Table SI. Sequences of the qPCR primers.

Primers	5'-3'
SOCS2-F	TGCAAGGATAAGCGGACAGG
SOCS2-R	CAGAGATGGTGCTGACGTGT
METTL3-F	CTTTGCCAGTTCGTTAGTCTC
METTL3-R	CTGACCTTCTTGCTCTGTTGTT
LGR5-F	CTACATGGTCGCTCTCATCTTG
LGR5-R	ATATTCTCCAGGTCTCCCTTGTC
CyclinB1-F	ATACTGCCTCTCCAAGCCCAATG
CyclinB1-R	GATCAGCTCCATCTTCTGCATCCA
P21-F	TCAAATCGTCCAGCGACCTTCC
P21-R	TCCATAGCCTCTACTGCCACCAT
SOX2-F	ACATGATGGAGACGGAGCTGAAG
SOX2-R	GGGACCACACCATGAAGGCATT
PCNA-F	CGTGAACCTCACCAGTATGTCCAA
PCNA-R	ACTTTCTCCTGGTTTGGTGCTTCA
Ki67-F	CCTAGAAGACTTGGCTGGCTTGAA
Ki67-R	GGACTGTGGCTTGAAGATTGTTGG
CTNNB1-F	AGAGTGCTGAAGGTGCTATCTGT
CTNNB1-R	TCCTGAGAGTCCAAAGACAGTTC
GAPDH-F	TGCACCACCAACTGCTTAGC
GAPDH-R	GGCATGGACTGTGGTCATGAG
LGR5 promoter-F	CGAGCTCCACACGTATTTTTATTGCATCTCAGTTC
LGR5 promoter-R	CCCTCGAGAAAGCGCTCCAGCCCGA

F, forward; R, reverse; SOCS2, suppressor of cytokine signaling 2; METTL3, methyltransferase like 3; LGR5, leucine-rich repeat-containing G protein-coupled receptor 5; SOX2, SRY-box transcription factor 2; PCNA, proliferating cell nuclear antigen; CTNNB1, catenin β1; GAPDH, glyceraldehyde 3-phosphate dehydrogenase.

Table SII. Bioinformatics analysis of METTL3.

A, GO analysis reveals these candidates that are sorted into multiple bioprocesses

GO terms (Biological process)	Count	P-value
Positive regulation of transcription from RNA polymerase II promoter	18	9.30E-11
Primary miRNA processing	5	4.70E-09
Negative regulation of transcription from RNA polymerase II promoter	12	1.40E-06
Positive regulation of gene expression	8	4.10E-06
Positive regulation of transcription, DNA-templated	10	5.00E-06
Negative regulation of apoptotic process	9	1.70E-05
Cell cycle arrest	6	2.90E-05
Cellular response to mechanical stimulus	5	3.20E-05
mRNA methylation	3	9.50E-05
Transcription from RNA polymerase II promoter	8	3.00E-04
Positive regulation of fibroblast proliferation	4	3.50E-04
mRNA processing	5	1.10E-03
Negative regulation of protein catabolic process	3	3.00E-03
Cellular response to lipopolysaccharide	4	3.00E-03
Lipopolysaccharide-mediated signaling pathway	3	3.00E-03
Cytokine-mediated signaling pathway	4	4.60E-03
Positive regulation of epithelial cell proliferation	3	1.00E-02
Ras protein signal transduction	3	1.40E-02
Positive regulation of inflammatory response	3	1.50E-02
Canonical Wnt signaling pathway	3	1.90E-02
Regulation of gene expression	3	2.70E-02
Cell surface receptor signaling pathway	4	3.30E-02
Response to drug	4	4.30E-02
Positive regulation of NF-kappaB transcription factor activity	3	4.60E-02
Positive regulation of I-kappaB kinase/NF-kappaB signaling	3	6.40E-02
Cell proliferation	4	6.70E-02
Inflammatory response	4	7.30E-02
Positive regulation of ERK1 and ERK2 cascade	3	7.40E-02
Signal transduction	7	7.40E-02
Fc-epsilon receptor signaling pathway	3	7.60E-02
Positive regulation of cell migration	3	8.10E-02
In utero embryonic development	3	8.30E-02
Positive regulation of cell proliferation	4	1.20E-01
MAPK cascade	3	1.40E-01
Regulation of transcription, DNA-templated	5	5.50E-01

