SUPPLEMENTARY MATERIAL AND METHODS

DNA methylation profiling

Microarray-based DNA methylation profiling of MPN, MPNs transformed to acute myeloid leukaemia (MPN-AML) and control samples was performed using the HumanMethylation27 Beadchip (Illumina, Inc., San Diego, CA, USA), according to the manufacturer's instructions (1). The panel is developed to quantify the DNA methylation state of 27,578 CpG sites located within the proximal promoter regions (1 kb upstream and 500bp downstream of transcription start sites) of 14,475 well-annotated genes from the consensus coding sequence project, as well as known cancer genes and miRNAs. Briefly, genomic DNA is treated with sodium bisulfite and whole-genome amplified following manufacturer's instructions. Two bead types represent each CpG locus: one for the unmethylated (U) site and another for the methylated (M) site. After hybridization and single-base extension using labeled nucleotides, the intensity of the U and M beads is measured with a microarray reader. The methylation status of a CpG is determined by the beta-value (β value) calculation, which is based on the ratio of the fluorescent signals between the M bead to the total locus fluorescence intensity.

To avoid biological biases, 1092 CpGs located on chromosomes X and Y were excluded from the analysis. Thus, a total of 26,486 autosomal CpGs went into further statistical analyses.

Differential methylation analysis of microarray data

Initially, a global view of the DNA methylation profile of MPNs and healthy BM/PB control samples was obtained using an unsupervised hierarchical cluster analysis including only CpGs with standard deviation (SD) >0.25 among samples (Genesis Software, version 1.7.5) (2). Different methods have been described in the literature for the analysis of differentially methylated DNA between two groups and no consensus strategy has been reached. Therefore, in our study, each CpG in the array was classified as differentially methylated between groups if it was detected with a combination of quantitative and qualitative approaches: significant T-test analysis, Volcano analysis and Methylation threshold analysis as previously described (3). Besides, some modifications were included to improve the specificity of the analysis in the T-test and Volcano analysis. First, in order to include a CpG as differentially methylated between

groups an absolute difference of at least 0.2 between averaged ß values was required. Second, all the ß values were divided into three groups: hypomethylated (averaged ß value lower than 0.3), partially methylated (averaged β value between 0.3 and 0.7) or hypermethylated (averaged β value higher than 0.7). We considered to be differentially methylated only those CpGs that showed a β value group change between our groups of study.

Raw array data files were deposited in a MIAME compliant database Gene Expression Omnibus (GEO) and are available under the accession number GSE31600 (healthy PB/BM control samples) and GSE42042 (MPNs samples). For this study we also included data from cytogenetically normal Acute Myeloid Leukaemia (AML) samples publicly available under the accession number GSE32251 (4).

Methylation profiling of leukemic transformed MPNs.

To investigate whether MPNs transformed to AML have a specific DNA methylation signature, we compared the methylation profile of each MPNs to its transformed counterpart independently.

As stated above, differentially methylated genes were found between MPNs and MPNs transformed to AML samples by two statistical analyses: T-test analysis and Volcano analysis. The methylation threshold analysis was not performed due to the low number of samples of MPNs transformed to leukemia (4 PV, 4 ET and 5 PMF).

Bioinformatics pathway analysis

For these analyses we used all the differentially methylated genes that were found when comparing controls against MPNs as a whole entity, as well as those differentially methylated genes that were found when comparing each neoplasm with the control group.

Ingenuity Pathway Analysis software (IPA, www.ingenuity.com) was also used to identify deregulated gene networks containing differentially methylated genes between each group of interest. Functional enrichment analysis of Gene Ontology (GO) was performed using standard hypergeometric tests (5). All annotations were extracted from the Ensembl database (http://www.ensembl.org).

In order to study the biological meaning of the results, enrichment tests with respect to sets of related genes were carried out. To this end, the non-parametric Kolmogorov-Smirnoff rank test was used as implemented in the GSEA (Gene Set Enrichment Analysis) software (6). The p-values for each gene-set were computed based on 2000 permutation iterations. We calculated the enrichment of differentially methylated gene sets (chronic MPNs vs controls, $\beta > 0$; transformed MPNs vs controls, $\beta > 0$ and AML samples vs controls, $\beta > 0$) in the ranked gene lists generated using the value of the β statistics obtained from limma (chronic MPNs vs controls, transformed MPNs vs controls and AML samples vs controls). We analyzed the enrichment of transcription factor binding sites defined in TRANSFAC database as previously described, using Gene Set Enrichment Analysis (GSEA) pre-ranked algorithm and 1000 permutations (7).

DNA methylation analysis by Pyrosequencing

Using the criteria stated above, two genes, *GAS2* and *BHMT* that were statistically differentially methylated between chronic MPNs and control samples were selected for technical validation. *GAS2* is hypermethylated in MPNs samples whereas *BHMT* is hypomethylated. The methylation level of *GAS2* and *BHMT,* both genes differentially methylated between chronic MPNs and control samples was analyzed by bisulfite pyrosequencing as previously described (8) in a new independent set of 25 samples (13 ET, 8 PV and 4 PMF). Primer sequences of each gene and conditions for amplification are described in Supplementary Table 15. DNA extracted from the peripheral blood of healthy donors was used as control for methylation-specific assays. Human male genomic DNA universally methylated for all genes (Intergen Company, NY) was used as a positive control for methylated alleles. Water blanks were included with each assay.

REFERENCES

1. Bibikova M, Le J, Barnes B, Saedinia-Melnyk S, Zhou L, Shen R, et al. Genome-wide DNA methylation profiling using Infinium(R) assay. Epigenomics. 2009;1(1):177-200.
2. Sturn A, Quackenbush J, Trajanoski Z. Genesis: cluster analysis of microarray data. Bioinformatics. 2002;18(1):207-8.
3. Perez C, Martinez-Calle N, Martin-Subero JI, Segura V, Delabesse E, Fernandez-Mercado M, et al. TET2 mutations are associated with specific 5-methylcytosine and 5-hydroxymethylcytosine profiles in patients with chronic myelomonocytic leukemia. PloS one. 2012;7(2):e31605.

4. Deneberg S, Guardiola P, Lennartsson A, Qu Y, Gaidzik V, Blanchet O, et al. Prognostic DNA methylation patterns in cytogenetically normal acute myeloid leukemia are predefined by stem cell chromatin marks. Blood. 2011;118(20):5573-82.
5. Draghici S, Khatri P, Eklund AC, Szallasi Z. Reliability and reproducibility issues in DNA microarray measurements. Trends in genetics : TIG. 2006;22(2):101-9.
6. Subramanian A, Tamayo P, Mootha VK, Mukherjee S, Ebert BL, Gillette MA, et al. Gene set enrichment analysis: a knowledge-based approach for interpreting genome-wide expression profiles. Proceedings of the National Academy of Sciences of the United States of America. 2005;102(43):15545-50.
7. Nischal S, Bhattacharyya S, Christopeit M, Yu Y, Zhou L, Bhagat TD, et al. Methylome profiling reveals distinct alterations in phenotypic and mutational subgroups of myeloproliferative neoplasms. Cancer research. 2013;73(3):1076-85.
8. Vilas-Zornoza A, Agirre X, Martin-Palanco V, Martin-Subero JI, San Jose-Eneriz E, Garate L, et al. Frequent and simultaneous epigenetic inactivation of TP53 pathway genes in acute lymphoblastic leukemia. PloS one. 2011;6(2):e17012.

