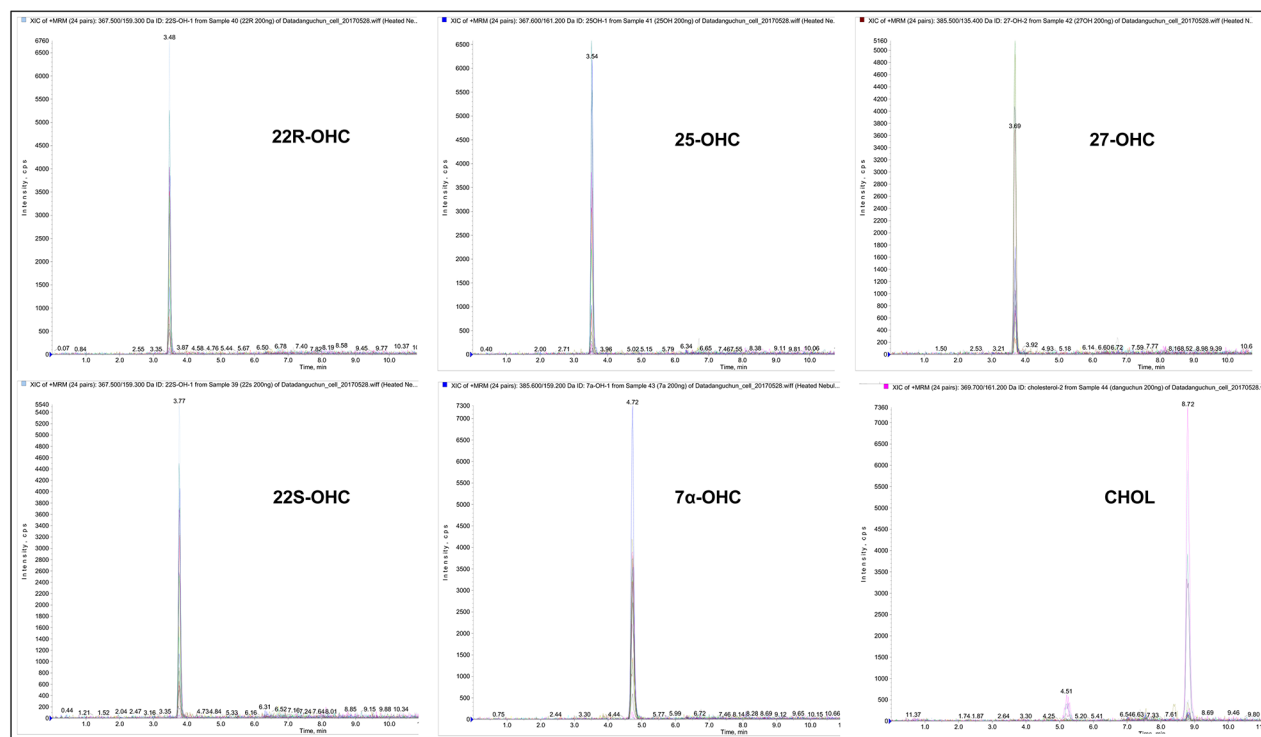
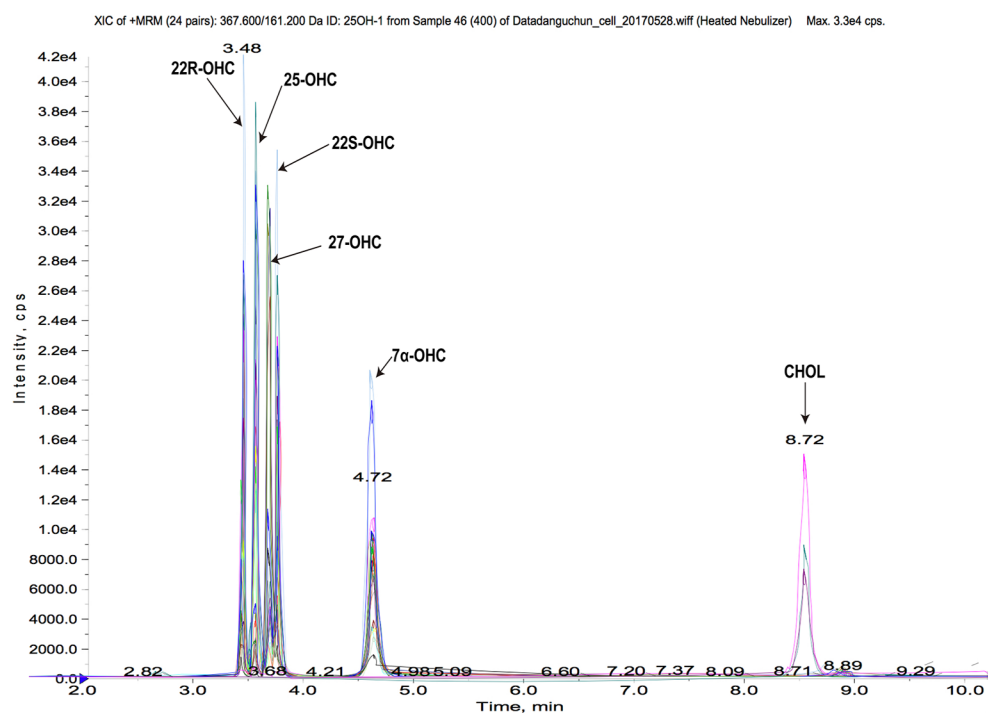
