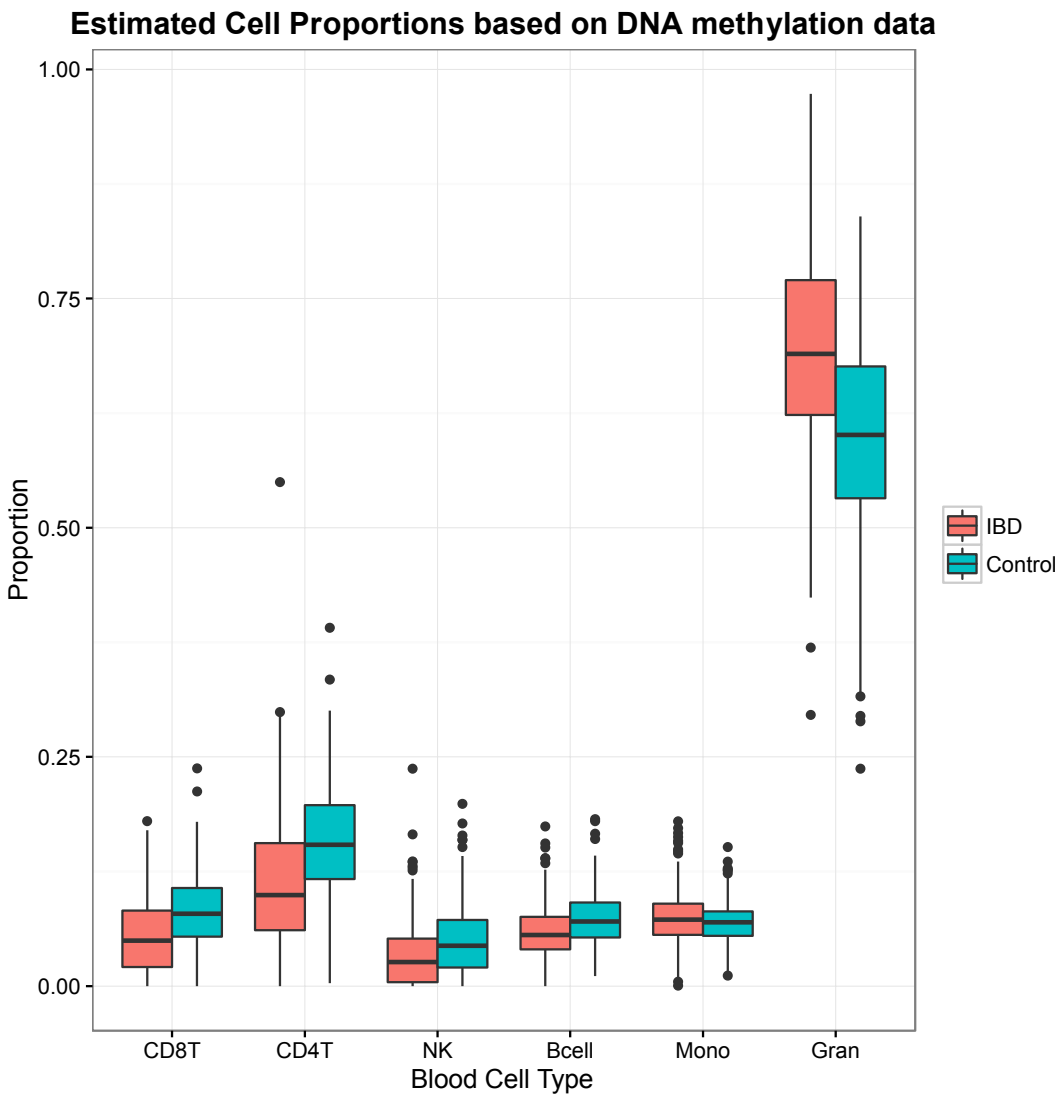
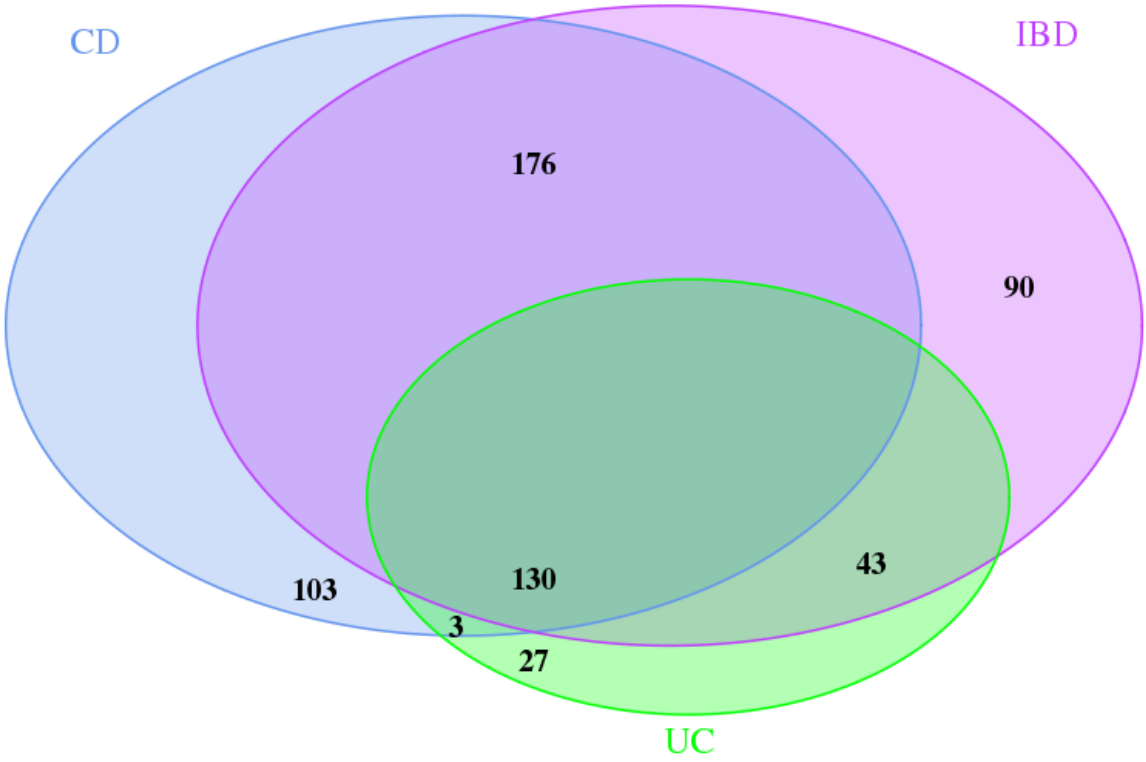
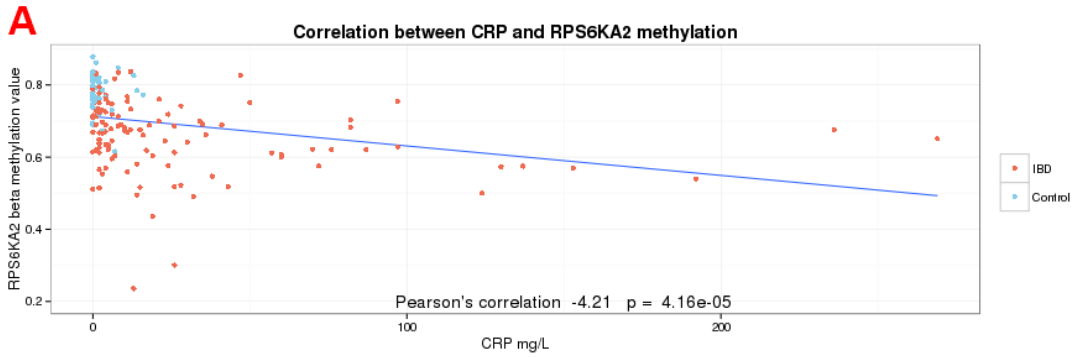


Supplementary Figure 1 - Estimated cell proportions as derived from Houseman[1] cell mixture deconvolution from DNA methylation data.CD8T=CD8⁺ T-cells, CD4T=CD4⁺ T-cells, NK=Natural-Killer Cells, Bcell=B-cell, Mono=Monocyte, Gran=Granulocytes, IBD=inflammatory bowel disease.

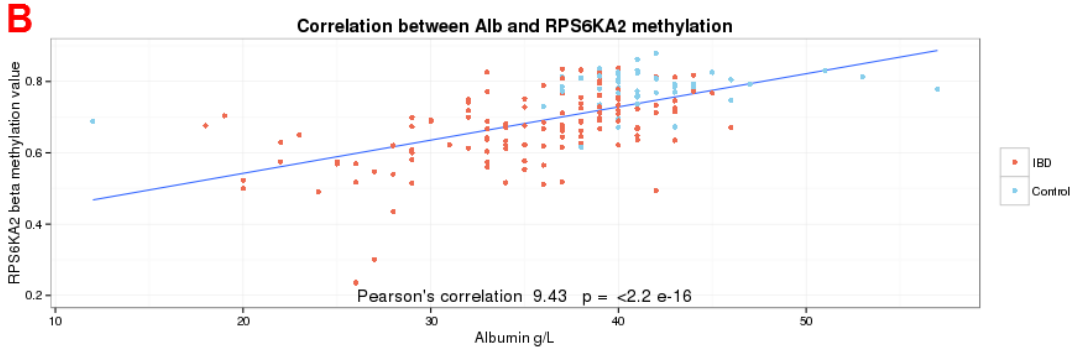


Supplementary Figure 2 – Venn diagram demonstrating overlap in differentially methylated positions (DMPs) seen in inflammatory bowel disease (IBD, purple), Crohn's disease (CD, blue) and ulcerative colitis (UC, green) versus controls.

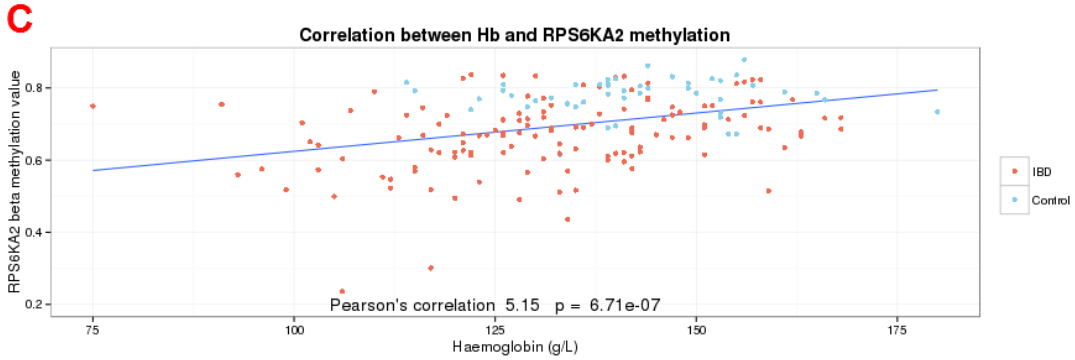
A

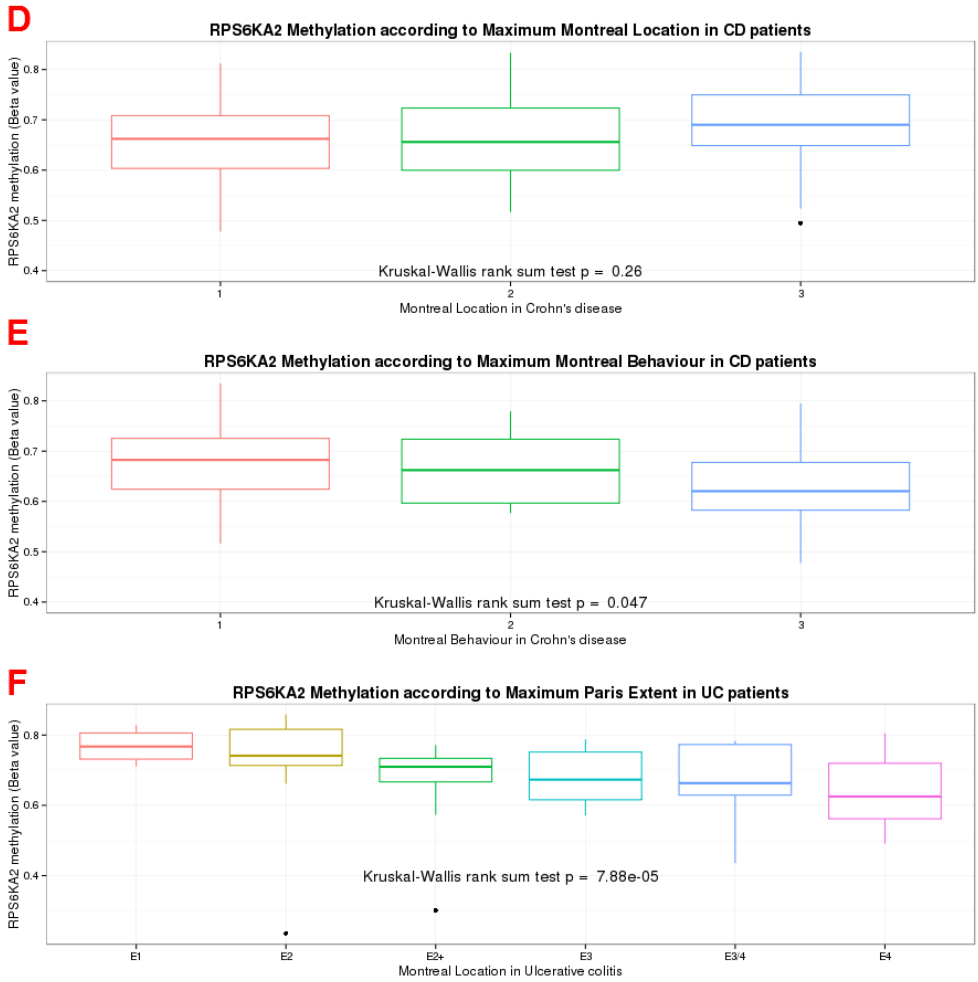

Correlation between CRP and RPS6KA2 methylation
RPS6KA2 beta methylation value
0.2
0.4
0.6
0.8
0
100
200
CRP mg/L
Pearson's correlation -4.21 p = 4.16e-05
IBD
Control