Table S1: Genes differentially methylated in chronic MPN patients vs BM/PB samples of healthy donors. Red: Genes hypermetylated in MPNs. Green: Genes hypometylated in MPNs.

UniqueID	GEN NAME	CpG ISLAND	CHROMOSOME
cg24949488	DNTT	TRUE	10
cg17078393	LCK	TRUE	1
cg13164537	CD226	FALSE	18
cg00911351	PCDHGB4	TRUE	5
cg02197293	FBXO27	TRUE	19
cg03918304	HOXD10	FALSE	2
cg04378886	RCN3	TRUE	19
cg06268694	CELSR1	TRUE	22
cg06653796	LIME1	TRUE	20
cg07665060	C19orf33	TRUE	19
cg08832227	KCNA1	TRUE	12
cg09188980	CALCA	TRUE	11
cg09547224	SLC5A1	TRUE	22
cg09582042	ITR	TRUE	13
cg12111714	ATP8A2	TRUE	13
cg12973651	CNFN	TRUE	19
cg13315147	CYP2E1	TRUE	10
cg13603171	MOXD1	TRUE	6
cg14456683	ZIC1	TRUE	3
cg15517609	RYR1	FALSE	19
cg15747595	TSPYL5	TRUE	8
cg16853982	ACTN2	TRUE	1
cg19564367	AFAP	TRUE	4
cg20807545	ADAMTS18	TRUE	16
cg25133685	OR2W1	FALSE	6
cg25782229	WT1	TRUE	11
cg26279025	IL11	TRUE	19
cg26465611	MEGF10	TRUE	5
cg27202708	C1orf65	TRUE	1
cg27243140	OTOP3	TRUE	17
cg01530101	KCNQ1DN	TRUE	11
cg04317399	HOXA4	TRUE	7
cg05436231	CD164L2	TRUE	1
cg05890484	BHMT	TRUE	5
cg06563300	SLC17A8	FALSE	12
cg07054641	WDR52	TRUE	3
cg08321346	ANKMY1	TRUE	2
cg11126134	FLJ14834	TRUE	13
cg15584813	SLC38A4	TRUE	12
cg16731240	ZNF577	TRUE	19
cg26267561	OXT	TRUE	20
cg09809672	EDARADD	FALSE	1
cg13185177	GP5	FALSE	3
cg12819826	PPAN	TRUE	19
cg06812844	TRPM2	FALSE	21

cg00174500	CMTM5	FALSE	14
cg01560871	C10orf27	FALSE	10
cg04230060	SUSD1	TRUE	9
cg05740244	LDHC	TRUE	11
cg12188860	TOP1MT	TRUE	8
cg19682367	FAM79B	FALSE	3
cg22580512	NCOR2	TRUE	12
cg26066361	CLEC7A	FALSE	12
cg06493930	GAS2	FALSE	11
cg07251788	CLTCL1	TRUE	22
cg08632701	SETD4	TRUE	21

Table S2: Genes differentially methylated in PV patients vs BM/PB samples of healthy donors. Red: Genes hypermetylated in PV. Green: Genes hypometylated in PV

UniqueID	GEN NAME	CpG ISLAND	CHROMOSOME
cg00160914	C1orf183	FALSE	1
cg00186701	TSPYL5	TRUE	8
cg00208967	OLFM2	TRUE	19
cg00911351	PCDHGB4	TRUE	5
cg01530101	KCNQ1DN	TRUE	11
cg02061229	MMP10	FALSE	11
cg02197293	FBXO27	TRUE	19
cg02757432	GPR26	TRUE	10
cg02844545	GCM2	TRUE	6
cg03086857	EDNRB	TRUE	13
cg03679734	CKMT1B	FALSE	15
cg03743584	PRAP1	FALSE	10
cg03918304	HOXD10	FALSE	2
cg04378886	RCN3	TRUE	19
cg05250458	ZNF177	TRUE	19
cg05294243	KLK13	FALSE	19
cg05436231	CD164L2	TRUE	1
cg05890484	BHMT	TRUE	5
cg06268694	CELSR1	TRUE	22
cg06653796	LIME1	TRUE	20
cg07621046	C10orf82	TRUE	10
cg07665060	C19orf33	TRUE	19
cg08321346	ANKMY1	TRUE	2
cg09188980	CALCA	TRUE	11
cg09547224	SLC5A1	TRUE	22
cg09582042	ITR	TRUE	13
cg11126134	FLJ14834	TRUE	13
cg11647681	PCDHGA12	TRUE	5
cg12111714	ATP8A2	TRUE	13
cg12973651	CNFN	TRUE	19
cg13282837	TCL1A	TRUE	14
cg13315147	CYP2E1	TRUE	10
cg14100184	GNG13	FALSE	16
cg15517609	RYR1	FALSE	19
cg15747595	TSPYL5	TRUE	8
cg16142218	CHMP7	FALSE	8
cg16731240	ZNF577	TRUE	19
cg16853982	ACTN2	TRUE	1
cg18059933	TP53INP1	TRUE	8
cg19125999	C1orf172	FALSE	1
cg19564367	AFAP	TRUE	4
cg20807545	ADAMTS18	TRUE	16
cg21053323	SUMO3	TRUE	21
cg21096915	MGC16291	TRUE	10
cg22136365	TAT	FALSE	16
cg23089840	LRRC3	FALSE	21

cg23191950	ALDH1A3	TRUE	15
cg23326689	STMN2	TRUE	8
cg25133685	OR2W1	FALSE	6
cg25500444	FLJ23514	TRUE	11
cg25782229	WT1	TRUE	11
cg26279025	IL11	TRUE	19
cg26465611	MEGF10	TRUE	5
cg27202708	C1orf65	TRUE	1
cg27243140	OTOP3	TRUE	17
cg27304754	CALB2	FALSE	16
cg00071250	FASLG	FALSE	1
cg01367992	LY9	FALSE	1
cg05535113	CHST4	FALSE	16
cg06563300	SLC17A8	FALSE	12
cg07054641	WDR52	TRUE	3
cg09830866	C16orf24	TRUE	16
cg13164537	CD226	FALSE	18
cg13461622	RUNX3	FALSE	1
cg13975369	TSGA14	TRUE	7
cg14920846	NAV1	TRUE	1
cg15584813	SLC38A4	TRUE	12
cg16404106	FLJ23514	TRUE	11
cg17078393	LCK	TRUE	1
cg24949488	DNTT	TRUE	10
cg26372517	TFAP2E	TRUE	1
cg00174500	CMTM5	FALSE	14
cg01560871	C10orf27	FALSE	10
cg05740244	LDHC	TRUE	11
cg06493930	GAS2	FALSE	11
cg08632701	SETD4	TRUE	21
cg11134443	KYNU	FALSE	2
cg19815376	FLJ34503	FALSE	6
cg20022541	C14orf152	FALSE	14
cg22580512	NCOR2	TRUE	12
cg26066361	CLEC7A	FALSE	12
cg26143719	C1QTNF6	FALSE	22
cg26264314	NALP5	TRUE	19
cg01441777	CSNK1E	TRUE	22
cg06812844	TRPM2	FALSE	21
cg07251788	CLTCL1	TRUE	22
cg09809672	EDARADD	FALSE	1
cg12819826	PPAN	TRUE	19
cg13185177	GP5	FALSE	3
cg22381196	DHODH	TRUE	16
cg26267561	OXT	TRUE	20