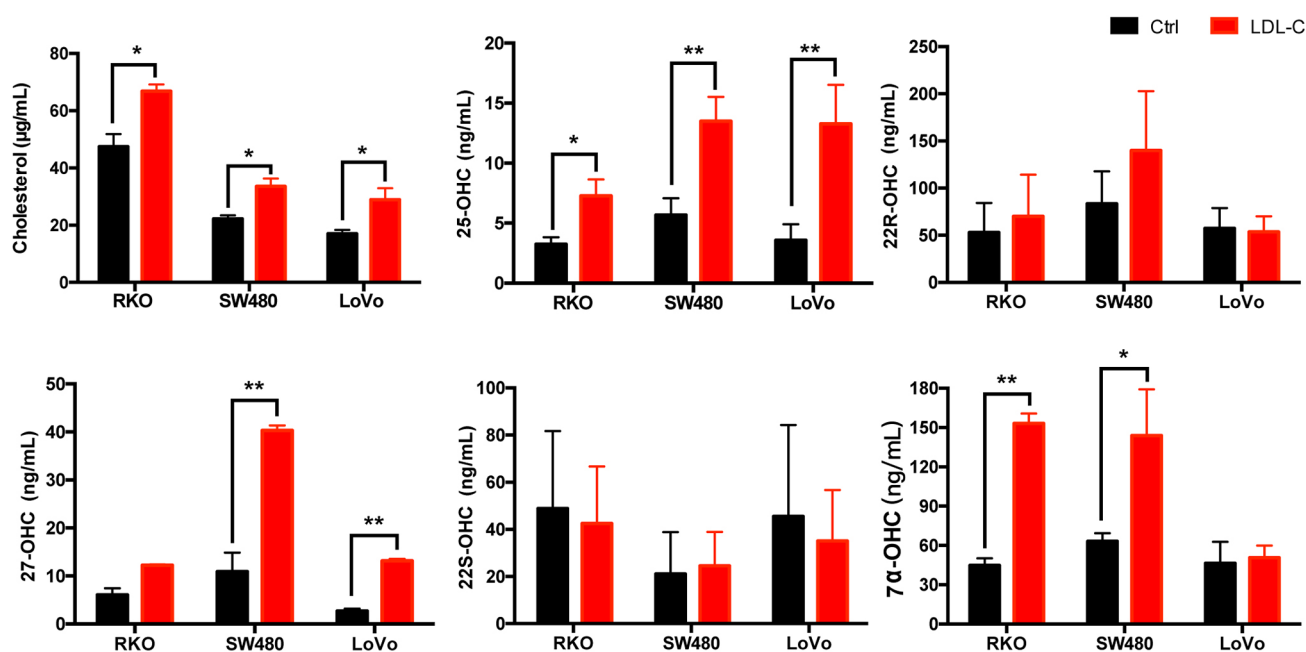


