Supplementary Data

| Table S1 Primers used in this study | | |
|-------------------------------------|---------------------------------|---------------------------------|
| Primer | | |
| ChIP assay | | |
| DTDST | GCT GGG ATT ACA AGC GTG AG | TTC CCC ATC AAA GAT TCC AG |
| ST6GalNAc6 | CCA CGA AAA ATG CTG GCT CC | CTG CTG TAG TGG TCT TGG CA |
| BGN exon 1 binding site | CAA ACT GCC CAG GAG TGA GT | AGG CGC AGG CTG ACT AGT TG |
| BGN p65 binding site | GGC CCT CTT TTT AAG GGA AG | GGT GGT TTC TCC AGG ATC AG |
| EZH2 p65 binding site | AGC ATA AAG CCA GAC CAG GC | TAG CTT CGC CTC TGA CGT TT |
| SUZ12 p65 binding site | GGT CCT TCT CTC CCC ACA AT | AGG GAA GGA GGG AGG AAA A |
| EED p65 binding site | AGG GGG AAG CAG GTT ACT GT | GGA CAG CGC TTC CTG ACT AT |
| Gene expression | | |
| EZH2 | TCA TGC AAC ACC CAA CAC TT | TTG GTG GGG TCT TTA TCC GC |
| SUZ12 | GCA AGA ATC TCA TAG CTT GTC AGC | GCA GGA CTT CCA GGG TAA CA |
| EED | AGC CAA ATG TAC AAC ACT GAC T | CAG CGC CAA ATA CTG GCA TC |
| ST6GalNAc6 | GAC GCC GGA GAG AAA TGA GT | GGG AGC CGT AAT GGA AGA CC |
| DTDST | CAG ATG CCT TGC TGA GTG GA | CCC ACA CCA TTA GTC CGA GG |
| BGN | AAC TAG TCA GCC TGC GCC T | CTC CCA GAA GCC TCT CTG CT |
| TLR2 | TGC TGC CAT TCT CAT TCT TCT G | AGG TCT TGG TGT TCA TTA TCT TCC |
| TLR4 | CAG AGT TGC TTT CAA TGG CAT C | AGA CTG TAA TCA AGA ACC TGG AGG |

Table S1. Primers used in this study.

