Supplementary Information

Material and Methods

*RNA/DNA extraction and real time PCR*

 AllPrep extraction kit (Qiagen, Hilden, Germany) was used to extract RNA and DNA. cDNA was obtained by reverse transcription using the high capacity cDNA reverse transcription kit (Applied Biosystems). RNA quality was checked by The Experion™ automated electrophoresis system (Bio-Rad Laboratories, Inc.) and RNA quality from all primary samples was of average quality. The expression of SOCSs as well as known marker genes was assessed by quantitative RT-PCR using TaqMan technology. TaqMan® chemistry-based primer/probe sets are recommended for use with RNA from microdissected samples, due to their improved specificity over primer only-based detection chemistries (e.g. SYBR) (Erickson *et al*, 2009). Reference numbers from Applied Biosystems are for *SOCS1*: Hs00864158_g1, *SOCS2*: HS 00919620_m1, *SOCS3*: Hs01000485_g1, *SOCS6*: Hs04272776_m1, *osteopontin/SPP1,*: Hs00959010_m1, *CDX1*: Hs00950423_g1, *KIAA1199*: Hs01552124_m1, *GR*: Hs00353740_m1 and *HPRT*: Hs02800695_m1. Briefly, TaqMan® Universal PCR Master Mix (Applied Biosystems) was used and the reaction was run on a cycler 7500 FAST Real time PCR Detection System (Applied Biosystems) with the following settings: 50° C 2 min, 95° C 10 min and 40x (15 sec 45° C and 1 min at 60°). Expression levels of the gene of interest were normalized against the house-keeping gene HPRT (Erickson *et al*, 2009). Absolute quantification analysis was used and the resulting expression data were presented as relative ratios to HPRT.

Supplementary Figure 1

A

B
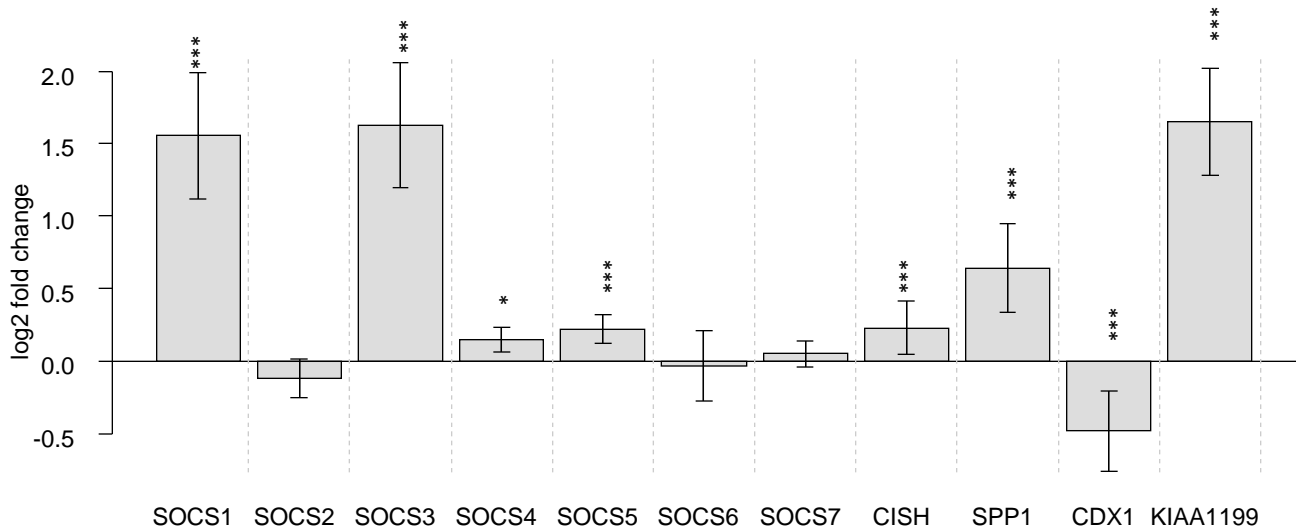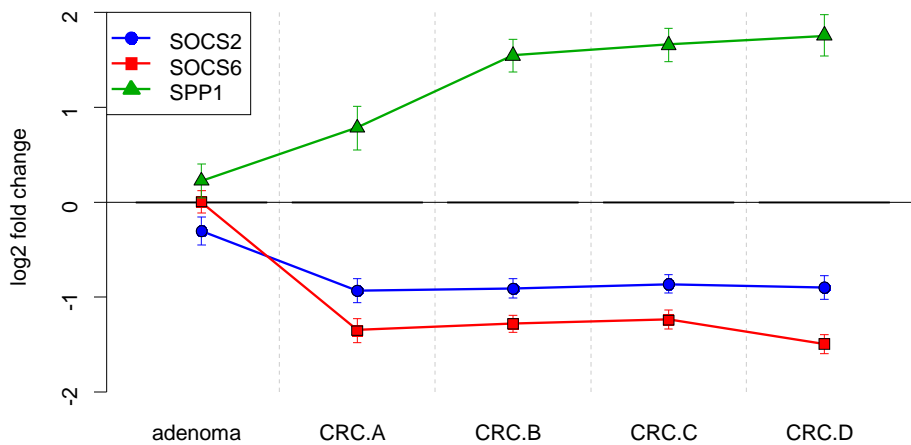
Supporting Information Figure 1.
(A) Expression of SOCS family members and marker genes in IBD samples. Bar plot showing the log2 FC values of the SOCS family genes and marker genes in IBD compared to normal colorectal mucosa. Error bars correspond to 95% confidence intervals for mean logFC. *FDR<0.05, **FDR<0.01, ***FDR<0.001.
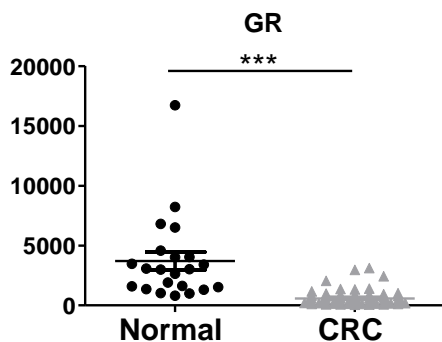**(B) Expression of SOCS2, SOCS6 and SPP1 in adenomas and CRC stages A-D.**

