

Supplementary Methods

Purification of intestinal epithelial cells

Samples were washed three times in Hank's Balanced Salt Solution (HBSS), followed by enzyme digestion using a mix of liberase and hyaluronidase in HBSS for 45 min at 37 °C. The cell suspension was passed through a 40 µM sieve, spun down at 1500 rpm at 4 °C for 7 min and re-suspended in phosphate-buffered saline (PBS) containing 10 % bovine serum albumin (BSA) and 100 IU/ml DNase. Cells were then stained with anti-CD326 magnetic microbeads and Fc-Receptor block for 30 min at 4 °C. A magnetic-associated, automated cell separation system (MACS, Miltenyi Biotec) was used to positively select for CD326+ cells. Sorted cells were re-suspended in RLT Plus lysis buffer (Qiagen) supplemented with 1 % β-Mercaptoethanol, passed through a Qiagen shredder column and stored at -80 °C until further processing.

T-cell contamination was assessed by flow cytometry with BD LSRFortessa (BD Bioscience) using FITC anti-human TCR α/β (BioLegend) with additional detection of dead cells by Zombie Aqua Fixable Viability Kit (BioLegend).

Bioinformatic analyses

DNA methylation data analyses: Raw Illumina Infinium HumanMethylation450 BeadChip data (i.e. IDAT files) were imported into R software for statistical analysis and the Bioconductor™ packages *minfi*¹ (and the annotation databases *IlluminaHumanMethylation450kmanifest*)² and *limma* were used for normalization and the majority of downstream analysis including generation of multidimensional scaling (MDS) plots and hierarchical clustering analysis. Imported IDAT files were background corrected and SWAN-corrected³ (subset-quantile-within array-normalization). Probes located on X and Y-chromosomes and probes with failed detection p-value (i.e. p > .001) were excluded. M-values (defined as the log2 ratio of

methylated probe intensity to the unmethylated probe intensity) were used for hierarchical clustering (ie. Euclidian distance of M-values with “ward” clustering method) and differential methylation analysis (as outlined below).

Distribution of unmethylated, partially and fully methylated probes was assessed using the *lumi*⁴ package as described previously⁵. This function calls the methylation status of each probe as either “unmethylated,” “marginal” (named as “partially methylated”) or “methylated.” Differential methylated positions (DMPs) were calculated on M-values using *limma*⁶ by fitting a linear model for each gene, computing estimated coefficients, standard errors for the contrast “Paediatric-Foetal” or “IBD-Control” and log-odds of differential expression by empirical Bayes moderation of the standard errors. Significantly different methylation positions were filtered out if the FDR-adjusted p-value < .01 and contrast log2 fold change greater than ±1.5.

DMPs were numerically grouped as differentially methylated or non-differentially methylated and ran in the *DMRfinder*⁷ grouping ≥ 3 differentially methylated positions with an interposition distance of <1kb and a maximum mismatch of 3 non-differentially methylated positions. DMRs were then converted into a RangedData object and annotated using the *ChIPpeakanno* Bioconductor package⁸ to the gene with nearest transcription start site (TSS).

Identification of rDMRs: Following identification and annotation of significantly differentially methylated regions (DMRs) and differentially expressed transcripts, rDMRs were defined as the overlap of both groups according to their unique gene symbol annotation (according to Ensembl database).

The significance of overlapping DMPs derived from the comparison between foetal and paediatric as well as IBD versus control datasets was calculated using a hypergeometric test

Gene expression data analyses: Raw Affymetrix data (i.e. CEL) files were read into R using the *affy*⁹ Bioconductor package. Data were normalized using the variance-stabilizing normalization algorithm, while the expression signal from probe sets representing exons was

summarized using robust multi-array analysis. These exon-level probe sets were mapped to known transcripts using *hugene10sttranscriptcluster.db*¹⁰. Differentially expressed genes were identified with *limma*⁶ in the same manner as for DMPs and the same significance levels for the contrast paediatric versus foetal (FDR adjusted $P < .01$ and log₂ fold-change $> \pm 1.5$).

Gene Expression primers

Target	Forward primer [5'-3']	Reverse primer [5'-3']
GAPDH	AGGTCGGAGTCACCGGATT	TGGAAGATGGTGATGGGATT
PIGR	CTGAGGAACAAGGTGGAAGC	CAAATCCCTGGAGTTCTCG
MUC2	GATTCGAAGTGAAGAGCAAG	CACTGGAGGAATAACTGG
TLR3	CCACACACTCCCTGATGAA	TGCAGTCAGCAACTTCATGG
IL6R	CTGGAAACTATTATGCTACC	GACTGTTCTGAAACTTCCTC
TET1	GAAAAGAGAGGGCTGCGATG	TGCACGGTCTCAGTGTACT
SLC5A1	ATCTATATTAAGGCTGGGTG	TCTTGGTGAATGTAGAGC

Pyrosequencing primers

GB=gene body, PR=promoter, [btn]=biotinylated

Name	Forward primer [5-3]	Reverse primer [5-3]	Sequencing primer
IL6R	GTTTGAGAGGAGTAGTGGGTAGAA	[btn]-ACCCCATTACCCACTAAAATCAACC	GTTGGGTAGAAAGATTG
MUC2	GTTTTTTGGTAGGGTTATATATGAG	[btn]-AACCTATTCCTAACTAACCTACTAC	GGAGAGTAGATTTGGG
PIGR GB	GATTTATGTTAGTTGGAGATAAAAGT	[btn]-TTAAAAAAATTAAAACCTAACAAACACACCT	ATTGTTTTAGTATTGTATAGG
PIGR PR	AGATAGGGAAGGAGGTGTTA	[btn]-TACCAAACCCCTTTACCAAT	ATTTTATTTAGTAGTTAGT
SGLT1	TGGGAGTATAGTGGGTTTTG	[btn]-AAAAAAACACCCACTAAACTATTAAC	GGTATTATTTGGTTG
TET1	AGATTTGGAGAGAGAATAGGATTAGTA	[btn]-ATACTCAAATAACTATTACCCCTACT	GGAGAGAGAATAGGATTAGGTATA
TLR3 GB	ATTTTTTATTTATTGTTGGG	[btn]-ACACAAAAATTCCACCCAATACTACA	TTTTTGAGAGTTAGTAGT
TLR3 PR	AGTTAATTGAATTGGGTATTGA	[btn]-TAAAAACCAATCCCCTACT	AATTTTTGGGTATATTGATT

Cloning primers

Target	Forward primer [5'-3']	Reverse primer [5'-3']	Restriction pair
PIGR	GAAGATCTGGCTTCACTTTGTC	CCCAAGCTTTCTCTCCCGTTGA	BglIII, HindIII
MUC2	GAAGATCTCCCACCATGAGTCAG	CCCAAGCTT GTGCTGCTCTCTC	BglIII, HindIII
TLR3	AAAAGTGCAGAACCACTCACCTC	CATGCCATGGGGATGACTGCTAG	PstI, NcoI

Antibodies used for Immunofluorescence

Host	Antigen	Supplier	Product number	Dilution
rabbit	MUC2	abcam	ab134119	1/200
rabbit	TLR3	abcam	ab62566	1/500
rabbit	PIGR	abcam	ab96196	1/200
goat	rabbit IgG	Life Technologies	R6394	1/1000
donkey	goat IgG	SantaCruz Biotechnologies	sc-2024	1/1000

Details of paediatric control and IBD samples

Patient#	Gender	Disease	Disease	Age	Segment	Macroscopic Inflammation score	Histological Inflammation score
1	Male	Control	Control	13	AC	0	0
1	Male	Control	Control	13	SC	0	0
7	Female	Control	Control	14	AC	0	0
7	Female	Control	Control	14	SC	0	0
23	Male	Control	Control	14	AC	0	0
23	Male	Control	Control	14	SC	0	0
39	Male	Control	Control	14	AC	0	0
39	Male	Control	Control	14	SC	0	0
56	Female	Control	Control	13	AC	0	0
56	Female	Control	Control	13	SC	0	0
28	Female	IBD	UC	14	AC	2	2
28	Female	IBD	UC	14	SC	0	0
6	Male	IBD	UC	12	AC	0	1
6	Male	IBD	UC	12	SC	2	3
24	Female	IBD	UC	14	AC	0	2
24	Female	IBD	UC	14	SC	0	2
47	Male	IBD	UC	13	AC	1	2
47	Male	IBD	UC	13	SC	1	2
40	Male	IBD	UC	14	AC	1	1
40	Male	IBD	UC	14	SC	2	1
35	Male	IBD	CD	13	AC	2	2
35	Male	IBD	CD	13	SC	1	0
13	Male	IBD	CD	13	AC	0	0
13	Male	IBD	CD	13	SC	0	0
26	Male	IBD	CD	13	AC	2	1
26	Male	IBD	CD	13	SC	0	1
34	Female	IBD	CD	13	AC	0	0
34	Female	IBD	CD	13	SC	2	2
41	Female	IBD	CD	13	AC	2	1
41	Female	IBD	CD	13	SC	1	1

IBD=Inflammatory Bowel Disease, UC=Ulcerative Colitis, CD=Crohn's Disease, AC=Ascending Colon, SC=Sigmoid Colon

Supplementary Methods: References

1. Aryee MJ, Jaffe AE, Corrada-Bravo H, et al. Minfi: a flexible and comprehensive Bioconductor package for the analysis of Infinium DNA methylation microarrays. *Bioinformatics* (Oxford, England) 2014;30:1363-9.
2. Hansen K, Aryee M. IlluminaHumanMethylation450kmanifest.
3. Maksimovic J, Gordon L, Oshlack A. SWAN: Subset-quantile within array normalization for illumina infinium HumanMethylation450 BeadChips. *Genome biology* 2012;13:R44-R44.
4. Du P, Kibbe WA, Lin SM. lumi: a pipeline for processing Illumina microarray. *Bioinformatics* (Oxford, England) 2008;24:1547-8.
5. Zilbauer M, Rayner TF, Clark C, et al. Genome-wide methylation analyses of primary human leukocyte subsets identifies functionally important cell-type-specific hypomethylated regions. *Blood* 2013;122:e52-60.
6. Smyth G. limma, 2005:pp. 397-420.
7. Slieker RC, Bos SD, Goeman JJ, et al. Identification and systematic annotation of tissue-specific differentially methylated regions using the Illumina 450k array. *Epigenetics Chromatin* 2013;6:26.
8. Zhu LJ, Gazin C, Lawson ND, et al. ChIPpeakAnno: a Bioconductor package to annotate ChIP-seq and ChIP-chip data. *BMC bioinformatics* 2010;11:237-237.
9. Gautier L, Cope L, Bolstad BM, et al. affy--analysis of Affymetrix GeneChip data at the probe level. *Bioinformatics* (Oxford, England) 2004;20:307-15.
10. MacDonald J. hugene10sttranscriptcluster.db.

Supplementary Table 1: Genomic location of identified regulatory Differentially Methylated Regions (rDMRs) mapped on the reference human genome (hg19). DMRs were annotated using Bioconductor package *ChIPpeakAnno*, providing start and end site, chromosomal locations and attributed gene (feature) based on nearest transcription start site.