### Serum cholesterol and oxysterols measurement

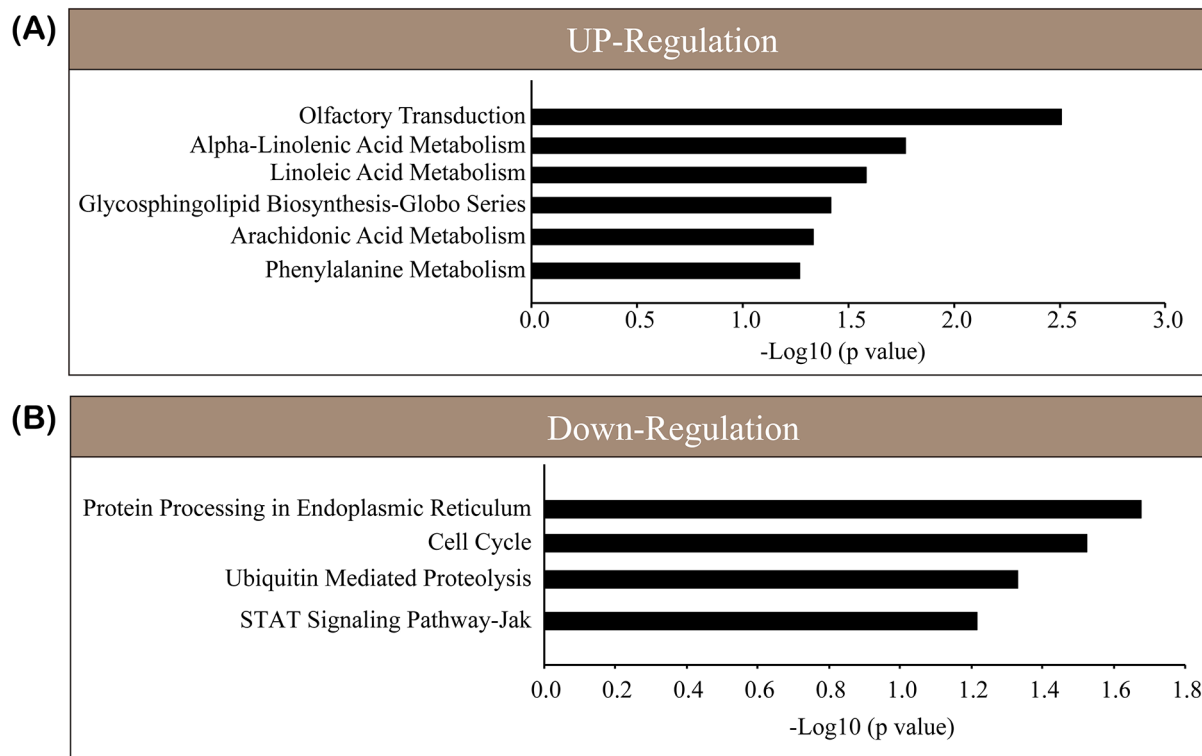
Informed consent was acquired from all the patients. Human serum samples were obtained from 129 individuals in the Department of Gastroenterology of the Second Affiliated Hospital of Zhejiang University School of Medicine. The serum cholesterol and oxysterols were quantified by using UPLC-MS/MS. Generally, the collected samples were stored at  $-80^{\circ}\text{C}$ , and equilibrated to room temperature within 15 mins. After homogeneity by repeatedly pipetting up and down, 200  $\mu\text{L}$  of serum were added drop-wise to 3 mL of the 1:1 mixture of dichloromethane (1060441000, Sigma-Aldrich): methanol (1060071000, Sigma-Aldrich) solution with 50  $\mu\text{g/mL}$  butylated hydroxytoluene (47168, Sigma-Aldrich) after sparged with  $\text{N}_2$  for 10 min. Then the sample tube was flushed with  $\text{N}_2$ , placed in a  $30^{\circ}\text{C}$  ultrasonic bath for 10 min and centrifuged at 3,500 rpm for 5 min at room temperature. After that, the organic layer was collected. For hydrolysis, an aliquot of KOH (10 N) were added directly to the extract to efficiently hydrolyzed sterol esters to free sterols after 1.5 hr incubation at  $35^{\circ}\text{C}$ . Following hydrolysis, 3 mL Dulbecco's phosphate-buffered saline (DPBS) was added to each sample. Following vortexing and centrifugation at 3,500 rpm for 5 min at  $25^{\circ}\text{C}$ , the organic layer was collected. Three mL dichloromethane was added to the remaining sample. After vortexing and centrifugation at 3,500 rpm for 5 min at  $25^{\circ}\text{C}$ , the organic layer was transferred to the initial sample as collected above. The hydrolyzed samples were dried under  $\text{N}_2$  overnight. The extracted and dried serum samples were dissolved in 1 mL hexane, and then transferred to the aminopropyl SPE column. Sterols were then eluted from the column with  $\text{CHCl}_3$ : methanol, and dried under  $\text{N}_2$  overnight. The dried samples were then dissolved in 500  $\mu\text{L}$  methanol to prepared for further analysis. Derivatization of sterols was performed by adding 100  $\mu\text{L}$  of 1:1 pyridine:MTBSTFA (1% TBDMCS) with 2 mg/mL  $\text{NH}_4\text{I}$  after 50  $\mu\text{L}$  sample was dried under  $\text{N}_2$ . Then, the derivatized sample was dried under  $\text{N}_2$ , and then dissolved in 200  $\mu\text{L}$  of hexane for further analysis. Quantitative analysis of cholesterol and oxysterols was performed using UPLC-MS-ESI.