Table S3. Genes differentially methylated in ET patients vs BM/PB samples of healthy donors. Red: Genes hypermetylated in ET. Green: Genes hypometylated in ET

UniqueID	GEN NAME	CpG ISLAND	CHROMOSOME
cg00186701	TSPYL5	TRUE	8
cg04378886	RCN3	TRUE	19
cg05373457	KCNS2	TRUE	8
cg05436231	CD164L2	TRUE	1
cg05890484	BHMT	TRUE	5
cg06653796	LIME1	TRUE	20
cg11126134	FLJ14834	TRUE	13
cg12973651	CNFN	TRUE	19
cg15747595	TSPYL5	TRUE	8
cg16853982	ACTN2	TRUE	1
cg25133685	OR2W1	FALSE	6
cg06563300	SLC17A8	FALSE	12
cg16731240	ZNF577	TRUE	19
cg24949488	DNTT	TRUE	10
cg26267561	OXT	TRUE	20
cg00174500	CMTM5	FALSE	14
cg01560871	C10orf27	FALSE	10
cg01820374	LAG3	FALSE	12
cg04230060	SUSD1	TRUE	9
cg06493930	GAS2	FALSE	11
cg06812844	TRPM2	FALSE	21
cg09809672	EDARADD	FALSE	1
cg13185177	GP5	FALSE	3
cg22580512	NCOR2	TRUE	12
cg24427660	PNPLA2	TRUE	11

Table S4: Genes differentially methylated in PMF patients vs BM/PB samples of healthy donors. Red: Genes hypermetylated in PMF. Green: Genes hypometylated in PMF

UniqueID	Symbol	CpG ISLAND	CHROMOSOME
cg00019495	HOP	FALSE	4
cg00503840	DLX5	TRUE	7
cg00767581	HOXD4	TRUE	2
cg00911351	PCDHGB4	TRUE	5
cg02197293	FBXO27	TRUE	19
cg02351381	C12orf34	FALSE	12
cg02757432	GPR26	TRUE	10
cg03918304	HOXD10	FALSE	2
cg04378886	RCN3	TRUE	19
cg04435420	SGCD	FALSE	5
cg05073035	ZIC1	TRUE	3
cg05337441	APOB	TRUE	2
cg05968233	ALKBH7	TRUE	19
cg06268694	CELSR1	TRUE	22
cg06572160	KCNC3	TRUE	19
cg06653796	LIME1	TRUE	20
cg06911084	DLX5	TRUE	7
cg06971096	PTPRN	TRUE	2
cg07549194	TIP39	FALSE	19
cg07612655	PTGIS	FALSE	20
cg07621046	C10orf82	TRUE	10
cg08126211	KAAG1	TRUE	6
cg08832227	KCNA1	TRUE	12
cg09001953	FLJ11200	TRUE	4
cg09188980	CALCA	TRUE	11
cg09547224	SLC5A1	TRUE	22
cg09871315	HOXA2	TRUE	7
cg10660256	BHMT	TRUE	5
cg10771262	TCF21	FALSE	6
cg11375102	C16orf30	TRUE	16
cg12029639	MAB21L1	TRUE	13
cg12061236	AKAP12	TRUE	6
cg12335708	DPP4	TRUE	2
cg12717203	FLJ90036	TRUE	4
cg13234863	KIAA1944	TRUE	12
cg13282837	TCL1A	TRUE	14
cg13315147	CYP2E1	TRUE	10
cg13749822	HHIP	TRUE	4
cg14100184	GNG13	FALSE	16
cg14605021	FGF20	TRUE	8
cg15517609	RYR1	FALSE	19
cg15522957	ALX4	TRUE	11
cg15792688	FLJ90036	TRUE	4
cg16853982	ACTN2	TRUE	1
cg17788832	PSKH2	TRUE	8
cg17963840	ADRA1A	TRUE	8

cg18182399	DES	TRUE	2
cg18691434	GPC2	TRUE	7
cg19125999	C1orf172	FALSE	1
cg19564367	AFAP	TRUE	4
cg19903229	C14orf105	FALSE	14
cg20134215	MCHR2	TRUE	6
cg20807545	ADAMTS18	TRUE	16
cg20893022	C19orf30	TRUE	19
cg20907471	PAX1	FALSE	20
cg21053323	SUMO3	TRUE	21
cg21096915	MGC16291	TRUE	10
cg21245372	NUP98	TRUE	11
cg22136365	TAT	FALSE	16
cg22341310	ZNF541	TRUE	19
cg22892110	MAPK15	TRUE	8
cg23713520	TM4SF11	TRUE	16
cg23917399	TNFAIP8	TRUE	5
cg24840099	MSX1	TRUE	4
cg24891133	FLJ14834	TRUE	13
cg25133685	OR2W1	FALSE	6
cg25315362	LSAMP	FALSE	3
cg25782229	WT1	TRUE	11
cg26069745	HOXA2	TRUE	7
cg26256793	COL11A1	TRUE	1
cg26279025	IL11	TRUE	19
cg26711820	MYF6	TRUE	12
cg27114120	PROKR2	TRUE	20
cg27196467	KCNIP4	FALSE	4
cg27202708	C1orf65	TRUE	1
cg00970325	PAQR9	TRUE	3
cg01530101	KCNQ1DN	TRUE	11
cg02212836	LY86	FALSE	6
cg04317399	HOXA4	TRUE	7
cg05194726	NRIP2	FALSE	12
cg05222924	WT1	TRUE	11
cg05436231	CD164L2	TRUE	1
cg05890484	BHMT	TRUE	5
cg06563300	SLC17A8	FALSE	12
cg07054641	WDR52	TRUE	3
cg07665060	C19orf33	TRUE	19
cg08321346	ANKMY1	TRUE	2
cg09009380	PKP1	TRUE	1
cg09582042	ITR	TRUE	13
cg09851465	C1orf87	TRUE	1
cg11126134	FLJ14834	TRUE	13
cg12111714	ATP8A2	TRUE	13
cg12782180	LEP	TRUE	7
cg12973651	CNFN	TRUE	19
cg13603171	MOXD1	TRUE	6
cg14456683	ZIC1	TRUE	3
cg14826456	ADRB1	TRUE	10
cg15584813	SLC38A4	TRUE	12
cg15747595	TSPYL5	TRUE	8

cg15748507	PRLHR	TRUE	10
cg16404106	FLJ23514	TRUE	11
cg16731240	ZNF577	TRUE	19
cg17078393	LCK	TRUE	1
cg19594666	LEP	TRUE	7
cg20264732	RBM35B	TRUE	16
cg21992250	SLC15A3	TRUE	11
cg22533573	WT1	TRUE	11
cg25500444	FLJ23514	TRUE	11
cg25802093	SPAG6	TRUE	10
cg26465611	MEGF10	TRUE	5
cg27243140	OTOP3	TRUE	17
cg02330106	MGMT	TRUE	10
cg05740244	LDHC	TRUE	11
cg08828036	ATP10A	TRUE	15
cg12188860	TOP1MT	TRUE	8
cg17267907	DEFA1	FALSE	8
cg19682367	FAM79B	FALSE	3
cg20022541	C14orf152	FALSE	14
cg21909391	FLJ42393	FALSE	3
cg22432908	KLRC2	FALSE	12
cg22580512	NCOR2	TRUE	12
cg24433189	SSTR5	TRUE	16
cg00466249	MGC15523	TRUE	17
cg06493930	GAS2	FALSE	11
cg06850526	MGC15523	TRUE	17
cg07251788	CLTCL1	TRUE	22
cg08632701	SETD4	TRUE	21
cg10106284	FAM49A	FALSE	2
cg12819826	PPAN	TRUE	19
cg17412560	CSEN	FALSE	2
cg17983064	IL3	FALSE	5
cg20507276	OR2L13	TRUE	1
cg26267561	OXT	TRUE	20