B

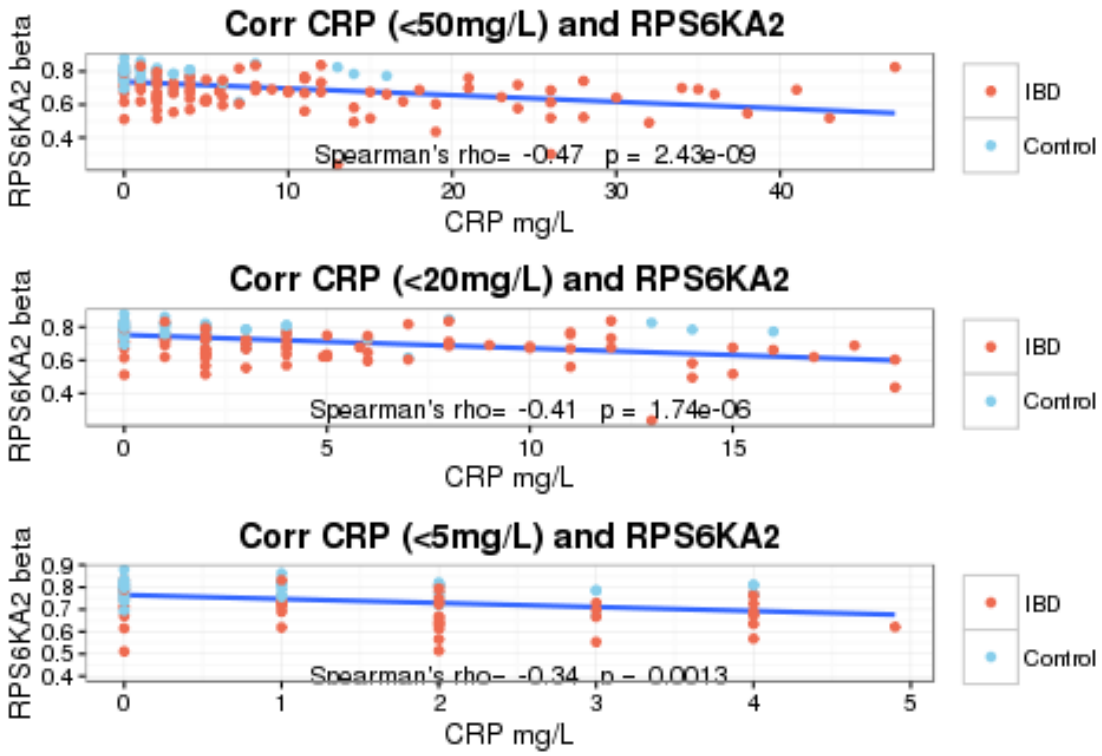

Correlation between Alb and RPS6KA2 methylation
RPS6KA2 beta methylation value
0.2
0.4
0.6
0.8
10
20
30
40
50
Albumin g/L
Pearson's correlation 9.43 p = <2.2 e-16
IBD
Control

C

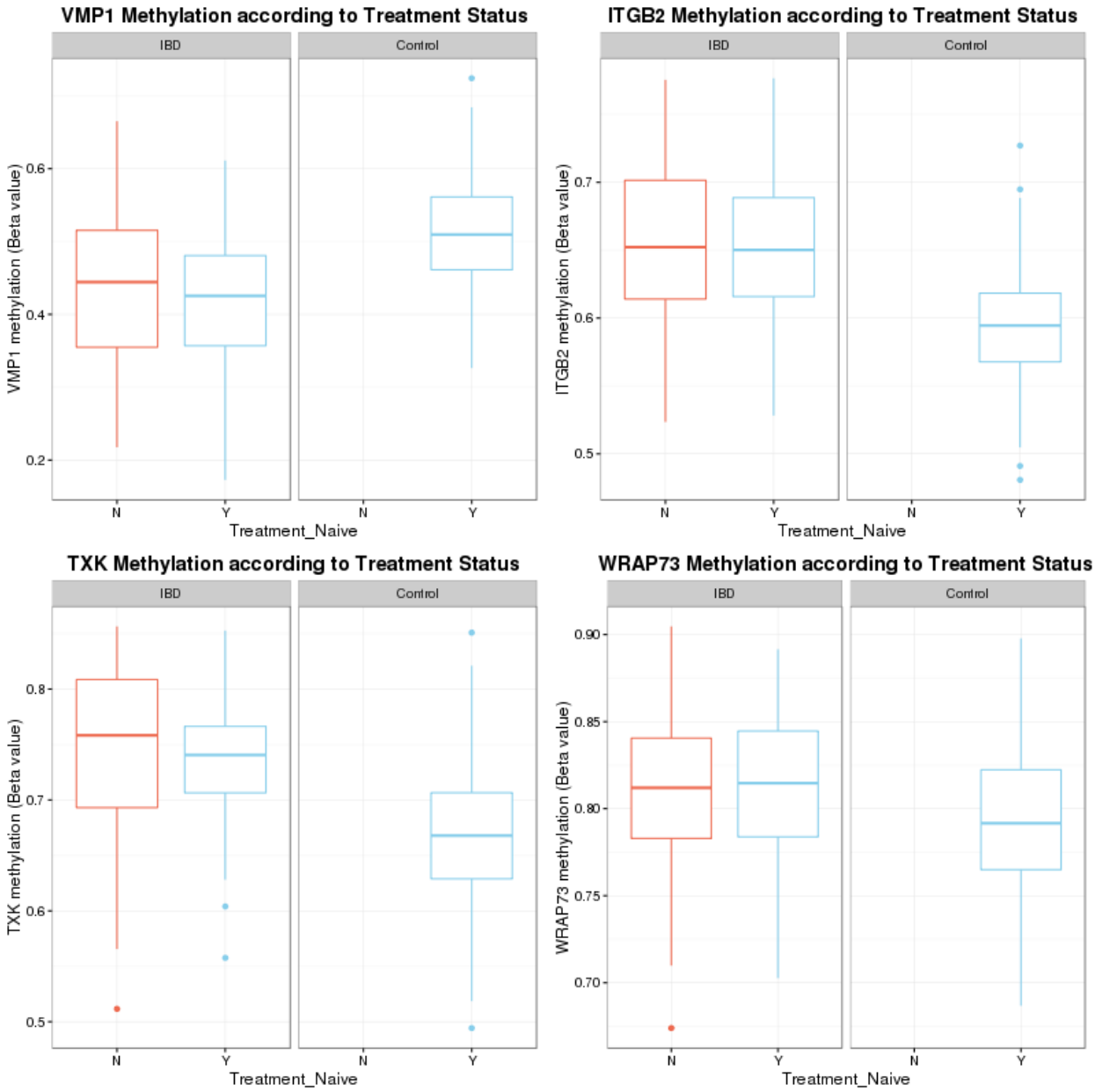

Correlation between Hb and RPS6KA2 methylation
RPS6KA2 beta methylation value
0.2
0.4
0.6
0.8
75
100
125
150
175
Haemoglobin (g/L)
Pearson's correlation 5.15 p = 6.71e-07
IBD
Control



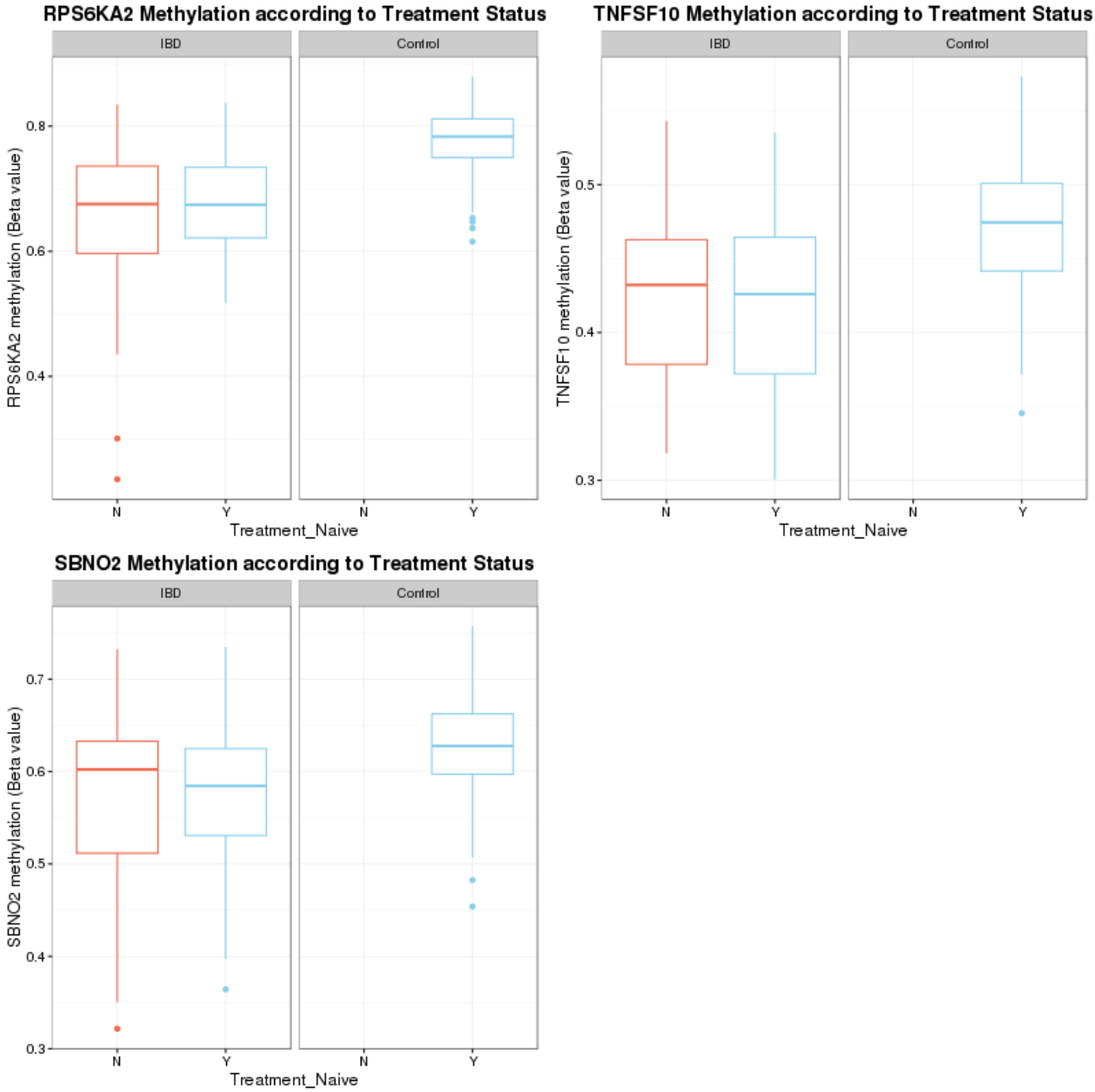
Supplementary Figure 3 - Correlation between RPS6KA2 methylation (beta value) and CRP (A, mg/L), Albumin (B, g/L) and Haemoglobin (C, Hb, g/L). Correlation and p values denote Pearson's test. Boxplots demonstrating RPS6KA2 methylation with maximum Montreal location in Crohn's disease (D, L1=Ileal disease, L2=Colonic disease, L3=Ileocolonic disease), Montreal behaviour in Crohn's disease (E, B1=inflammation only, B2=structuring disease, B3=penetrating disease) and Montreal Extent in Ulcerative colitis (F, E1=proctitis, E2 = left colonic disease, E3=extensive disease, E3/E4=extends beyond splenic flexure, E4=pancolitis). Statistical test = Kruskall Wallis rank sum test.



Supplementary Figure 4 - Correlation between C-Reactive Protein (CRP) and RPS6KA2 beta methylation at different ranges of CRP concentration. Correlation and p value denote Spearman's rank test.

