

Supplementary Table S1. Demographic and clinical characteristics of cohort I: methylation study in adipose-stem cells.

	Control	CD
n	5	7
Sex (male/female)	2/3	4/3
Age (y)	38 ± 4.6	36.1 ± 9.4
BMI (kg/m²)	24.65 ± 3.6	22.9 ± 4.8
Smoking, n (%)	3 (60)	5 (71.4)
Glucose (mg/dL)	81.5 ± 5.4	77 ± 7.7
Cholesterol (mg/dL)	115 ± 13.5	130 ± 20.3
HDL (mg/dL)	39.3 ± 5.5	41.8 ± 4.6
Triglycerides (mg/dL)	98.7 ± 4.5	95 ± 9.4
Insulin (µIU/mL)	2.1 ± 0.5	7.6 ± 2.4 ^a
HOMA-IR	0.51 ± 0.2	1.75 ± 0.55 ^a
Age of diagnosis	-	25.1 ± 9.4
Disease location, n (%)		
L1 ileal	-	6 (86)
L2 colonic	-	0 (0)
L3 ileocolonic	-	1(14)
Disease behavior,n (%)		
B1 nonstricturing, nonpenetrating	-	1 (14)
B2 stricturing	-	3 (43)
B3 penetraiting	-	3 (43)
Immunomodulator use	-	7/7
Biological agent treatment	-	1/7
Steroid treatment	-	6/7
C-reactive protein (mg/dL)	0.3 ± 0.10	3.3 ± 1.3 ^a
Fecal calprotectin (µg/g)	-	1560 ± 230 ^a

Abbreviations: CD; Crohn's Disease; BMI, body mass index; HDL, high-density lipoprotein cholesterol; HOMA-IR, insulin resistance index.

Results are presented as mean ± SD. ANOVA followed by *post hoc* Bonferroni test was used to compare means between groups.

^a*p* < 0.01 versus control-adipose stem cells.

Supplementary Table S2. Demographic and clinical characteristics of cohort II: gene expression study in adipose-stem cells.

	Control	Inactive CD	Active CD
n	10	10	10
Sex (male/female)	4/6	5/5	5/5
Age (years)	40 ± 5.3	38.2 ± 3.4	36.8 ± 10.4
BMI (kg/m²)	25.15 ± 2.1	24.59 ± 3.3	23.3 ± 3.3
Smoking, n (%)	5 (50)	6 (60)	5 (50)
Glucose (mg/dL)	81.3 ± 3.9	86 ± 11.4	75 ± 10.7
Cholesterol (mg/dL)	115 ± 12.3	121 ± 20.4	141 ± 16.3 ^a
HDL (mg/dL)	36.7 ± 5.6	44.7 ± 3.2 ^a	41.4 ± 5.4
Triglycerides (mg/dL)	100 ± 5.3	116 ± 13.1	95 ± 8.9
Insulin (μU/mL)	2.07 ± 0.9	5.05 ± 1.2	7.5 ± 1.4 ^{a,b}
HOMA-IR	0.49 ± 0.1	1.3 ± 0.5	1.65 ± 0.35 ^a
Age at diagnosis (years)	-	38 ± 8.6	27.9 ± 9.4
Last attack (months)		21 ± 7.4	
Disease location, n (%)			
L1 ileal	-	6/10 (60)	7/10 (70)
L2 colonic	-	3/10 (30)	2/10 (20)
L3 ileocolonic	-	2/10 (20)	1/10 (10)
Disease behavior, n (%)			
B1 nonstricturing, nonpenetrating	-	0/10 (0)	0/10 (0)
B2 stricturing	-	5/10 (50)	4/10 (40)
B3 penetrating	-	5/10 (50)	6/10 (60)
Indication of surgery	CoH	CoH	4SCD/6FCD
Immunomodulator use	-	10/10	10/10
Biological agent treatment	-	2/10	2/10
Steroid treatment	-	4/10	8/10
C-reactive protein (mg/dL)	0.2 ± 0.04	0.3 ± 0.13	3.4 ± 1.6 ^{a,b}
Fecal calprotectin (μg/g)	-	81.25 ± 20.3	2132.4 ± 159.1 ^b

Abbreviations: BMI, body mass index; HDL, high-density lipoprotein cholesterol; CoH, cholecystectomy or hernia; CD; Crohn's Disease; SCD, stenotic Crohn's disease; FCD, fistulizing Crohn's disease.