DMR start s of signif icant	end	width	strand	feature	start position	end position	inside Feature	distance to feature (nearest TSS)	symbol	genename	
1	19599516 are fr 27189298	19600817 27190330	1302 1033	- +	ENSG00000211454 ENSG00000175793	19592478 27189653	19600688 27190947	overlapStart overlapStart	1172 -355	AKR7L SFN	aldo-keto reductase family 7-like stratin
1	31845904	31846110	207	-	ENSG00000121769	31838472	31849697	inside	3793	FABP3	fatty acid binding protein 3, muscle and heart (mammary-derived growth inhibitor)
1	38022359	38022718	360	+	ENSG00000163879	38022520	38032458	overlapStart	-161	DNAL1	dynein, axonemal, light intermediate chain 1
1	47655599	47656423	825	-	ENSG00000162366	47649265	47656716	inside	1117	PDZK1IP1	PDZK1 interacting protein 1
1	64937345	64937528	184	+	ENSG00000158966	64936428	65158741	inside	917	CACHD1	cache domain containing 1
1	79085250	79086197	948	+	ENSG00000137959	79085607	79108484	overlapStart	-357	IFI44L	interferon-induced protein 44-like
1	79472282	79472452	171	-	ENSG00000162618	79355449	79472495	inside	213	ELTD1	EGF, latrophilin and seven transmembrane domain containing 1
1	85512957	85513191	235	-	ENSG00000055732	85483765	85514182	inside	1225	MCOLN3	mucolipin 3
1	86047227	86047433	207	+	ENSG00000142871	86046444	86049645	inside	783	CYR61	cysteine-rich, angiogenic inducer, 61
1	89664338	89664782	445	-	ENSG00000162654	89646831	89664615	overlapStart	277	GBP4	guanylate binding protein 4
1	110254662	110255096	435	+	ENSG00000134201	110254877	110260888	overlapStart	-215	GSTM5	glutathione S-transferase mu 5
1	114429815	114430903	1089	-	ENSG00000188761	114420790	114430203	overlapStart	388	BCL2L15	BCL2-like 15
1	114521775	114522185	411	+	ENSG00000116774	114522063	114524876	overlapStart	-288	OLFM13	olfactomedin-like 3
1	117529619	117530099	391	+	ENSG00000134256	117544382	117579167	upstream	-14763	CD101	CD101 molecule
1	145714010	145714143	134	-	ENSG00000117281	145695798	145715614	inside	1604	CD160	CD160 molecule
1	151343840	151346400	2561	-	ENSG00000143436	151336778	151345209	overlapStart	1369	SELENBP1	selenom binding protein 1
1	151804260	151805634	1375	-	ENSG00000143365	151778547	151804348	overlapStart	88	RORC	RAR-related orphan receptor C
1	154377091	154377429	339	+	ENSG00000160712	154377669	154441926	upstream	-578	IL6R	interleukin 6 receptor
1	156261200	156261403	204	-	ENSG00000189815	156248142	156265463	inside	4263	C1orf85	chromosome 1 open reading frame 85
1	160854954	160855148	195	-	ENSG00000179914	160846329	160854960	overlapStart	6	ITLN1	inteletin 1 (galactofuranose binding)
1	161193393	161195180	1788	-	ENSG00000158874	161192082	161193421	overlapStart	28	APOA2	apolipoprotein A-II
1	207119784	207120628	845	-	ENSG00000162896	207101863	207119811	overlapStart	27	PIGR	polymeric immunoglobulin receptor
1	217311993	217312478	486	-	ENSG00000196482	216676588	217311097	upstream	-896	ESRRG	estrogen-related receptor gamma
1	217313699	217314284	586	-	ENSG00000196482	216676588	217311097	upstream	-2602	ESRRG	estrogen-related receptor gamma
2	1690592	1691165	574	-	ENSG00000130508	1635659	1748624	inside	58032	PXDN	peroxidasin homolog (Drosophila)
2	61371880	61372256	377	-	ENSG00000212978	61368913	61372104	overlapStart	224	LOC339803	uncharacterized LOC339803
2	79347474	79347699	226	+	ENSG00000115386	79347488	79350545	overlapStart	-14	REG1A	regenerating islet-derived 1 alpha
2	85361959	85362480	522	+	ENSG000001522284	85360533	85357511	inside	1426	TCF7L1	transcription factor 7-like 1 (T-cell specific, HMG-box)
2	87018944	87018966	23	-	ENSG00000153563	87011729	87035519	inside	16575	CD8A	CD8a molecule
2	102608155	102608349	195	+	ENSG00000115590	102608306	102645006	overlapStart	-151	IL1R2	interleukin 1 receptor, type II
2	103239106	103240272	1167	+	ENSG00000115616	103236166	103327777	inside	2940	SLC9A2	solute carrier family 9, subfamily A (NHE2, cation proton antiporter 2), member 2
2	108993737	108994528	792	+	ENSG00000198075	108994367	109006667	overlapStart	-630	SULT1C4	sulfotransferase family, cytosolic, 1C, member 4
2	186603398	186603639	242	+	ENSG00000188738	186603622	186698017	overlapStart	-224	FSIP2	fibrous sheath interacting protein 2
2	190044504	190044983	480	-	ENSG00000204262	189896622	190044605	overlapStart	101	COL5A2	collagen, type V, alpha 2
2	198540518	198540621	104	-	ENSG00000162944	198435524	198540769	inside	251	RFTN2	raftlin family member 2
2	202047246	202048100	855	+	ENSG0000003400	202047604	202094129	overlapStart	-358	CASP10	caspase 10, apoptosis-related cysteine peptidase
2	206551364	206551844	481	+	ENSG00000118257	206546714	206662857	inside	4650	NRP2	neuropilin 2
2	216299448	216299856	409	-	ENSG00000115414	216225163	216300895	inside	1447	FN1	fibronectin 1
2	233877857	233877814	858	-	ENSG00000066248	233743396	233877982	overlapStart	125	NGEF	neuronal guanine nucleotide exchange factor
2	234526077	234526295	219	+	ENSG00000242366	234526291	234681956	overlapStart	-214	UGTA1A1	UDP glucuronosyltransferase 1 family, polypeptide A1
2	242710939	242711046	108	+	ENSG00000154252	242716240	242750403	upstream	-5301	GAL3ST2	galactose-3-O-sulfotransferase 2
2	242715549	242716559	1011	+	ENSG00000154252	242716240	242750403	overlapStart	-691	GAL3ST2	galactose-3-O-sulfotransferase 2
3	49907468	49907692	225	-	ENSG00000164076	49895421	49907655	overlapStart	187	CAMKV	CaM kinase-like vesicle-associated
3	52568323	52569169	847	-	ENSG00000162868	52558386	52569070	overlapStart	747	NT5DC2	5'-nucleotidase domain containing 2
3	58652346	58653593	1248	-	ENSG00000198643	58619673	58652575	overlapStart	229	FAM3D	family with sequence similarity 3, member D
3	108475765	108476878	1114	-	ENSG00000163515	108462271	108476231	overlapStart	466	RETNLB	resistin like beta
3	118892125	118892330	116	+	ENSG00000114638	118892364	118924000	upstream	-149	UPK1B	uroplakin 1B
3	119422161	119422359	199	+	ENSG00000183833	119421869	119485949	inside	292	MAATS1	MYCBP-associated, testis expressed 1
3	139257713	139257907	195	-	ENSG00000114115	139236276	139258671	inside	958	RBP1	retinol binding protein 1, cellular
3	164911744	164912664	921	-	ENSG00000121871	164904508	164914897	inside	3153	SLTRK3	SLT1 and NTRK-like family, member 3
3	187009486	187010344	859	-	ENSG00000127241	186935942	187009810	overlapStart	324	MASP1	mannan-binding lectin serine peptidase 1 (C4/C2 activating component of Ra-reactive factor)
4	15480643	15481269	627	+	ENSG00000048342	15471489	15603180	inside	9154	CC2D2A	coiled-coil and C2 domain containing 2A
4	40752838	40753247	410	+	ENSG00000179299	40751914	40812002	inside	924	NSUN7	NOP2/Sun domain family, member 7
4	41646293	41646672	380	-	ENSG00000109132	41746099	41750987	downstream	104694	PHOX2B	paired-like homeobox 2b
4	41746947	41749443	2497	-	ENSG00000109132	41746099	41750987	inside	4040	PHOX2B	paired-like homeobox 2b
4	100736658	100738011	1354	+	ENSG00000070190	100737981	100791344	overlapStart	-1323	DAPP1	dual adaptor of phosphotyrosine and 3-phosphoinositides
4	121991345	121991672	328	-	ENSG00000173376	121995678	121993569	inside	2224	NDNF	neuron-derived neurotrophic factor
4	151500192	151501739	1548	+	ENSG00000181541	151503077	151505843	upstream	-2885	MAB21L2	mab-21-like 2 (<i>C. elegans</i>)
4	151502935	151505467	2533	+	ENSG00000181541	151503077	151505843	overlapStart	-142	MAB21L2	mab-21-like 2 (<i>C. elegans</i>)
4	155533784	155534149	366	-	ENSG00000171557	155525286	155534119	overlapStart	335	FGG	fibrinogen gamma chain
4	156298166	156298332	167	-	ENSG00000164114	156263810	156298122	upstream	-44	MAP9	microtubule-associated protein 9
4	157996959	157997086	128	+	ENSG00000109738	157997277	158093242	upstream	-318	GLRB	glycine receptor, beta
4	186990006	186990425	420	+	ENSG00000164342	186990309	187006250	overlapStart	-303	TLR3	toll-like receptor 3
4	188916865	188918218	1354	-	ENSG00000179059	188916925	188926199	overlapStart	-60	ZFP42	ZFP42 zinc finger protein
5	32712237	32713112	876	+	ENSG00000113389	32709513	32787252	inside	2724	NPR3	natriuretic peptide receptor 3
5	40680670	40682333	1664	+	ENSG00000171522	40680033	40693837	inside	637	PTGER4	prostaglandin E receptor 4 (subtype EP4)
5	4339653	43397572	620	-	ENSG00000151882	43376747	43412493	inside	15540	CCL28	chemokine (C-C motif) ligand 28
5	43411929	43413879	1951	-	ENSG00000151882	43376747	43412493	overlapStart	564	CCL28	chemokine (C-C motif) ligand 28
5	71014918	71015523	606	+	ENSG00000164326	71014994	71016875	overlapStart	-76	CARTPT	CART prepropeptide
5	74162771	74162880	110	-	ENSG00000198780	74073399	74162663	upstream	-108	FAM169A	family with sequence similarity 169, member A
5	127871927	127873106	1180	-	ENSG00000138829	127593601	127873735	inside	1808	FBN2	fibrillin 2
5	127874466	127874825	360	-	ENSG00000138829	127593601	127873735	upstream	-731	FBN2	fibrillin 2

5	149792390	149792840	451	-	ENSG0000019582	149781206	149792332	upstream	-58	CD74	CD74 molecule, major histocompatibility complex, class II invariant chain
5	150284416	150284600	185	-	ENSG00000145908	150273961	150284540	overlapStart	124	ZNF300	zinc finger protein 300
6	5994743	5995150	408	-	ENSG00000124785	5998232	6007200	downstream	12457	NRN1	neuritin 1
6	6004686	6004897	212	-	ENSG00000124785	5998232	6007200	inside	2514	NRN1	neuritin 1
6	6006398	6006770	373	-	ENSG00000124785	5998232	6007200	inside	802	NRN1	neuritin 1
6	11044877	11044894	18	-	ENSG00000197977	10980992	11044547	upstream	-330	ELOVL2	ELOVL fatty acid elongase 2
6	25218680	25218855	176	-	ENSG00000168405	25081295	25218698	overlapStart	18	CMAHP	cytidine monophospho-N-acetylneuraminc acid hydroxylase, pseudogene
6	26440101	26440610	510	+	ENSG00000111801	26440700	26453643	upstream	-599	BTN3A3	butyrophilin, subfamily 3, member A3
6	29527870	29528119	250	-	ENSG00000213886	29523292	29527702	upstream	-168	UBD	ubiquitin D
6	29690766	29690893	128	+	ENSG00000204642	29690552	29706305	inside	214	HLA-F	major histocompatibility complex, class I, F
6	30079203	30079307	105	-	ENSG00000204616	30070674	30080883	inside	1680	TRIM31	tripartite motif containing 31
6	30080495	30081408	914	-	ENSG00000204616	30070674	30080883	overlapStart	388	TRIM31	tripartite motif containing 31
6	30458586	30458730	145	+	ENSG00000204592	30457231	30461982	inside	1355	HLA-E	major histocompatibility complex, class I, E
6	30459512	30460244	733	+	ENSG00000204592	30457231	30461982	inside	2281	HLA-E	major histocompatibility complex, class I, E
6	31238245	31238751	507	-	ENSG00000204525	31236526	31239907	inside	1662	HLA-C	major histocompatibility complex, class I, C
6	31239063	31239158	96	-	ENSG00000204525	31236526	31239907	inside	844	HLA-C	major histocompatibility complex, class I, C
6	31466722	31466821	100	+	ENSG00000204516	31465863	31478901	inside	859	MICB	MHC class I polypeptide-related sequence B
6	32407289	32407689	401	+	ENSG00000204287	32407619	32412823	overlapStart	-330	HLA-DRA	major histocompatibility complex, class II, DR alpha
6	32798417	32798510	94	-	ENSG00000204267	32781544	32806599	inside	8182	TAP2	transporter 2, ATP-binding cassette, sub-family B (MDR/TAP)
6	32800429	32800541	113	-	ENSG00000204267	32781544	32806599	inside	6170	TAP2	transporter 2, ATP-binding cassette, sub-family B (MDR/TAP)
6	32812933	32813154	222	-	ENSG00000204264	32808494	32812480	upstream	-453	PSMB8	proteasome (prosome, macropain) subunit, beta type, 8
6	32819858	32820586	729	-	ENSG00000168394	32812986	32821755	inside	1897	TAP1	transporter 1, ATP-binding cassette, sub-family B (MDR/TAP)
6	32822346	32823116	771	-	ENSG00000168394	32812986	32821755	upstream	-591	TAP1	transporter 1, ATP-binding cassette, sub-family B (MDR/TAP)
6	32825040	32825360	321	-	ENSG00000168394	32812986	32821755	upstream	-3285	TAP1	transporter 1, ATP-binding cassette, sub-family B (MDR/TAP)
6	32828996	32829208	213	-	ENSG00000168394	32812986	32821755	upstream	-7241	TAP1	transporter 1, ATP-binding cassette, sub-family B (MDR/TAP)
6	32920735	32921200	466	-	ENSG00000242574	32902406	32920899	overlapStart	164	HLA-DMB	major histocompatibility complex, class II, DM beta
6	32942710	32942808	99	-	ENSG00000204257	32916390	32938493	upstream	-4217	HLA-DMA	major histocompatibility complex, class II, DM alpha
6	32945234	32945423	190	-	ENSG00000204257	32916390	32938493	upstream	-6741	HLA-DMA	major histocompatibility complex, class II, DM alpha
6	33047944	33048919	976	-	ENSG00000231389	33032346	33048552	overlapStart	608	HLA-DPA1	major histocompatibility complex, class II, DP alpha 1
6	33264834	33265133	300	-	ENSG00000237441	33259431	33267101	inside	2267	RGL2	ral guanine nucleotide dissociation stimulator-like 2
6	33267989	33267996	8	-	ENSG00000237441	33259431	33267101	upstream	-888	RGL2	ral guanine nucleotide dissociation stimulator-like 2
6	34498918	34499504	587	-	ENSG00000124664	34505579	34524091	downstream	25173	SPDEF	SAM pointed domain containing ETS transcription factor
6	52858459	52859107	649	-	ENSG00000170899	52842751	52860176	inside	1717	GSTA4	glutathione S-transferase alpha 4
7	1022471	1022675	205	+	ENSG00000073067	1022835	1029276	upstream	-364	CYP2W1	cytochrome P450, family 2, subfamily W, polypeptide 1
7	2551598	2551996	399	+	ENSG00000106003	2552163	2568811	upstream	-565	LFNG	LFNG O-fucosylpeptide 3-beta-N-acetylglucosaminyltransferase
7	2557028	2557358	331	+	ENSG00000106003	2552163	2568811	inside	4865	LFNG	LFNG O-fucosylpeptide 3-beta-N-acetylglucosaminyltransferase
7	2564966	2566750	1785	+	ENSG00000106003	2552163	2568811	inside	12803	LFNG	LFNG O-fucosylpeptide 3-beta-N-acetylglucosaminyltransferase
7	5292696	5293333	638	+	ENSG00000164638	5314000	5343696	upstream	-21304	SLC29A4	solute carrier family 29 (equilibrative nucleoside transporter), member 4
7	30950813	30951801	989	+	ENSG00000240583	30951468	30965131	overlapStart	-655	AQP1	aquaporin 1 (Colton blood group)
7	44580809	44581105	297	-	ENSG0000015520	44552134	44580914	overlapStart	105	NPC1L1	NPC1-like 1
7	48129797	48130197	401	+	ENSG00000183696	48128225	48148330	inside	1572	UPP1	uridine phosphorylase 1
7	92747308	92747455	148	-	ENSG00000205413	92728829	92747336	overlapStart	28	SAMD9	sterile alpha motif domain containing 9
7	99277394	99277978	585	-	ENSG00000106258	99245817	99277619	overlapStart	225	CYP3A5	cytochrome P450, family 3, subfamily A, polypeptide 5
7	102574445	102574504	60	+	ENSG00000128606	102553438	102585396	inside	21007	LRRC17	leucine rich repeat containing 17
7	134832221	134833299	1079	+	ENSG00000146859	134832824	134850650	overlapStart	-603	TMEM140	transmembrane protein 140
7	150211761	150211939	179	+	ENSG00000179144	150211918	150218161	overlapStart	-157	GIMAP7	GTPase, IMAP family member 7
8	24771326	24773060	1735	+	ENSG00000104722	24770525	24776606	inside	801	NEFM	neurofilament, medium polypeptide
8	30300142	30300306	165	+	ENSG00000157110	30241944	30429734	inside	58198	RBPM5	RNA binding protein with multiple splicing
8	41165699	41166738	1040	-	ENSG00000104432	41119483	41166992	inside	1293	SFRP1	secreted frizzled-related protein 1
8	80523320	80523413	94	+	ENSG00000104435	80523361	80578313	overlapStart	-41	STMN2	stathmin-like 2
8	98289745	98290574	830	-	ENSG00000180543	98285717	98290176	overlapStart	431	TSPY5L	TSPY-like 5
8	145048235	145048767	533	-	ENSG00000178209	144989321	145049543	inside	1308	PLEC	plectin
8	145051668	145052304	637	-	ENSG00000178209	144989321	145049543	upstream	-2125	PLEC	plectin
8	145727318	145728526	1209	+	ENSG00000167701	145729465	145732554	upstream	-2147	GPT	glutamic-pyruvate transaminase (alanine aminotransferase)
8	145729106	145729799	694	+	ENSG00000167701	145729465	145732554	overlapStart	-359	GPT	glutamic-pyruvate transaminase (alanine aminotransferase)
9	112970404	112970590	187	-	ENSG00000188959	112952328	112970469	overlapStart	65	C9orf152	chromosome 9 open reading frame 152
9	120466493	120466837	345	+	ENSG00000136869	120466610	120479149	overlapStart	-117	TLR4	toll-like receptor 4
10	70319645	70319783	139	+	ENSG00000138336	70320413	70454239	upstream	-768	TET1	tet methylcytosine dioxygenase 1
10	70321554	70322874	1321	+	ENSG00000138336	70320413	70454239	inside	1141	TET1	tet methylcytosine dioxygenase 1
10	85952296	85953798	1503	+	ENSG00000188373	85933494	85945050	overlapStart	-1198	C10orf99	chromosome 10 open reading frame 99
10	85956635	85958834	2200	+	ENSG00000148600	85954410	85979377	inside	2225	CDHR1	cadherin-related family member 1
10	90611782	90613015	1234	-	ENSG00000152766	90581889	90611575	upstream	-207	ANKRD22	ankyrin repeat domain 22
10	90749920	90750176	257	+	ENSG00000026103	90749226	90775542	inside	694	FAS	Fas cell surface death receptor
10	91061115	91061583	469	+	ENSG00000119922	91061712	91069033	upstream	-597	IFIT2	interferon-induced protein with tetratricopeptide repeats 2