Table S5: Common genes differentially methylated in the group of three MPN patients vs BM/PB samples of healthy donors. Red: Genes hypermetylated in MPNs. Green: Genes hypometylated in MPNs

UniqueID	GEN NAME	CpG ISLAND	CHROMOSOME
cg04378886	RCN3	TRUE	19
cg05436231	CD164L2	TRUE	1
cg05890484	BHMT	TRUE	5
cg06563300	SLC17A8	FALSE	12
cg06653796	LIME1	TRUE	20
cg11126134	FLJ14834	TRUE	13
cg12973651	CNFN	TRUE	19
cg15747595	TSPYL5	TRUE	8
cg16731240	ZNF577	TRUE	19
cg16853982	ACTN2	TRUE	1
cg25133685	OR2W1	FALSE	6
cg26267561	OXT	TRUE	20
cg06493930	GAS2	FALSE	11
cg22580512	NCOR2	TRUE	12

Table S6: Uncommon genes differentially methylated in the group of three MPN patients vs BM/PB samples of healthy donors. Red: hypermetylated genes in MPNs. Green: hypometylated genes in MPNs.

UniqueID	GEN NAME	CpG ISLAND	CHROMOSOME
cg00160914	C1orf183	FALSE	1
cg00208967	OLFM2	TRUE	19
cg02061229	MMP10	FALSE	11
cg02844545	GCM2	TRUE	6
cg03086857	EDNRB	TRUE	13
cg03679734	CKMT1B	FALSE	15
cg03743584	PRAP1	FALSE	10
cg05250458	ZNF177	TRUE	19
cg05294243	KLK13	FALSE	19
cg11647681	PCDHGA12	TRUE	5
cg16142218	CHMP7	FALSE	8
cg18059933	TP53INP1	TRUE	8
cg23089840	LRRC3	FALSE	21
cg23191950	ALDH1A3	TRUE	15
cg23326689	STMN2	TRUE	8
cg27304754	CALB2	FALSE	16
cg00071250	FASLG	FALSE	1
cg01367992	LY9	FALSE	1
cg05535113	CHST4	FALSE	16
cg09830866	C16orf24	TRUE	16
cg13164537	CD226	FALSE	18
cg13461622	RUNX3	FALSE	1
cg13975369	TSGA14	TRUE	7
cg14920846	NAV1	TRUE	1
cg26372517	TFAP2E	TRUE	1
cg05373457	KCNS2	TRUE	8
cg17963840	ADRA1A	TRUE	10
cg14826456	ADRB1	TRUE	6
cg12061236	AKAP12	TRUE	19
cg05968233	ALKBH7	TRUE	11
cg15522957	ALX4	TRUE	2
cg05337441	APOB	TRUE	5
cg10660256	BHMT	FALSE	12
cg02351381	C12orf34	FALSE	14
cg19903229	C14orf105	TRUE	16

cg11375102	C16orf30	TRUE	19
cg20893022	C19orf30	TRUE	1
cg09851465	C1orf87	TRUE	1
cg26256793	COL11A1	FALSE	2
cg18182399	DES	TRUE	7
cg06911084	DLX5	TRUE	2
cg12335708	DPP4	FALSE	2
cg14605021	FGF20	TRUE	4
cg09001953	FLJ11200	TRUE	13
cg15792688	FLJ90036	TRUE	4
cg18691434	GPC2	TRUE	7
cg13749822	HHIP	TRUE	4
cg00019495	HOP	FALSE	4
cg26069745	HOXA2	TRUE	7
cg04317399	HOXA4	TRUE	7
cg00767581	HOXD4	TRUE	2
cg08126211	KAAG1	TRUE	6
cg08832227	KCNA1	TRUE	12
cg06572160	KCNC3	TRUE	19
cg27196467	KCNIP4	FALSE	4
cg13234863	KIAA1944	TRUE	12
cg12782180	LEP	TRUE	7
cg25315362	LSAMP	FALSE	3
cg02212836	LY86	FALSE	6
cg12029639	MAB21L1	TRUE	13
cg22892110	MAPK15	TRUE	8
cg20134215	MCHR2	TRUE	6
cg13603171	MOXD1	TRUE	6
cg24840099	MSX1	TRUE	4
cg26711820	MYF6	TRUE	12
cg05194726	NRIP2	FALSE	12
cg21245372	NUP98	TRUE	11
cg00970325	PAQR9	TRUE	3
cg20907471	PAX1	FALSE	20
cg09009380	PKP1	TRUE	1
cg15748507	PRLHR	TRUE	10
cg27114120	PROKR2	TRUE	20
cg17788832	PSKH2	TRUE	8
cg07612655	PTGIS	FALSE	20
cg06971096	PTPRN	TRUE	2
cg20264732	RBM35B	TRUE	16
cg04435420	SGCD	FALSE	5

cg21992250	SLC15A3	TRUE	11
cg25802093	SPAG6	TRUE	10
cg10771262	TCF21	FALSE	6
cg07549194	TIP39	FALSE	19
cg23713520	TM4SF11	TRUE	16
cg23917399	TNFAIP8	TRUE	5
cg14456683	ZIC1	TRUE	11
cg22341310	ZNF541	TRUE	19
cg11134443	KYNU	FALSE	2
cg19815376	FLJ34503	FALSE	6
cg26066361	CLEC7A	FALSE	12
cg26143719	C1QTNF6	FALSE	22
cg26264314	NALP5	TRUE	19
cg01441777	CSNK1E	TRUE	22
cg22381196	DHODH	TRUE	16
cg01820374	LAG3	FALSE	12
cg04230060	SUSD1	TRUE	9
cg24427660	PNPLA2	TRUE	11
cg17412560	CSEN	FALSE	8
cg17267907	DEFA1	TRUE	2
cg10106284	FAM49A	FALSE	3
cg19682367	FAM79B	TRUE	8
cg21909391	FLJ42393	FALSE	3
cg17983064	IL3	FALSE	5
cg22432908	KLRC2	FALSE	12
cg06850526	MGC15523	TRUE	17
cg02330106	MGMT	TRUE	10
cg20507276	OR2L13	TRUE	1
cg24433189	SSTR5	TRUE	16
cg12188860	TOP1MT	TRUE	8

Table S7A: Transcription factor-binding sites enriched in hypermethylated genes in chronic MPNs.