| | | | | | | | | log2 | FC | | | | | | | |
|-----------------|------------|---------|---------|--------|---------|---------|--------|-------|--------------|--------|--------|--------|---------------|--------|--------|--------|
| | | | | | | | | -3 | | | | | | 3 | | |
| | | | TI DA 1 | icondo | rolotiv | e genes | | | | | | | | | | |
| Tissues | STéGaINAcé | SLC26A2 | BGW | HSPD1 | | | | TNC | HYALI | HYAL2 | SDC2 | HSPG2 | HASI | HAS2 | HAS3 | SFTPAI |
| All | -0.768 | -0.197 | 0.41 | 0.403 | 0.275 | 0.758 | 1.213 | 0.537 | -1.398 | ns ns | -0.453 | 0.316 | -0.309 | 0.126 | -0.351 | -0.294 |
| Adipose | TAS | TIS | ns | 0.364 | TIS | TIS | T.S. | ns | 1.550 Its | ns | TLS | ns | 70.505 TrS | 1.12.0 | TIS | ns |
| Advenal Gland | -0.722 | TAS . | ns | T/S | ns | ns | -1.911 | ns | -0.841 | -0.772 | ns | ns | ns | ns | 0.998 | ns |
| Bladder | ns ns | T/S | 1.01 | 0.809 | 0.659 | ns | 1.886 | TLS | TLS | 0.714 | TLS | 1.039 | T/S | ns | 0.983 | ns |
| Blood | ns | -0.266 | 0.715 | 0.444 | 0.383 | 0.425 | 0.515 | 0.864 | ns | 0.26 | 0.971 | 1.471 | 0.29 | 0.552 | -0.794 | 0.293 |
| Bone | TLS | TLS | TLS | TLS | T/S | TLS | ns. | TLS | ns | ns | TLS | T/S | T/S | T/S | T/S | TLS |
| Brain | -1.15 | 1.257 | 0.831 | 0.51 | 0.167 | 0.541 | 1.07 | 2.609 | -0.764 | 0.813 | TLS | 1.984 | -2.01 | 1.648 | 0.182 | -0.513 |
| Breast | -0.648 | -0.146 | 1.528 | 0.284 | -0.061 | 1.048 | 1.049 | ns | -1.616 | -0.256 | -0.539 | ns | TLS | -0.331 | -1.063 | ns - |
| Cervix | ns | TLS | TLS | 0.715 | ns. | TLS | TLS | TLS | TLS | ns | TLS. | ns | ns. | ns. | ns | ns |
| Colon | -2.703 | -3.317 | 2.274 | 0.703 | 0.416 | 1.654 | 2.314 | 1.195 | -0.481 | 0.789 | 0.469 | 0.734 | 0.385 | 0.147 | ns. | ns. |
| Endometaium | -1.621 | ns | 0.723 | 0.434 | T/S | 1.764 | 2.175 | TLS | TLS | -0.364 | -0.829 | ns. | T/S | 0.803 | T/S | -0.879 |
| Esophagus | -1.323 | TLS | TLS | ns | ns | TLS | ns | ns | ns | -0.398 | -1.435 | -1.82 | ns | TLS | ns. | ns |
| Eye | ns | JLS | TLS | ns | TLS | TLS | ns | ns | ns | ns | TLS | ıs | T/S | TLS | TLS | ns |
| Gallbladdex | ns | TLS | TLS | ns. | TLS | TLS | ns | ns | ns. | ns | TLS | ns | ns. | TLS | ns | ns |
| Head and Neck | TLS | -1.649 | 1.001 | ns. | TLS | TLS. | ns | ns | TLS. | ns | 1.22 | 1.139 | TLS | 1.16 | 1.673 | ns - |
| Kidney | -0.435 | 0.196 | 0.347 | -0.364 | 0.117 | 0.67 | 0.868 | 1.728 | -2.024 | ns | 0.152 | 1.136 | 0.39 | 0.349 | ns | 0.537 |
| Liver | -0.366 | 1.101 | -1.155 | TLS | 0.142 | -0.818 | TLS | 0.312 | -1.362 | 0.302 | TLS | ıs | ns. | ıs | ns | ns |
| Lung | -0.691 | -0.553 | 0.631 | 0.421 | -0.181 | -0.821 | T/S | 0.554 | -1.385 | -0.726 | -0.277 | -0.508 | -0.421 | ıs | 0.707 | -1.375 |
| Lymph Node | ns | TLS | TLS | ns | ns | ns. | ns | TLS | ns | ns | TLS | ıs | ns | ns | ns | ns |
| Muscle | ns | TLS | TLS | ns . | ns | TLS | ns | ns | ns | ns . | TLS | ns | ns | TLS | ns | ns |
| Oral | -1.263 | ns | 0.969 | 0.711 | TLS | TLS | ns | ns | ns | ns | TLS | າເຣ | TLS | TLS | 1.963 | ns |
| Overy | ns . | 0.605 | 1.489 | TLS | 0.222 | 1.032 | 3.903 | 1.277 | -1.026 | 1.282 | -0.477 | 2.231 | -1.441 | 0.745 | -0.526 | ns. |
| Panciesse | ns | -0.34 | 0.901 | TLS | 0.229 | -1.203 | TLS | TLS | ILS | ns . | -0.751 | 0.879 | ns. | ILS | ns | ns . |
| Pharynx | ns | JLS | TLS | TLS | 0.732 | ILS | TLS | TLS | TLS | TLS | ILS | ns | TLS | TLS | ns | ns |
| Placenta | ns | ns | TLS | TLS | T/S | TLS | TLS | ns | ıs | ns. | TLS | ns | T/S | TLS | ns | ns |
| Prostate | ns - | TLS | TLS | TLS | T/S | ILS | -2.556 | TLS | TLS | -0.456 | TLS | ns | ns. | ns. | 1.414 | T/S |
| Skin | -0.638 | JLS | 0.4 | 0.635 | TLS | TLS | TLS | 0.994 | -1.177 | TLS | TLS | TLS | -0.36 | TLS | 0.441 | 0.366 |
| Small_Intestine | ns - | TLS | TLS | TLS | T/S | TLS | T/S | TLS | TLS | T/S | TLS | ns | ns. | ns. | ns | ns |
| Spleen | ns . | TLS | TLS | T/S | T/S | Is | T/S | TLS | Is | T/S | T/S | īs | T/S | T/S | TiS. | T/S |
| Stomach | ns | TLS | 1.07 | 0.74 | 0.864 | ns. | TLS | 0.815 | ns. | 0.697 | 0.62 | 0.816 | ns | 0.478 | ns | -1.099 |
| Teeth | ns | TLS | ILS | TLS | TLS | TLS | TLS | TLS | TLS | ns | 2.946 | ns | ns. | ns. | ns | ns |
| Testis | ns . | T/S | IS | 1.733 | ns | TLS | T/S | ILS | T/S | T/S | TLS | ns | ns. | T/S | ns | T/S |
| Thyroid | 0.341 | 0.374 | 0.838 | ILS | T/S | 0.687 | 1.067 | 2.26 | -0.713 | 0.424 | -1.126 | 0.295 | T/S | 1.341 | -0.514 | 1.31 |
| Tongue | ns | ıs | TLS | 0.832 | Ts. | TLS | ns | 2.791 | ns | -0.718 | -1.365 | -1.089 | T/S | ħS. | 2.402 | -3.068 |
| Uterus | ns . | ıs | TLS | ns | TLS | TLS | ns | TLS | ns | 0.732 | TLS | ıs | 1.171 | 1.322 | -1.373 | TLS |
| Vagina | ıs | ıs | TLS | T/S | T/S | TLS | T/S | TLS | ns. | T/S | T/S | ıs | T/S | T/S | T/S | T/S |
| Vulva | ns | ILS | ILS | T/S | T/S | ILS | T/S | 1.19 | ILS | T/S | ILS | ns | ns. | ILS | ns | ILS |