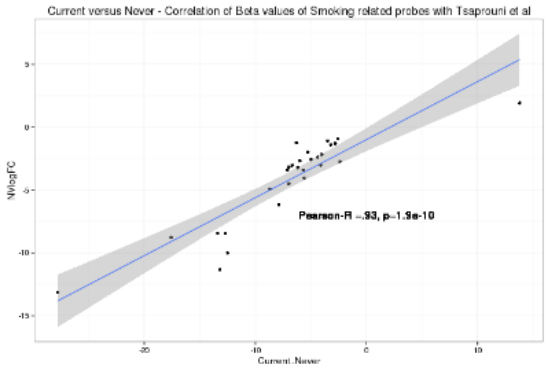


Supplementary Figure 5 - Boxplot demonstrating the impact of treatment on methylation of top differentially methylated regions (DMRs). y axis denotes methylation beta value for each DMR, and x axis denotes treatment naivety(N=not treatment naïve, y=yes treatment naïve). Facets denote case status IBD= inflammatory bowel disease, Control)

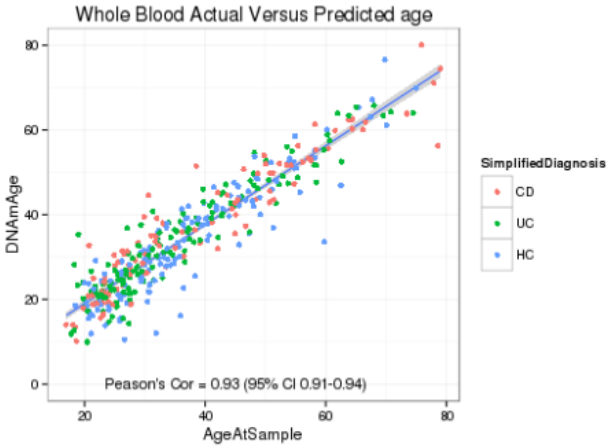


Supplementary Figure 6 - Boxplot demonstrating the impact of treatment on methylation of top differentially methylated positions (DMPs). y axis denotes methylation beta value for each DMR, and x axis denotes treatment naivety(N=not treatment naïve, y=yes treatment naïve). Facets denote case status IBD= inflammatory bowel disease, Control)

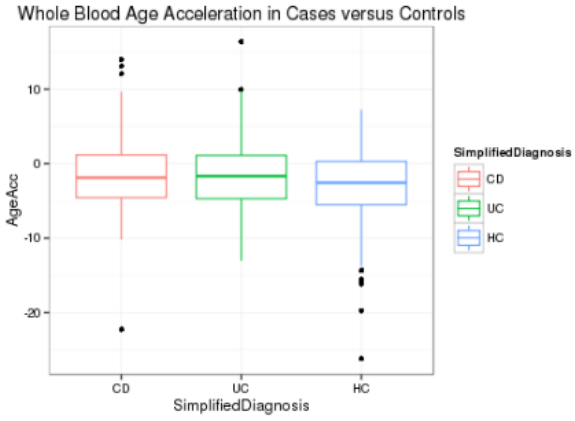
A



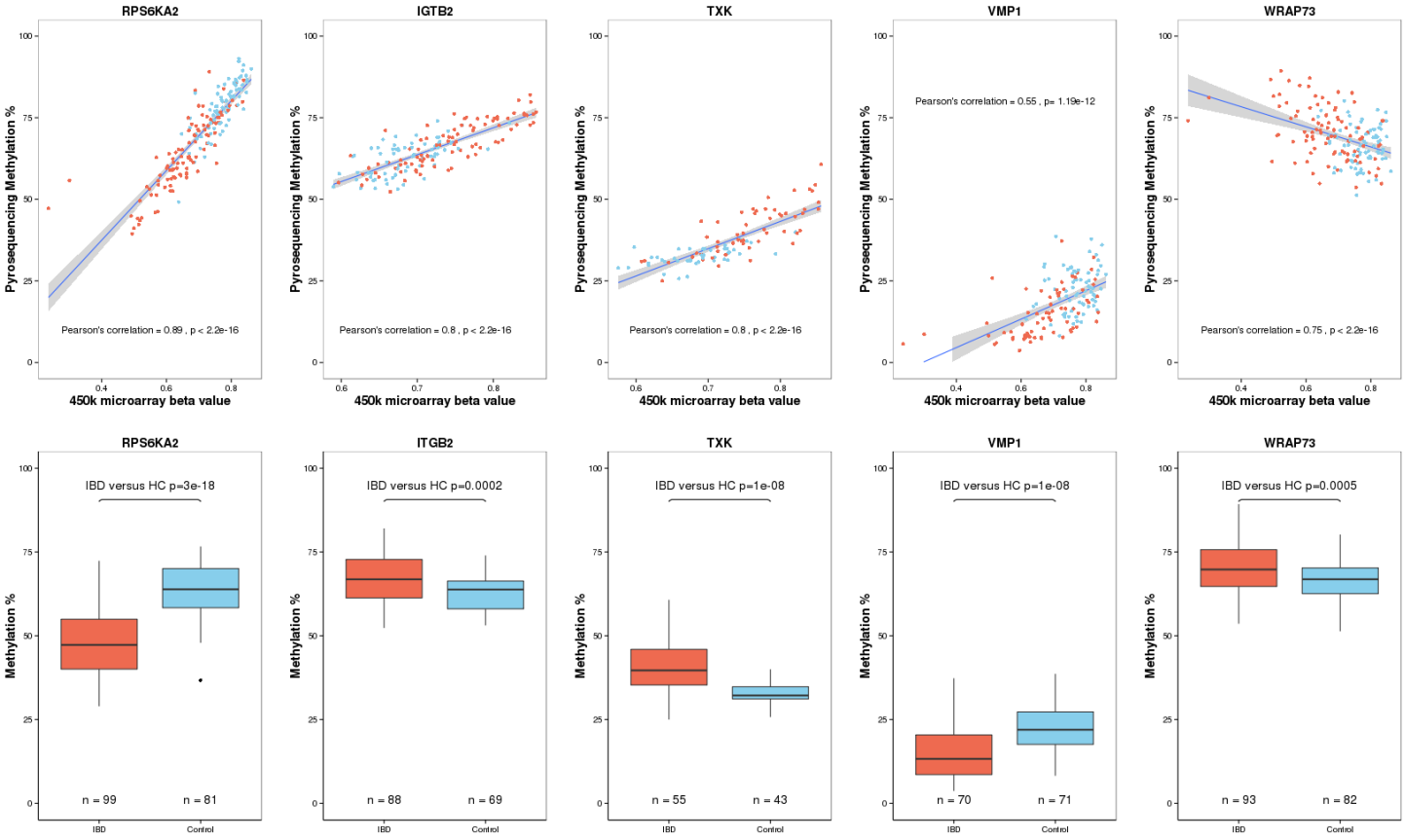
B



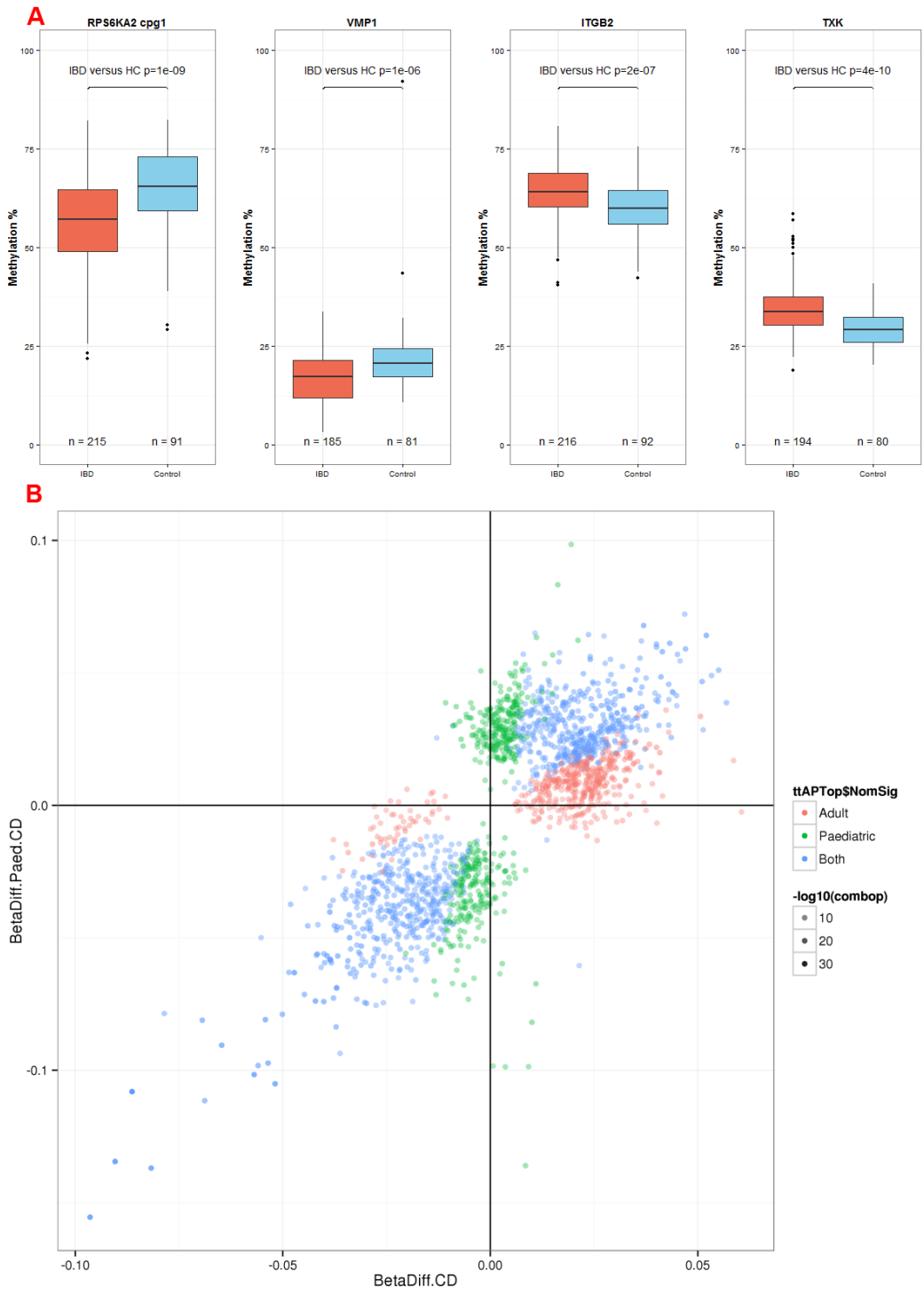
C



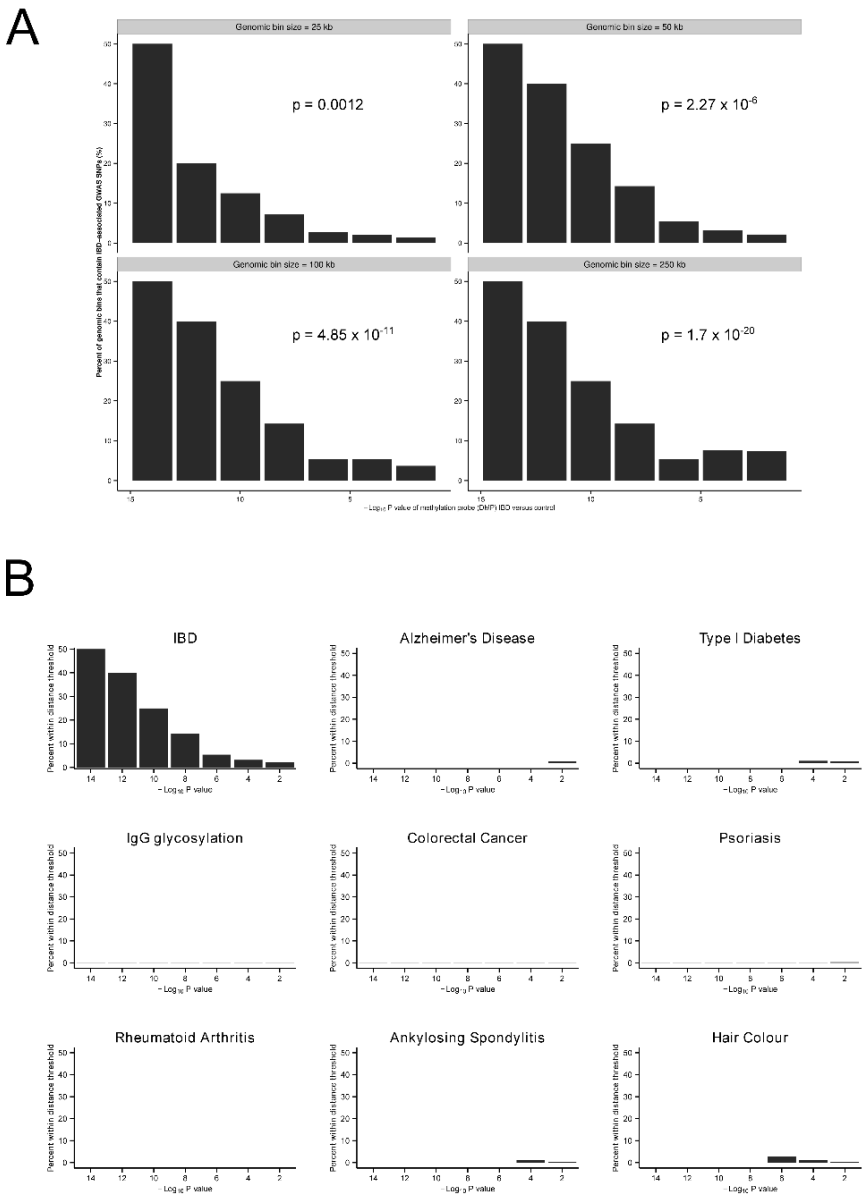
Supplementary Figure 7 - A - Correlation between smoking related DNA methylation probes in the present dataset (Smokers versus non-smokers) and the previously published dataset by Taylor/Tsapouroni et al.[2] Correlation and p values denotes Pearson's test. B - Correlation between actual age of whole blood samples obtained from patients in this study and estimated age using a modification of the Horvath method[3] Correlation and p values denotes Pearson's test. C – Estimated age acceleration in IBD cases compared with controls using a modification of the Horvath method[3] (CD= Crohn's disease, UC = ulcerative colitis, HC = healthy controls).Y-axis=age acceleration.