10	114134550	114136073	1524	+	ENSG00000197142	114133776	114188138	inside	774	ACSL5	acyl-CoA synthetase long-chain family member 5
10	133793477	133794454	978	-	ENSG00000176171	133781578	133795435	inside	1958	BNIP3	BCL2/adenovirus E1B 19kDa interacting protein 3
11	1060659	1060710	52	+	ENSG00000198788	1074875	1104416	upstream	-14216	MUC2	mucin 2, oligomeric mucus/gel-forming
11	1073496	1073641	146	+	ENSG00000198788	1074875	1104416	upstream	-1379	MUC2	mucin 2, oligomeric mucus/gel-forming
11	2170831	2171026	196	-	ENSG00000167244	2150342	2170833	overlapStart	2	IGF2	insulin-like growth factor 2 (somatomedin A)
11	2481206	2481965	760	+	ENSG00000053918	2466221	2870221	inside	14985	KCNQ1	potassium voltage-gated channel, KQT-like subfamily, member 1
11	2482223	2482401	179	+	ENSG00000053918	2466221	2870221	inside	16002	KCNQ1	potassium voltage-gated channel, KQT-like subfamily, member 1
11	2485050	2485409	360	+	ENSG00000053918	2466221	2870221	inside	18829	KCNQ1	potassium voltage-gated channel, KQT-like subfamily, member 1
11	2548920	2548989	70	+	ENSG00000053918	2466221	2870221	inside	82699	KCNQ1	potassium voltage-gated channel, KQT-like subfamily, member 1
11	2571399	2571525	127	+	ENSG00000053918	2466221	2870221	inside	105178	KCNQ1	potassium voltage-gated channel, KQT-like subfamily, member 1
11	2596300	2596606	307	+	ENSG00000053918	2466221	2870221	inside	130079	KCNQ1	potassium voltage-gated channel, KQT-like subfamily, member 1
11	2612781	2612876	96	+	ENSG00000053918	2466221	2870221	inside	146560	KCNQ1	potassium voltage-gated channel, KQT-like subfamily, member 1
11	2920617	2922068	1452	+	ENSG00000110628	2920951	2946476	overlapStart	-334	SLC22A18	solute carrier family 22, member 18
11	5248218	5248566	349	-	ENSG00000244734	5246694	5250625	inside	2407	HBB	hemoglobin, beta
11	27015592	27015991	400	+	ENSG00000176971	27015628	27018630	overlapStart	-36	FIBIN	fin bud initiation factor homolog (zebrafish)
11	30605411	30605797	387	-	ENSG00000066382	30406040	30607930	inside	2519	MPPED2	metallophosphoesterase domain containing 2
11	36422377	36422557	181	+	ENSG00000135362	36397555	36486753	inside	24822	PRR5L	proline rich 5 like
11	60869760	60869969	210	+	ENSG00000110448	60869930	60895319	overlapStart	-170	CD5	CD5 molecule
11	633040948	63304614	517	+	ENSG00000133221	63304273	63313929	overlapStart	-175	RARRE3	retinoic acid receptor responder (tazarotene induced) 3
11	68607622	68607737	116	-	ENSG00000110090	68522090	68609399	inside	1777	CPT1A	carnitine palmitoyltransferase 1A (liver)
11	68621650	68622263	614	-	ENSG00000110090	68522090	68609399	upstream	-12251	CPT1A	carnitine palmitoyltransferase 1A (liver)
11	75428198	75429059	862	+	ENSG00000166391	75428888	75442660	overlapStart	-690	MOGAT2	monoacylglycerol O-acyltransferase 2
11	87908783	87908938	156	-	ENSG00000123892	87846448	87908635	upstream	-148	RAB38	RAB38, member RAS oncogene family
11	102187898	102187976	79	+	ENSG0000023445	102188194	102208448	upstream	-296	BIRC3	baculoviral IAP repeat containing 3
11	104915759	104916331	573	-	ENSG00000204397	104912053	104916051	overlapStart	292	CARD16	caspase recruitment domain family, member 16
11	114548872	114549291	420	+	ENSG00000204361	114549200	114578285	overlapStart	-328	NXPE2	neurexophilin and PC-esterase domain family, member 2
11	117069780	117070046	267	+	ENSG00000149591	117070040	117075507	overlapStart	-260	TAGLN	transgelin
11	124621829	124622815	987	-	ENSG00000019102	124617368	124622134	overlapStart	305	VSIG2	V-set and immunoglobulin domain containing 2
12	3862575	3862597	23	-	ENSG00000130038	3724494	3862366	upstream	-209	EFCAB4B	EF-hand calcium binding domain 4B
12	4488749	4488893	145	-	ENSG00000118972	4477393	4488894	inside	145	FGF23	fibroblast growth factor 23
12	6473299	6473643	345	-	ENSG00000111319	6456015	6484715	inside	11416	SCNN1A	sodium channel, non-voltage-gated 1 alpha subunit
12	6484219	6484607	389	-	ENSG00000111319	6456015	6484715	inside	496	SCNN1A	sodium channel, non-voltage-gated 1 alpha subunit
12	6486639	6487080	442	-	ENSG00000111319	6456015	6484715	upstream	-1924	SCNN1A	sodium channel, non-voltage-gated 1 alpha subunit
12	13348429	13349724	1296	+	ENSG00000134531	13349602	13369708	overlapStart	-1173	EMP1	epithelial membrane protein 1
12	49687715	49688316	602	+	ENSG00000135406	49687485	49692465	inside	230	PRPH	peripherin
12	53497074	53497306	233	+	ENSG00000167780	53497274	53518323	overlapStart	-200	SOAT2	sterol O-acyltransferase 2
12	54412506	54413384	879	+	ENSG00000197757	54410642	54424607	inside	1864	HOXC6	homeobox C6
12	56329615	56329903	289	+	ENSG00000065357	56324946	56347805	inside	4669	DGKA	diacylglycerol kinase, alpha 80kDa
12	65515276	65515470	195	-	ENSG00000156076	65444047	65515116	upstream	-160	WIF1	WNT inhibitory factor 1
12	65672031	65672174	144	+	ENSG00000174099	65672488	65860678	upstream	-457	MSRB3	methionine sulfoxide reductase B3
12	103355190	103356060	871	+	ENSG00000139352	103351452	103354287	downstream	3738	ASCL1	achaete-scute family bHLH transcription factor 1
12	113343409	113343603	195	+	ENSG00000089127	113344739	113369794	upstream	-1330	OAS1	2'-5'-oligoadenylate synthetase 1, 40/46kDa
12	113415883	113416518	636	+	ENSG00000111335	113416274	113449528	overlapStart	-391	OAS2	2'-5'-oligoadenylate synthetase 2, 69/71kDa
13	20768138	20768560	423	-	ENSG00000165474	20761609	20767037	upstream	-1101	GJB2	gap junction protein, beta 2, 26kDa
13	36050844	36053408	2565	-	ENSG00000180660	36048322	36050832	upstream	-12	MAB21L1	mab-21-like 1 (C. elegans)
13	53602385	53603286	902	+	ENSG00000102837	53602830	53626196	overlapStart	-445	OLFM4	olfactomedin 4
13	113704976	113705742	767	+	ENSG00000057593	113760105	113774995	upstream	-55129	F7	coagulation factor VII (serum prothrombin conversion accelerator)
13	113743564	113744601	1038	+	ENSG00000057593	113760105	113774995	upstream	-16541	F7	coagulation factor VII (serum prothrombin conversion accelerator)
13	113776126	113777013	888	+	ENSG00000126218	113777128	113803843	upstream	-1002	F10	coagulation factor X
14	94576831	94577514	684	+	ENSG00000165949	94577079	94580333	overlapStart	-248	IFI27	interferon, alpha-inducible protein 27
15	35086890	35086967	78	-	ENSG00000159291	35080296	35087911	inside	1021	ACTC1	actin, alpha, cardiac muscle 1
15	37398943	37399798	856	-	ENSG00000134138	37183222	37393500	upstream	-5443	MEIS2	Meis homeobox 2
15	45407818	45410236	2419	-	ENSG00000140279	45384848	45406537	upstream	-1281	DUOX2	dual oxidase 2
15	59908999	59909035	37	+	ENSG00000140297	59903983	59913023	inside	5016	GCNT3	glucosaminyl (N-acetyl) transferase 3, mucin type
15	78933807	78933902	96	-	ENSG00000117971	78916461	78933587	upstream	-220	CHRN8	cholinergic receptor, nicotinic, beta 4 (neuronal)
16	2879998	2880359	362	+	ENSG00000162078	2880170	2882285	overlapStart	-172	ZG16B	zymogen granule protein 16B
16	3067500	3068085	586	-	ENSG00000184697	3064713	3070072	inside	2572	CLDN6	claudin 6
16	3114986	3115809	824	+	ENSG00000085817	31151313	3119668	overlapStart	-327	IL32	interleukin 32
16	23765258	23765381	124	+	ENSG00000166869	23765948	23770272	upstream	-690	CHP2	calcineurin-like EF-hand protein 2
16	28549923	28550637	715	-	ENSG00000176046	28548606	28550495	overlapStart	572	NUPR1	nuclear protein, transcriptional regulator, 1
16	30198370	30198509	140	+	ENSG00000102879	30194892	30200397	inside	3478	CORO1A	coronin, actin binding protein, 1A
16	30485383	30485966	584	+	ENSG0000005844	30483983	30534505	inside	1400	ITGAL	integrin, alpha L (antigen CD11A (p180), lymphocyte function-associated antigen 1; alpha polypeptide)
16	56665855	56666334	480	+	ENSG00000205364	56666534	56667897	upstream	-679	MT1M	metallothionein 1M
16	56669038	56669778	741	+	ENSG00000205364	56666534	56667897	downstream	2504	MT1M	metallothionein 1M
16	66982435	66982803	369	+	ENSG00000172828	66995138	67008999	upstream	-12703	CES3	carboxylesterase 3
16	68676451	68676806	356	+	ENSG00000062038	68678151	68732971	upstream	-1700	CDH3	cadherin 3, type 1, P-cadherin (placental)
16	74734876	74735490	615	-	ENSG00000168404	74705755	74734789	upstream	-87	MLKL	mixed lineage kinase domain-like
17	3847872	3848506	635	-	ENSG00000074370	3822943	3867736	inside	19864	ATP2A3	ATPase, Ca++ transporting, ubiquitous
17	4463911	4464400	490	-	ENSG00000167741	4460224	4463876	upstream	-35	GGT6	gamma-glutamyltransferase 6