Table S2. TLR4 ligand expression level in cancers. The data were retrieved from the GENT2 database (GPL570 platform), and are only shown according to significant test results by t-test (p < 0.001). ns, not significant.

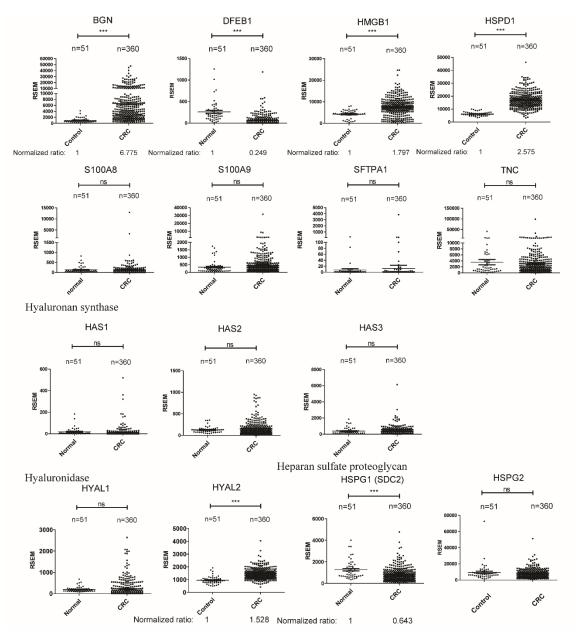


Figure S1. Large-scale RNA-Seq transcriptome analysis of TLR4 potential ligands—BGN, DEFB1, HMGB1, HSPD1, S100A8, S100A9, SFTPA1, TNC, hyaluronan synthase (HAS1, HAS2, and HAS3), and heparan sulfate proteoglycan responsive enzymes (SDC2 also called HSPG1, and HSPG2) in normal colorectal tissues and tissues from colorectal cancer from the TCGA database. n, number of patients; ***, p < 0.001.