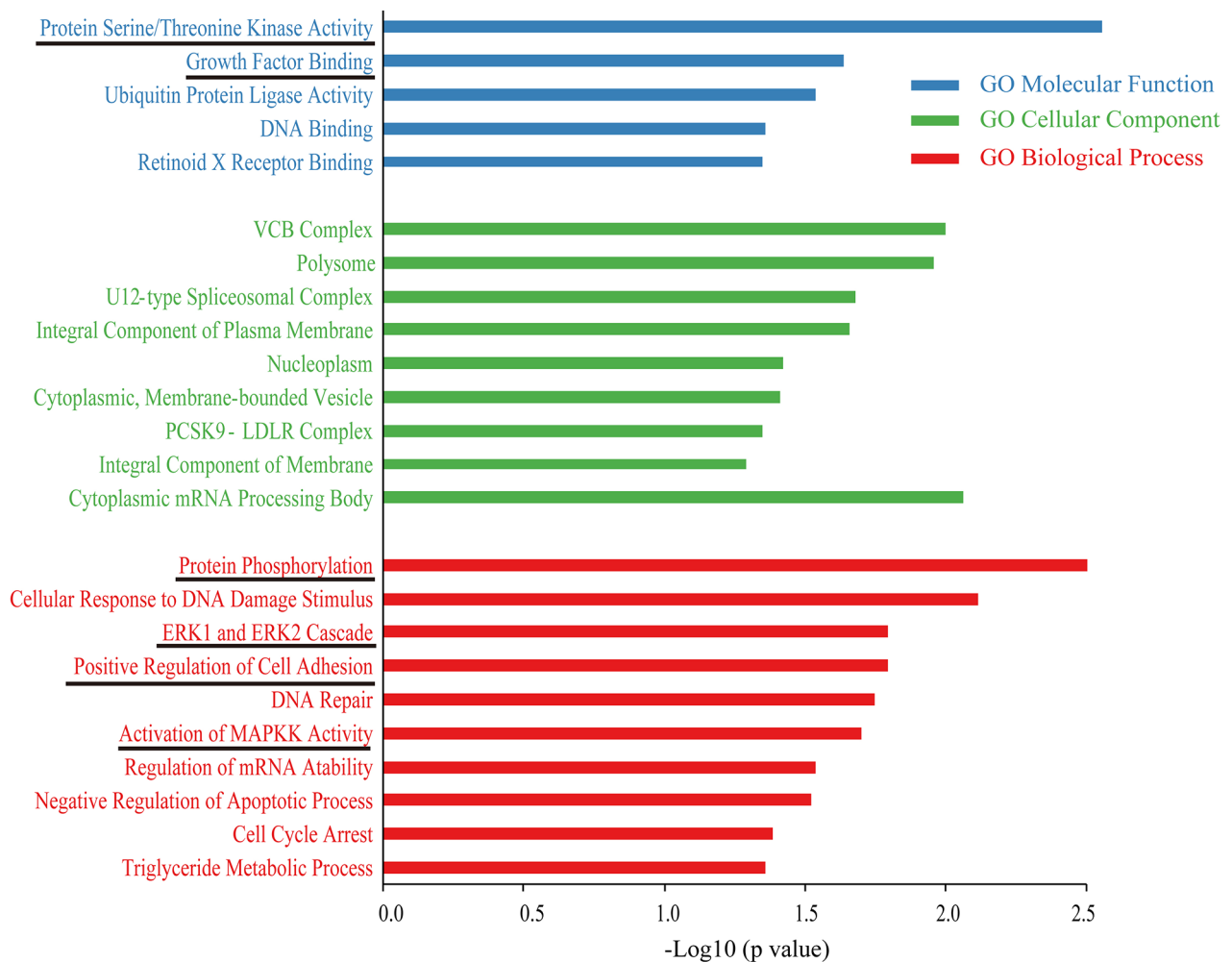
**Supplement Figure 1** Chromatograms for cholesterol (CHOL), 22R-OHC, 22S-OHC, 25-OHC, 27-OHC and 7α-OHC. (A-B) Chromatograms for cholesterol (CHOL), 22R-OHC, 22S-OHC, 25-OHC, 27-OHC and 7α-OHC together and individually.