B, KEGG analysis indicates that these candidates are involved in numerous signal pathways, and in benign and malignant diseases

KEGG pathway	Count	P-value
Chagas disease (*American trypanosomiasis*)	8	9.90E-08
Signaling pathways regulating pluripotency of stem cells	8	7.60E-07
Proteoglycans in cancer	8	8.30E-06
Hepatitis C	7	9.60E-06
FoxO signaling pathway	7	1.00E-05
Hepatitis B	7	1.60E-05
HTLV-I infection	8	4.10E-05
Toxoplasmosis	6	8.00E-05
Pancreatic cancer	5	1.10E-04
Prolactin signaling pathway	5	1.50E-04
Pertussis	5	1.90E-04
Salmonella infection	5	2.80E-04
ErbB signaling pathway	5	3.30E-04
MAPK signaling pathway	7	3.70E-04
Influenza A	6	4.90E-04
Bladder cancer	4	5.10E-04

Table SII. Continued.

B, KEGG analysis indicates that these candidates are involved in numerous signal pathways, and in benign and malignant diseases

KEGG pathway	Count	P-value
Tuberculosis	6	5.30E-04
Pathways in cancer	8	6.00E-04
Herpes simplex infection	6	6.20E-04
Toll-like receptor signaling pathway	5	7.00E-04
Sphingolipid signaling pathway	5	1.10E-03
Osteoclast differentiation	5	1.50E-03
Colorectal cancer	4	1.70E-03
Inflammatory bowel disease (IBD)	4	1.90E-03
Epithelial cell signaling in *Helicobacter pylori* infection	4	2.20E-03
Leishmaniasis	4	2.50E-03
Chronic myeloid leukemia	4	2.70E-03
NF-κB signaling pathway	4	4.50E-03
Prostate cancer	4	4.70E-03
GnRH signaling pathway	4	5.10E-03
Epstein-Barr virus infection	5	5.90E-03
HIF-1 signaling pathway	4	6.30E-03
TNF signaling pathway	4	7.90E-03
PI3K-Akt signaling pathway	6	9.80E-03
Neurotrophin signaling pathway	4	1.10E-02
Cell cycle	4	1.20E-02
Endometrial cancer	3	1.70E-02
Legionellosis	3	1.90E-02
NOD-like receptor signaling pathway	3	1.90E-02
Hippo signaling pathway	4	2.00E-02
Acute myeloid leukemia	3	2.00E-02
Central carbon metabolism in cancer	3	2.60E-02
Glioma	3	2.60E-02
Shigellosis	3	2.60E-02
Transcriptional misregulation in cancer	4	2.70E-02
Fc epsilon RI signaling pathway	3	2.90E-02
Adipocytokine signaling pathway	3	3.00E-02
RIG-I-like receptor signaling pathway	3	3.00E-02
Adherens junction	3	3.10E-02
Melanoma	3	3.10E-02
TGF-β signaling pathway	3	4.20E-02

METTL3, methyltransferase like 3; GO, Gene Ontology; KEGG, Kyoto Encyclopedia of Genes and Genomes.

Table SIII. Expression profiles of METTL3, SOCS2 and LGR5 in CRC through the Oncomine database.