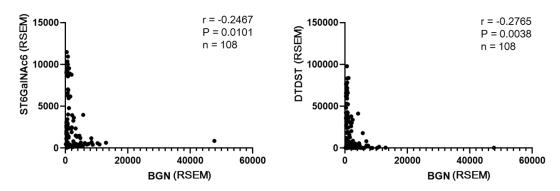


Figure S2. ST6GalNAc6 and DTDST mRNA levels were inversely correlated with BGN. Large-scale RNA-Seq transcriptome analysis of the relationship between ST6GalNAc6 and DTDST and BGN in healthy control colonic and rectal tissues and in colorectal cancer samples (stage 1) from the TCGA database. ST6GalNAc6 and DTDST each showed a significant inverse correlation with BGN mRNAs.

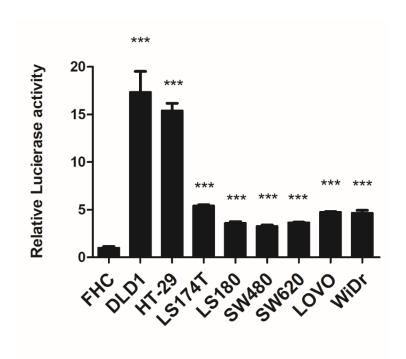


Figure S3. Relative NF- κ B activity in normal intestinal cells and some colon cancer cells. Promoter analysis of NF- κ B activity in normal intestinal cells—FHC—and colon cancer cells—DLD1, HT-29, LS174T, LS180, SW480, SW620, LOVO, and WiDr cells. Cells were transfected with 0.2 μg/well of the pGL4.32 (luc2P/NF- κ B-RE/Hygro) vector (Promega Corporation, Madison, WI, USA), and incubated for 24 h for the subsequent dual luciferase reporter assay. Firefly luciferase activity was normalized to Renilla luciferase activity. Data are presented as the relative fold increase compared with FHC. ***, p < 0.001; (n = 3 with mean ± SD shown).

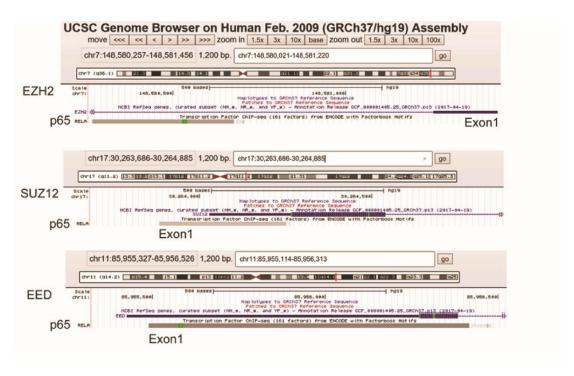


Figure S4. Identification of p65 binding regions in EZH2, SUZ12, and EED through multi-omics data analysis. Locations of p65 show gray blocker in EZH2, SUZ12, and EED. The genomic positions in this figure are based on the UCSC Genome Browser, Assembly GRCh37/hg19.

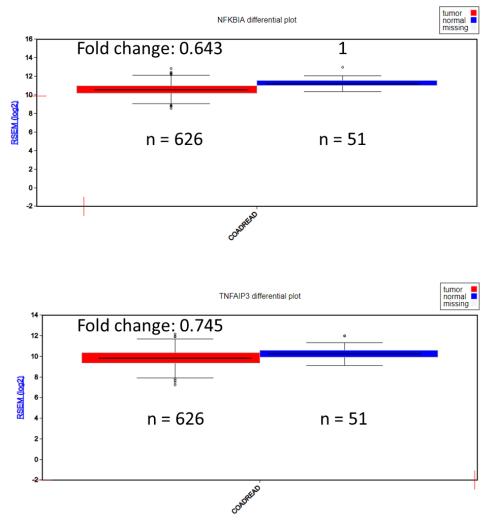


Figure S5. NFKBIA and TNFAIP3 differential plots for colorectal cancer in the TCGA database.