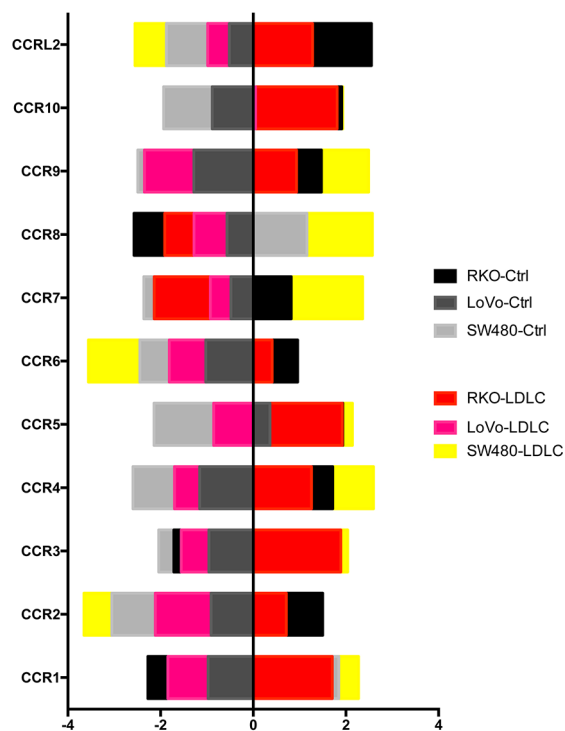
**Supplement Figure 2** Low-density lipoprotein cholesterol (LDL-C) significantly increased the intracellular levels of 25-OHC, 27-OHC and 7α-OHC in RKO, SW480, and LoVo colon cancer cells. \* p<0.05, \*\* p<0.01.



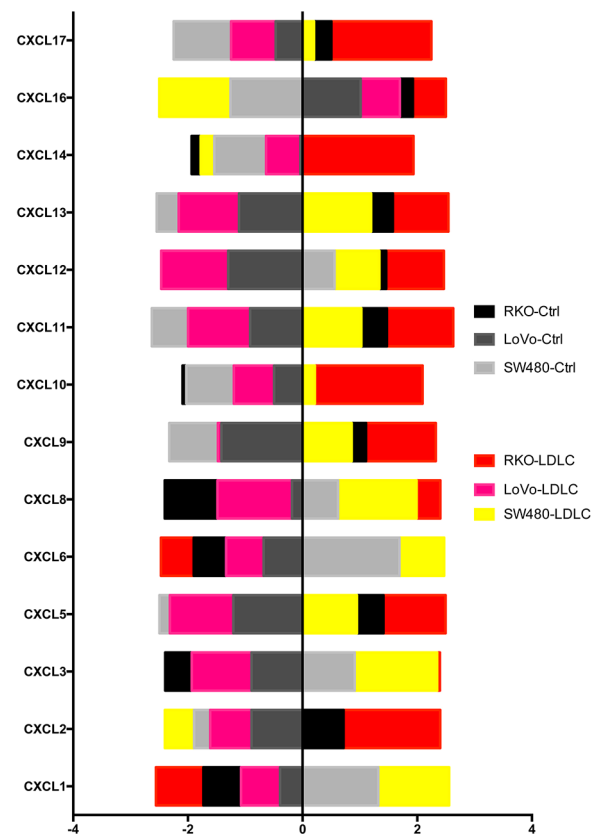
**Supplement Figure 3** Significantly enriched KEGG terms (P<0.05) in the up-regulated or down-regulated genes. KEGG terms were sorted based on P-values.