Results are presented as mean ± SD. ANOVA followed by *post hoc* Bonferroni test was used to compare means between groups.

^a*p* < 0.01 versus control-adipose stem cells.

^b*p* < 0.05 versus inactive CD-adipose stem cells.

Supplementary Table S3. Demographic and clinical characteristics of cohort III: gene expression study in peripheral blood mononuclear cells.

	Control	Inactive CD	Active CD
n	10	10	10
Sex (male/female)	5/5	5/5	5/5
Age (y)	39.3 ± 6.9	38.8 ± 14.14	45.14 ± 18.14
BMI (kg/m²)	24.4 ± 1.4	25.52 ± 5.22	23.06 ± 3.37
Smoking, n (%)			
Active	3 (30)	5 (50)	3 (30)
Ex	3 (30)	2 (20)	3 (30)
No	4 (40)	3 (30)	4 (40)
Glucose (mg/dL)	75 ± 3.9	86.6 ± 10.13 ^a	84.33 ± 11.29 ^a
Cholesterol (mg/dL)	139 ± 11.3	198 ± 52.09 ^a	164.75 ± 22.8 ^a
Cholesterol-HDL (mg/dL)	60.61 ± 20.15	64.22 ± 22.52	42 ± 15.55 ^{a,b}
Triglycerides	123 ± 35.6	141 ± 43.8	106 ± 25.45
Age of diagnosis	-	19 ± 4.7	22 ± 5.8
Last attack (months)	-	20 ± 3.8	-
Disease location, n (%)			
L1 ileal	-	8 (80)	10 (100)
L2 colonic	-	1 (10)	0 (0)
L3 ileocolonic	-	1 (10)	0 (0)
Disease behavior, n (%)			
B1 nonstricturing, nonpenetrating	-	6 (60)	4 (40)
B2 stricturing	-	3 (30)	3 (30)
B3 penetrating	-	1 (10)	3 (30)
Immunomodulator use	-	8/10	7/10
Biological agent treatment	-	7/10	6/10
Steroid treatment	-	4/10	4/10
C-reactive protein (mg/dL)	0.14 ± 0.04	0.21 ± 0.07	3.4 ± 1.1 ^{a,b}
Fecal calprotectin (µg/g)	-	178.75 ± 23.4	2219 ± 117.15 ^b

Abbreviations: BMI, body mass index; HDL, high-density lipoprotein cholesterol; CoH, cholecystectomy or hernia; CD; Crohn's Disease.

Results are presented as mean ± SD. ANOVA followed by *post hoc* Bonferroni test was used to compare means between groups.

^a*p* < 0.01 versus control-peripheral mononuclear cells (PBMCs).

^b*p* < 0.01 versus inactive CD-PBMCs.

Supplementary Table S4. Immunophenotypic characterization of hASCs isolated from healthy control subjects, active CD and inactive CD patients. The values reflect the mean \pm SD percentage surface positive staining of hASCs for a part of surface antigens including hematopoietic and stromal markers.

