0.003463	0.017499
GOTERM_CC_DIRECT	chylomicron	7	3.78E-12	5.18E-11
GOTERM_CC_DIRECT	very-low-density lipoprotein particle	7	6.70E-11	8.04E-10
GOTERM_MF_DIRECT	protein binding	56	0.01252	0.076564
GOTERM_MF_DIRECT	identical protein binding	20	7.95E-06	1.58E-04
GOTERM_MF_DIRECT	receptor binding	15	1.75E-10	1.21E-08
GOTERM_MF_DIRECT	serine-type endopeptidase inhibitor activity	10	1.36E-10	1.21E-08
GOTERM_MF_DIRECT	heparin binding	9	2.19E-07	8.72E-06
GOTERM_MF_DIRECT	endopeptidase inhibitor activity	8	2.28E-10	1.21E-08
GOTERM_MF_DIRECT	phospholipid binding	7	4.71E-06	1.07E-04
GOTERM_MF_DIRECT	heme binding	5	0.00232	0.033528
GOTERM_MF_DIRECT	lipid binding	5	0.004354	0.046696
GOTERM_MF_DIRECT	serine-type endopeptidase activity	5	0.005367	0.048378

**Table S2** Functional enrichment analysis in downregulated genes and KEGG pathway analysis of downregulated genes.

Category	Term	Count	PValue	FDR
GOTERM_MF_DIRECT	serine-type endopeptidase activity	4	0.001040782	0.036947749
GOTERM_MF_DIRECT	fibronectin binding	3	5.25E-04	0.036947749
GOTERM_MF_DIRECT	collagen binding	3	0.002287891	0.054146742
GOTERM_MF_DIRECT	endopeptidase activity	3	0.003736562	0.066323975
GOTERM_MF_DIRECT	metalloendopeptidase activity	3	0.006914653	0.098188076
GOTERM_MF_DIRECT	peptidase activator activity	2	0.011661676	0.1379965
GOTERM_CC_DIRECT	extracellular space	12	7.73E-07	6.34E-05
GOTERM_CC_DIRECT	extracellular region	12	2.16E-06	8.85E-05
GOTERM_CC_DIRECT	extracellular exosome	8	0.005551036	0.113796234
GOTERM_CC_DIRECT	extracellular matrix	6	5.47E-06	1.49E-04
GOTERM_CC_DIRECT	myosin filament	2	0.016539939	0.271255002
GOTERM_BP_DIRECT	extracellular matrix organization	6	4.20E-06	0.001399286
GOTERM_BP_DIRECT	collagen catabolic process	4	9.66E-06	0.001608987
GOTERM_BP_DIRECT	extracellular matrix disassembly	4	3.70E-05	0.004102275
GOTERM_BP_DIRECT	proteolysis	4	0.008631591	0.346430155
GOTERM_BP_DIRECT	cellular response to UV-A	3	5.00E-05	0.004160911
GOTERM_BP_DIRECT	muscle contraction	3	0.004961167	0.275344781
GOTERM_BP_DIRECT	cellular protein metabolic process	3	0.009362977	0.346430155
GOTERM_BP_DIRECT	leukocyte migration	3	0.015588099	0.403155842
GOTERM_BP_DIRECT	negative regulation of canonical Wnt signaling pathway	3	0.015738817	0.403155842
GOTERM_BP_DIRECT	positive regulation of cell migration	3	0.026085994	0.620473996
GOTERM_BP_DIRECT	cytokine-mediated signaling pathway	3	0.039404819	0.731117395
GOTERM_BP_DIRECT	mesenchyme migration	2	0.004900687	0.275344781
GOTERM_BP_DIRECT	intramembranous ossification	2	0.006854584	0.326082344
GOTERM_BP_DIRECT	positive regulation of peptidase activity	2	0.013664639	0.403155842
GOTERM_BP_DIRECT	response to beta-amyloid	2	0.014633885	0.403155842
GOTERM_BP_DIRECT	regulation of heart contraction	2	0.032879011	0.729914036
GOTERM_BP_DIRECT	embryo implantation	2	0.039519859	0.731117395
GOTERM_BP_DIRECT	regulation of cytosolic calcium ion concentration	2	0.039519859	0.731117395
GOTERM_BP_DIRECT	negative regulation of cell adhesion	2	0.048931885	0.857595677
KEGG_PATHWAY	Rheumatoid arthritis	3	0.006686261	0.334313028
KEGG_PATHWAY	Coronavirus disease - COVID-19	3	0.037788377	0.904089086

**Table S3** C5 expression in COAD patients based on individual cancer stages via UALCAN analysis

Comparison	Statistical significance
Normal-vs-Stage1	4.27E-02
Normal-vs-Stage2	7.74E-05
Normal-vs-Stage3	6.28E-07
Normal-vs-Stage4	4.42E-03
Stage1-vs-Stage2	2.33E-01
Stage1-vs-Stage3	8.38E-01
Stage1-vs-Stage4	6.43E-01
Stage2-vs-Stage3	1.09E-02
Stage2-vs-Stage4	2.00E-01
Stage3-vs-Stage4	6.18E-01