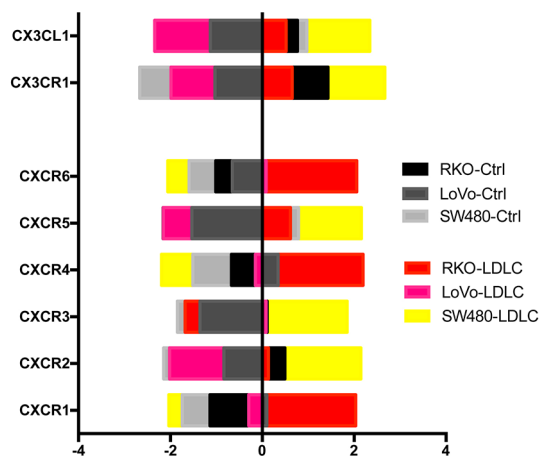
**Supplement Figure 4** Significantly enriched Gene ontology (GO) terms ( $P < 0.05$ ) in the down-regulated genes. GO terms belong to molecular functions, cellular components, and biological processes were shown in blue, green, and red, respectively. GO terms were sorted based on P-values.



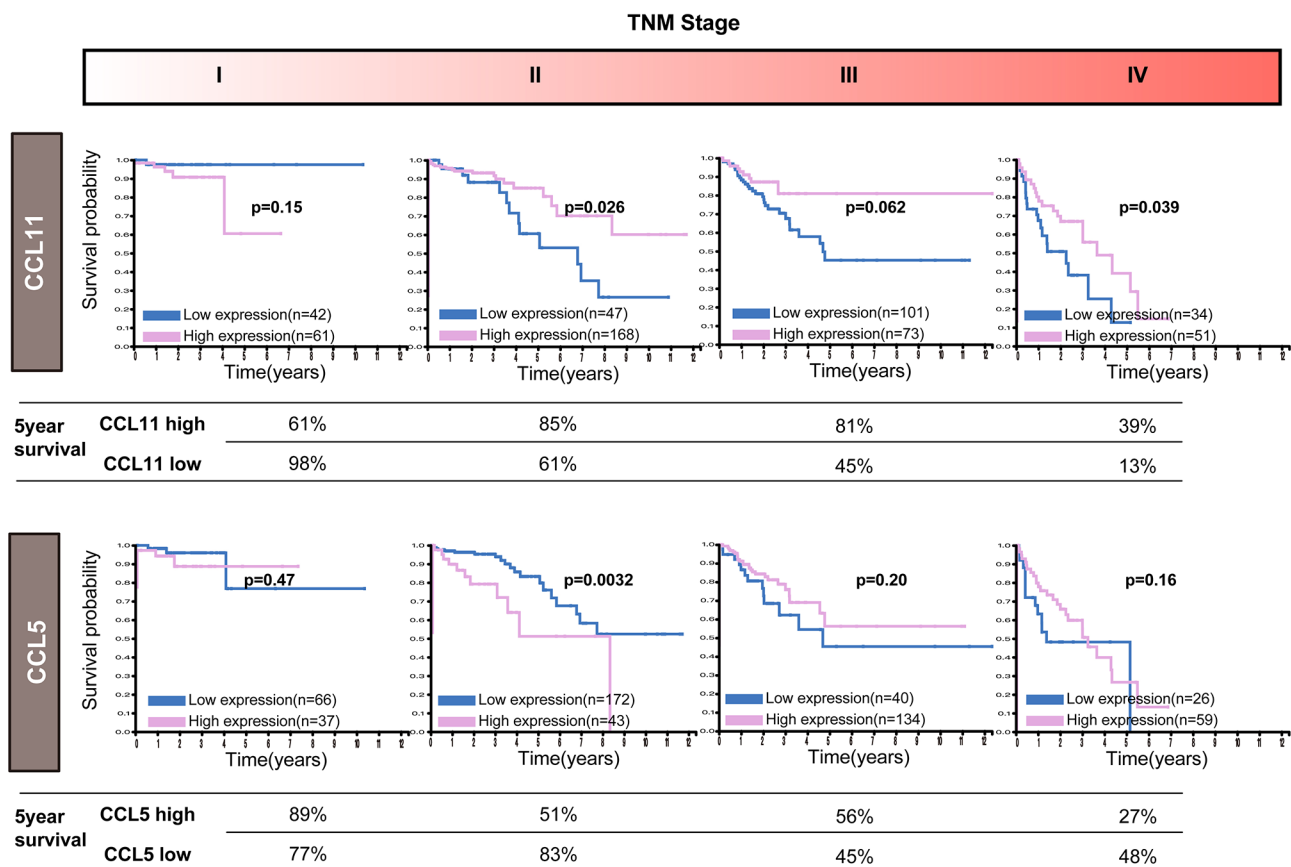
**Supplement Figure 5** Low-density lipoprotein cholesterol (LDL-C) had no influence on CCL chemokine family receptors (CCR). The changes of CCR when incubated with LDL-C (100 µg/ml).