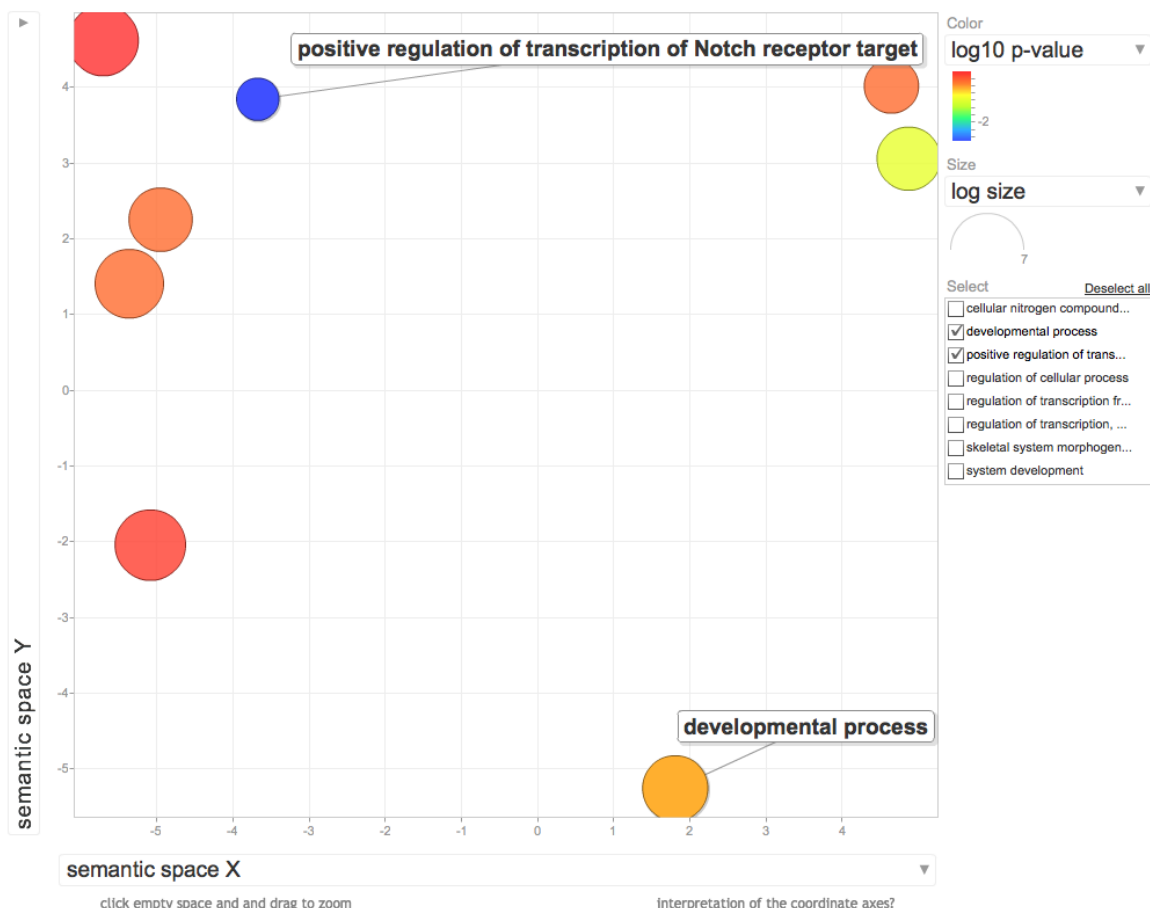
Surface markers	Control		Inactive CD		Active CD	
	%	MFI	%	MFI	%	MFI
CD34	0.2 \pm 0.1	80 \pm 9.2	0.91 \pm 0.4	125 \pm 10.7 ^a	0.9 \pm 0.5	200 \pm 16.4 ^a
CD45	0.3 \pm 0.25	110 \pm 10.4	0.3 \pm 0.19	87 \pm 8.3	0.2 \pm 0.15	90 \pm 9.5
CD90	95.3 \pm 2.1	18800 \pm 725.2	97.3 \pm 2.4	22400 \pm 888	97.9 \pm 2	31000 \pm 1025
CD73	90 \pm 7.2	9880 \pm 200	86.5 \pm 6.6	8400 \pm 176	87.5 \pm 8.1	5900 \pm 110 ^a
CD36	40 \pm 10.3	700 \pm 25	32.5 \pm 10.3	190 \pm 30 ^a	30.5 \pm 10.3	200 \pm 45 ^a

Abbreviations: hASCs, human adipose derived stem cells; MFI, median fluorescence intensity.

ANOVA followed by post hoc Bonferroni test was used to compare means between groups. * P < 0.05 versus Control-hASCs.

Gene name	Detector
C2	Hs00918862_m1
CHID1	Hs01061050_m1
DLX5	Hs00193291_m1
EBF3	Hs01008793_m1
EN1	Hs00154977_m1
FGF1	Hs01092738_m1
FGF13	Hs01381548_m1
FGFR2	Hs01552918_m1
G6PD	Hs00166169_m1
HOXB5	Hs00357820_m1
HOXB6	Hs00980016_m1
IKBKE	Hs01063858_m1
IKBKG	Hs00415849_m1
LTBR	Hs01101194_m1
NOTCH4	Hs00965889_m1
PRDM8	Hs00220274_m1
PRDM16	Hs00223161_m1
PTPRN2	Hs00243067_m1
RIPK1	Hs01041869_m1
SHROOM3	Hs01068190_m1
SPON2	Hs00202813_m1
TNF	Hs00174128_m1
WT1	Hs01103751_m1

Supplemental Table S5. Human gene expression analysis. Results were calculated using the comparative Ct method and expressed relative to the expression of the housekeeping gene 18S (Hs03928985_g1).