Transcription factor	FDR p-val
CP2	<10E-12
PAX4	<10E-12
SP1	<10E-12
OCT1	0.019
GATA1	0.036
YY1	0.004
LHX3	0.006
TCF1P	0.007
HNF3B	0.012
FAC1	0.013
MYC	0.014

Table S7B: Transcription factor-binding sites enriched in hypomethylated genes in chronic MPNs.

Transcription factor	FDR p-val
PEA3	0.009
SMAD	0.019
ETS1	0.034

Table S7C: Transcription factor-binding sites enriched in hypomethylated genes in transformed MPNs.

Transcription factor	FDR p-val
FAC1	<10E-12
PAX	<10E-12
ATF3	<10E-12
PAX4	<10E-12
CHX10	<10E-12
PITX2	<10E-12
NF1	0.001
Oct-01	0.002
LEF1	0.004
MEF2	0.027
CP2	0.037
LMO2	0.039
CEBP	0.045
LEF1	0.047

Table S8: MPN patients data and description of *JAK2*, *TET2* and *EZH2* gene mutations. WT: Wild Type; NI: No Information; NA: No analysed.

Patient	Age	Time of sampling	Cytogenetics	JAK2	TET2	EZH2
PV1	67	At diagnosis	46,XX,del(20)(q12)	JAKV617F- HOMO	WT	NA
PV2	72	At diagnosis	46,XX	JAKV617F- HOMO	WT	NA
PV3	79	At diagnosis	NI	JAKV617F- HOMO	WT	NA
PV4	67	At diagnosis	46,XY	JAKV617F- HOMO	WT	NA
PV5	76	At diagnosis	NI	JAKV617F- HOMO	WT	NA
PV6	82	At diagnosis	NI	JAKV617F- HET	WT	NA
PV7	85	At diagnosis	46,XY	JAKV617F- HOMO	WT	NA
PV8	78	At diagnosis	NI	JAKV617F- HOMO	WT	NA
PV9	85	At diagnosis	NI	JAKV617F- HOMO	WT	NA
PV10	NI	At diagnosis	NI	JAKV617F- HOMO	WT	NA
PV11	62	At diagnosis	NI	JAKV617F- HOMO	WT	NA
PV12	76	At diagnosis	46,XX	JAKV617F- HOMO	R1516X	NA
PV13	54	At diagnosis	NI	JAKV617F-HET	WT	NA
PV14	46	At diagnosis	NI	JAKV617F-HET	WT	NA
PV15	63	At diagnosis	NI	JAKV617F-HET	WT	NA
PV16	NI	At diagnosis	NI	JAKV617F-HET	WT	NA
PV17	80	At diagnosis	NI	JAKV617F-HET	WT	NA
PV18	68	At diagnosis	NI	JAKV617F-HET	WT	NA
PV19	55	At diagnosis	NI	JAKV617F-HET	WT	NA
PV20	NI	At diagnosis	NI	JAKV617F-HET	WT	NA
PV21	82	At diagnosis	46,XX	JAKV617F-HET	WT	NA
PV22	74	At diagnosis	NI	JAKV617F-HET	WT	NA
PV23	87	At diagnosis	NI	JAKV617F-HET	WT	NA
PV24	64	At diagnosis	NI	JAKV617F-HET	V1395L	NA
ET1	78	At diagnosis	NI	JAKV617F- HOMO	WT	NA
ET2	71	At diagnosis	NI	WT	WT	NA
ET3	80	At diagnosis	NI	WT	WT	NA
ET4	80	At diagnosis	NI	WT	WT	NA
ET5	80	At diagnosis	NI	WT	WT	NA
ET6	61	At diagnosis	46,XY	JAKV617F- HOMO	WT	NA
ET7	61	At diagnosis	NI	JAKV617F- HOMO	WT	NA
ET8	87	At diagnosis	NI	JAKV617F- HOMO	WT	NA
ET9	61	At diagnosis	NI	WT	WT	NA
ET10	55	At diagnosis	46,XY	WT	WT	NA
ET11	55	At diagnosis	NI	WT	NI	NA
ET12	81	At diagnosis	46,XX	JAKV617F- HOMO	WT	NA
ET13	50	At diagnosis	NI	WT	WT	NA
ET14	65	At diagnosis	NI	WT	WT	NA
ET15	71	At diagnosis	NI	JAKV617F- HOMO	WT	NA
ET17	60	At diagnosis	NI	JAKV617F-HET	WT	NA
ET18	28	At diagnosis	NI	JAKV617F-HET	WT	NA
ET19	84	At diagnosis	NI	JAKV617F-HET	ins/del	NA
ET20	NI	At diagnosis	46,XY	WT	WT	NA
ET21	31	At diagnosis	NI	WT	WT	NA
ET22	65	At diagnosis	NI	JAKV617F-HET	WT	NA
ET23	60	At diagnosis	46,XX	JAKV617F-HET	WT	NA
ET24	90	At diagnosis	NI	JAKV617F-HET	WT	NA

PMF1	77	At diagnosis	NI	JAKV617F-HET	T1372I	WT
PMF2	79	At diagnosis	NI	JAKV617F-HOMO	WT	73980T>TG;660L>L/V
PMF3	70	At diagnosis	46,XY	JAKV617F-HOMO	WT	WT
PMF4	77	At diagnosis	46,XX	JAKV617F-HET	WT	WT
PMF5	47	At diagnosis	NI	JAKV617F-HOMO	WT	WT
PMF6	59	At diagnosis	46,XY,t(8;12)(q12;p11) [7%]	JAKV617F-HET	ins/del	WT
PMF7	52	At diagnosis	47,XX,+8 [63%]	JAKV617F-HET	WT	WT
PMF8	70	At diagnosis	NI	JAKV617F-HET	WT	WT
PMF9	61	At diagnosis	NI	JAKV617F-HOMO	WT	WT
PMF10	60	At diagnosis	46,XY	JAKV617F-HET	WT	WT
PMF11	48	At diagnosis	NI	JAKV617F-HET	WT	WT
PMF12	69	At diagnosis	NI	JAKV617F-HET	WT	WT
PMF13	63	At diagnosis	NI	WT	NI	WT
PMF14	67	At diagnosis	46,XX	WT	WT	WT
PMF15	NI	At diagnosis	NI	WT	WT	WT
PMF16	57	At diagnosis	NI	WT	WT	WT
PMF17	NI	At diagnosis	47,XX,del(13)(q12q21) [37%]	WT	WT	WT
PMF18	65	At diagnosis	NI	WT	WT	WT
PMF19	69	At diagnosis	NI	WT	WT	WT
PMF20	74	At diagnosis	46,XY	WT	WT	WT
PMF21	61	At diagnosis	46,XY	WT	WT	WT
PMF22	72	At diagnosis	46,XY	WT	WT	WT
PMF23	43	At diagnosis	46,XY	WT	WT	WT
PMF24	78	At diagnosis	47,XY,+8 [3%]	WT	NI	WT
TRANSFORMED PV1	73	At the moment of transformation	59,X,Y,+1,+2,+6,+8,+9,+13,+14,+15,+19,+20,+4mar [80%] 45,X,-Y [20%]	JAKV617F-HET	NA	NA
TRANSFORMED PV2	80	At the moment of transformation	46,XY,der(20)t(1;20)(q21,q1)	JAKV617F-HET	NA	NA
TRANSFORMED PV3	75	At the moment of transformation	44,X,-Y,-17,der(19)t(17;19)(p13;q12) [54%] 45,X,-Y [46%].	JAKV617F-HET	NA	NA
TRANSFORMED PV4	76	At the moment of transformation	44,XY,del(2)(q?),-4,del(5)(q13q32)-17 [43%] 45,XY,del(5)(q13q32),del(12)(p13)-17 [47%] 46,XY [30%]	JAKV617F-HET	NA	NA
TRANSFORMED ET1	77	At the moment of transformation	46,XY,-5,add(6)(p25),+mar[20]	JAKV617F-HET	NA	NA
TRANSFORMED ET2	60	At the moment of transformation	47,XX,del(20)(q13)x2 [10%] 46,XX [90%]	JAKV617F-HOMO	NA	NA
TRANSFORMED ET3	46	At the moment of transformation	46,XX,del(5)(q15q31),del(20)(q11)[50]	WT	NA	NA
TRANSFORMED ET4	68	At the moment of transformation	47,XX,del(5)(q13q32),-13,-17,+21,+2mar [57%] 46,XX [43%]	JAKV617F-HET	NA	NA
TRANSFORMED PMF1	47	At the moment of transformation	46,XY,del(1)(p33) [77%] 46,XY[23%]	WT	NA	NA
TRANSFORMED PMF2	75	At the moment of transformation	46,XY,add(12)(p13) [40%] 46,XY[60%]	WT	NA	NA
TRANSFORMED PMF3	NI	At the moment of transformation	46,XX,-7,+mar	JAKV617F-HET	NA	NA
TRANSFORMED PMF4	62	At the moment of transformation	46,XY,del(1)(p32),-7,-8, 12, add(16)(q24), +3mar [80%] 46,XY[20%]	WT	NA	NA
TRANSFORMED PMF5	64	At the moment of transformation	46,XY,+der(1)del(1)(p21),-7	WT	NA	NA