17	6659070	6659562	493	+	ENSG00000132530	6659156	6678962	overlapStart	-86	XAF1	XIAP associated factor 1
17	25958267	25958673	407	+	ENSG00000168961	25956824	25976586	inside	1443	LGALS9	lectin, galactoside-binding, soluble, 9
17	26127438	26127542	105	-	ENSG00000007171	26083792	26127555	inside	117	NOS2	nitric oxide synthase 2, inducible
17	37782302	37782685	384	+	ENSG00000131771	37783179	37792879	upstream	-877	PPP1R1B	protein phosphatase 1, regulatory (inhibitor) subunit 1B
17	38346960	38347816	857	+	ENSG00000108352	38333309	38351908	inside	13651	RAPGEFL1	Rap guanine nucleotide exchange factor (GEF)-like 1
17	39019545	39019978	434	-	ENSG00000187242	39017195	39023462	inside	3917	KRT12	keratin 12
17	39041110	39041602	493	-	ENSG00000171431	39030852	39041479	overlapStart	369	KRT20	keratin 20
17	39969264	39970091	828	+	ENSG00000141756	39968962	39979465	inside	302	FKBP10	FK506 binding protein 10, 65 kDa
17	47089952	47091521	1570	+	ENSG00000159217	47074774	47133507	inside	15178	IGF2BP1	insulin-like growth factor 2 mRNA binding protein 1
17	47093489	47094252	764	+	ENSG00000159217	47074774	47133507	inside	18715	IGF2BP1	insulin-like growth factor 2 mRNA binding protein 1
17	47113407	47113596	190	+	ENSG00000159217	47074774	47133507	inside	38633	IGF2BP1	insulin-like growth factor 2 mRNA binding protein 1
17	58226085	58226981	897	+	ENSG00000167434	58227297	58236901	upstream	-1212	CA4	carbonic anhydrase IV
17	73719885	73720840	956	+	ENSG00000132470	73717516	73753898	inside	2369	ITGB4	integrin, beta 4
17	73727879	73728061	183	+	ENSG00000132470	73717516	73753898	inside	10363	ITGB4	integrin, beta 4
17	80289500	80290217	718	-	ENSG00000141574	80278900	80291921	inside	2421	SECTM1	secreted and transmembrane 1
18	56528679	56531159	2481	+	ENSG00000074657	56529832	56653712	overlapStart	-1153	ZNF532	zinc finger protein 532
19	310296	310512	217	-	ENSG00000141934	281048	291435	upstream	-18861	PPAP2C	phosphatidic acid phosphatase type 2C
19	4326975	4327350	376	-	ENSG00000178078	4324041	4338847	inside	11872	STAP2	signal transducing adaptor family member 2
19	4328745	4328818	74	-	ENSG00000178078	4324041	4338847	inside	10102	STAP2	signal transducing adaptor family member 2
19	5838729	5838999	271	-	ENSG00000156413	5830637	5839742	inside	1013	FUT6	fucosyltransferase 6 (alpha (1,3)fucosyltransferase)
19	5846552	5846599	48	-	ENSG00000171124	5842900	5851485	inside	4933	FUT3	fucosyltransferase 3 (galactoside 3(4)-L-fucosyltransferase, Lewis blood group)
19	5851255	5851762	508	-	ENSG00000171124	5842900	5851485	overlapStart	230	FUT3	fucosyltransferase 3 (galactoside 3(4)-L-fucosyltransferase, Lewis blood group)
19	13120987	13123217	2231	+	ENSG00000008441	13106584	13209610	inside	14403	NFIX	nuclear factor I/X (CCAAT-binding transcription factor)
19	13124604	13125851	1248	+	ENSG00000008441	13106584	13209610	inside	18020	NFIX	nuclear factor I/X (CCAAT-binding transcription factor)
19	13127389	13127873	485	+	ENSG00000008441	13106584	13209610	inside	20805	NFIX	nuclear factor I/X (CCAAT-binding transcription factor)
19	15783239	15783848	610	+	ENSG00000186204	15783886	15807984	upstream	-647	CYP4F12	cytochrome P450, family 4, subfamily F, polypeptide 12
19	16045708	16046185	478	-	ENSG00000171903	16023180	16045676	upstream	-32	CYP4F11	cytochrome P450, family 4, subfamily F, polypeptide 11
19	18539756	18539843	88	-	ENSG00000105655	18545625	18548943	downstream	9187	ISYNA1	inositol-3-phosphate synthase 1
19	18543829	18545062	1234	-	ENSG00000105655	18545625	18548943	downstream	5114	ISYNA1	inositol-3-phosphate synthase 1
19	22234992	22235199	208	+	ENSG00000197134	22235266	22273901	upstream	-274	ZNF257	zinc finger protein 257
19	35530755	35531417	663	+	ENSG00000105707	35531410	35557475	overlapStart	-655	HPN	hepsin
19	37096148	37096588	441	+	ENSG00000161298	37095719	37119744	inside	429	ZNF382	zinc finger protein 382
19	40421453	40421743	291	-	ENSG00000090920	40353964	40440533	inside	19080	FCGBP	Fc fragment of IgG binding protein
19	45150513	45150725	213	+	ENSG00000073008	45147098	45169429	inside	3415	PVR	poliovirus receptor
19	45315572	45316682	1111	+	ENSG00000187244	45312338	45324677	inside	3234	BCAM	basal cell adhesion molecule (Lutheran blood group)
19	46917018	46917255	238	-	ENSG00000169515	46914451	46916067	upstream	-951	CCDC8	coiled-coil domain containing 8
19	49685846	49686254	409	+	ENSG00000130529	49661052	49715091	inside	24794	TRPM4	transient receptor potential cation channel, subfamily M, member 4
19	49713645	49714044	400	+	ENSG00000130529	49661052	49715091	inside	52593	TRPM4	transient receptor potential cation channel, subfamily M, member 4
19	57276642	57276917	276	-	ENSG00000198300	57285930	57352075	downstream	75433	PEG3	paternally expressed 3
19	58220080	58220837	758	-	ENSG00000179909	58208735	58220579	overlapStart	499	ZNF154	zinc finger protein 154
20	1310425	1310884	460	-	ENSG00000125775	1290619	1309883	upstream	-542	SDCBP2	syndecan binding protein (syntenin) 2
20	33451149	33451427	279	+	ENSG00000131069	33459949	33515765	upstream	-8800	ACSS2	acyl-CoA synthetase short-chain family member 2
20	36148133	36148275	143	+	ENSG00000053438	36149617	36152092	upstream	-1484	NNAT	neuronatin
20	36148615	36149194	580	+	ENSG00000053438	36149617	36152092	upstream	-1002	NNAT	neuronatin
20	36149452	36150061	610	+	ENSG00000053438	36149617	36152092	overlapStart	-165	NNAT	neuronatin
20	62167942	62168955	1014	-	ENSG00000101213	62159778	62168695	overlapStart	753	PTK6	protein tyrosine kinase 6
21	15645787	15646635	849	+	ENSG00000243064	15646120	15735075	overlapStart	-333	ABCC13	ATP-binding cassette, sub-family C (CFTR/MRP), member 13, pseudogene
21	22369485	22370237	753	+	ENSG00000154654	22370633	22915650	upstream	-1148	NCAM2	neural cell adhesion molecule 2
21	42797588	42797953	366	+	ENSG00000157601	42792231	42831141	inside	5357	MX1	myxovirus (influenza virus) resistance 1, interferon-inducible protein p78 (mouse)
21	43736736	43737065	330	-	ENSG00000160180	43726682	43735761	upstream	-975	TFF3	trefoil factor 3 (intestinal)
22	32438947	32439052	106	+	ENSG00000100170	32439019	32509016	overlapStart	-72	SLC5A1	solute carrier family 5 (sodium/glucose cotransporter), member 1
22	36044151	36044792	642	+	ENSG00000221963	36044442	36057404	overlapStart	-291	APOL6	apolipoprotein L, 6
22	36648832	36649144	313	+	ENSG00000100342	36649056	36663576	overlapStart	-224	APOL1	apolipoprotein L, 1

Supplementary Table 2: Differentially methylated positions (DMP) comparing purified colonic intestinal epithelium obtained from children newly diagnosed with IBD and matched healthy controls. Differential methylation analyses were performed using *minfi* and *limma* Bioconductor packages (see methods) contrasting IBD versus control samples (adjusted p<0.01 and logfold change (logFC) >±1.5). A negative logFC indicates lower methylation levels in IBD compared to control samples.

ID	logFC	AveExpr	t	P.Value	adj.P.Val	B	UCSC_RefGene_Name	UCSC_RefGene_Accession	CHR	UCSC_CpG_Islands_Name (Genome Build 37)	Relation_to_ UCSC_CpG_Isl and			
cg00095326	-1.732	-0.792	-4.656	5.619E-05	7.573E-03	1.860			1					
cg01081168	1.509	-1.033	4.836	3.357E-05	7.055E-03	2.331			1					
cg07111834	-1.915	1.491	-5.341	7.831E-06	6.184E-03	3.664	PTPN22;PTPN22	NM_012411;NM_015967	1					
cg07978304	1.805	0.696	4.488	9.089E-05	8.435E-03	1.420	KIF26B	NM_018012	1	chr1:245316547-245320247	S_Shore			
cg09183124	-1.746	0.230	-5.544	4.355E-06	5.954E-03	4.200			1					
cg13300480	-1.806	-0.933	-5.768	2.289E-06	5.192E-03	4.787	ROR1;ROR1	NM_005012;NM_001083592	1					
cg13950674	2.281	-0.539	4.394	1.187E-04	9.068E-03	1.176	SPRR2B;SPRR2B	NM_001017418;NM_001017	1					
cg16734875	-1.776	0.949	-5.191	1.206E-05	6.319E-03	3.268	GRHL3;GRHL3;GRHL3	NM_198173;NM_198174;N	1	M_021180				
cg18377941	-1.553	2.494	-4.742	4.390E-05	7.298E-03	2.086	ABCA4	NM_000350	1					
cg19269426	-2.437	0.346	-5.764	2.317E-06	5.192E-03	4.776	GGPS1;GGPS1;GGPS1	NM_004837;NM_001037278	1	;NM_001037277				
cg19274341	-2.128	-0.201	-4.351	1.341E-04	9.374E-03	1.064			1					
cg19693031	1.845	-0.192	5.372	7.150E-06	6.134E-03	3.747	TXNIP	NM_006472	1					
cg20416874	1.812	0.102	5.140	1.398E-05	6.498E-03	3.133	RERE;RERE	NM_012102;NM_001042681	1					
cg21172278	-1.908	3.307	-5.365	7.297E-06	6.139E-03	3.728	MIR942;TTF2	NR_030640;NM_003594	1					
cg21837069	-1.674	-0.160	-4.502	8.720E-05	8.347E-03	1.457	VWA1;VWA1	NM_199121;NM_022834	1	chr1:1370767-1371449	N_Shore			
cg22341908	-1.962	-0.866	-6.676	1.728E-07	2.331E-03	7.134			1	chr1:197743931-197744788	S_Shelf			
cg22718139	1.688	0.387	4.405	1.149E-04	9.009E-03	1.205	HMGCS2;HMGCS2	NM_001166107;NM_005518	1					
cg26894297	-1.556	1.998	-5.357	7.473E-06	6.152E-03	3.706			1	chr1:23750508-23751663	S_Shelf			
cg27229484	-1.546	3.748	-4.891	2.859E-05	7.010E-03	2.478	ZC3H12A	NM_025079	1					
cg04745820	1.529	0.351	4.754	4.239E-05	7.271E-03	2.118	LTBP1	NM_206943	2					
cg05267204	-1.647	0.426	-4.928	2.571E-05	6.957E-03	2.576			2					
cg07986907	-2.044	2.595	-5.725	2.587E-06	5.264E-03	4.676	SLC20A1	NM_005415	2					
cg15150396	2.620	2.101	4.463	9.750E-05	8.578E-03	1.355	DYSF;DYSF;DYSF;DYSF;DYSF; DYSF;DYSF;DYSF;DYSF;DYSF; DYSF;DYSF;DYSF;DYSF;	NM_001130455;NM_001130	2	979;NM_001130980;NM_00	1130982;NM_001130976;N	chr2:71787430-71787897	Island	
cg16908938	1.817	1.877	4.460	9.821E-05	8.595E-03	1.349	GREB1;GREB1;GREB1	NM_148903;NM_014668;N	2	M_033090				
cg22122098	-1.943	1.451	-6.624	2.001E-07	2.548E-03	7.001	UBR3	NM_172070	2					
cg22957691	-1.968	2.071	-5.177	1.255E-05	6.377E-03	3.232	FEZ2;FEZ2	NM_005102;NM_001042548	2					
cg25058482	-1.707	-2.694	-5.657	3.147E-06	5.472E-03	4.497	TANK;TANK	NM_004180;NM_133484	2					
cg27092594	-2.256	-0.553	-5.102	1.560E-05	6.607E-03	3.033			2					
cg00959259	-1.528	-0.739	-5.167	1.291E-05	6.407E-03	3.206	PARP9;PARP9;DTX3L;PARP9; PARP9;PARP9;PARP9	NM_001146106;NM_001146	3	104;NM_138287;NM_03145	8;NM_001146103;NM_0011	46105;NM_001146102	chr3:122283002-122283594	N_Shore
cg09729182	-1.709	-1.905	-5.015	2.001E-05	6.753E-03	2.805	CASR	NM_000388	3					
cg15954263	2.841	3.149	5.422	6.200E-06	6.014E-03	3.877	FNDC3B;FNDC3B	NM_001135095;NM_022763	3					
cg20917322	1.573	4.347	4.703	4.904E-05	7.406E-03	1.984	CCDC51	NM_024661	3					
cg22844232	-1.509	-1.493	-5.625	3.458E-06	5.579E-03	4.411			3	chr3:193776091-193776308	N_Shore			
cg22930808	-1.995	1.358	-5.266	9.719E-06	6.241E-03	3.466	PARP9;PARP9;DTX3L;PARP9; PARP9;PARP9;PARP9	NM_001146106;NM_001146	3	104;NM_138287;NM_03145	8;NM_001146103;NM_0011	46105;NM_001146102	chr3:122283002-122283594	N_Shore
cg05366050	2.686	1.526	4.407	1.144E-04	8.989E-03	1.209			4	chr4:164087461-164088146	S_Shelf			
cg05571448	-1.565	2.223	-4.392	1.193E-04	9.074E-03	1.171	PPP3CA;PPP3CA;PPP3CA	NM_001130691;NM_000944	4	;NM_001130692				
cg06855422	-1.918	2.100	-4.400	1.165E-04	9.030E-03	1.192	GRID2	NM_001510	4					
cg07394914	-1.517	-1.207	-5.944	1.382E-06	4.443E-03	5.247	IRF2	NM_002199	4					
cg10397389	-1.816	1.234	-5.316	8.415E-06	6.227E-03	3.598	DAPP1;DAPP1	NM_014395;NM_014395	4					
cg12833118	-1.509	3.287	-4.742	4.396E-05	7.298E-03	2.084			4					
cg12998503	-1.609	0.805	-5.631	3.395E-06	5.574E-03	4.428	WWC2	NM_024949	4					
cg14506696	-1.866	0.783	-5.369	7.216E-06	6.134E-03	3.738	DAPP1	NM_014395	4					
cg21614638	-1.885	1.374	-4.919	2.638E-05	6.998E-03	2.552	DAPP1	NM_014395	4					
cg23421166	-1.562	0.806	-5.277	9.410E-06	6.241E-03	3.496	ART3	NM_001130017	4					
cg01595951	-2.241	0.015	-5.878	1.671E-06	4.670E-03	5.074			5	chr5:54830148-54831120	S_Shelf			
cg06653140	-3.329	-4.385	-5.661	3.117E-06	5.465E-03	4.505	SKP2;SKP2	NM_032637;NM_005983	5					
cg15375424	-1.522	1.140	-5.204	1.163E-05	6.273E-03	3.302	IRF1	NM_002198	5	chr5:131825842-131826935	N_Shelf			
cg16349093	-1.909	0.969	-5.280	9.331E-06	6.241E-03	3.503			5					
cg00119778	-2.898	-1.141	-7.360	2.578E-08	9.839E-04	8.845			6					
cg00440797	-2.287	-1.349	-6.311	4.850E-07	3.180E-03	6.199	HLA-DRB5	NM_002125	6	chr6:32489742-32490128	S_Shelf			
cg00533183	-1.573	1.815	-5.406	6.494E-06	6.014E-03	3.835	PSMB8;PSMB8	NM_004159;NM_148919	6	chr6:32811494-32811839	N_Shore			