While parsing your data, warning(s) were encountered:
 Could not parse GO ID from line: '#term ID false discovery rate'. Line will be skipped.

Hide/show dispensable GO terms

Export results to text table (CSV) Make R script for plotting

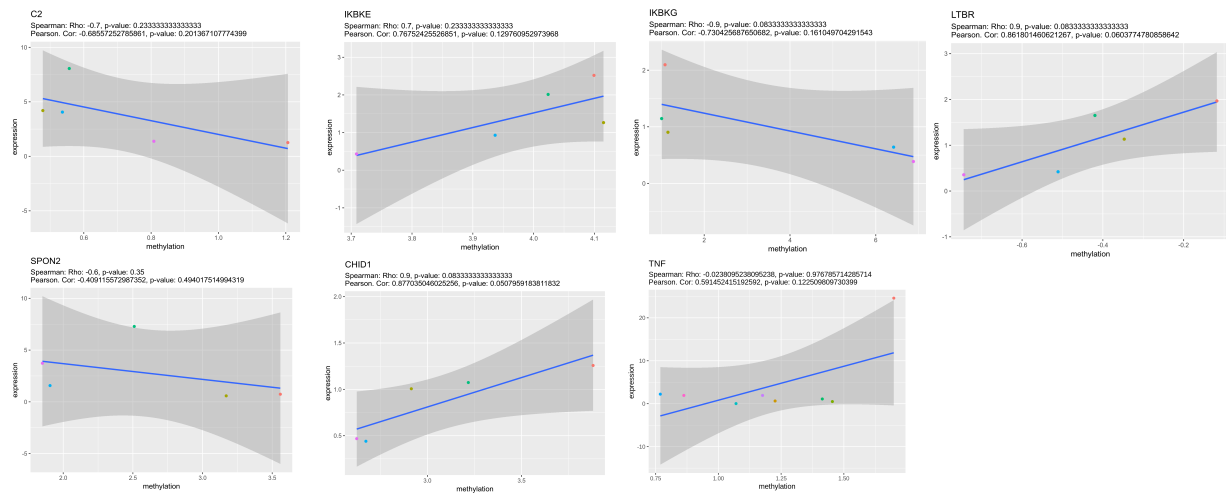
term ID	description	frequency	pin?	log ₁₀ p-value	uniqueness	dispensability
GO:0007221	positive regulation of transcription of Notch receptor target	0.002 %		-2.2596	0.58	0.00
GO:0032502	developmental process	2.812 %		-1.5243	0.89	0.00
GO:0048731	system development	1.264 %		-1.6799	0.43	0.05
GO:0009653	anatomical structure morphogenesis	1.542 %	📌	-1.3125	0.46	0.84
GO:0007389	pattern specification process	0.147 %	📌	-1.4271	0.49	0.75
GO:0030154	cell differentiation	1.133 %	📌	-1.4271	0.43	0.79
GO:0007399	nervous system development	0.582 %	📌	-1.4271	0.45	0.86
GO:0007275	multicellular organism development	1.559 %	📌	-1.6615	0.43	0.92
GO:0044271	cellular nitrogen compound biosynthetic process	22.502 %		-1.3363	0.59	0.13
GO:0050794	regulation of cellular process	18.840 %		-1.3054	0.49	0.21
GO:0006357	regulation of transcription from RNA polymerase II promoter	1.273 %		-1.4271	0.42	0.55
GO:0006355	regulation of transcription, DNA-templated	9.917 %		-1.4271	0.32	0.66
GO:0019219	regulation of nucleobase-containing compound metabolic process	10.258 %	📌	-1.4271	0.37	0.86
GO:0031326	regulation of cellular biosynthetic process	10.816 %	📌	-1.4271	0.36	0.89
GO:0051252	regulation of RNA metabolic process	10.029 %	📌	-1.3696	0.35	0.89
GO:0006351	transcription, DNA-templated	10.659 %	📌	-1.4271	0.47	0.88
GO:2000112	regulation of cellular macromolecule biosynthetic process	10.683 %	📌	-1.4271	0.35	0.88
GO:0048705	skeletal system morphogenesis	0.053 %		-1.4271	0.51	0.69

Did you find REVIGO useful in your work? Feel free to share it with your colleagues.