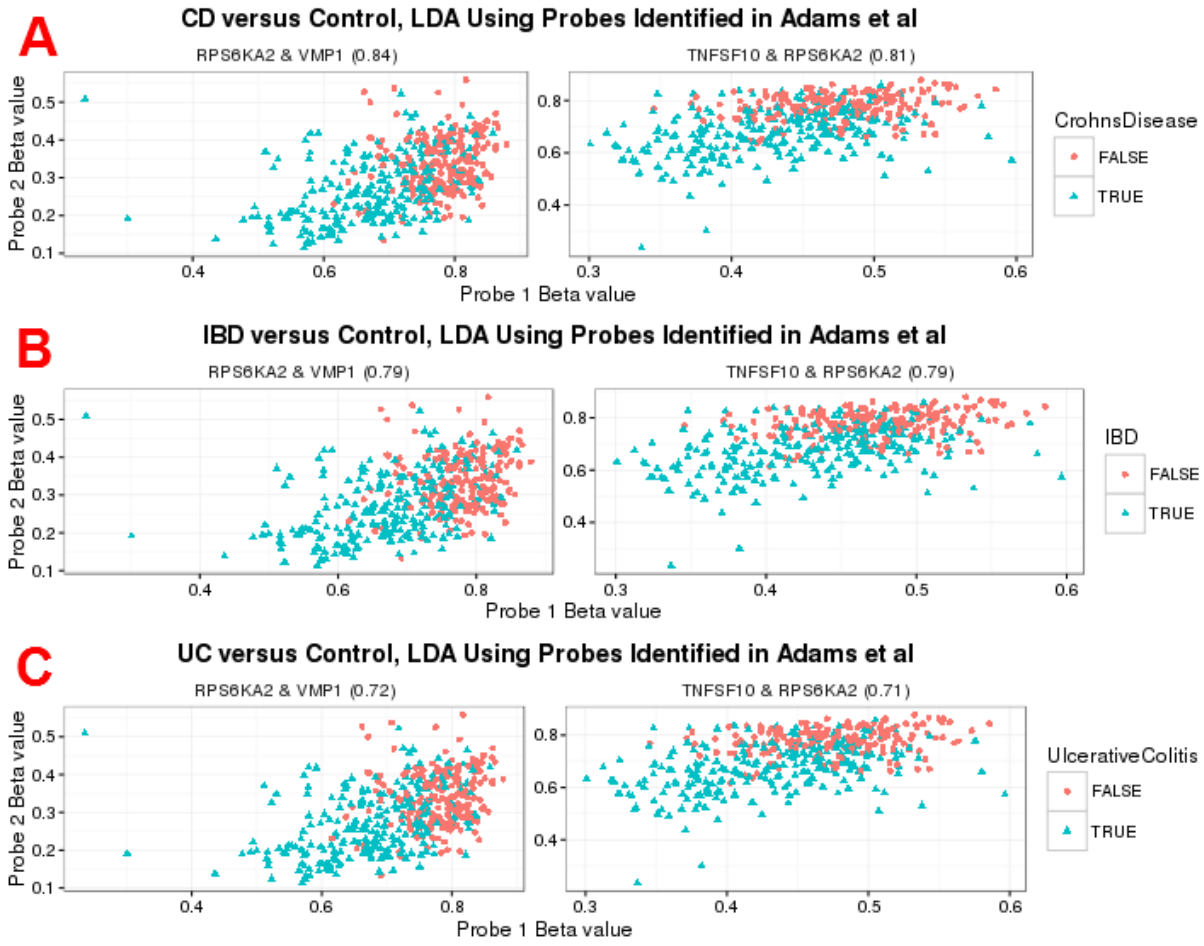
Supplementary Figure 8 - Technical validation of 450k microarray results using pyrosequencing. The top panel demonstrates correlation between methylation percentage (pyrosequencing) and beta values (450k microarray). The red points represent IBD cases, and the blue points represent controls. The bottom panel demonstrates the methylation difference (%) between IBD cases (red) and controls (blue) using pyrosequencing. P values calculated using Wilcoxon test. Correlation using Pearson's test.



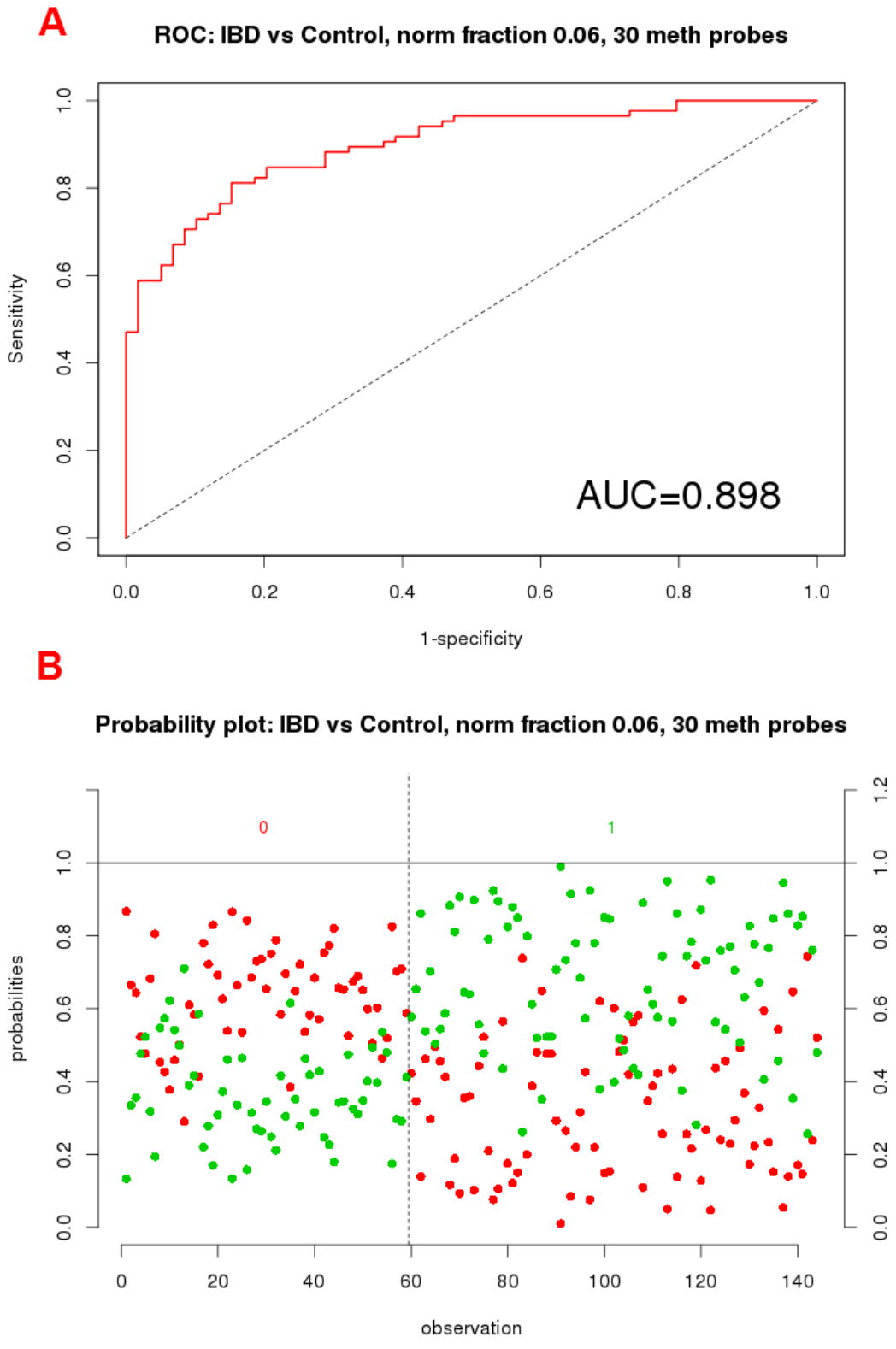
Supplementary Figure 9 – A= Pyrosequencing validation of top DMP (RPS6KA2) and DMRs (VMP1, ITGB2, TXK) in inflammatory bowel disease cases (IBD, red) and controls (blue). P values calculated using Wilcoxon test. B= Correlation between differentially methylated positions in the present (adult) dataset and previously published paediatric data set. Blue points = methylation probes rank in top 10000 in both adult and paediatric datasets, Red points = methylation probes rank in top 10000 in adult dataset only, Green points = methylation probes rank in top 10000 in paediatric dataset only. Transparency of points denotes the statistical significance (-log10 p value). Pearson's correlation 0.28, p-value < 2.2×10^{16}.



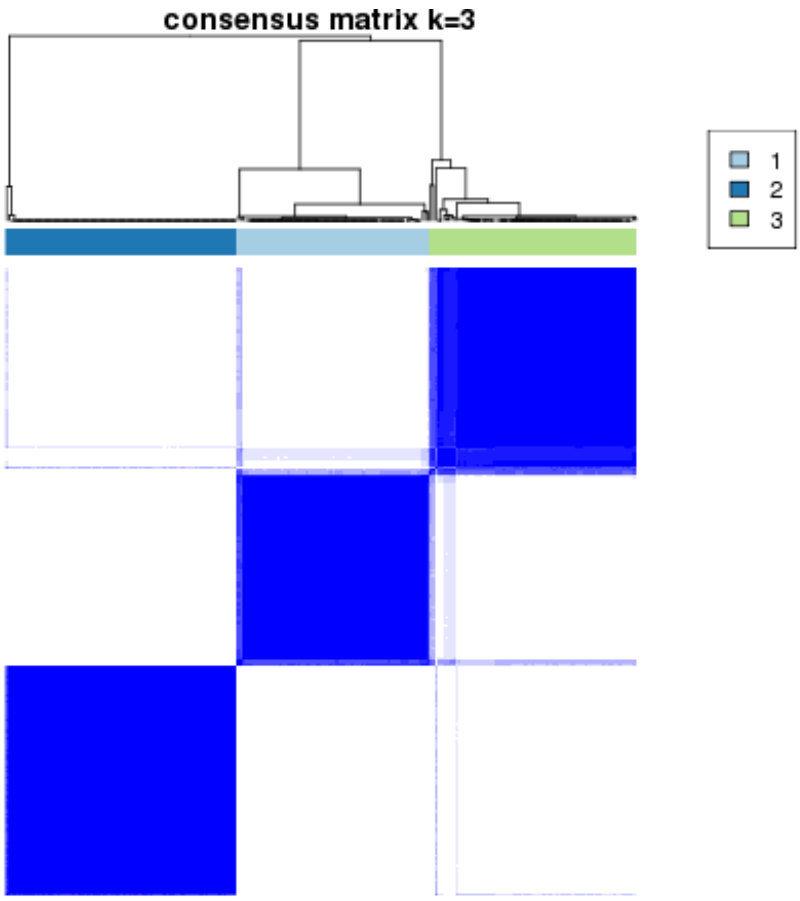
Supplementary Figure 10- Co-localisation of statistically significant IBD-associated differentially methylated positions (DMP) and IBD GWAS loci. A -Each facet represents a different genomic bin size (25kb, 50kb, 100kb and 250kb). There was co-localisation of IBD-associated SNPs (y-axis) within genomic regions (i.e. defined bin) containing highly statistically significant DNA methylation probes compared those regions containing methylation probes with lower levels of statistical significance (x axis, -log 10 p value). P values denote Wilcoxon rank sum comparison with randomly generated bins with similar probe density. B – Enrichment of IBD-associated SNPs but not of SNPs associated with other complex immune traits and diseases within 50kb regions containing IBD-associated differentially methylated positions.