cg00579921	1.678	-0.135	4.645	5.801E-05	7.647E-03	1.831	HLA-DRB5	NM_002125	6	chr6:32489742-32490128	Island
cg00750366	-1.619	2.843	-4.299	1.551E-04	9.783E-03	0.931	HLA-DPB1	NM_002121	6	chr6:33048416-33048814	N_Shelf
cg01016122	1.549	-1.963	6.390	3.875E-07	3.050E-03	6.403	PSORS1C1	NM_014068	6		
cg01132696	1.536	-1.951	5.279	9.371E-06	6.241E-03	3.499	HLA-DPB1	NM_002121	6	chr6:33048416-33048814	Island
cg01673307	-2.296	1.493	-5.707	2.729E-06	5.274E-03	4.627	TAP1	NM_000593	6	chr6:32820849-32822370	N_Shore
cg01745539	-1.608	-1.430	-4.968	2.296E-05	6.872E-03	2.679	HLA-DQB1	NM_002123	6	chr6:32632158-32633027	Island
cg01804934	-2.284	1.044	-5.003	2.076E-05	6.756E-03	2.771	HLA-DPA1	NM_033554	6		
cg02181920	-1.529	0.424	-4.940	2.486E-05	6.944E-03	2.606	TAP1	NM_000593	6	chr6:32820849-32822370	N_Shore
cg02756056	-1.528	1.479	-5.999	1.179E-06	4.361E-03	5.392	TAP1;PSMB8	NM_000593;NM_004159	6	chr6:32811494-32811839	S_Shore
cg02806715	-1.978	0.407	-5.783	2.192E-06	5.104E-03	4.827	HLA-DMA	NM_006120	6		
cg03009030	-1.632	1.590	-5.342	7.806E-06	6.184E-03	3.666	HLA-DPA1	NM_033554	6		
cg04461101	-2.455	-0.305	-5.597	3.742E-06	5.749E-03	4.339			6		
cg05358170	-1.639	2.530	-4.912	2.697E-05	7.010E-03	2.532	HLA-F;HLA-F;HLA-F	NM_001098478;NM_001098479;NM_018950	6	chr6:29691106-29692093	S_Shore
cg05938207	1.718	-1.227	5.454	5.659E-06	6.014E-03	3.961	HLA-DRB5	NM_002125	6	chr6:32489742-32490128	Island
cg06032479	1.589	-0.576	5.835	1.888E-06	4.767E-03	4.963	HLA-DRB1	NM_002124	6	chr6:32551851-32552331	Island
cg06271046	-2.189	-0.992	-4.894	2.841E-05	7.010E-03	2.484			6		
cg06422189	-1.847	1.515	-5.194	1.195E-05	6.303E-03	3.277	HLA-B	NM_005514	6	chr6:31323946-31325211	N_Shore
cg06504039	1.635	1.739	4.583	6.914E-05	7.947E-03	1.670	HLA-DOA	NM_002119	6	chr6:32975684-32975926	S_Shelf
cg06791592	-1.715	2.464	-5.056	1.778E-05	6.630E-03	2.913	PSMB9;PSMB9	NM_002800;NM_148954	6	chr6:32820849-32822370	S_Shore
cg07156249	-2.534	0.267	-5.511	4.795E-06	5.961E-03	4.112	PSMB9;PSMB9;TAP1	NM_002800;NM_148954;N_M_000593	6	chr6:32820849-32822370	S_Shore
cg07218288	-2.386	-1.653	-6.318	4.757E-07	3.180E-03	6.217	PSMB8;PSMB8;TAP1	NM_004159;NM_148919;N_M_000593	6	chr6:32811494-32811839	S_Shore
cg07984380	-3.802	-1.899	-4.551	7.584E-05	8.092E-03	1.585	HLA-DRB1	NM_002124	6		
cg08735211	-1.848	1.367	-5.708	2.721E-06	5.274E-03	4.629	HLA-DMA	NM_006120	6		
cg08845336	2.396	-0.337	4.812	3.593E-05	7.119E-03	2.269	HLA-DRB1	NM_002124	6	chr6:32551851-32552331	Island
cg09139047	2.451	-1.398	5.330	8.073E-06	6.186E-03	3.636	HLA-DRB1	NM_002124	6	chr6:32551851-32552331	Island
cg09234582	1.733	-0.463	7.150	4.599E-08	1.413E-03	8.326	HLA-DRB1	NM_002121	6	chr6:33048416-33048814	N_Shore
cg09321817	-2.614	0.854	-5.711	2.698E-06	5.264E-03	4.637	HLA-DPA1	NM_033554	6		
cg10180404	-1.556	-1.032	-4.772	4.033E-05	7.230E-03	2.163	HLA-DQB1	NM_002123	6	chr6:32632158-32633027	Island
cg10466124	-2.583	-4.173	-6.770	1.326E-07	2.247E-03	3.737	HLA-DRB5	NM_002125	6		
cg10518264	-1.886	1.340	-5.682	2.928E-06	5.360E-03	4.563	HLA-DMB	NM_002118	6		
cg10817441	-1.892	1.273	-6.105	8.708E-07	3.953E-03	5.668	PSMB9;PSMB9	NM_002800;NM_148954	6	chr6:32820849-32822370	S_Shore
cg10921592	-1.968	2.827	-5.322	8.260E-06	6.216E-03	3.615	HLA-DPA1	NM_033554	6		
cg11404906	2.515	-0.906	5.737	2.499E-06	5.252E-03	4.707	HLA-DRB1	NM_002124	6	chr6:32551851-32552331	N_Shore
cg115451043	-1.545	-1.961	-5.340	7.847E-06	6.184E-03	3.662	HLA-DPA1	NM_033554	6		
cg11594821	-1.509	1.420	-5.330	8.077E-06	6.186E-03	3.635	HLA-E	NM_005516	6	chr6:30457369-30458175	S_Shore
cg11617938	-1.560	0.554	-5.706	2.736E-06	5.274E-03	4.624	HLA-F;HLA-F;HLA-F	NM_001098478;NM_001098479;NM_018950	6	chr6:29691106-29692093	S_Shore
cg11706729	-1.999	-1.402	-6.273	5.398E-07	3.491E-03	6.102	PSMB8;PSMB8;TAP1	NM_004159;NM_148919;N_M_000593	6	chr6:32811494-32811839	S_Shore
cg12537337	-1.930	-1.030	-5.186	1.223E-05	6.327E-03	3.256	BTN3A3;BTN3A3	NM_197974;NM_006994	6		
cg12736254	-1.640	0.652	-5.849	1.815E-06	4.762E-03	4.999	HLA-DRB1	NM_002124	6		
cg13065507	-1.617	2.087	-7.074	5.686E-08	1.413E-03	8.135			6		
cg14140375	-1.694	1.651	-5.996	1.191E-06	4.361E-03	5.382	HLA-F;HLA-F;HLA-F	NM_001098478;NM_001098479;NM_018950	6	chr6:29691106-29692093	S_Shore
cg14645244	2.586	-2.181	5.968	1.290E-06	4.415E-03	5.310	HLA-DRB1	NM_002124	6	chr6:32551851-32552331	Island
cg14870156	2.454	-0.920	6.208	6.491E-07	3.648E-03	5.935	HLA-DRB1	NM_002121	6	chr6:33048416-33048814	Island
cg15575880	-2.305	0.412	-5.044	1.840E-05	6.663E-03	2.882	HLA-DPA1	NM_033554	6		
cg16186435	-1.694	1.165	-5.554	4.241E-06	5.901E-03	4.224	PSMB8;PSMB8	NM_004159;NM_148919	6	chr6:32811494-32811839	N_Shore
cg16465027	-2.335	-0.363	-6.442	3.340E-07	2.970E-03	6.537			6		
cg16890093	-1.663	1.390	-5.769	2.285E-06	5.192E-03	4.789	PSMB8;PSMB8;TAP1	NM_004159;NM_148919;N_M_000593	6	chr6:32811494-32811839	S_Shore
cg17022232	-1.557	2.097	-5.020	1.973E-05	6.743E-03	2.818	HLA-DMB	NM_002118	6		
cg17159161	-1.839	-4.107	-6.361	4.210E-07	3.180E-03	6.328	HLA-B	NM_005514	6	chr6:31323946-31325211	N_Shore
cg17316649	1.813	-1.280	6.728	1.493E-07	2.326E-03	7.266	HLA-DRB1	NM_002124	6	chr6:32551851-32552331	Island
cg17369694	-5.034	-2.751	-6.711	1.567E-07	2.326E-03	7.222	HLA-DRB5	NM_002125	6		
cg17626301	-2.112	0.677	-5.113	1.509E-05	6.580E-03	3.064	TAP1	NM_000593	6	chr6:32820849-32822370	N_Shore
cg19300401	-4.688	1.600	-4.757	4.202E-05	7.271E-03	2.126			6		
cg19455396	-2.905	3.607	-7.674	1.098E-08	9.839E-04	9.606	TAP2;TAP2	NM_000544;NM_018833	6		
cg19575208	2.077	-0.310	4.352	1.336E-04	9.365E-03	1.068	HLA-DRB1	NM_002124	6	chr6:32551851-32552331	Island
cg19990651	1.564	-1.735	4.941	2.478E-05	6.944E-03	2.609	HLA-DRB1	NM_002121	6	chr6:33048416-33048814	Island
cg20907136	-1.664	-0.714	-4.548	7.642E-05	8.098E-03	1.578	HLA-DPA1	NM_033554	6		
cg22731440	-2.073	0.344	-7.399	2.320E-08	9.839E-04	8.939	HLA-B	NM_005514	6	chr6:31323946-31325211	N_Shore
cg232322773	-1.574	-0.122	-5.520	4.667E-06	5.959E-03	4.137	HCP5	NM_006674	6		
cg23923934	-1.589	2.010	-5.145	1.377E-05	6.464E-03	3.147	HLA-B	NM_005514	6	chr6:31323946-31325211	N_Shore
cg24111025	-2.103	1.841	-4.896	2.820E-05	7.010E-03	2.491	TAP1	NM_000593	6	chr6:32820849-32822370	N_Shore
cg24129356	-2.027	0.320	-5.746	2.441E-06	5.241E-03	4.729	HLA-DMA	NM_006120	6		
cg24287218	-1.672	0.515	-4.965	2.316E-05	6.874E-03	2.671	HLA-DPA1	NM_033554	6		
cg24421410	-1.889	0.721	-5.414	6.348E-06	6.014E-03	3.856	HLA-DMA	NM_006120	6		
cg24638099	-3.248	0.131	-4.677	5.294E-05	7.498E-03	1.914	HLA-DRB6	NR_001298	6		
cg24898914	-1.505	2.838	-5.407	6.471E-06	6.014E-03	3.838	PSMB8;PSMB8	NM_004159;NM_148919	6	chr6:32811494-32811839	N_Shore
cg25042789	-2.726	-0.077	-5.622	3.481E-06	5.579E-03	4.404	TAP1	NM_000593	6	chr6:32820849-32822370	N_Shore
cg25045942	1.810	-0.145	7.087	5.486E-08	1.413E-03	8.167	HLA-DRB1	NM_002121	6	chr6:33048416-33048814	N_Shore
cg25824217	-1.865	1.531	-4.427	1.079E-04	8.838E-03	1.262	HLA-DPA1	NM_033554	6		
cg25954539	-2.604	-2.361	-7.440	2.073E-08	9.839E-04	9.039	HLA-B	NM_005514	6	chr6:31323946-31325211	N_Shore
cg26033526	-2.201	0.928	-5.572	4.023E-06	5.827E-03	4.272	TAP1	NM_000593	6	chr6:32820849-32822370	N_Shore
cg26234900	-1.896	0.706	-5.151	1.352E-05	6.438E-03	3.164	TAP1	NM_000593	6	chr6:32820849-32822370	N_Shore
cg26465432	1.765	-0.045	5.906	1.539E-06	4.539E-03	5.149	HLA-DRB1	NM_002121	6	chr6:33048416-33048814	Island
cg26725201	-1.509	1.332	-6.423	3.528E-07	2.970E-03	6.488			6		
cg27543214	-2.860	0.201	-5.575	3.994E-06	5.825E-03	4.279			6		
cg00733385	1.596	0.881	4.799	3.734E-05	7.145E-03	2.234	ZNF775	NM_173680	7	chr7:150093636-150095229	N_Shore
cg07878625	3.838	2.309	5.391	6.785E-06	6.116E-03	3.795	ZNF783	NR_015357	7	chr7:148978762-148979390	N_Shore
cg19453938	-1.974	-1.274	-4.454	1.001E-04	8.653E-03	1.332					