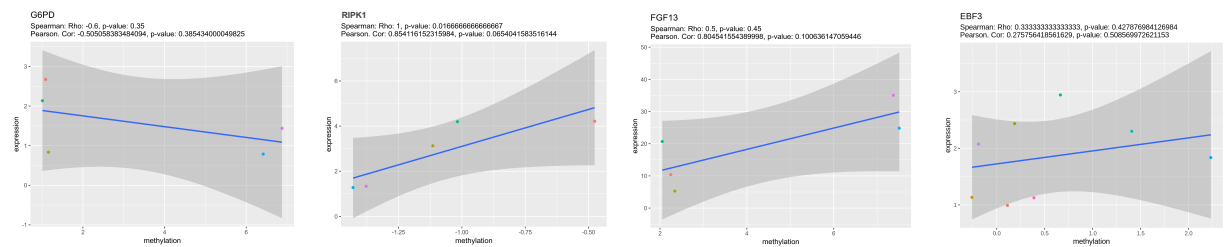
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Supplementary Figure S2. Functional analysis and visualization of genes down-regulated in adipose-stem cells isolated of CD patients. The enriched pathways were visualized and the network analysis performed using REVIGO (<https://http://revigo.irb.hr/>), which summarizes and visualizes lists of gene ontology [GO] terms.