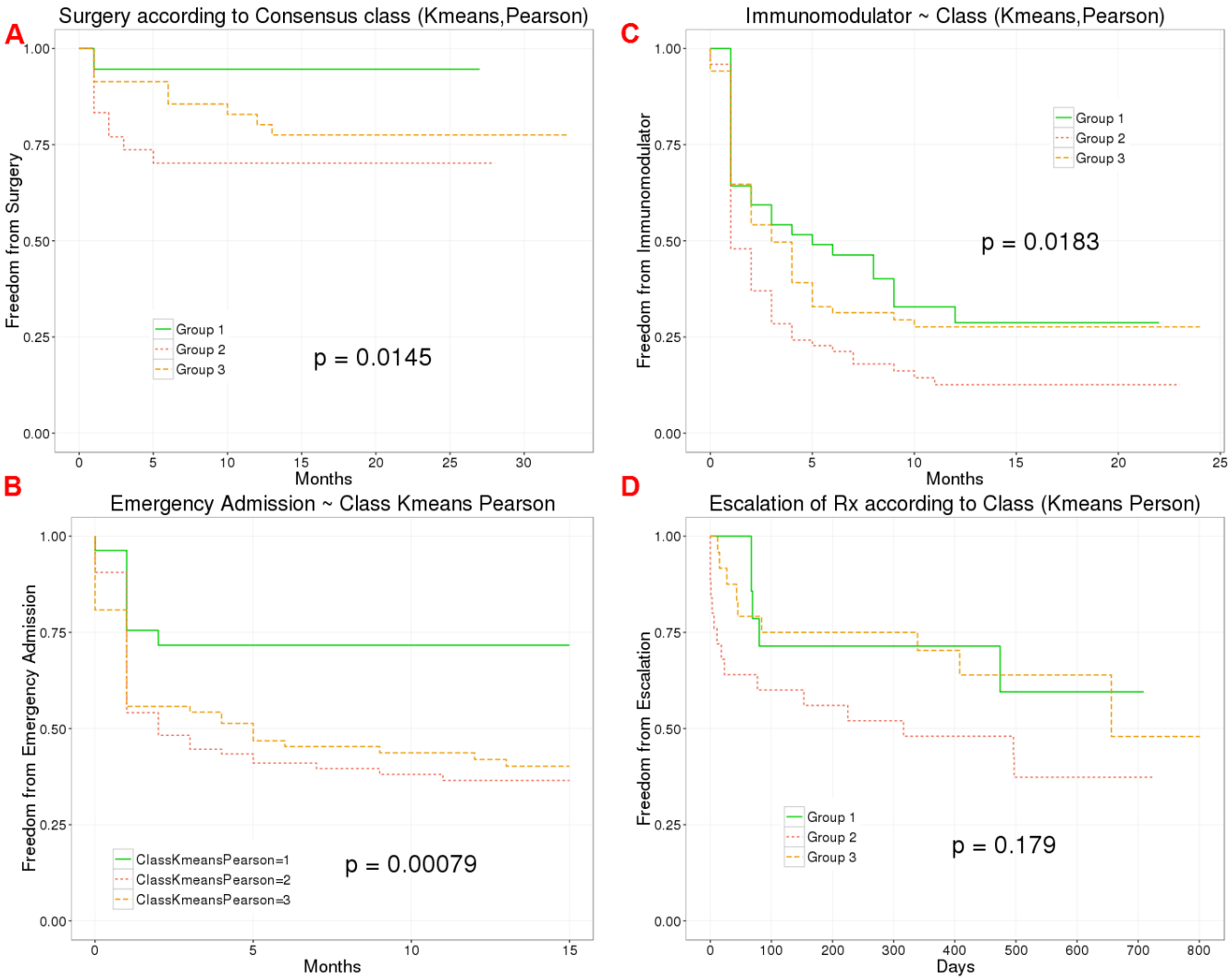
Supplementary Figure 11 - Validation of 2 methylation probe biomarkers described in Adams et al.[4] The top two performing 2-marker probe sets were validated in the present dataset using linear discriminant analysis (without cross validation) for Crohns disease (CD, blue points, panel A), inflammatory bowel disease (IBD blue points, panel C) and ulcerative colitis (UC blue points, panel C) versus control (red points). The figures in brackets denote the area under receiver operator curve (AUC).



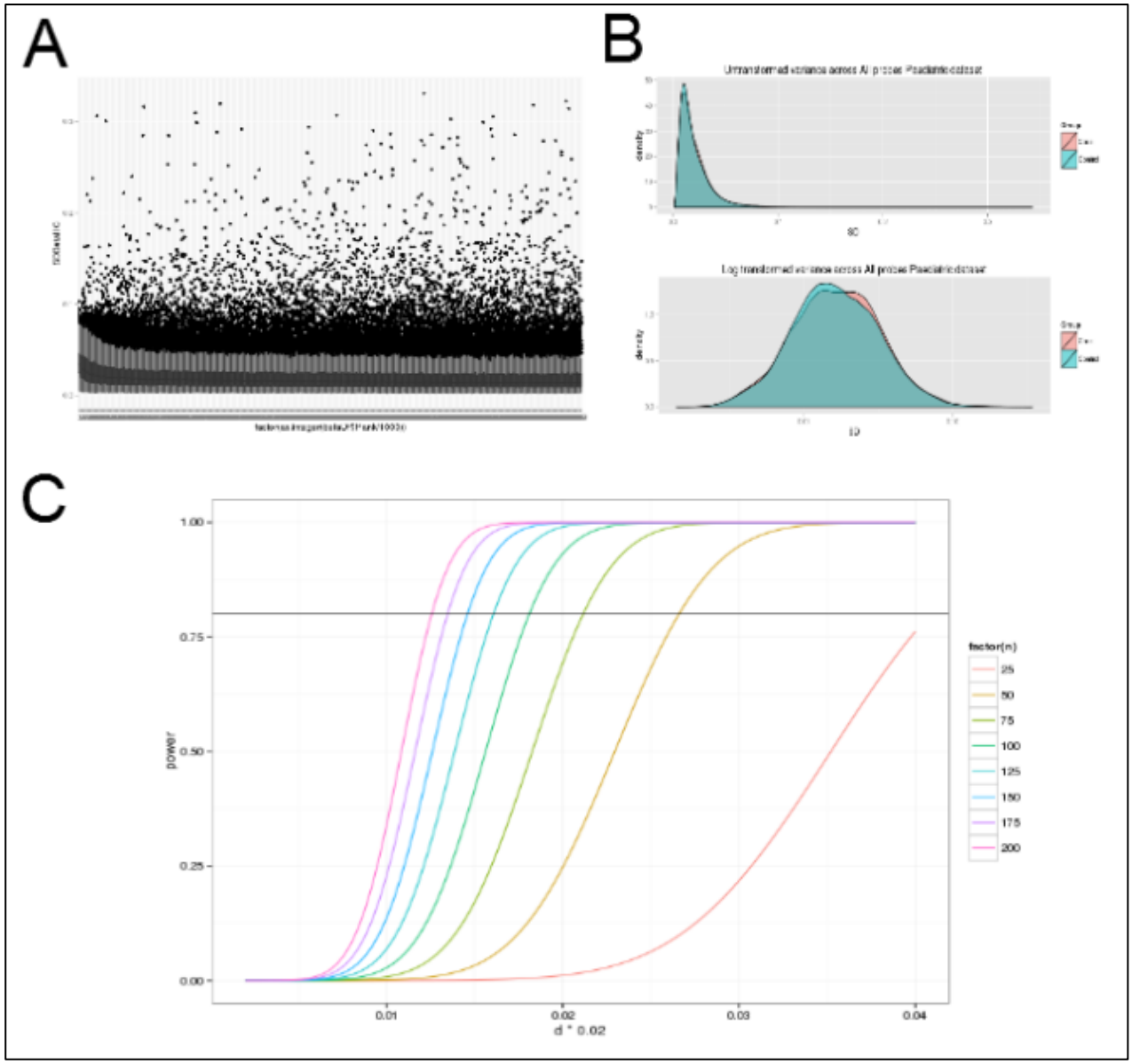
Supplementary Figure 12 – A: Receiver operating characteristic (ROC) curve for 30 methylation probes selected using L1 penalized regression analysis (Lasso) distinguish IBD from controls. B: Probability plot. 0/red = controls, 1/green = IBD cases. `



Supplementary Figure 13- Unsupervised Consensus Clustering to identify IBD subclasses based on DNA methylation data. Three stable clusters were formed.



Supplementary Figure 14 - Survival analysis according to DNA methylation consensus class. A– Time to surgery in months. B – Time until emergency admission in months. C – Time until requirement for Immunomodulator in months (oral or IV steroid, anti-TNFalpha drug, ciclosporin, Methotrexate, thiopurine). D – Criteria of treatment escalation defined by Lee et al[5] in days (surgery, step up to 2 or more immunmodulators). P values denote ChiSquared test for difference between survival curves with 2 degrees of freedom. The coloured lines denoted the three different groups (green =Group 1, low risk, yellow = Group 3, intermediate risk, red= Group 2 high risk).



Supplementary Figure 15 – Power A – Boxplot of median variance across all probes on 450K array. B – Distribution of beta values and log transformed beta values. C – Power curves used to determine numbers per group required to detect a difference of one standard deviation. Y axis = power, X axis = effect size, different colour lines represent number (n) in each group.

		CD (n=121)	**UC (n=119)**	P value CD vs UC	**Symptomatic controls (n=74)**	P value SC vs CD	P value SC vs UC	**Healthy volunteers (n=117)**	P value HL vs CD	P value HL vs UC
Age [median(IQR)]		32.4 (24.9-50.7)	34.3 (25.5-47.8)	1†	32.8 (26.4-45.5)	0.9†	0.9†	32.3 26.4-40.6)	0.4†	0.3†
Females (%)		58 (47.9)	51 (42.9)	0.5 ◊	39 (52.7)	0.6 ◊	0.2 ◊	59 (50.4)	0.8◊	0.3◊
Smoking status	Current	53	13	Current versus ex/never 5×10^{-8}	17	Current versus ex/never 0.005	Current versus ex/never 0.05	24	Current versus ex/never 0.0005	Current versus ex/never 0.5
	Ex	29	45		17			32		
	Never	39	58		40			56		
	Unknown	0	3		0			5		
CRP		8(2-23)	11.5 (2-31)	0.8†	0 (0-3.5)	0.006†	0.004†			
ESR		18 (5-39)	5.5 (4.3-9.8)	0.03†	6 (4.5-7.5)	0.002†	1†			
FC		495 (135-828)	760 (660-950)	0.2	19 (19-37)	0.0001†	1.0×10^{-6}†			
Time between diagnosis & sample (days, median [IQR])		48 [7-90.8)	32 [1-71]							
Treatment Naïve (denominator number with available data)		27/69	37/70							
Oral/IV steroids at sample (duration of therapy days, median [IQR])		10/69 (8[2-14])	10/70 (2[1-6.5])							
Biologic at sample (duration of therapy in days, median [IQR])		4/69 (4 [2.75-5.25])	-							
Aza/6MP at sample (duration of therapy in days, median [IQR])		10/69 (5[2-10])	4/70 (5[2-10])							

Topical therapy at sample (duration of therapy in days, median [IQR])	1/69 (1 DAY)	11/70 (5[2.75-13.25])				
Oral 5ASA at sample (duration of therapy in days, median [IQR])	3/69 (2[1-5])	16/70 (2[1-5)				

Supplementary Table 1 - Patient Demographics (CD= Crohn's disease, UC= Ulcerative colitis, SC= Symptomatic controls, HL=Healthy Lab volunteers, IQR=interquartile range, CRP=C-reactive protein, ESR=Erythrocyte sedimentation rate, FC= faecal calprotectin † = Wilcoxon rank sum test, ǂ = Welch two sample t test, ◊ = χ^2 test)

category	No. genes differentially expressed in category	Total No of genes in category	GO term	P Val	FDR Adj P Val
GO:0080134	47	1293	regulation of response to stress	1.27E-07	0.003
GO:0048518	119	4815	positive regulation of biological process	3.41E-07	0.003
GO:0044763	213	10900	single-organism cellular process	8.02E-07	0.005
GO:0044699	227	11972	single-organism process	1.02E-06	0.005
GO:0009607	32	816	response to biotic stimulus	1.61E-06	0.005
GO:0001775	34	853	cell activation	1.70E-06	0.005
GO:0002252	29	675	immune effector process	1.93E-06	0.005
GO:0048583	86	3212	regulation of response to stimulus	2.38E-06	0.005
GO:0048522	104	4164	positive regulation of cellular process	2.50E-06	0.005
GO:0051179	120	5016	localization	2.59E-06	0.005
GO:0031347	29	699	regulation of defense response	2.80E-06	0.005
GO:0002376	66	2336	immune system process	3.56E-06	0.006
GO:0043207	30	783	response to external biotic stimulus	5.01E-06	0.007
GO:0051707	30	783	response to other organism	5.01E-06	0.007
GO:0002366	13	171	leukocyte activation in immune response	5.27E-06	0.007
GO:0045321	27	635	leukocyte activation	5.86E-06	0.007
GO:0002263	13	173	cell activation involved in immune response	6.12E-06	0.007
GO:0002682	44	1365	regulation of immune system process	1.11E-05	0.012

GO:0006810	99	4044	transport	1.23E-05	0.013
GO:0051234	101	4156	establishment of localization	1.45E-05	0.014
GO:0070887	67	2444	cellular response to chemical stimulus	1.81E-05	0.017
GO:0006897	24	546	endocytosis	2.86E-05	0.026
GO:0030099	17	316	myeloid cell differentiation	3.18E-05	0.027
GO:0006952	47	1610	defense response	3.27E-05	0.027
GO:0045638	8	77	negative regulation of myeloid cell differentiation	3.93E-05	0.031
GO:0051049	48	1584	regulation of transport	4.45E-05	0.034
GO:0046632	8	75	alpha-beta T cell differentiation	4.72E-05	0.035
GO:0009891	49	1645	positive regulation of biosynthetic process	5.25E-05	0.037
GO:0009611	33	950	response to wounding	6.13E-05	0.040
GO:0010646	71	2666	regulation of cell communication	6.27E-05	0.040
GO:0050776	31	885	regulation of immune response	6.40E-05	0.040
GO:0002684	29	818	positive regulation of immune system process	6.41E-05	0.040
GO:0044422	150	7205	organelle part	7.51E-05	0.042
GO:1902578	89	3663	single-organism localization	7.54E-05	0.042
GO:0002521	19	413	leukocyte differentiation	7.56E-05	0.042
GO:0044765	86	3512	single-organism transport	7.67E-05	0.042
GO:0051641	69	2638	cellular localization	7.72E-05	0.042
GO:0046637	6	43	regulation of alpha-beta T cell differentiation	8.18E-05	0.042