**Supplement Figure 6** Low-density lipoprotein cholesterol (LDL-C) had no influence on CXCL chemokine family. The changes of CXCL when incubated with LDL-C (100 µg/ml).



**Supplement Figure 7** Low-density lipoprotein cholesterol (LDL-C) had no influence on CXCL chemokine family receptors (CXCR), CX3CL1 and CX3CR1. The changes of CXCR, CX3CL1 and CX3CR1 when incubated with LDL-C (100  $\mu$ g/ml).

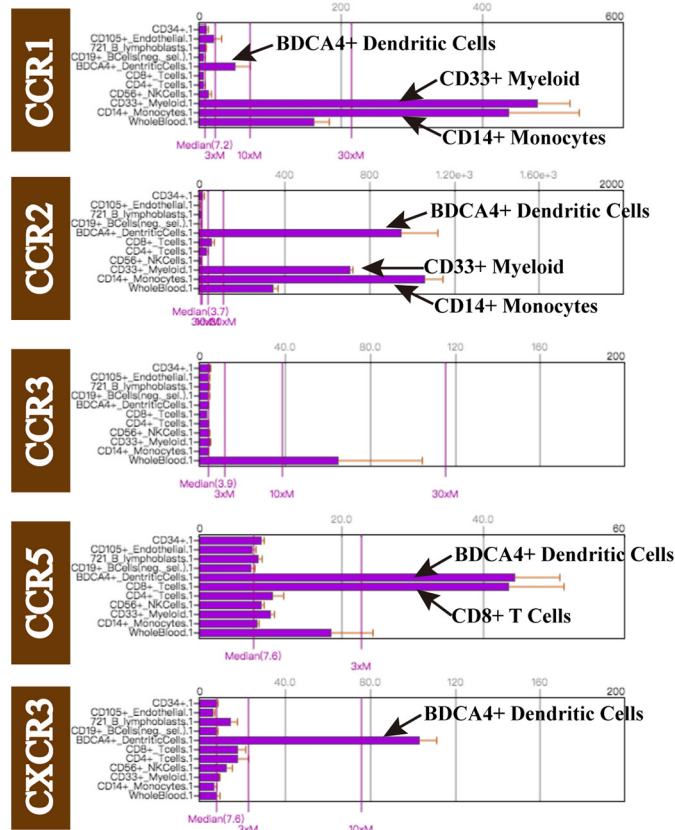


**Supplement Figure 8** The decreased CCL11 expression and increased CCL5 expression were negatively correlated with 5-year overall survival of colorectal cancer patients.

(A)

Chemokine	Receptor	
	Agonistic	Antagonistic
CCL5	CCR1, CCR3, CCR5	
CCL11	CCR3, CCR5	CXCR3, CCR2

(B)



**Supplement Figure 9** Decreased CCL11 and increased CCL5 might lead to the recruitment and activation of BDCA4+ Dendritic Cells, CD33+ Myeloid, and CD14+ Monocytes. (A) Chemokines bind receptors of CCL5 and CCL11, such CCL5 binds to CCR1/3/5 and CCL11 binds to CCR3/5 (agonistic receptor) and CCR2, CXCR3 (antagonistic receptor). (B) The tissue-specific pattern of CCR1, CCR2, CCR3, CCR5, and CXCR3 mRNA expression. Data from BioGPS. (CCR1 expression pattern: <http://ds.biogps.org/?dataset=GSE1133&gene=1230>; CCR2 expression pattern: <http://ds.biogps.org/?dataset=GSE1133&gene=729230>; CCR3 expression pattern: <http://ds.biogps.org/?dataset=GSE1133&gene=1232>; CCR5 expression pattern: <http://ds.biogps.org/?dataset=GSE1133&gene=1234>; CXCR3 expression pattern: <http://ds.biogps.org/?dataset=GSE1133&gene=2833>).