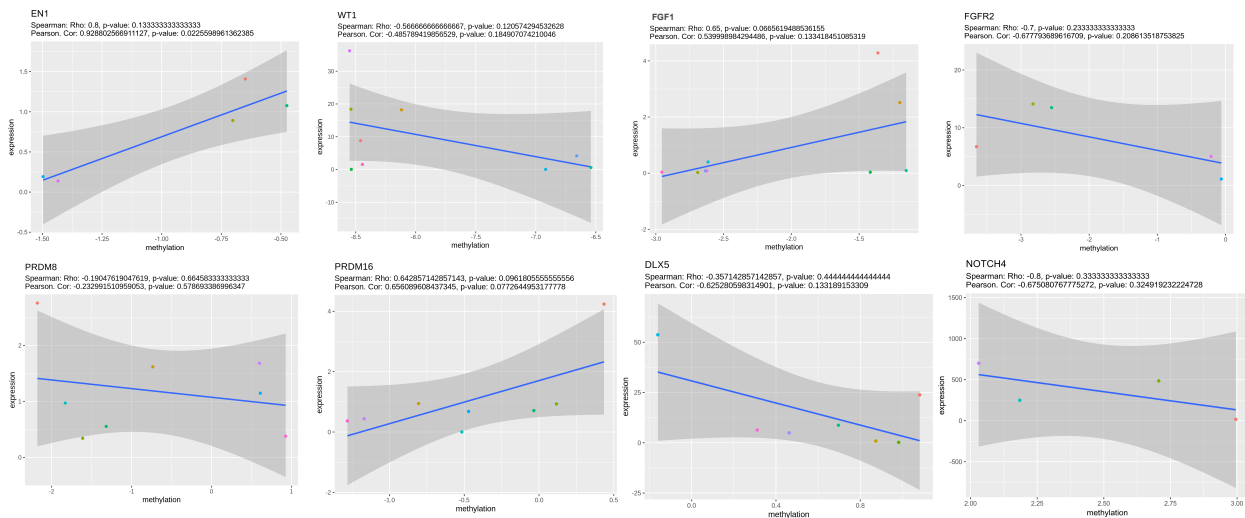
A. Immune system



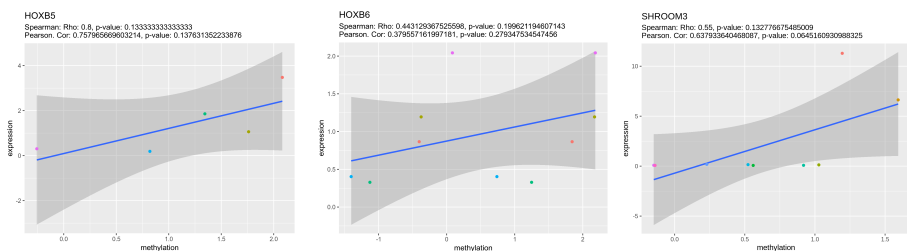
B. Metabolic process



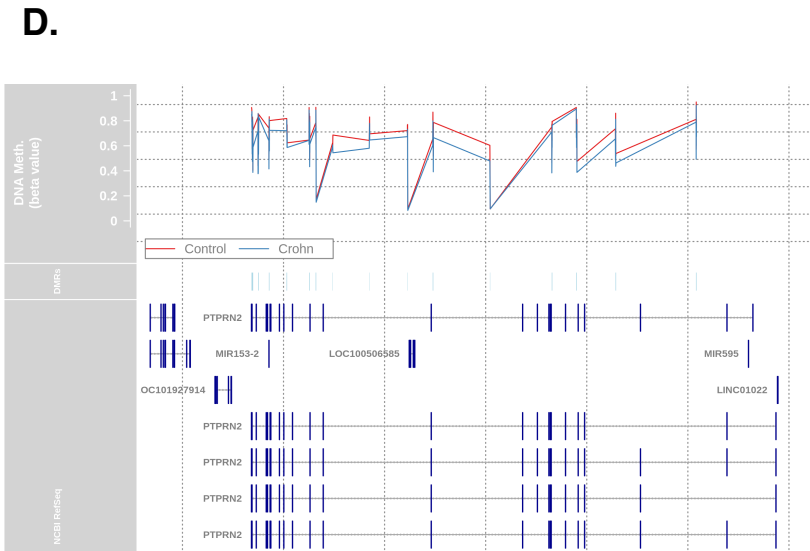
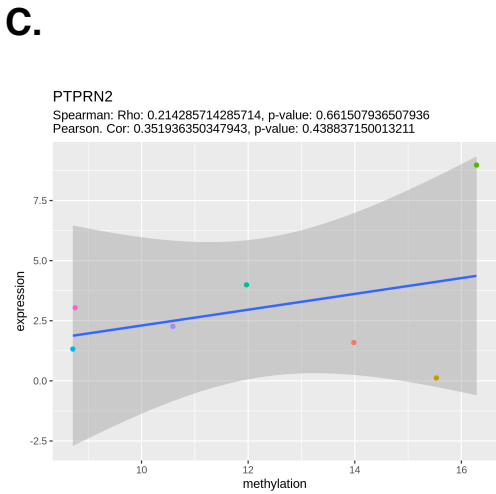
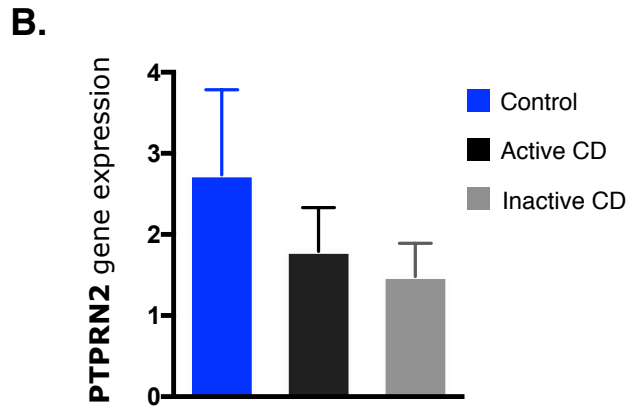
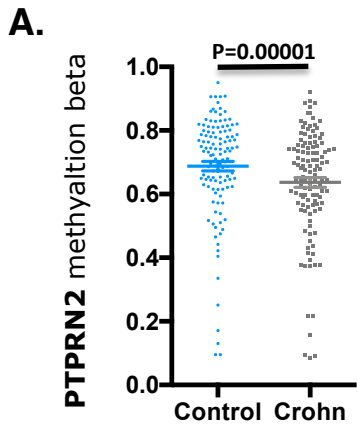
C. Cell Differentiation



D. Development process



Supplementary Figure S3. Pearson and Spearman correlations between gene expression and methylation data of candidate genes obtained from differentially methylated regions. (A) Genes involved in immune system response: *C2*, *IKBKE*, *IKBKG*, *LTBR*, *SPON2*, *CHD1* and *TNFA*. (B) Genes related to the regulation of metabolism: *G6PD*, *FGF13*, *EBF3*, *RIPK1*. (C) Genes related to cell differentiation: *EN1*, *WT1*, *FGF1*, *FGFR2*, *PRDM8*, *PRDM16* and *DLX5*.



Supplementary Figure S4. *PTPNR2* is hypomethylated in human adipose stem cells of patients with Crohn's disease but there is no correlation with gene expression. Methylation (a) and mRNA levels (b) of *PTPNR2* in hASCs. (c) Spearman and Person's correlation between methylation and gene expression data. (d) DMR plot in *PTPNR2* gene.