Table S9: Genes differentially methylated in transformed MPN patients vs MPN patients in the chronic phase. Red: Genes hypermetylated in transformed MPNs. Green: Genes hypometylated in transformed MPNs.

UniqueID	GEN NAME	CpG ISLAND	CHROMOSOME
cg25346576	CCDC55	TRUE	17
cg07369274	DNASE1L3	FALSE	3
cg25944100	MS4A3	FALSE	11
cg06196379	TREM1	FALSE	6
cg24641737	DENND2D	FALSE	1
cg26538116	LRPPRC	TRUE	2
cg08713365	C20orf98	TRUE	20
cg20542800	LTB4R	FALSE	14
cg04545708	C11orf1	FALSE	11
cg22381196	DHODH	TRUE	16
cg12836863	BRCA2	TRUE	13
cg20119051	R3HDM1	TRUE	2
cg10095719	NRP1	TRUE	10
cg23328404	ChGn	FALSE	8
cg02332073	TSGA13	FALSE	7
cg09001777	FUT3	FALSE	19
cg07525077	RNASE3	FALSE	14
cg23696618	SERPINB10	FALSE	18
cg21969640	GPR84	FALSE	12
cg13311440	CD48	FALSE	1
cg22933847	MRGPRF	FALSE	11
cg13471990	ENTPD1	FALSE	10
cg01980222	TREM2	FALSE	6
cg07211259	PDCD1LG2	FALSE	9
cg03600318	SFTPD	FALSE	10
cg00615241	PRTN3	FALSE	19
cg11098259	AQP9	FALSE	15
cg20070090	S100A8	FALSE	1
cg14178895	C6orf105	FALSE	6
cg26366091	CHI3L2	FALSE	1
cg26701826	MGC26963	FALSE	4
cg21126943	CEACAM6	FALSE	19
cg11916609	IL1RL1	FALSE	2
cg13064571	C8orf44	FALSE	8
cg07300408	RNASE11	FALSE	14
cg10636246	AIM2	FALSE	1
cg19764555	AHNAK	TRUE	11
cg02863947	NR1I2	FALSE	3
cg26861460	PARVG	FALSE	22
cg09047884	TTLL1	TRUE	22
cg12125117	GPR97	FALSE	16
cg04182865	RNF14	FALSE	5
cg16967583	AGXT	FALSE	2
cg04451770	ENTPD1	FALSE	10
cg20748065	POR	TRUE	7

cg21932814	CSTA	FALSE	3
cg05252264	FCAR	TRUE	19
cg10218646	ZBTB11	TRUE	3
cg05697976	MLSTD1	FALSE	12
cg19963522	PIP3-E	FALSE	6
cg09418321	DYRK4	FALSE	12
cg09134726	PRTN3	FALSE	19
cg23219570	FGF23	FALSE	12
cg17496921	TSPAN16	FALSE	19
cg18463686	CLEC5A	FALSE	7
cg15958424	ACPP	FALSE	3
cg01402255	GATAD2B	FALSE	1
cg23181133	CEACAM3	FALSE	19
cg23347958	DHX8	TRUE	17
cg17356733	IFNGR2	TRUE	21
cg08458487	SFTPD	FALSE	10
cg20760063	NBR2	TRUE	17
cg27485921	ATP6V1E2	FALSE	2
cg26105232	IL2RA	FALSE	10
cg08872742	CDH5	FALSE	16
cg00974864	FCGR3B	FALSE	1
cg01982833	SURB7	FALSE	12
cg05000446	MGC41945	FALSE	9
cg22825487	VNN3	FALSE	6
cg24926276	LRG1	FALSE	19
cg21492378	CEP1	FALSE	9
cg07384961	CLDN6	TRUE	16
cg18951427	ACYP2	FALSE	2
cg05157725	COL21A1	TRUE	6
cg09076077	FLJ33860	TRUE	20
cg15248035	CCIN	TRUE	9
cg26928972	CSTA	FALSE	3
cg16826718	HRK	TRUE	12
cg24092914	VHL	TRUE	3
cg12315311	UNQ3033	TRUE	19
cg21410991	ISL1	TRUE	5
cg22242539	SERPINF1	TRUE	17
cg16509045	TRPM6	FALSE	9
cg21991396	CIAS1	FALSE	1
cg22262140	FLJ36046	TRUE	22
cg06317209	AVIL	FALSE	12
cg20287234	GPR55	TRUE	2
cg06645778	HSPC159	TRUE	2
cg24489015	LPO	FALSE	17
cg08130265	C15orf5	FALSE	15
cg20720686	POR	FALSE	7
cg15052901	SLC24A4	FALSE	14
cg16097772	LYZ	FALSE	12
cg07409200	FLJ40919	FALSE	13
cg21935083	RAD50	TRUE	5
cg08044694	BRD4	TRUE	19
cg06812844	TRPM2	FALSE	21
cg09646392	TNFSF13B	FALSE	13