cg18486231	3.282	-0.056	4.706	4.867E-05	7.399E-03	1.991	RNASE4;ANG;ANG;RNASE4	NM_194431;NM_001097577 ;NM_001145;NM_002937	14	chr14:21152483-21152740	S_Shelf
cg01637789	1.816	-0.124	4.551	7.588E-05	8.092E-03	1.585	THBS1	NM_003246	15	chr15:39872527-39873567	S_Shelf
cg03472130	-1.777	1.397	-5.619	3.519E-06	5.579E-03	4.395	THSD4	NM_024817	15		
cg04827020	1.678	-0.635	4.572	7.136E-05	8.014E-03	1.641	THBS1	NM_003246	15	chr15:39872527-39873567	S_Shelf
cg06272045	-1.711	0.400	-5.850	1.808E-06	4.762E-03	5.002			15		
cg09782560	-1.908	-0.188	-5.223	1.100E-05	6.241E-03	3.353			15		
cg10760299	1.803	-0.708	4.916	2.667E-05	7.010E-03	2.542	GATM	NM_001482	15	chr15:45669970-45671029	N_Shore
cg19348484	-1.648	0.680	-4.645	5.803E-05	7.647E-03	1.830	FURIN	NM_002569	15	chr15:91414311-91415427	N_Shore
cg19997662	-1.805	3.078	-4.840	3.316E-05	7.055E-03	2.343	CHSY1	NM_014918	15		
cg21954370	-1.535	0.598	-4.852	3.199E-05	7.011E-03	2.375			15		
cg22700246	-1.801	0.876	-6.152	7.623E-07	3.725E-03	5.788			15		
cg23387863	-1.607	2.302	-5.409	6.425E-06	6.014E-03	3.845	SGK269	NM_024776	15		
cg26261358	-4.421	-2.626	-4.555	7.505E-05	8.072E-03	1.595			15		
cg01351032	-1.623	0.064	-7.121	4.990E-08	1.413E-03	8.253	CIITA	NM_000246	16	chr16:10972782-10973305	N_Shore
cg04599946	-1.721	0.815	-5.228	1.085E-05	6.241E-03	3.365	IRF8	NM_002163	16	chr16:85932121-85932942	S_Shelf
cg05450979	-3.241	2.805	-4.812	3.597E-05	7.119E-03	2.268	NUBP1	NM_002484	16		
cg07839457	-2.246	-0.516	-5.511	4.798E-06	5.961E-03	4.111	NLRCS	NM_032206	16	chr16:57023190-57023768	N_Shore
cg08159663	-1.963	0.500	-5.599	3.720E-06	5.749E-03	4.344	NLRCS	NM_032206	16	chr16:57023190-57023768	N_Shore
cg08714975	-1.755	2.294	-5.350	7.637E-06	6.153E-03	3.687			16		
cg08985333	-1.530	-0.540	-6.768	1.333E-07	2.247E-03	7.368	CIITA	NM_000246	16	chr16:10972782-10973305	N_Shore
cg09015246	-2.306	-0.131	-7.572	1.446E-08	9.839E-04	9.361	CIITA;CIITA	NM_000246;NM_000246	16	chr16:10972782-10973305	N_Shore
cg10466548	-1.659	-0.347	-5.412	6.380E-06	6.014E-03	3.851			16		
cg26239233	-1.893	-0.974	-6.426	3.495E-07	2.970E-03	6.496	CIITA	NM_000246	16	chr16:10972782-10973305	N_Shore
cg00679763	-1.695	2.867	-5.711	2.696E-06	5.264E-03	4.638	UBE2Z	NM_023079	17		
cg01401135	1.513	-0.836	4.830	3.415E-05	7.063E-03	2.316	DNAH17	NM_173628	17		
cg01697487	-1.610	0.889	-5.277	9.402E-06	6.241E-03	3.496	MYCBPAP	NM_032133	17	chr17:48585385-48586167	S_Shelf
cg02753187	-1.610	0.087	-5.928	1.444E-06	4.472E-03	5.207	CALCOCO2	NM_005831	17		
cg15601264	-2.142	0.150	-4.957	2.366E-05	6.898E-03	2.652			17		
cg15965301	-1.720	2.393	-5.630	3.400E-06	5.574E-03	4.426			17		
cg17445097	-1.917	1.254	-5.635	3.353E-06	5.535E-03	4.439	PHF12;PHF12	NM_020889;NM_001033561	17		
cg21463898	1.604	0.878	5.030	1.920E-05	6.717E-03	2.843	OSBPL7	NM_145798	17	chr17:45890956-45891165	N_Shelf
cg24166450	-1.633	-1.357	-4.464	9.729E-05	8.576E-03	1.357			17		
cg05941652	1.555	1.826	5.112	1.514E-05	6.580E-03	3.060	LAMA3;LAMA3	NM_198129;NM_001127717	18	chr18:21269269-21270349	S_Shelf
cg10565645	2.492	2.901	4.457	9.918E-05	8.624E-03	1.340	GALNT1;GALNT1	NM_020474;NM_020474	18		
cg00428638	-1.667	1.333	-4.302	1.542E-04	9.761E-03	0.936	INSR;INSR	NM_000208;NM_001079817	19		
cg01254505	-2.421	-2.898	-6.675	1.733E-07	2.331E-03	7.131	BST2	NM_004335	19		
cg01329005	-2.386	0.211	-5.148	1.367E-05	6.438E-03	3.154	BST2	NM_004335	19		
cg09993699	-1.595	-0.393	-5.702	2.764E-06	5.286E-03	4.615	BST2	NM_004335	19		
cg10680514	-1.951	-3.472	-4.399	1.170E-04	9.034E-03	1.189	LGALS13	NM_013268	19		
cg11558551	-2.861	-2.151	-5.979	1.251E-06	4.396E-03	5.338	BST2	NM_004335	19		
cg12123019	-1.672	-0.422	-5.712	2.691E-06	5.264E-03	4.640	IL12RB1;IL12RB1	NM_005535;NM_153701	19		
cg20092122	-1.537	1.098	-4.652	5.685E-05	7.608E-03	1.849	BST2	NM_004335	19		
cg22316634	2.246	2.026	4.555	7.504E-05	8.072E-03	1.595	COMP	NM_000095	19	chr19:18896515-18896860	N_Shore
cg23281436	1.775	-0.849	5.004	2.068E-05	6.756E-03	2.775	KANK3	NM_198471	19	chr19:8397958-8400461	S_Shelf
cg24272870	-1.841	-2.593	-5.868	1.720E-06	4.674E-03	5.048			19		
cg26588045	-1.540	0.646	-5.036	1.887E-05	6.716E-03	2.859	MIA;RAB4B	NM_006533;NM_016154	19	chr19:41283880-41284276	N_Shore
cg14359894	-2.073	-3.757	-5.229	1.080E-05	6.241E-03	3.370	RASSF2	NM_014737	20	chr20:4803013-4804146	Island
cg15488794	-2.040	-0.906	-6.058	9.961E-07	4.123E-03	5.545	BCL2L1;BCL2L1	NM_138578;NM_001191	20		
cg17343385	1.925	3.253	5.070	1.710E-05	6.607E-03	2.949	DNAJC5	NM_025219	20	chr20:62550713-62551523	S_Shore
cg18740175	-1.603	2.407	-5.108	1.531E-05	6.583E-03	3.050	NFATC2;NFATC2;NFATC2	NM_001136021;NM_173091 ;NM_012340	20	chr20:50108795-50109456	S_Shore
cg00243527	4.163	0.622	5.930	1.438E-06	4.472E-03	5.211	LIF	NM_002309	22	chr22:30642437-30642671	N_Shore
cg00539347	-1.832	-1.539	-4.291	1.589E-04	9.850E-03	0.909			22		

Supplementary Table 3: Summary of existing/published evidence on the functional implication of rDMR-associated genes in the intestinal epithelium. Genes were grouped into the following main categories: Development and differentiation, Intestinal epithelial immune function, Involvement in GI disease, Metabolic function. For each gene, reported function and, where applicable, modulation by environmental factors and/or relevance to disease pathogenesis is summarised.

Gene symbol	Gene name	Function in the intestinal epithelium	Modulation by epigenetic factors/ impacted by environmental factors and/or relevance for disease	Reference
Development and differentiation				
KCNQ1	potassium voltage-gated Channel, KQT-like subfamily, member 1	Voltage-gated potassium channel	Tissue-specific imprinting, role in GI cancer	1, 2
LFNG	LFNG O-fucosyl-peptide 3-beta-N-acetylglucosaminyltransferase	Notch signaling involvement	Differentially regulated in the mouse intestinal epithelium with development	3
SFRP	secreted frizzled-related protein1	Wnt modulator. Dynamically expressed, controls apicobasal polarity in the developing gut		4, 5
SPDEF	SAM pointed domain containing ETS transcription factor	Transcription Factor, Tumor suppressor, Wnt inhibitor	Functions as a colorectal tumor suppressor by inhibiting β-catenin activity.	6
TCF7L1	transcription factor 7-like 1	Intestinal homeostatic self-renewal, Wnt signaling		7, 8
TET1	tet methylcytosine dioxygenase 1	Regulation of cell lineage commitment. Erasure of genomic imprinting	Modulated by Vitamin C	9-11,12
WIF1	WNT inhibitory factor 1	Tumor suppressor gene, negative Wnt regulator	Increased with maternal vitamin B supplementation. Methylation as marker for colorectal cancer	13,14,15
ZFP42	zinc finger protein 42	Pluripotency marker	Rex1/Zfp42 as an epigenetic regulator for genomic imprinting. Potential role in preimplantation development	16, 17,
Intestinal epithelial immune function				
BIRC3	baculoviral IAP repeat containing 3	Regulator of innate immune signaling, antiapoptotic	Upregulated in Caco-2 cell by <i>L. salivarius</i> . Upregulation in regenerating colonocytes in UC. May be regulated by DNA methylation	18, 19, 20
IL32	interleukin 32	Cytokine signaling	Induced by Toll-like receptor agonists. Stimulated by butyrate. Overexpressed in IBD	21, 22, 23
ITLN1	intelectin 1	Expression in enterocytes and goblet cells. Intestinal homeostasis by protecting against apoptosis		24, 25
LGALS9	lectin, galactoside-binding, soluble, 9	Modulator of cell-cell and cell-matrix interactions	Involved in immunomodulating effects of nondigestible oligosaccharides	26, 27
MUC2	mucin 2	Mucus layer, antimicrobial defense	Epigenetic regulation by DNA methylation in colorectal and pancreatic cancer. Gene transcription influenced by type of bacterial colonization in neonatal mice. Depletion in necrotizing enterocolitis	28, 29-34
OAS1, OAS2	2'-5'-oligoadenylate synthetase	Involvement in innate immune response	Inverse correlation between promoter methylation and expression level in glioblastomas, Diagnostic biomarker for systemic lupus erythematosus	34, 35, 36
PTGER4	prostaglandin E receptor 4	PGE2 signaling, T-cell factor signaling	Gastric colonisation with restricted commensal microbiota replicates the promotion of neoplastic lesions. Risk variant affecting PTGER4 for CD	37, 38
PIGR	polymeric immunoglobulin receptor	Transepithelial IgA transport	altered DNA methylation in Barrett's oesophagus and Plasmodium infection (liver)	39, 40
TFF3	trefoil-factor 3	Mucosal layer protection	UC-associated TLR2-R753Q variant leads to TFF3 deficiency. Epigenetic control in human retinoblastoma cell lines	41, 42
TLR3, TLR4	toll-like receptor 3, toll-like receptor 4	Pattern recognition receptor	Gut flora required for the control of intestinal infection by poly (I:C) administration in neonates. Microbial cell components induce tolerance to flagellin-stimulated inflammation	43, 44
			TLR4 signaling reduced by amniotic fluid. Partially repressed by DNA methylation in cell lines.	45, 46
HLA-C, HLA-DMA, HLA-DMB, HLA-DRA	major histocompatibility complex, class II	Antigen presentation in epithelial cells	HLA-DRA bound by histone methyl and acetyltransferase complex components. HLA-DRA is protected against epigenetic silencing by DNA methylation by RFX	47, 48, 49
Involvement in GI disease				
BNIP3	BCL2/adenovirus E1B 19kDa interacting protein 3	Mediator of cell survival	Epigenetic silencing in control of expression in human colorectal cancer cells	50
CCL28	chemokine (C-C motif) Ligand 28	Mucosal tissue protection, antibacterial	Increased expression in ileal crohns disease	51, 52
HOXC6	homeobox C6	Tumor suppressor gene	Predictive significance in esophageal squamous cell carcinoma. Upregulation associated with poor gastric cancer survival. Inactivated by methylation and somatic mutations in head and neck cancer	53, 54, 55
DUOX2	dual oxidase 2	Generation of hydrogen peroxide	Induction by gut microbiota, increased expression in paediatric CD associated with Proteobacteria	56, 57
MICB	MHC class I polypeptide-related sequence B	Mediation of enterocyte apoptosis	Tumor-associated expression, linked to stress and Coeliac Disease. Linked to UC in Chinese population	58-60
OLFM4	olfactomedin-4	Cell adhesion, growth, self-renewal	Secreted into mucus in active IBD	61
PRPH	peripherin	Cytoskeletal protein	Tumor suppressor gene in hepatocellular carcinoma	62
REG1A	regenerating gene 1A	Antimicrobial defense	Epigenetic regulation of REG1A in cutaneous melanoma. Altered expression in UC mucosa, returned to normal in remission	63, 64
SELENBP1	selenium-binding protein 1	role in protein degradation (likely)	Modulated by epigenetic mechanisms in colorectal cancer. Altered protein level in Ulcerative Colitis	65, 66, 67
SFRP	secreted frizzled-related protein1	Modulator of Wnt signaling	Frequent epigenetic inactivation of SFRP genes in gastric cancer, expression leads to antitumor synergy of HDAC and methyltransferase inhibitors in chemoresistant cancers	68, 69
TAP1, TAP2	transporter 1 and 2 of ATP-binding cassette, sub-family B (MDR/TAP)	Antigen presentation	TAP polymorphism in inflammatory bowel diseases. Downregulation linked to a loss of inflammatory response in colorectal cancer	70, 70
UBD	ubiquitin D	Protein modification	Selectively expressed in the follicle-associated epithelium. Proteins modified by UBD are involved in NF-κB activation. Epigenetic marker for liver preneoplasia in a mouse model	71, 72, 73
XAF1	XIAP associated factor 1	Regulation of apoptosis	Alteration in human CRC and gastric cancer. Correlation between CpG methylation and silencing	74-76