GO:0048534	27	706	hematopoietic or lymphoid organ development	8.27E-05	0.042
GO:0016192	39	1186	vesicle-mediated transport	8.42E-05	0.042
GO:0050896	152	7392	response to stimulus	8.59E-05	0.042
GO:0048771	10	132	tissue remodeling	8.89E-05	0.042
GO:0033365	27	744	protein localization to organelle	9.73E-05	0.044
GO:0050778	23	587	positive regulation of immune response	9.78E-05	0.044
GO:0002274	10	143	myeloid leukocyte activation	0.000103	0.046
GO:0009605	61	2303	response to external stimulus	0.000108	0.046
GO:0045087	32	974	innate immune response	0.000109	0.046
GO:0009893	80	3185	positive regulation of metabolic process	0.000111	0.046
GO:0002697	17	371	regulation of immune effector process	0.000115	0.046
GO:0006955	42	1454	immune response	0.000117	0.046
GO:0023051	69	2620	regulation of signaling	0.00012	0.046
GO:0032101	27	763	regulation of response to external stimulus	0.00012	0.046
GO:1903707	9	119	negative regulation of hemopoiesis	0.000123	0.046
GO:0006950	85	3582	response to stress	0.000123	0.046

Supplementary Table 2 – GO term analysis of DMPs in IBD versus control in whole blood

Gene	Position	CHR	Δβ	P Value	Holm adj P value
RPS6KA2	166970252	chr6	-0.09	1.26E-29	5.63E-24
SBNO2	1130866	chr19	-0.09	3.61E-26	1.62E-20
VMP1	57915665	chr17	-0.11	3.04E-23	1.36E-17
SBNO2	1130965	chr19	-0.05	1.15E-22	5.16E-17
VMP1	57915717	chr17	-0.10	3.52E-22	1.58E-16
NA	50327986	chr22	-0.05	4.81E-21	2.15E-15
NA	101901234	chr3	-0.06	2.73E-18	1.22E-12
SOCS3	76354621	chr17	-0.07	3.63E-18	1.63E-12
NA	12890029	chr19	-0.06	1.92E-17	8.62E-12
FKBP5	35654363	chr6	-0.07	3.42E-17	1.53E-11
NA	35696870	chr6	-0.04	7.67E-17	3.44E-11
VMP1	57915773	chr17	-0.06	1.09E-16	4.90E-11

Supplementary Table 3 - Top table of differentially methylated positions (DMPs) between Crohn's disease (CD) cases and controls in whole blood. NA denotes methylation probes with no annotated gene symbol. $\Delta\beta$ = difference in methylation beta value. Holm adjusted p value derived from linear models with age, sex and estimated cell proportions as co-variates. Chr= chromosome.

Gene	Position	CHR	Δβ	P Value	Holm adj P value
NA	35696870	chr6	-0.04	1.12E-16	5.02E-11
NA	101901234	chr3	-0.06	1.35E-16	6.07E-11
TNFSF10	172235808	chr3	-0.05	2.85E-16	1.28E-10
SBNO2	1130866	chr19	-0.06	1.42E-15	6.36E-10
NA	12890029	chr19	-0.06	1.57E-15	7.03E-10
AIM2	159047163	chr1	-0.06	6.96E-15	3.12E-09
ICA1	8201134	chr7	0.04	1.45E-14	6.48E-09
RPS6KA2	166970252	chr6	-0.07	2.22E-14	9.95E-09
VMP1	57915665	chr17	-0.09	2.48E-14	1.11E-08
ZEB2	145172035	chr2	-0.08	5.65E-14	2.53E-08
NA	50327986	chr22	-0.04	2.11E-13	9.45E-08
FRMD4A	13913931	chr10	0.05	2.45E-13	1.10E-07

Supplementary Table 4 - Top table of differentially methylated positions (DMPs) between Ulcerative colitis (UC) cases and controls in whole blood. NA denotes methylation probes with no annotated gene symbol. $\Delta\beta$ = difference in methylation beta value. Holm adjusted p value derived from linear models with age, sex and estimated cell proportions as co-variates. Chr= chromosome.

Gene	Probe	Position	CHR	Δβ	P Value	Holm Adj P value
MNDA	cg05304729	158800024	chr1	-0.06	3.44E-07	0.15
NA	cg19683494	74908142	chr5	-0.06	5.94E-07	0.27
ZEB2	cg10502206	145182344	chr2	0.02	1.08E-06	0.49
NA	cg02573091	74908125	chr5	-0.07	1.97E-06	0.88
NLRC5	cg07839457	57023022	chr16	-0.06	2.81E-06	1
TK1	cg25069807	76171191	chr17	0.03	4.75E-06	1
NA	cg25730685	2375010	chr1	0.01	7.07E-06	1
SPG7	cg04879696	89574810	chr16	0.01	7.66E-06	1
TK1	cg06098276	76171208	chr17	0.04	1.30E-05	1
CENPV	cg05238069	16257135	chr17	0.01	1.56E-05	1
CAPN5	cg08103551	76777993	chr11	0.00	1.67E-05	1
ADK	cg23198334	76179907	chr10	0.01	2.10E-05	1

Supplementary Table 5 - Top table of differentially methylated positions (DMPs) between Crohn's disease (CD) and Ulcerative colitis (UC) in whole blood. NA denotes methylation probes with no annotated gene symbol. Δβ = difference in methylation beta value. Holm adjusted p value derived from linear models with age, sex and estimated cell proportions as co-variates. Chr= chromosome.

Gene	Probe	Position	CHR	Δβ	P Value	Holm adj P value
ROCK1	cg09449490	18690843	chr18	0.01	1.17E-06	0.52
PFKFB3	cg27545615	6249748	chr10	0.03	1.55E-06	0.69
PIK3R6	cg00409104	8762014	chr17	0.02	1.55E-06	0.70
CELF2	cg11832281	11211022	chr10	0.01	1.83E-06	0.82
NA	cg01686975	138816336	chr7	0.02	2.19E-06	0.98
NA	cg24448340	179921042	chr1	0.03	3.00E-06	1
TXNDC11	cg03382501	11794641	chr16	0.02	3.06E-06	1
EFHD2	cg25978218	15738732	chr1	0.02	3.08E-06	1
CPD	cg23344321	28707212	chr17	0.02	4.57E-06	1
XPO6	cg26730763	28205389	chr16	0.01	5.56E-06	1
KIAA1033	cg13622209	105501127	chr12	0.01	5.75E-06	1
NA	cg08900384	72546168	chr11	0.02	6.03E-06	1

Supplementary Table 6 - Top table of differentially methylated positions (DMPs) between Symptomatic controls and healthy volunteers in whole blood. NA denotes methylation probes with no annotated gene symbol. $\Delta\beta$ = difference in methylation beta value. Holm adjusted p value derived from linear models with age, sex and estimated cell proportions as co-variates. Chr= chromosome.

Differentially methylated regions (DMRs)	
VMP1/ microRNA-21	Vaculole membrane protein1 (VMP1) encodes a transmembrane protein within the golgi body, endoplastic reticulum.[6] VMP1 is an inducer of autophagy via interactions with BECN1.[7,8] microRNA-21, is a microRNA is encoded at the 3' end of VMP1,[9] where the change in methylation is concentrated at in IBD.[4] microRNA-21 has been linked with several types of cancer including colorectal cancer.[10] microRNA-21 has been widely implicated in pathogenesis of IBD.[11] microRNA-21 knockout mice have improve survival following chemically (Dextran sulphate sodium) induced colitis in two studies,[12] but exacerbation in TBNS (2,4,6-trinitrobenzenesulfonic acid) and T-cell transfer models of murine colitis.[13] Several microRNA screens have identified upregulation of microRNA-21 in IBD, notably in cases with active inflammation.[14–18]
WDR8/WRAP 73	WD (trp-asp) repeat protein family, antisense to Trp73. The WD gene repeat motif make up a large family of genes involved in several cellular and gene regulatory processes, including cell cycle progression, apoptosis and signal transduction.[19] Murine studies suggest a role for WRAP73 in the process of ossification.[19]
ITGB2 (CD18)	Integrin Beta 2 subunit. Cell adhesion and cell surface mediated signalling.[20] Heritable defects in this gene cause leukocyte adhesion deficiency type I characterised by severe recurrent infections.[21,22] Aberrant DNA methylation at the ITGB2 locus has previous been demonstrated in IBD[23] and other diseases.[24,25] Anti-integrin antibodies have attracted interest as therapeutics in IBD. Natalizumab is an anti-alpha4 integrin antibody is efficacious in multiple sclerosis and CD, but is associated an unacceptable risk of PML (progressive multifocal leukoenchepalopathy).[26] Vedolizumab is a gut-specific anti-α4β7 integrin antibody efficacious for inducing and maintaining remission in UC (GEMINI-1)[27] and CD.[28]
TXK	TXK is a member of the Tec family of tyrosine kinases.[29] T cells express TXK and the other tec kinases, which serve as modulators of T-cell receptor signalling and assist in cytokine production by CD4+ effector T-cells.[30] TXK may also have role in T-cell development in the thymus. TXK has been shown to be over expressed in the circulating leucocytes in Behcet's disease [31] including in Th1 lymphocytes accumulating within intestinal lesions.[32] An IBD-associated GWAS locus.[33]
HDAC4	Histone Deacetylase class II. Histone modifications are an important epigenetic mechanism that are associated with alternative conformations of chromatin. Acetylation of lysine on histones H3 and H4 is associated with transcriptional activity.[34] The extent of acetylation are regulated by the relative activity of the HDAC enzymes, together with the HAT (histone acetyl transferases).[34] Non-specific HDAC inhibitors such as butyrate are associated with amelioration of colitis.[35] Alternative methylation of HDAC4 has previously been described in other situations.[25,36,37]
Differentially methylated positions (DMPs)	
RPS6KA2	Ribsomal S6 kinase A2 is a ribosomal kinase in the serine/threonine kinase family.[38] Acts on the intracellular MAP

(RSK3)	kinase signaling pathway (interacts with MAPK1 and 3).[39] Thought to have a role in cell growth, cell motility, proliferation[39] and cell cycle progression,[40] although may also act as a tumour suppressor gene in ovarian cancer.[41] Alternatively spliced isoforms exist.[41] An IBD-associated GWAS locus.[33]
SBNO2	Strawberry notch homologue 2 has an anti-inflammatory effect, by acting in the IL-10 downstream pathway.[42] IL-10 induced SNBNO2 expression was found to repress NF-κβ (but not IRF7) selectively within macrophages.[42] A susceptibility locus in IBD GWAS.[43]
TNFSF10 (TRAIL, CD253, Apo2L)	Tumour necrosis factor superfamily member 10/TRAIL acts as a ligand in the TNF family.[44] This widely investigated cytokine induces caspase-8-dependent apoptosis in tumour but not normal cells;[45] this property has led to extensive investigation as a chemotherapeutic agent.[46] TRAIL has been implicated in intestinal inflammation and demonstrated to be over-expressed in intestinal epithelial cell lines[47] and in human mononuclear cells in inflamed intestinal sections.[48]
BCL3	B-cell CLL/lymphoma 3 is a proto-oncogene acting as a co-activator through NF-κβ and is associated with translocation in a specific form of B-cell leaukaemia (t(14;19)(q32;q13)) [49]
IL23A	Interleukin 23 subunit A. The T-helper (Th)17 and interleukin (IL)12-23 pathway is well established in IBD pathogenesis, with susceptibility gene loci IL23R, IL12B, JAK2, and STAT3 identified in both UC and CD.[50,51]

Supplementary Table 7 - Selected candidate genes in differentially methylated regions and positions.

Illumina 450k Probe id	Chr	Gene symbol	Δβ	P.Value	FDR adj.P.Val
cg17501210	chr6	RPS6KA2	-0.07	2.09E-21	9.38E-16
cg18608055	chr19	SBNO2	-0.07	2.20E-20	9.84E-15
cg16936953	chr17	VMP1	-0.08	1.20E-18	5.36E-13
cg09349128	chr22	NA	-0.04	6.81E-18	3.05E-12
cg12170787	chr19	SBNO2	-0.04	6.96E-18	3.12E-12
cg25114611	chr6	NA	-0.04	1.19E-17	5.35E-12
cg12992827	chr3	NA	-0.05	3.58E-17	1.60E-11
cg19821297	chr19	NA	-0.06	1.79E-16	8.04E-11
cg12054453	chr17	VMP1	-0.07	4.29E-16	1.92E-10
cg01059398	chr3	TNFSF10	-0.04	1.78E-15	7.98E-10
cg26804423	chr7	ICA1	0.04	4.04E-15	1.81E-09
cg02716826	chr9	NA	-0.03	8.06E-15	3.61E-09
cg13619623	chr7	BBS9	0.04	1.00E-14	4.49E-09
cg18942579	chr17	VMP1	-0.05	1.05E-14	4.70E-09
cg03546163	chr6	FKBP5	-0.06	1.72E-14	7.70E-09
cg07398517	chr3	NA	-0.03	1.95E-14	8.73E-09
cg26470501	chr19	BCL3	-0.03	2.19E-14	9.82E-09
cg22959742	chr10	FRMD4A	0.04	5.91E-14	2.65E-08
cg02448796	chr1	KCNAB2	0.04	1.15E-13	5.14E-08
cg16724148	chr1	AGL	0.03	3.11E-13	1.39E-07

Supplementary Table 8 - Top table of differentially methylated positions (DMPs) between inflammatory bowel disease (IBD) cases and controls in whole blood with smoking included as a covariate along with age, sex and the estimated blood cell proportions. NA denotes methylation probes with no annotated gene symbol. $\Delta\beta$ = difference in methylation beta value. FDR = false discovery rate p value. Chr= chromosome.