cg15739581	GALNT3	FALSE	2
cg23242898	DCC	TRUE	18
cg12343777	ALOX15B	FALSE	17
cg08368934	GPR97	FALSE	16
cg25341726	IL27	FALSE	16
cg03801286	KCNE1	FALSE	21
cg07979357	IL27RA	TRUE	19
cg12380764	IL19	FALSE	1
cg15831515	ANXA3	FALSE	4
cg02490034	MEST	TRUE	7
cg21283680	SH3BP5	FALSE	3
cg00415993	F2RL2	FALSE	5
cg21561173	C21orf81	TRUE	21
cg17241310	BARHL2	TRUE	1
cg01081263	SCUBE2	TRUE	11
cg27067618	CYP4F3	FALSE	19
cg25799986	WFDC2	TRUE	20
cg18390025	ELOVL3	TRUE	10
cg09997082	GIPR	FALSE	19
cg11935638	EHHADH	FALSE	3
cg15361231	GLRX2	FALSE	1
cg12535715	HTRA4	TRUE	8
cg13035743	PRRT1	TRUE	6
cg24427660	PNPLA2	TRUE	11
cg24777950	CTSG	FALSE	14
cg17527798	LTF	TRUE	3
cg05556717	CCL26	FALSE	7
cg17214107	FGF2	TRUE	4
cg12819826	PPAN	TRUE	19
cg21771250	FAM83F	TRUE	22
cg03064067	SLC6A15	TRUE	12
cg22183706	CALCA	TRUE	11
cg08965527	LRRC50	TRUE	16
cg01820374	LAG3	FALSE	12
cg04747322	SNCAIP	TRUE	5
cg23213217	DEGS1	TRUE	1
cg14189571	ZFP42	TRUE	4
cg06295856	CALCA	TRUE	11
cg25044651	FLJ90650	TRUE	5
cg18084554	ARID3A	FALSE	19
cg01718139	UNQ3033	TRUE	19
cg03627896	LOC283932	TRUE	16
cg08793459	PTRH2	TRUE	17
cg23889010	SLPI	FALSE	20
cg26252167	GPR6	TRUE	6
cg26306976	ITGB1BP1	FALSE	2
cg21402071	CHRNB4	FALSE	15
cg15799267	ALOX15B	FALSE	17
cg17279839	RARRES2	TRUE	7
cg23653187	ADPN	TRUE	22
cg25094569	WT1	TRUE	11
cg22584138	SLC6A4	TRUE	17
cg08145590	C3orf15	TRUE	3

cg22524514	CST6	TRUE	11
cg09068492	CALCA	TRUE	11
cg20191453	AMT	TRUE	3
cg14348532	CALCA	TRUE	11
cg02628202	LGMN	TRUE	14
cg19646028	C19orf30	TRUE	19
cg17586860	SSTR4	TRUE	20
cg10978355	CKMT2	TRUE	5
cg10660256	BHMT	TRUE	5
cg09656934	TDRD5	TRUE	1
cg11511443	LMO3	FALSE	12
cg16731240	ZNF577	TRUE	19
cg17607231	SP140	FALSE	2
cg26093148	TNRC4	TRUE	1
cg08046471	CXCL11	FALSE	4
cg17452257	KIAA0753	FALSE	17
cg23154064	C3orf63	FALSE	3
cg17338258	SHBG	FALSE	17
cg14074641	ABCC12	FALSE	16
cg08585897	TERF2IP	TRUE	16
cg08124030	TM4SF1	TRUE	3

Table S10: Genes differentially methylated in transformed PV patients vs PV samples in the chronic phase. Red: Genes hypermetylated in transformed PV. Green: Genes hypometylated in transformed PV.

UniqueID	GEN NAME	CpG ISLAND	CHROMOSOME
cg02491012	SPIN1	TRUE	16
cg25346576	CCDC55	TRUE	17
cg07369274	DNASE1L3	FALSE	3
cg14262937	OPRM1	FALSE	6
cg25944100	MS4A3	FALSE	11
cg23219570	FGF23	FALSE	12
cg14117297	MGC23244	FALSE	19
cg26538116	LRPPRC	TRUE	2
cg01602416	GCSH	TRUE	16
cg18943195	RAB11FIP5	TRUE	2
cg20867633	GOLT1A	TRUE	1
cg13311440	CD48	FALSE	1
cg21042619	EED	TRUE	11
cg23179321	RPP38	TRUE	10
cg04790129	ITGB2	FALSE	21
cg10261191	MGC39545	TRUE	11
cg26215727	SCNN1A	FALSE	12
cg24641737	DENND2D	FALSE	1
cg24926276	LRG1	FALSE	19
cg14178895	C6orf105	FALSE	6
cg01402255	GATAD2B	FALSE	1
cg20287234	GPR55	TRUE	2
cg25559243	AAMP	TRUE	2
cg27217148	PCGF6	TRUE	10
cg20542800	LTB4R	FALSE	14
cg04545708	C11orf1	FALSE	11
cg07220939	SLC22A12	TRUE	11
cg26701826	MGC26963	FALSE	4
cg13035743	PRRT1	TRUE	6
cg10636246	AIM2	FALSE	1
cg12836863	BRCA2	TRUE	13
cg08840010	TNFRSF9	FALSE	1
cg03025569	TRIM16	FALSE	17
cg26861460	PARVG	FALSE	22
cg23328404	ChGn	FALSE	8
cg13064571	C8orf44	FALSE	8
cg06196379	TREM1	FALSE	6
cg09001777	FUT3	FALSE	19
cg21504624	IL11RA	FALSE	9
cg17166812	NDUFS2	FALSE	1
cg07300408	RNASE11	FALSE	14
cg20119051	R3HDM1	TRUE	2
cg08837884	LRG1	FALSE	19
cg21004129	IL8RA	FALSE	2
cg13807496	ALX4	TRUE	11

cg20760063	NBR2	TRUE	17
cg00415993	F2RL2	FALSE	5
cg14145194	ICAM3	FALSE	19
cg19963522	PIP3-E	FALSE	6
cg11916609	IL1RL1	FALSE	2
cg24092914	VHL	TRUE	3
cg22082462	CPNE6	TRUE	14
cg15447486	GPR109B	FALSE	12
cg04182865	RNF14	FALSE	5
cg03547797	GAS2	FALSE	11
cg23696618	SERPINB10	FALSE	18
cg04988978	MPO	FALSE	17
cg03600318	SFTPD	FALSE	10
cg14859417	PTPRE	TRUE	10
cg22252999	ART3	FALSE	4
cg22381196	DHODH	TRUE	16
cg13650156	PILRA	FALSE	7
cg10044101	VNN2	FALSE	6
cg24489015	LPO	FALSE	17
cg11921829	FCRL2	FALSE	1
cg14448145	DNAJC5	TRUE	20
cg22262140	FLJ36046	TRUE	22
cg23547429	SLC43A3	FALSE	11
cg01718139	UNQ3033	TRUE	19
cg02863947	NR1I2	FALSE	3
cg00400028	ACPL2	TRUE	3
cg21578541	TLR9	FALSE	3
cg14700707	NOTCH4	FALSE	6
cg21935083	RAD50	TRUE	5
cg21126943	CEACAM6	FALSE	19
cg05461841	LOC124220	FALSE	16
cg09571369	P2RY14	FALSE	3
cg06521852	HRIHFB2122	TRUE	22
cg24471894	KIAA0020	FALSE	9
cg08872742	CDH5	FALSE	16
cg13053608	LGP1	FALSE	17
cg11919271	P2RY12	FALSE	3
cg12167564	LYST	FALSE	1
cg16967583	AGXT	FALSE	2
cg01980222	TREM2	FALSE	6
cg21624359	FFAR3	FALSE	19
cg04425624	TNF	FALSE	6
cg09047884	TTLL1	TRUE	22
cg22242539	SERPINF1	TRUE	17
cg06812844	TRPM2	FALSE	21
cg17122311	IL27	FALSE	16
cg04845628	MINA	TRUE	3
cg15775914	CHML	FALSE	1
cg21969640	GPR84	FALSE	12
cg05886367	BTNL9	FALSE	5
cg07211259	PDCD1LG2	FALSE	9
cg13765621	CD1D	FALSE	1
cg26105232	IL2RA	FALSE	10