Metabolic Function				
NPC1L1	Niemann-Pick C1-like 1	Cholesterol absorption	Epigenetic modulation by DNA methylation	77
SLC5A1	solute carrier family 5 (sodium/glucose cotransporter), member 1	Sodium-dependent glucose transport	Dietary and nutrient-dependent regulation	78, 79
SLC9A2	solute carrier family 9 (sodium/hydrogen exchanger), member 2	Sodium/hydrogen exchanger	Regulation by butyrate in rat ileum	80

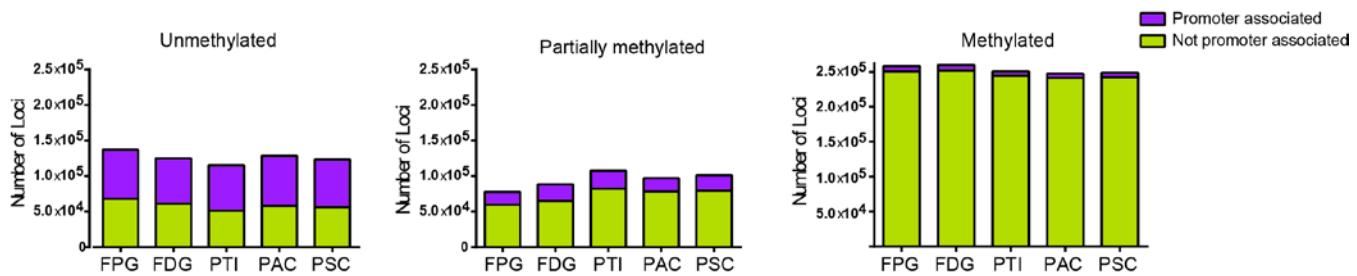
Supplementary Table 2 References

- Than BLN, Goos JACM, Sarver AL, et al. The role of KCNQ1 in mouse and human gastrointestinal cancers. *Oncogene* 2014;33:3861-8.
- Rapetti-Mauss R, O'Mahony F, Sepulveda FV, et al. Oestrogen promotes KCNQ1 potassium channel endocytosis and postendocytic trafficking in colonic epithelium. *The Journal of physiology* 2013;591:2813-31.
- Schröder N, Gossler A. Expression of Notch pathway components in fetal and adult mouse small intestine. *Gene expression patterns : GEP* 2002;2:247-50.
- Matsuyama M, Aizawa S, Shimono A. Sfrp controls apicobasal polarity and oriented cell division in developing gut epithelium. *PLoS genetics* 2009;5:e1000427-e1000427.
- Pézeron G, Anselme I, Laplante M, et al. Duplicate sfrp1 genes in zebrafish: sfrp1a is dynamically expressed in the developing central nervous system, gut and lateral line. *Gene expression patterns : GEP* 2006;6:835-42.
- Noah TK, Lo Y-H, Price A, et al. SPDEF functions as a colorectal tumor suppressor by inhibiting β-catenin activity. *Gastroenterology* 2013;144:1012-1023.e6.
- van Es JH, Haegebarth A, Kujala P, et al. A critical role for the Wnt effector Tcf4 in adult intestinal homeostatic self-renewal. *Molecular and cellular biology* 2012;32:1918-27.
- Shy BR, Wu C-I, Khratmsova GF, et al. Regulation of Tcf7l1 DNA binding and protein stability as principal mechanisms of Wnt/β-catenin signaling. *Cell reports* 2013;4:1-9.
- Blaschke K, Ebata KT, Karimi MM, et al. Vitamin C induces Tet-dependent DNA demethylation and a blastocyst-like state in ES cells. *Nature* 2013;500:222-6.
- Lee K, Hamm J, Whitworth K, et al. Dynamics of TET family expression in porcine preimplantation embryos is related to zygotic genome activation and required for the maintenance of NANOG. *Developmental biology* 2014;386:86-95.
- Yamaguchi S, Shen L, Liu Y, et al. Role of Tet1 in erasure of genomic imprinting. *Nature* 2013;504:460-4.
- Ficz G, Branco MR, Seisenberger S, et al. Dynamic regulation of 5-hydroxymethylcytosine in mouse ES cells and during differentiation. *Nature* 2011;473:398-402.
- Roperch J-P, Incitti R, Forbin S, et al. Aberrant methylation of NPY, PENK, and WIF1 as a promising marker for blood-based diagnosis of colorectal cancer. *BMC cancer* 2013;13:566-566.
- Amiot A, Mansour H, Baumgaertner I, et al. The detection of the methylated Wif-1 gene is more accurate than a fecal occult blood test for colorectal cancer screening. *PloS one* 2014;9:e99233-e99233.
- Ciappio ED, Liu Z, Brooks RS, et al. Maternal B vitamin supplementation from preconception through weaning suppresses intestinal tumorigenesis in Apc1638N mouse offspring. *Gut* 2011;60:1695-702.
- Kim JD, Kim H, Ekram MB, et al. Rex1/Zfp42 as an epigenetic regulator for genomic imprinting. *Hum Mol Genet* 2011;20:1353-62.
- Climent M, Alonso-Martin S, Perez-Palacios R, et al. Functional analysis of Rex1 during preimplantation development. *Stem Cells Dev* 2013;22:459-72.
- O'Callaghan J, Buttó LF, MacSharry J, et al. Influence of adhesion and bacteriocin production by *Lactobacillus salivarius* on the intestinal epithelial cell transcriptional response. *Applied and environmental microbiology* 2012;78:5196-203.
- Seidelin JB, Vainer B, Andresen L, et al. Upregulation of clAP2 in regenerating colonocytes in ulcerative colitis. *Virchows Archiv : an international journal of pathology* 2007;451:1031-8.
- Puto LA, Reed JC. Daxx represses RelB target promoters via DNA methyltransferase recruitment and DNA hypermethylation. *Genes & development* 2008;22:998-1010.
- Li W, Sun W, Liu L, et al. IL-32: a host proinflammatory factor against influenza viral replication is upregulated by aberrant epigenetic modifications during influenza A virus infection. *Journal of immunology (Baltimore, Md. : 1950)* 2010;185:5056-65.
- Kobori A, Bamba S, Imaeda H, et al. Butyrate stimulates IL-32alpha expression in human intestinal epithelial cell lines. *World journal of gastroenterology : WJG* 2010;16:2355-61.
- Shioya M, Nishida A, Yagi Y, et al. Epithelial overexpression of interleukin-32alpha in inflammatory bowel disease. *Clinical and experimental immunology* 2007;149:480-6.
- Wruckmeyer U, Hansen GH, Seya T, et al. Intelectin: a novel lipid raft-associated protein in the enterocyte brush border. *Biochemistry* 2006;45:9188-97.
- Washimi K, Yokose T, Yamashita M, et al. Specific expression of human intelectin-1 in malignant pleural mesothelioma and gastrointestinal goblet cells. *PloS one* 2012;7:e39889-e39889.
- de Kvit S, Saeland E, Kraneveld AD, et al. Galectin-9 induced by dietary synbiotics is involved in suppression of allergic symptoms in mice and humans. *Allergy* 2012;67:343-52.
- de Kvit S, Kraneveld AD, Knippels LMJ, et al. Intestinal epithelium-derived galectin-9 is involved in the immunomodulating effects of nondigestible oligosaccharides. *Journal of innate immunity* 2013;5:625-38.
- Siedow A, Szyf M, Gratchev A, et al. De novo expression of the Muc2 gene in pancreas carcinoma cells is triggered by promoter demethylation. *Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine*;23:54-60.
- Hanski C, Riede E, Gratchev A, et al. MUC2 gene suppression in human colorectal carcinomas and their metastases: in vitro evidence of the modulatory role of DNA methylation. *Laboratory investigation; a journal of technical methods and pathology* 1997;77:685-95.
- Gratchev A, Siedow A, Bumke-Vogt C, et al. Regulation of the intestinal mucin MUC2 gene expression in vivo: evidence for the role of promoter methylation. *Cancer letters* 2001;168:71-80.
- Mesquita P. Role of site-specific promoter hypomethylation in aberrant MUC2 mucin expression in mucinous gastric carcinomas. *Cancer Letters* 2003;189:129-136.
- Yamada N, Hamada T, Goto M, et al. MUC2 expression is regulated by histone H3 modification and DNA methylation in pancreatic cancer. *International journal of cancer. Journal international du cancer* 2006;119:1850-7.
- Vincent A, Perrais M, Desseyne JL, et al. Epigenetic regulation (DNA methylation, histone modifications) of the 11p15 mucin genes (MUC2, MUC5AC, MUC5B, MUC6) in epithelial cancer cells. *Oncogene* 2007;26:6566-76.
- Okudaira K, Kakar S, Cun L, et al. MUC2 gene promoter methylation in mucinous and non-mucinous colorectal cancer tissues. *International journal of oncology* 2010;36:765-75.
- Etcheverry A, Aubry M, de Tayrac M, et al. DNA methylation in glioblastoma: impact on gene expression and clinical outcome. *BMC genomics* 2010;11:701-701.