Supplementary Figure 2

A

B
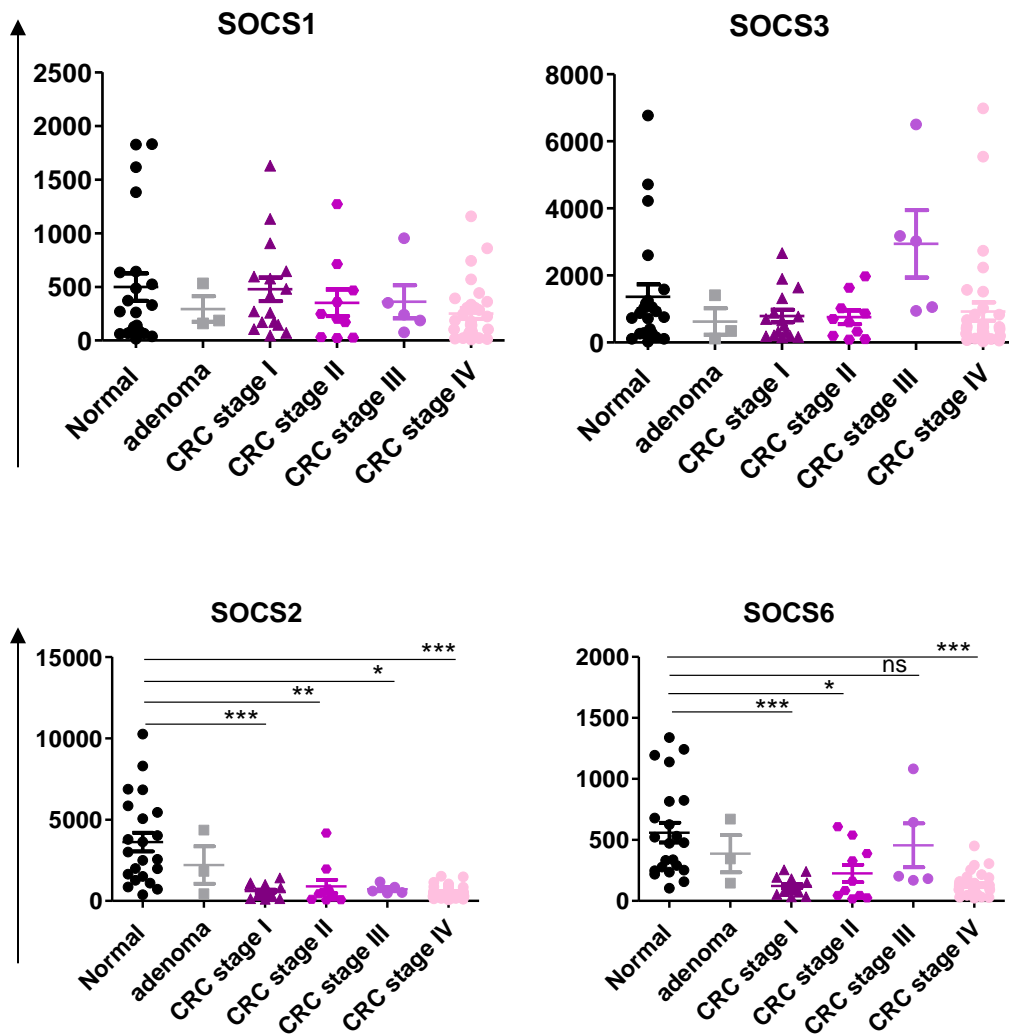
Supporting Information Figure 2.
(A) Expression of SOCS family members in primary human samples. SOCS1, 2, 3 and 6 mRNA levels in adenomas and along CRC progression in CRC samples from stage 1 to stage 4. *FDR<0.05, **FDR<0.01, ***FDR<0.001.
(B) Expression of the glucocorticoid receptor in primary human CRC samples. ***FDR<0.001