Illumina 450k Probe id	Chr	Gene symbol	Δβ	P.Value	Holm adj.P.Val
cg16936953	chr17	VMP1	-0.11	1.71E-16	7.68E-11
cg01059398	chr3	TNFSF10	-0.06	2.83E-16	1.27E-10
cg18608055	chr19	SBNO2	-0.08	3.65E-16	1.64E-10
cg19821297	chr19	NA	-0.07	9.37E-15	4.20E-09
cg09349128	chr22	NA	-0.05	2.09E-14	9.37E-09
cg12054453	chr17	VMP1	-0.09	6.02E-14	2.70E-08
cg12992827	chr3	NA	-0.06	3.00E-13	1.35E-07
cg12269535	chr6	SRF	-0.05	8.07E-13	3.62E-07
cg12170787	chr19	SBNO2	-0.05	1.43E-12	6.41E-07
cg02650017	chr17	PHOSPHO1	-0.02	2.44E-12	1.09E-06
cg16292768	chr8	CLU	-0.05	3.22E-12	1.44E-06
cg17501210	chr6	RPS6KA2	-0.07	3.80E-12	1.70E-06
cg02716826	chr9	NA	-0.04	9.09E-12	4.07E-06
cg10472711	chr7	HEATR2	-0.06	2.62E-11	1.17E-05

Supplementary Table 9 - Top table of differentially methylated positions (DMPs) between inflammatory bowel disease (IBD) cases and controls in whole blood with treatment status included as a covariate along with age, sex and the estimated blood cell proportions. NA denotes methylation probes with no annotated gene symbol. $\Delta\beta$ = difference in methylation beta value.

	IBD (n=130)	**Control** (n=101)	p Value
Female	51 (50.5%)	47 (36.2%)	0.3◊
Age (median, IQR)	29.2 (25.9-42.4)	30.7 (26 - 38.9)	0.9†
Current Smokers (%)	36 (27.7%)	20 (19.8%)	0.2◊
CRP	8.5 (3-33.5)	2 (1-4.5)	1.7e-05†
Albumin	34 (26.3-38)	41 (38-43)	2.3e-07†
WCC	8.3 (5.8-12.3)	5.7 (4.8-12.3)	6.1e-07†

Supplementary Table 10 - Patient demographics of subset of adult cohort used for technical validation studies using pyrosequencing (Results are median and interquartile range unless stated, WCC=white cell count, CRP=C-reactive protein, IQR= interquartile range, IBD=inflammatory bowel disease, † = Wilcoxon rank sum test, ◊ = $\chi 2$ test)

	Pearson's correlation	Lower CI	Upper CI	P value
RPS6KA2	0.89	0.86	0.92	2.2e-16
IGTB2	0.8	0.73	0.85	2.2e-16
TXK	0.8	0.71	0.86	2.2e-16
VMP1	0.55	0.43	0.66	1.2e-12
WRAP73	0.75	0.68	0.81	2.2e-16

Supplementary Table 11 - Technical replication: Correlation between Methylation 450k microarray and pyrosequencing for same samples. CI = 95% confidence interval

		CD (n=121)	UC (n=119)	Controls (n= 98)
Age		36.5 (26.4-47.8)	36.6 (27.1-46.7)	34.9 (27.3-55.5)
Females *(%)*		68 *(57)*	74 *(62)*	65 *(66)*
Smoking status	Current *(%)*	18 *(15)*	7 *(6)*	14 *(14)*

Supplementary Table 12 - Patient demographics of Independent pyrosequencing cohort (data presented are medians (interquartile range) except where specified)

Rank IBD	Rank CD	Probe ID	Chr	Gene Symbol	Δβ IBD	Holm adj P Value IBD	Δβ CD	Holm adj P Value CD		Paed CD rank	Paed CD Δβ	Paed Holm adj P Value
1	1	cg17501210	chr6	RPS6KA2	-0.07	3.08E-13	-0.09	3.82E-19		2	-0.11	1.0E-09
2	2	cg18608055	chr19	SBNO2	-0.07	4.52E-13	-0.08	1.00E-16		29	-0.14	7.5E-05
3	6	cg09349128	chr22	NA	-0.04	1.19E-11	-0.05	7.82E-13		20	-0.06	6.3E-05
4	3	cg12170787	chr19	SBNO2	-0.04	1.19E-11	-0.05	2.91E-14		39	-0.11	1.9E-04
5	5	cg16936953	chr17	VMP1	-0.08	2.15E-11	-0.10	1.19E-13		4	-0.16	3.0E-08
6	7	cg12992827	chr3	NA	-0.05	4.15E-11	-0.06	7.74E-11		3	-0.10	2.4E-08
7	12	cg25114611	chr6	NA	-0.04	4.64E-11	-0.04	6.84E-09		102	-0.04	1.3E-03
8	10	cg02448796	chr1	KCNAB2	0.05	3.02E-10	0.05	2.98E-09		2005	0.05	7.7E-02
9	4	cg12054453	chr17	VMP1	-0.07	7.25E-10	-0.09	1.15E-13		1	-0.13	8.9E-10
10	21	cg07398517	chr3	NA	-0.04	8.21E-10	-0.04	3.40E-08		27	-0.06	7.4E-05
11	19	cg13619623	chr7	BBS9	0.04	1.07E-09	0.04	2.31E-08		13925	0.03	3.2E-01
12	65	cg16724148	chr1	AGL	0.03	2.70E-09	0.03	1.47E-06		45887	0.01	5.2E-01
13	16	cg26804423	chr7	ICA1	0.04	3.14E-09	0.04	1.25E-08		13175	0.03	3.1E-01
14	17	cg19821297	chr19	NA	-0.05	7.26E-09	-0.05	1.83E-08		9	-0.08	9.2E-06
15	60	cg22959742	chr10	FRMD4A	0.05	7.26E-09	0.04	1.08E-06		6879	0.04	2.1E-01
16	13	cg03546163	chr6	FKBP5	-0.06	7.96E-09	-0.07	6.84E-09		59	-0.08	6.0E-04
17	64	cg01059398	chr3	TNFSF10	-0.04	1.31E-08	-0.04	1.44E-06		12	-0.07	1.2E-05
18	25	cg26955383	chr10	CALHM1	0.03	1.31E-08	0.04	4.04E-08		38423	0.01	4.9E-01
19	32	cg10636246	chr1	AIM2	-0.04	1.74E-08	-0.04	1.41E-07		1736	-0.05	6.7E-02
20	24	cg18942579	chr17	VMP1	-0.05	2.14E-08	-0.05	4.04E-08		15	-0.10	2.5E-05
21	30	cg01101459	chr1	NA	0.04	3.15E-08	0.04	1.04E-07		1145	0.06	4.3E-02
22	48	cg17953136	chr2	LAPTM4A	0.04	4.37E-08	0.04	4.84E-07		24081	0.03	4.1E-01
23	38	cg26020069	chr6	TRAM2	-0.03	6.43E-08	-0.03	2.13E-07		1683	-0.03	6.5E-02
24	15	cg02716826	chr9	NA	-0.04	6.54E-08	-0.04	1.07E-08		17	-0.06	6.3E-05
25	8	cg25132241	chr14	FBLN5	0.02	6.54E-08	0.03	1.64E-10		2545	0.03	9.9E-02
26	247	cg27087650	chr19	BCL3	-0.03	6.85E-08	-0.02	0.000106		5666	-0.02	1.8E-01
27	54	cg23172671	chr1	NA	0.03	8.25E-08	0.03	7.99E-07		5548	0.03	1.8E-01
28	72	cg26470501	chr19	BCL3	-0.03	8.29E-08	-0.03	1.80E-06		114	-0.04	1.6E-03
29	26	cg12670943	chr22	POLDIP3	0.02	8.29E-08	0.02	4.80E-08		20023	0.02	3.8E-01
30	75	cg07035242	chr1	UBIAD1	0.03	9.22E-08	0.03	2.01E-06		65975	0.02	5.8E-01

Supplementary Table 13 - Table comparing top DMPs in present adult 450k dataset (yellow, left of figure) with same probes in previously published paediatric Crohn's disease data from Adams et al (orange, right of figure). The hatched areas related to results for Crohn's disease versus controls. Paed = Paediatric, adj = adjusted, CD = Crohn's disease, IBD – Inflammatory bowel disease

Illumina 450k Probe id	Chr	Gene Symbol	Δβ	P.Value	FDR. adj.P.Val
cg24854010	chr12	WNT5B	0.04	3.22E-10	0.0001
cg03411579	chr12	NA	0.06	2.02E-08	0.002
cg00709979	chr16	NA	0.04	2.61E-08	0.002
cg17990365	chr11	IFITM3	-0.09	3.02E-08	0.002
cg18214661	chr8	PDGFRL	-0.05	3.91E-08	0.002
cg23755933	chr12	GOLGA3	0.17	3.98E-08	0.002
cg02508743	chr8	LYN	0.08	4.22E-08	0.002
cg19849557	chr6	C6orf136	0.08	4.63E-08	0.002
cg19590591	chr12	GOLGA3	0.10	4.88E-08	0.002
cg02143778	chr16	NA	0.04	5.45E-08	0.002
cg19045191	chr11	NAT10	0.05	6.87E-08	0.003
cg01668008	chr8	NA	0.03	1.25E-07	0.004
cg06730953	chr3	NA	0.03	1.36E-07	0.004
cg24773560	chr12	IL23A	0.05	1.47E-07	0.004
cg13067095	chr11	EHD1	0.04	1.80E-07	0.004
cg18959422	chr1	MYBPH	0.05	1.98E-07	0.004
cg06715330	chr17	CCDC57	0.05	2.02E-07	0.004

Supplementary Table 14- Top Table of differentially methylated positions (DMPs) in inflammatory bowel disease (IBD) cases and controls in CD14+ monocytes.

Illumina 450k Probe id	Chr	Gene Symbol	Δβ	P.Value	FDR. adj.P.Val
cg09977980	chr17	EVPLL	0.02	3.70E-08	0.006
cg02498382	chr2	SNRNP27	0.02	3.97E-08	0.006
cg22268279	chr12	FLJ12825	0.06	6.21E-08	0.006
cg11823551	chr5	NA	0.01	7.06E-08	0.006
cg17572191	chr11	HRAS	0.02	7.43E-08	0.006
cg02478369	chr17	NA	0.01	7.43E-08	0.006
cg04587829	chr17	FN3K	0.05	1.97E-07	0.010
cg26481249	chr4	SORBS2	0.01	2.04E-07	0.010
cg14031265	chr4	NA	0.01	2.28E-07	0.010
cg05195566	chr15	ISLR	0.02	2.40E-07	0.010
cg18608055	chr19	SBNO2	-0.07	2.43E-07	0.010
cg16123202	chr7	NA	0.03	2.63E-07	0.010
cg08835956	chr7	POU6F2	0.07	3.10E-07	0.011
cg01243924	chr1	CNTN2	0.02	3.35E-07	0.011
cg14811319	chr6	SPACA1	0.05	3.63E-07	0.011
cg02465427	chr22	GUCD1	0.01	4.36E-07	0.011
cg22617703	chr20	DNAJC5	0.02	4.56E-07	0.011

Supplementary Table 15- Top Table of differentially methylated positions (DMPs) in inflammatory bowel disease (IBD) cases and controls in CD4+ lymphocytes. NA denotes methylation probes with no annotated gene symbol.

Illumina 450k Probe id	Chr	Gene Symbol	Δβ	P.Value	FDR. adj.P.Val
cg02985240	chr1	ARID4B	0.07	1.34E-07	0.059
cg27299024	chr15	NA	-0.02	3.89E-07	0.087
cg07395000	chr7	TECPR1	-0.01	7.71E-07	0.114
cg11093149	chr8	UNC5D	-0.03	2.28E-06	0.209
cg15390816	chr12	NCOR2	0.01	2.35E-06	0.209
cg26949055	chr15	RYR3	-0.01	3.28E-06	0.210
cg26448609	chr7	LAMB1	-0.02	4.73E-06	0.210
cg07827038	chr13	NA	-0.01	5.28E-06	0.210
cg25496181	chr12	KSR2	0.02	5.48E-06	0.210
cg21069500	chr5	CXXC5	0.07	5.60E-06	0.210
cg01454538	chr2	PXDN	0.01	5.97E-06	0.210
cg00505381	chr2	CAPN10	0.01	6.72E-06	0.210
cg14189551	chr2	NA	0.01	7.13E-06	0.210
cg15093556	chr7	POLD2	0.01	7.14E-06	0.210
cg21356040	chr6	MOG	0.02	7.30E-06	0.210
cg22708961	chr1	MORN1	-0.02	7.53E-06	0.210
cg05324393	chr6	NA	0.06	8.94E-06	0.234

Supplementary Table 16- Top Table of differentially methylated positions (DMPs) in inflammatory bowel disease (IBD) cases and controls in CD8+ lymphocytes. NA denotes methylation probes with no annotated gene symbol.