36. Feng X, Huang J, Liu Y, et al. Identification of interferon-inducible genes as diagnostic biomarker for systemic lupus erythematosus. *Clinical rheumatology* 2014.
37. Glas J, Seiderer J, Czamara D, et al. PTGER4 expression-modulating polymorphisms in the 5p13.1 region predispose to Crohn's disease and affect NF- κ B and XBP1 binding sites. *PloS one* 2012;7:e52873-e52873.
38. Lertpiriyapong K, Whary MT, Muthupalani S, et al. Gastric colonisation with a restricted commensal microbiota replicates the promotion of neoplastic lesions by diverse intestinal microbiota in the Helicobacter pylori INS-GAS mouse model of gastric carcinogenesis. *Gut* 2014;63:54-63.
39. Alvi MA, Liu X, O'Donovan M, et al. DNA methylation as an adjunct to histopathology to detect prevalent, inconspicuous dysplasia and early-stage neoplasia in Barrett's esophagus. *Clinical cancer research : an official journal of the American Association for Cancer Research* 2013;19:878-88.
40. Al-Quraishy S, Dkhil MA, Abdel-Baki AAS, et al. Genome-wide screening identifies Plasmodium chabaudi-induced modifications of DNA methylation status of Tlr1 and Tlr6 gene promoters in liver, but not spleen, of female C57BL/6 mice. *Parasitology research* 2013;112:3757-70.
41. Podolsky DK, Gerken G, Eyking A, et al. Colitis-associated variant of TLR2 causes impaired mucosal repair because of TFF3 deficiency. *Gastroenterology* 2009;137:209-20.
42. Philippot C, Busch M, Dünker N. Epigenetic control of trefoil factor family (TFF) peptide expression in human retinoblastoma cell lines. *Cellular physiology and biochemistry : international journal of experimental cellular physiology, biochemistry, and pharmacology* 2014;34:1001-14.
43. Lacroix-Lamandé S, Guesdon W, Drouet F, et al. The gut flora is required for the control of intestinal infection by poly(I:C) administration in neonates. *Gut microbes* 2014;5:533-40.
44. Li N, Quidgley MC, Kobeissy FH, et al. Microbial cell components induced tolerance to flagellin-stimulated inflammation through Toll-like receptor pathways in intestinal epithelial cells. *Cytokine* 2012;60:806-11.
45. Takahashi K, Sugi Y, Hosono A, et al. Epigenetic regulation of TLR4 gene expression in intestinal epithelial cells for the maintenance of intestinal homeostasis. *Journal of immunology (Baltimore, Md. : 1950)* 2009;183:6522-9.
46. Good M, Siggers RH, Sodhi CP, et al. Amniotic fluid inhibits Toll-like receptor 4 signaling in the fetal and neonatal intestinal epithelium. *Proceedings of the National Academy of Sciences of the United States of America* 2012;109:11330-5.
47. Byrne B, Madrigal-Estebas L, McEvoy A, et al. Human duodenal epithelial cells constitutively express molecular components of antigen presentation but not costimulatory molecules. *Human immunology* 2002;63:977-86.
48. Hershberg RM, Cho DH, Youakim A, et al. Highly polarized HLA class II antigen processing and presentation by human intestinal epithelial cells. *The Journal of clinical investigation* 1998;102:792-803.
49. Seguín-Estévez Q, De Palma R, Krawczyk M, et al. The transcription factor RFX protects MHC class II genes against epigenetic silencing by DNA methylation. *Journal of immunology (Baltimore, Md. : 1950)* 2009;183:2545-53.
50. Swiderek E, Kalas W, Wysokinska E, et al. The interplay between epigenetic silencing, oncogenic KRas and HIF-1 regulatory pathways in control of BNIP3 expression in human colorectal cancer cells. *Biochemical and biophysical research communications* 2013;441:707-12.
51. Hieshima K, Ohtani H, Shibano M, et al. CCL28 has dual roles in mucosal immunity as a chemokine with broad-spectrum antimicrobial activity. *Journal of immunology (Baltimore, Md. : 1950)* 2003;170:1452-61.
52. Berri M, Virlogeux-Payant I, Chevaleyre C, et al. CCL28 involvement in mucosal tissues protection as a chemokine and as an antibacterial peptide. *Developmental and comparative immunology* 2014;44:286-90.
53. Du Y-B, Dong B, Shen L-Y, et al. The survival predictive significance of HOXC6 and HOXC8 in esophageal squamous cell carcinoma. *The Journal of surgical research* 2014;188:442-50.
54. Zhang Q, Jin XS, Yang ZY, et al. Upregulated Hoxc6 expression is associated with poor survival in gastric cancer patients. *Neoplasma* 2013;60:439-45.
55. Guerrero-Preston R, Michailidi C, Marchionni L, et al. Key tumor suppressor genes inactivated by "greater promoter" methylation and somatic mutations in head and neck cancer. *Epigenetics : official journal of the DNA Methylation Society* 2014;9:1031-46.
56. Haberman Y, Tickle TL, Dexheimer PJ, et al. Pediatric Crohn disease patients exhibit specific ileal transcriptome and microbiome signature. *The Journal of clinical investigation* 2014;124:3617-33.
57. Sommer F, Bäckhed F. The gut microbiota engages different signaling pathways to induce Duox2 expression in the ileum and colon epithelium. *Mucosal immunology* 2014.
58. Groh V, Rhinehart R, Sechrist H, et al. Broad tumor-associated expression and recognition by tumor-derived gamma delta T cells of MICA and MICB. *Proceedings of the National Academy of Sciences of the United States of America* 1999;96:6879-84.
59. Lü M, Xia B, Li J, et al. MICB microsatellite polymorphism is associated with ulcerative colitis in Chinese population. *Clinical immunology (Orlando, Fla.)* 2006;120:199-204.
60. Allegretti YL, Bondar C, Guzman L, et al. Broad MICA/B expression in the small bowel mucosa: a link between cellular stress and celiac disease. *PloS one* 2013;8:e73658-e73658.
61. Gersmann M, Becker S, Nuding S, et al. Olfactomedin-4 is a glycoprotein secreted into mucus in active IBD. *J Crohns Colitis* 2012;6:425-34.
62. Revill K, Wang T, Lachenmayer A, et al. Genome-wide methylation analysis and epigenetic unmasking identify tumor suppressor genes in hepatocellular carcinoma. *Gastroenterology* 2013;145:1424-35.e1-25.
63. Sato Y, Marzese DM, Ohta K, et al. Epigenetic regulation of REG1A and chemosensitivity of cutaneous melanoma. *Epigenetics : official journal of the DNA Methylation Society* 2013;8:1043-52.
64. Planell N, Lozano JJ, Mora-Buch R, et al. Transcriptional analysis of the intestinal mucosa of patients with ulcerative colitis in remission reveals lasting epithelial cell alterations. *Gut* 2013;62:967-76.
65. Silvers AL, Lin L, Bass AJ, et al. Decreased selenium-binding protein 1 in esophageal adenocarcinoma results from posttranscriptional and epigenetic regulation and affects chemosensitivity. *Clinical cancer research : an official journal of the American Association for Cancer Research* 2010;16:2009-21.
66. Wang N, Chen Y, Yang X, et al. Selenium-binding protein 1 is associated with the degree of colorectal cancer differentiation and is regulated by histone modification. *Oncology reports* 2014;31:2506-14.
67. Hsieh S-Y, Shih T-C, Yeh C-Y, et al. Comparative proteomic studies on the pathogenesis of human ulcerative colitis. *Proteomics* 2006;6:5322-31.
68. Nojima M, Suzuki H, Toyota M, et al. Frequent epigenetic inactivation of SFRP genes and constitutive activation of Wnt signaling in gastric cancer. *Oncogene* 2007;26:4699-713.
69. Cooper SJ, von Roemeling CA, Kang KH, et al. Reexpression of tumor suppressor, sFRP1, leads to antitumor synergy of combined HDAC and methyltransferase inhibitors in chemoresistant cancers. *Molecular cancer therapeutics* 2012;11:2105-15.
70. Heresbach D, Alizadeh M, Bretagne JF, et al. TAP gene transporter polymorphism in inflammatory bowel diseases. *Scandinavian journal of gastroenterology* 1997;32:1022-7.
71. Kobayashi A, Donaldson DS, Kanaya T, et al. Identification of novel genes selectively expressed in the follicle-associated epithelium from the meta-analysis of transcriptomics data from multiple mouse cell and tissue populations. *DNA Res* 2012;19:407-22.
72. Oliva J, Bardag-Gorce F, French BA, et al. Fat10 is an epigenetic marker for liver preneoplasia in a drug-primed mouse model of tumorigenesis. *Experimental and molecular pathology* 2008;84:102-12.
73. Buchsbaum S, Bercovich B, Ziv T, et al. Modification of the inflammatory mediator LRRKIP2 by the ubiquitin-like protein FAT10 inhibits its activity during cellular response to LPS. *Biochemical and biophysical research communications* 2012;428:11-6.
74. Byun D-S, Cho K, Ryu B-K, et al. Hypermethylation of XIAP-associated factor 1, a putative tumor suppressor gene from the 17p13.2 locus, in human gastric adenocarcinomas. *Cancer research* 2003;63:7068-75.
75. Zou B, Chim CS, Zeng H, et al. Correlation between the single-site CpG methylation and expression silencing of the XAF1 gene in human gastric and colon cancers. *Gastroenterology* 2006;131:1835-43.

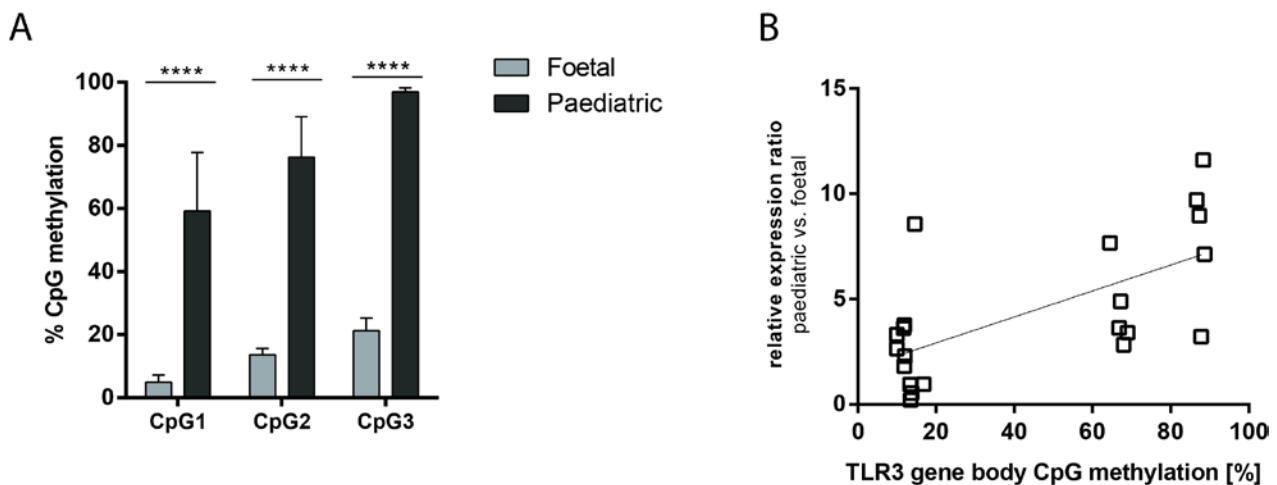
76. Chung S-K, Lee M-G, Ryu B-K, et al. Frequent alteration of XAF1 in human colorectal cancers: implication for tumor cell resistance to apoptotic stresses. *Gastroenterology* 2007;132:2459-77.
77. Malhotra P, Soni V, Kumar A, et al. Epigenetic modulation of intestinal cholesterol transporter Niemann-Pick C1-like 1 (NPC1L1) gene expression by DNA methylation. *The Journal of biological chemistry* 2014;289:23132-40.
78. Dyer J, Hosie KB, Shirazi-Beechey SP. Nutrient regulation of human intestinal sugar transporter (SGLT1) expression. *Gut* 1997;41:56-9.
79. Wiśniewski JR, Friedrich A, Keller T, et al. The Impact of High Fat Diet on Metabolism and Immune Defense in Small Intestine Mucosa. *Journal of proteome research* 2014.
80. Subramanya SB, Rajendran VM, Srinivasan P, et al. Differential regulation of cholera toxin-inhibited Na-H exchange isoforms by butyrate in rat ileum. *American journal of physiology. Gastrointestinal and liver physiology* 2007;293:G857-63.

Supplementary Figures



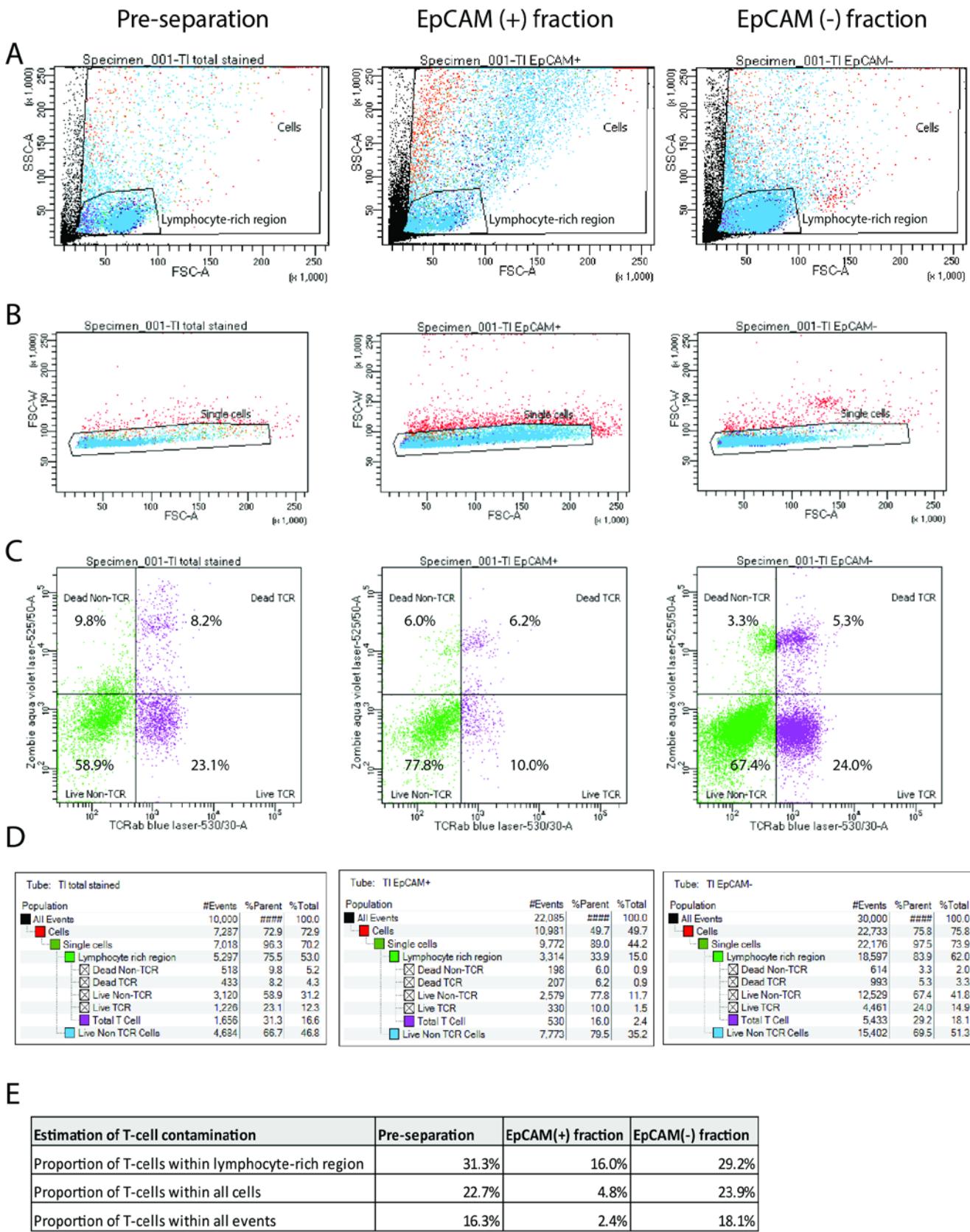
Supplementary Figure 1

Genome-wide DNA methylation pattern of purified intestinal foetal and paediatric epithelial cells analysed by 450K array. Number of promoter-associated loci stratified according to their DNA methylation status (unmethylated, partially methylated and methylated). Shown is the average number of loci per sample in each sample group. Overall, unmethylated probes were more frequently found to be associated with gene promoter regions compared to partially methylated probes. In contrast, the majority of fully methylated probes were not associated with promoter regions. This distribution pattern did not vary significantly between individual samples. Abbreviations: FPG=Foetal proximal gut, FDG=Foetal distal gut, PTI=Paediatric terminal ileum, PAC=Paediatric ascending colon, PSC=Paediatric sigmoid colon. n=3 (foetal) and 2 (paediatric).



Supplementary Figure 2:

(A) DNA methylation profile of 3 CpGs located in the 3rd intron of the TLR3 gene was assessed in foetal and paediatric intestinal epithelium assessed using pyrosequencing on bisulfite converted DNA. In contrast to the upstream promoter regions, this intragenic region was found to be significantly hypermethylated in paediatric compared to foetal intestinal epithelium. Two-way analysis of variance, post-test: Sidak, **** $p<0.0001$, $n=12-16$, measured in duplicate. (B) A positive correlation of intragenic DNA methylation with TLR3 mRNA expression was observed.



Supplementary Figure 3

Estimation of T-cell contamination pre- and post- magnetic bead sorting (MACS) assessed by flow cytometry. (A) Forward- and side scatterplots of cells prior to MACS-separation (left) and post-separation; EpCAM-positive fraction (centre; containing purified intestinal epithelium) and EpCAM-negative fraction (right). Displayed are all events with indicated gating for total cellular population and the population containing the highest lymphocyte proportion (lymphocyte-rich region) (B) Gatings for single cells in each fraction, based on forward scatter. (C) Fluorescent intensity scatters within lymphocyte-rich region for T-cell receptor (TCR) and live-dead cell staining (Zombie Aqua) in each fraction. Percentages of cells in each quadrant as a proportion of total cells within lymphocyte-rich region are indicated. (D) Gating hierarchy summarising number of events within each gate and the respective percentage of total events. (E) Estimation of T-cell contamination by calculating proportion of T-cells within lymphocyte-rich region as well as proportion of cells and total events. Proportion of T-cells within EPCAM (+) fraction estimated to be <5%. Displayed data are representative of regularly performed T -cell contamination testing.