Supplementary Figure 3
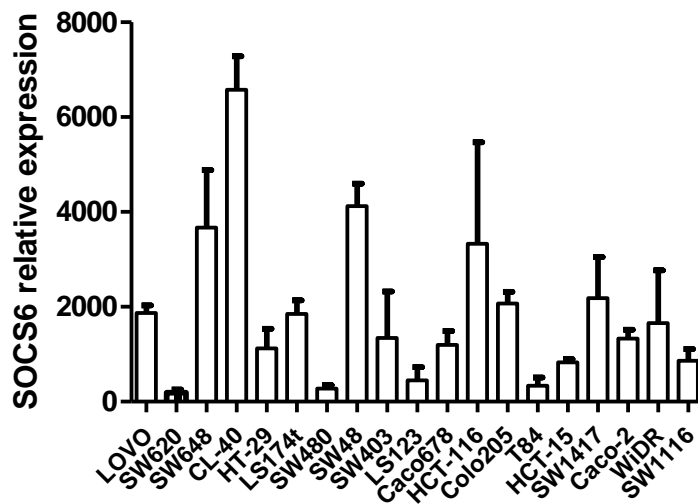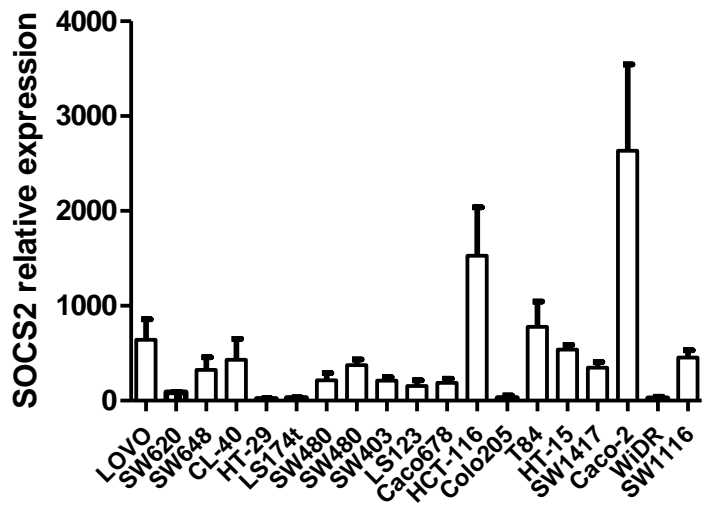
Supporting Information Figure 3.
Expression of SOCS2 and SOCS6 nRNA levely by real time PCR in colon cancer cell lines.

Supplementary Table 1

TNM	Tumor	Normal tissue
Adenoma: high dysplasia	3	3
Stage I	16	3
Stage II	10	10
Stage III	6	6
Stage IV	31	2
TOTAL	**66**	**23**

Gender	35 males	31 females
Age: median	65	69
range	30-89	45-89

Supplementary Table 1. Clinical characteristics of patients.