Illumina 450k Probe id	Chr	Gene Symbol	Δβ	P.Value	FDR. adj.P.Val
cg24854010	chr12	WNT5B	0.05	6.65E-11	2.98E-05
cg19515108	chr12	NA	0.05	3.94E-09	0.0009
cg01029592	chr17	SOX15	0.03	9.87E-09	0.001
cg21408624	chr7	GRB10	0.01	1.43E-08	0.001
cg18959422	chr1	MYBPH	0.05	1.45E-08	0.001
cg07532744	chr12	MON2	-0.02	2.33E-08	0.002
cg22017309	chr11	RAB3IL1	-0.05	3.84E-08	0.002
cg24127866	chr17	ABCA5	-0.01	6.32E-08	0.003
cg01368219	chr3	CACNA2D3	0.07	6.64E-08	0.003
cg18470101	chr4	NA	0.05	6.78E-08	0.003
cg06179971	chr17	TBC1D16	0.02	8.05E-08	0.003
cg15603957	chr4	CCSER1	-0.03	8.59E-08	0.003
cg19786988	chr15	TLN2	0.02	8.69E-08	0.003
cg24521869	chr17	ABI3	0.06	1.56E-07	0.005
cg01943221	chr1	PIK3CD	0.03	2.09E-07	0.006
cg22856496	chr12	ITGA7	0.07	2.19E-07	0.006
cg10985810	chr7	PTPRN2	0.03	2.21E-07	0.006

Supplementary Table 17 - Top table of differentially methylated positions (DMPs) between Crohn's disease (CD) cases and controls in CD14+ monocytes

Illumina 450k Probe id	Chr	Gene Symbol	Δβ	P.Value	FDR. adj.P.Val
cg20219381	chr8	RGS22	0.04	1.52E-07	0.0369
cg11467680	chr2	NA	0.02	1.64E-07	0.0369
cg00345704	chr17	KRTAP2-3	0.01	2.59E-07	0.0387
cg01243924	chr1	CNTN2	0.03	4.76E-07	0.0422
cg26089160	chr10	PSD	0.03	5.58E-07	0.0422
cg04587829	chr17	FN3K	0.06	7.55E-07	0.0422
cg18413240	chr3	NA	-0.01	7.80E-07	0.0422
cg00618291	chr1	SKI	0.02	8.82E-07	0.0422
cg09866283	chr14	NA	0.01	9.19E-07	0.0422
cg08503808	chr8	TRAPPC9	0.03	9.79E-07	0.0422
cg14053997	chr9	ASS1	0.04	1.06E-06	0.0422
cg02769267	chr7	MAD1L1	0.02	1.13E-06	0.0422
cg18560366	chr3	DPPA4	-0.04	1.68E-06	0.0478
cg16051685	chr1	TRIM63	0.04	1.83E-06	0.0478
cg15287594	chr20	FITM2	-0.03	1.85E-06	0.0478
cg00466500	chr20	CDH22	0.03	2.29E-06	0.0478
cg10721834	chr19	NA	0.06	2.38E-06	0.0478

Supplementary Table 18- Top table of differentially methylated positions (DMPs) between Crohn's disease (CD) cases and controls in CD4+ lymphocytes

Illumina 450k Probe id	Chr	Gene Symbol	Δβ	P.Value	FDR. adj.P.Val
cg08113002	chr19	ASPDH	-0.09	1.40E-08	0.01
cg08122156	chr11	SYT9	0.07	1.32E-06	0.15
cg26716902	chr17	CNTNAP1	0.10	1.66E-06	0.15
cg17296166	chr19	PNMAL1	0.04	1.90E-06	0.15
cg22428858	chr1	NA	-0.01	2.41E-06	0.15
cg20947775	chr4	SCD5	0.01	2.61E-06	0.15
cg09789252	chr19	ASPDH	-0.08	2.77E-06	0.15
cg11870206	chr19	ASPDH	-0.08	2.81E-06	0.15
cg10702818	chr3	NA	0.05	3.08E-06	0.15
cg07370771	chr10	VENTX	0.05	4.50E-06	0.19
cg16575998	chr2	C2orf61	0.07	5.07E-06	0.19
cg09794923	chr2	GPC1	0.02	5.59E-06	0.19
cg13830646	chr11	FOSL1	0.01	5.69E-06	0.19
cg02985240	chr1	ARID4B	0.07	5.91E-06	0.19
cg16429080	chr2	EXOC6B	-0.02	6.32E-06	0.19
cg14178705	chr6	SKIV2L	-0.02	6.86E-06	0.19
cg20573616	chr10	MMRN2	-0.02	7.86E-06	0.21

Supplementary Table 19 - Top table of differentially methylated positions (DMPs) between Crohn's disease (CD) cases and controls in CD8+ lymphocytes

Illumina 450k Probe id	Chr	Gene Symbol	Δβ	P.Value	FDR. adj.P.Val
cg08208133	chr11	HTR3A	0.09	1.67E-09	0.0007
cg08272368	chr3	NA	-0.04	9.74E-08	0.013
cg11277662	chr8	TSNARE1	-0.09	9.75E-08	0.013
cg07665063	chr12	NA	0.07	1.14E-07	0.013
cg02508743	chr8	LYN	0.10	2.02E-07	0.017
cg03411579	chr12	NA	0.07	2.54E-07	0.017
cg01799015	chr19	PALM	-0.08	2.62E-07	0.017
cg02230964	chr8	TSNARE1	-0.09	3.07E-07	0.017
cg23004985	chr15	PDE8A	-0.01	3.33E-07	0.017
cg24985772	chr11	NA	0.11	4.54E-07	0.017
cg07842062	chr16	MEFV	0.04	4.97E-07	0.017
cg13300202	chr8	TSNARE1	-0.05	5.43E-07	0.017
cg26663590	chr16	NA	0.10	5.50E-07	0.017
cg04119529	chr16	NTHL1	0.04	5.77E-07	0.017
cg12411704	chr7	ELFN1	0.06	5.77E-07	0.017
cg02023138	chr12	BIN2	0.02	7.21E-07	0.019
cg09678340	chr16	CMIP	0.03	7.21E-07	0.019
cg25189873	chr13	SERPINE3	0.03	7.97E-07	0.020
cg25653947	chr8	NA	0.05	8.84E-07	0.020
cg08208133	chr11	HTR3A	0.09	1.67E-09	0.0007

Supplementary Table 20 - Top table of differentially methylated positions (DMPs) between Ulcerative colitis (UC) cases and controls in CD14+ Monocytes

Illumina 450k Probe id	Chr	Gene Symbol	Δβ	P.Value	FDR. adj.P.Val
cg02498382	chr2	SNRNP27	0.02	7.95E-09	0.004
cg09977980	chr17	EVPLL	0.02	4.60E-08	0.005
cg05654304	chr1	VPS13D	0.03	5.21E-08	0.005
cg22268279	chr12	FLJ12825	0.08	5.39E-08	0.005
cg18074189	chr12	TMTC1	-0.06	6.09E-08	0.005
cg23753748	chr10	CALHM2	0.06	8.68E-08	0.005
cg18803306	chr20	NA	0.07	1.10E-07	0.005
cg19063856	chr17	RAPGEFL1	-0.05	1.16E-07	0.005
cg03638432	chr16	NA	-0.02	1.16E-07	0.005
cg16677399	chr6	NA	-0.19	1.16E-07	0.005
cg02886589	chr2	TMEM178A	-0.04	1.26E-07	0.005
cg22217176	chr18	ATP9B	0.04	1.56E-07	0.005
cg11670802	chr10	DIP2C	0.01	1.68E-07	0.005
cg10359807	chr16	USP7	-0.06	1.74E-07	0.005
cg15986326	chr10	EPC1	-0.06	1.82E-07	0.005
cg22566355	chr12	KCNH3	0.04	2.09E-07	0.006
cg26120842	chr10	NA	0.04	2.75E-07	0.006
cg09621572	chr6	LTA	-0.05	2.76E-07	0.006
cg01620082	chr3	NA	-0.08	2.77E-07	0.006
cg02498382	chr2	SNRNP27	0.02	7.95E-09	0.004

Supplementary Table 21 - Top table of differentially methylated positions (DMPs) between Ulcerative colitis (UC) cases and controls in CD4+ Lymphocytes

Illumina 450k Probe id	Chr	Gene Symbol	Δβ	P.Value	FDR. adj.P.Val
cg00904852	chr10	NA	-0.04	2.90E-08	0.013
cg04444506	chr17	KIF2B	-0.03	2.49E-07	0.036
cg03160145	chr18	RAX	0.03	5.56E-07	0.036
cg04254389	chr19	NA	-0.07	7.94E-07	0.036
cg05438837	chr13	CRYL1	-0.02	8.09E-07	0.036
cg12977937	chr17	NA	-0.06	8.15E-07	0.036
cg01362776	chr3	NA	-0.02	8.86E-07	0.036
cg19925178	chr5	NA	-0.04	9.46E-07	0.036
cg08639523	chr1	NA	-0.03	1.08E-06	0.036
cg22821931	chr7	GRB10	-0.02	1.11E-06	0.036
cg21543123	chr14	NA	-0.04	1.35E-06	0.036
cg09852744	chr6	TULP4	-0.07	1.39E-06	0.036
cg04351185	chr7	NA	-0.04	1.43E-06	0.036
cg08763102	chr4	HTT	-0.08	1.51E-06	0.036
cg16624521	chr5	NA	0.04	1.57E-06	0.036
cg02985240	chr1	ARID4B	0.08	1.59E-06	0.036
cg25117822	chr6	NA	-0.07	1.61E-06	0.036
cg03791799	chr6	MDC1	-0.02	1.65E-06	0.036
cg04898195	chr1	NPHP4	0.02	1.68E-06	0.036
cg00904852	chr10	NA	-0.04	2.90E-08	0.013

Supplementary Table 22 – Top table of differentially methylated positions (DMPs) between Ulcerative colitis (UC) cases and controls in CD8+ Lymphocytes

	CD	UC	IBD	Control	IBD versus Control
n	22	22	44	24	
Females (%)	10 (45.5)	10 (45.5)	20 (45.5)	8 (33)	0.5
Age At Diagnosis (median, IQR)	26 (22-32)	36.5 (26-50)	28.2 (24.8-38.8)	31.5 (25.7 – 41.3)	0.7
Smoking (current or Ex)	13 (59)	12 (57)	25 (58.1)	7 (32)	0.08

Supplementary Table 23 - Patient demographics of patients included in whole blood gene expression microarray (p values denote Fishers exact test for categorical variables, and Wilcoxon test for continuous variable)

	EntrezID (Seed)	Symbol (Seed)	Number of genes in network	Modularity	FDR p Value
1	56616	DIABLO	30	3.628882	0.009
2	80331	DNAJC5	38	2.701339	0.043
3	5265	SERPINA1	14	4.457891	0.006
4	1991	ELANE	59	4.583397	0
5	4353	MPO	66	3.873013	0
6	3082	HGF	12	5.652254	0.002
7	566	AZU1	13	4.021772	0.016
8	3674	ITGA2B	17	4.495567	0.004
9	1053	CEBPE	12	3.682455	0.032
10	966	CD59	46	2.791665	0.026
11	4318	MMP9	17	5.140515	0.002

Supplementary Table 24- Functional epigenetic module for IBD versus control in whole blood. Modularity=average of edge weights. P Values are calculated using the Monte-Carlo procedure (a permutation test, n=1000)

	Group 1 (low risk) (n=62)	**Group 2** (High risk) (n=91)	Wilcox p value (high risk versus low risk)	**Group 3** (intermediate risk) (n=87)	Kruskal-Wallis p value (all three groups)
Age	37.6 (27-50.3)	30.8 (24.6-47.7)	0.1	33.4 (25-47.4)	0.3
Female (%)	31 (50)	36 (39.6)	0.3	42 (48.3)	0.4*
Follow up length	18 (13-28)	19 (7-25)	0.6	20 (10-29)	0.4
CRP	3.5 (1.25-5.75)	14.5 (4-37.5)	0.002	11 (2.25-26)	0.004
Albumin	40 (37.25-41)	34 (29-36.75)	1.7E-5	37 (33-39)	1.89E-5
Haemoglobin	141 (127-149.5)	132.5 (115.5 – 142)	0.02	130 (122-144)	0.06

*Supplementary Table 25 - Demographics of three IBD subgroups generated by Unsupervised consensus clustering (data presented as medians (interquartile range), * = chi squared test)*

ITGB2forward	GGATAAAGAGGTGGGAATAGGTAAG	
ITGB2reverse	ATCCCTAATTAACAAAACCTCATCC	Biotin 5'
ITGB2Sequencing	GTATTGATATTTATTTGTATGTGA	
TXKforward	ATAGGAAAATAGGTGGGGTTAA	
TXKreverse	CAAAAAAAAAAAATCATAATAACCCCTTCT	Biotin 5'
TXKsequencing	ATAGGTGGGGTTAATTT	
WRAP73forward	TTTTTTTTTAGGGGTTTTTAGAAGGTG	
WRAP73reverse	TACCTAAACCAAATCCAACACATC	Biotin 5'
WRAP73sequencing	AGAAGGTGTTTAGATTTTAAG	
RPS6KA2forward	GGTGGAGTTTATTGGAAGGTTGTG	
RPS6KA2reverse	ACAAAATCCCTCTAAATCCAACTATCT	Biotin 5'
RPS6KA2sequencing	TGGGTGGTTTATTTAGAAT	
SBNO2forward	AGGAAAGAAGTTAGGGTTTGAT	Biotin 5'
SBNO2reverse	ACTCAATTACCCTCTCCTTTTTT	
SBNO2sequencing	CCTAAAAAACTAAATCACCAT	
VMP1forward	TGGGTTATTGTATTTTGTTTTTAGTGTTG	
VMP1reverse	ACTAACAAACCAACTTCACTTATTTAC	Biotin 5'
VMP1sequencing	GTATTTTGTTTTTAGTGTTGTT	

Supplementary Table 26 - Pyrosequencing primer sequences

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