			METTL3			SOCS2			LGR5			
DATASET	Normal (cases)	Tumor (cases)	Fold change	t-test	P-value	Fold change	t-test	P-value	Fold change	t-test	P-value	(Refs.)
TCGA colorectal	Colon (19)	Rectosigmoid adenocarcinoma (3)	/	/	/	**-2.068**	**-9.460**	**1.39E-07**	/	/	/	
	Rectum (3)	Rectal adenocarcinoma (60)	**2.208**	**10.413**	**9.18E-14**	**-2.788**	**-10.792**	**9.45E-17**	**3.229**	**7.800**	**1.04E-11**	
		Cecum adenocarcinoma (22)	**2.321**	**7.333**	**6.37E-09**	**-2.570**	**-7.867**	**1.52E-09**	**4.497**	**8.109**	**3.94E-09**	
		Colon adenocarcinoma (101)	**2.052**	**9.863**	**1.39E-13**	**-2.926**	**-13.179**	**9.53E-19**	**4.533**	**12.473**	**1.89E-22**	
Skrzypczak colorectal 2	Colon (10)	Colon adenoma (5)	**1.940**	**6.343**	**1.56E-05**	**-4.196**	**-11.681**	**5.35E-07**	**29.997**	**13.880**	**3.85E-09**	(43)
	Colon (10)	Colon adenoma (5)	**1.446**	**4.118**	**7.41E-04**	**-5.076**	**-8.298**	**1.02E-06**	/	/	/	
	Colon (10)	Colon carcinoma (5)	1.007	0.059	4.77E-01	**-2.769**	**-12.047**	**1.73E-08**	**8.264**	**8.338**	**8.15E-07**	
	Colon (10)	Colon carcinoma (5)	-1.011	-0.191	5.72E-01	/	/	/	/	/	/	
Graudens colon	Colon (12)	Colorectal carcinoma (18)	1.072	0.903	1.88E-01	**-2.018**	**-7.086**	**7.52E-08**	/	/	/	(44)
Sabates-bellver colon	Ascending colon (4)	Colon adenoma (25)	**1.704**	**5.354**	**1.50E-06**	-1.125	-1.314	9.80E-02	**5.873**	**13.611**	**1.06E-15**	(45)
	Descending colon (5)	Rectal adenoma (7)	**1.598**	**2.679**	**1.50E-02**	-1.106	-0.458	3.31E-01	/	/	/	
	Rectum (7)											
	Sigmoid colon (15)											
	Transverse colon (1)											
Skrzypczak colorectal	Colorectal Tissue (24)	Colorectal adenocarcinoma (45)	**1.242**	**3.063**	**2.00E-03**	**-1.372**	**-3.742**	**2.03E-04**	**4.745**	**15.225**	**1.17E-23**	(43)
		Colorectal carcinoma (36)	1.041	0.793	2.15E-01	**-1.261**	**-2.510**	**7.00E-03**	**4.871**	**6.879**	**3.57E-09**	
Kaiser colon	Colon (5)	Rectosigmoid adenocarcinoma (10)	1.534	2.107	3.00E-02	/	/	/	/	/	/	(46)
		Rectal adenocarcinoma (8)	1.375	1.934	5.30E-02	/	/	/	/	/	/	
		Colon adenocarcinoma (41)	**1.604**	**2.904**	**1.50E-02**	**-2.028**	**-7.166**	**1.74E-05**	**6.905**	**12.859**	**5.21E-14**	
		Cecum adenocarcinoma (17)	**1.482**	**2.397**	**2.80E-02**	/	/	/	/	/	/	
		Rectal mucinous adenocarcinoma (4)	1.281	1.917	5.60E-02	/	/	/	/	/	/	
		Colon mucinous adenocarcinoma (13)	**1.199**	**2.253**	**2.80E-02**	/	/	/	/	/	/	
Hong colorectal	Colon (12)	Colorectal carcinoma (70)	**1.476**	**2.100**	**2.80E-02**	**-3.314**	**-11.710**	**1.07E-18**	**6.431**	**8.671**	**5.28E-13**	(47)
Gaedcke colorectal	Rectum (65)	Rectal adenocarcinoma (65)	**1.030**	**0.443**	**3.29E-01**	**-1.590**	**-6.537**	**2.02E-09**	**1.854**	**7.407**	**1.32E-10**	(48)
Alon colon	Colon (22)	Colon adenocarcinoma (39)	/	/	/	1.024	0.253	5.99E-01	/	/	/	(49)
Notterman colon	Colon (18)	Colon adenocarcinoma (18)	/	/	/	-1.059	-0.524	3.02E-01	/	/	/	(50)
Ki colon	Colon (28) liver (13)	Colon adenocarcinoma (50)	/	/	/	1.319	-3.013	2.00E-03	1.379	3.602	2.76E-04	(51)
Gaspar colon	Intestinal mucosa (22)	Colorectal adenoma (56)	/	/	/	-1.062	-0.427	3.36E-01	1.397	2.626	6.00E-03	(52)

Elevated mRNA expression levels of METTL3 and LGR5 were found in CRC. Meanwhile, downregulation of SOCS2 mRNA was observed in these clinical data. Those that gained statistical significance ($P<0.05$) are highlighted in bold print. CRC, colorectal cancer; METTL3, methyltransferase like 3; SOCS2, suppressor of cytokine signaling 2; LGR5, leucine-rich repeat-containing G protein-coupled receptor 5.