Supplementary Table 2

	GSE 8671	GSE 9254	GSE 20916	GSE 10714	GSE 14333	GSE17538	GSE21510	GSE15960	GSE 4183	GSE10961	Total
Normal	32	19	22	3			25	6	8		115
IBD				7					15		22
Adenoma	32			5				6	15		58
CRC-A					44	28	15				87
CRC-B				3	94	72	46				215
CRC-C					91	76	39				206
CRC-D					61	56	23				140
Profiling performed by	Sabates-Bellver et al., 2007	LaPointe et al., 2008	Skrzypczak et al., 2010	Galamb et al., 2008	Jorissen et al., 2009	Smith et al., 2010	Tsukamoto et al., 2011	Galamb et al., 2010	Gyorffy et al., 2009	Pantaleo et al., 2008	843

SupplementaryTable 2. Initial GEO Data sets included.

Supplementary Table 3

	IBD	Adenoma	CRC-A	CRC-B	CRC-C	CRC-D	CRC-all
	n=22	n=58	n=87	n=215	n=206	n=140	n=648
SOCS Genes							
SOCS1	2.94 (***)	1.22 (***)	1.10 (**)	ns	ns	0.84 (***)	ns
SOCS2	ns	0.81 (***)	0.52 (***)	0.53 (***)	0.55 (***)	0.53 (***)	0.55 (***)
SOCS3	3.10 (***)	1.26 (***)	1.14 (**)	1.19 (***)	1.22 (***)	ns	1.19 (***)
SOCS4	1.11(*)	1.16 (***)	1.11 (***)	1.13 (***)	1.17 (***)	1.13 (***)	1.14 (***)
SOCS5	1.17 (***)	ns	1.11 (***)	1.13 (***)	1.25 (***)	1.19 (***)	1.18 (***)
SOCS6	ns	ns	0.39 (***)	0.41 (***)	0.42 (***)	0.35 (***)	0.41 (***)
SOCS7	ns	1.22 (***)	1.43 (***)	1.43 (***)	1.42 (***)	1.53 (***)	1.42 (***)
CIS	1.17 (***)	ns	ns	0.95 (*)	0.94 (**)	0.92 (***)	0.95 (*)
STAT1	2.80 (***)	1.17 (**)	1.60 (***)	1.48 (***)	1.43 (***)	1.26 (***)	1.48 (***)
STAT2	1.26 (***)	ns	0.86 (***)	0.87 (***)	0.88 (***)	0.82 (***)	0.86 (***)
STAT3	1.51 (***)	1.10 (***)	0.79 (***)	0.76 (***)	0.75 (***)	0.73 (***)	0.76 (***)
STAT4	1.52 (***)	0.68 (***)	0.82 (***)	0.78 (***)	0.79 (***)	0.73 (***)	0.78 (***)
STAT5A	1.61 (***)	1.12 (**)	1.12 (***)	1.10 (***)	1.13 (***)	1.12 (***)	1.12 (***)
STAT5B	1.15 (***)	ns	1.06 (***)	1.06 (***)	1.07 (***)	1.08 (***)	1.07 (***)
STAT6	ns	1.07 (**)	0.73 (***)	0.71 (***)	0.72 (***)	0.72 (***)	0.72 (***)
Marker Genes							
CDX1	0.72 (***)	0.88 (***)	0.70 (***)	0.64 (***)	0.62 (***)	0.65 (***)	0.65 (***)
SPP1	1.56 (***)	1.18 (*)	1.72 (***)	2.98 (***)	3.14 (***)	3.54 (***)	2.83 (***)
KIAA1199	3.15 (***)	7.32 (***)	4.40 (***)	4.79 (***)	4.05 (***)	4.68 (***)	4.48 (***)

Supplementary Table 3. Linear FC values of significantly regulated SOCS and STAT family genes as well as marker genes compared to normal colorectal mucosa samples. linear FC=1, n: normal tissue array controls=103; n: total arrays=831; *up-regulated genes (grey); down-regulated genes (white); (ns) not significant. CRC-A to CRC-D: different CRC Dukes stages; CRC-all: all the CRC samples pooled together;* * FDR < 0.05, ** FDR < 0.01, *** FDR<0.001.