cg23043245	PACSIN1	TRUE	6
cg21197871	C8orf38	TRUE	8
cg22421766	SCNN1D	FALSE	1
cg26912636	TMEPAI	FALSE	20
cg17496921	TSPAN16	FALSE	19
cg19836808	S100A7	FALSE	1
cg17356733	IFNGR2	TRUE	21
cg08241785	F2RL2	FALSE	5
cg22438810	LCN2	FALSE	9
cg08130265	C15orf5	FALSE	15
cg09405083	C10orf26	FALSE	10
cg07073964	PRSSL1	TRUE	19
cg00333528	GABRR1	FALSE	6
cg00294382	IL23A	FALSE	12
cg08510456	BSN	TRUE	3
cg01525376	LCK	FALSE	1
cg03565081	C14orf93	FALSE	14
cg15739581	GALNT3	FALSE	2
cg17607231	SP140	FALSE	2
cg10095719	NRP1	TRUE	10
cg13615963	CCR6	FALSE	6
cg21492378	CEP1	FALSE	9
cg19560287	GEMIN5	TRUE	5
cg19764555	AHNAK	TRUE	11
cg07525077	RNASE3	FALSE	14
cg08623383	C1orf38	FALSE	1
cg09983885	TRIM21	TRUE	11
cg06233503	KCNQ1	TRUE	11
cg23181133	CEACAM3	FALSE	19
cg27236973	KRT17	TRUE	17
cg23347958	DHX8	TRUE	17
cg12125117	GPR97	FALSE	16
cg11098259	AQP9	FALSE	15
cg09744051	A4GALT	TRUE	22
cg20541456	CYFIP2	FALSE	5
cg22825487	VNN3	FALSE	6
cg12315311	UNQ3033	TRUE	19
cg02829654	LYST	FALSE	1
cg15958424	ACPP	FALSE	3
cg00615241	PRTN3	FALSE	19
cg22933847	MRGPRF	FALSE	11
cg11905488	CLEC12A	FALSE	12
cg08713365	C20orf98	TRUE	20
cg02836529	NEUROD1	TRUE	2
cg06645778	HSPC159	TRUE	2
cg14611112	LCN6	FALSE	9
cg15831515	ANXA3	FALSE	4
cg21932814	CSTA	FALSE	3
cg09418321	DYRK4	FALSE	12
cg18752880	C1QTNF3	FALSE	5
cg21522988	MLSTD1	FALSE	12
cg04036898	POMGNT1	TRUE	1
cg13473336	SLC5A2	FALSE	16

cg09646392	TNFSF13B	FALSE	13
cg02626929	PAQR4	FALSE	16
cg07713493	PCTK3	FALSE	1
cg09076077	FLJ33860	TRUE	20
cg06317209	AVIL	FALSE	12
cg20098659	CLEC9A	TRUE	12
cg18934187	STARD6	FALSE	18
cg11752275	GNLY	FALSE	2
cg10849854	GREB1	FALSE	2
cg27485921	ATP6V1E2	FALSE	2
cg15248035	CCIN	TRUE	9
cg19342782	ANKRD13C	FALSE	1
cg14519515	ADRBK1	TRUE	11
cg01377911	NTF5	TRUE	19
cg09533063	ALDH8A1	FALSE	6
cg14740251	SIGLEC5	FALSE	19
cg12662162	C6orf106	TRUE	6
cg12696750	DNALI1	TRUE	1
cg22791453	ASS	TRUE	9
cg08176694	PITPNM2	TRUE	12
cg03169527	C3orf31	TRUE	3
cg20320468	LAIR1	FALSE	19
cg04340502	GSTA3	FALSE	6
cg10218646	ZBTB11	TRUE	3
cg21771250	FAM83F	TRUE	22
cg20070090	S100A8	FALSE	1
cg14119236	FGF23	TRUE	12
cg15551881	TRAF1	FALSE	9
cg24059075	PRPH	FALSE	12
cg17518962	GAL3ST4	FALSE	7
cg23242898	DCC	TRUE	18
cg04451770	ENTPD1	FALSE	10
cg12380764	IL19	FALSE	1
cg19317715	AOC2	FALSE	17
cg19504245	TNNT1	FALSE	19
cg23213217	DEGS1	TRUE	1
cg17071957	GSN	TRUE	9
cg00145118	GNPDA1	FALSE	5
cg23771661	B3GNT3	TRUE	19
cg18675600	PTP4A3	TRUE	8
cg03627896	LOC283932	TRUE	16
cg13619990	ACSM1	FALSE	16
cg16046376	PC	FALSE	11
cg25651505	VAMP5	TRUE	2
cg16708981	ZNF677	TRUE	19
cg10126923	NKG7	FALSE	19
cg09848074	FLJ44186	FALSE	7
cg26366091	CHI3L2	FALSE	1
cg20748065	POR	TRUE	7
cg09134726	PRTN3	FALSE	19
cg10787197	C6orf105	FALSE	6
cg07384961	CLDN6	TRUE	16
cg08020808	CMA1	FALSE	14

cg12966875	SLPI	FALSE	20
cg21198021	PHC2	FALSE	1
cg21282997	IL18RAP	FALSE	2
cg01982833	SURB7	FALSE	12
cg09147222	CPNE4	TRUE	3
cg08044694	BRD4	TRUE	19
cg08458487	SFTPD	FALSE	10
cg03875678	GZMB	FALSE	14
cg07979357	IL27RA	TRUE	19
cg16415058	SORCS1	TRUE	10
cg02990612	GATA4	TRUE	8
cg25341726	IL27	FALSE	16
cg00666746	SYDE1	TRUE	19
cg01946401	RUNX2	FALSE	6
cg20938359	SLC6A12	FALSE	12
cg04355435	TMEM125	FALSE	1
cg18468842	SLC13A3	TRUE	20
cg02490034	MEST	TRUE	7
cg08209724	ZNF207	TRUE	17
cg06785429	DCUN1D1	FALSE	3
cg06270401	DYRK4	FALSE	12
cg11320084	RNF2	TRUE	1
cg12205591	CRYAA	TRUE	21
cg20018806	TCN1	FALSE	11
cg11207564	CCL3L3	FALSE	17
cg18463686	CLEC5A	FALSE	7
cg09298484	TSGA10	FALSE	2
cg01031251	RPS6KA1	TRUE	1
cg09358725	LMO2	FALSE	11
cg11024597	ECRG4	FALSE	2
cg18951427	ACYP2	FALSE	2
cg12968903	FLJ32028	FALSE	4
cg12343777	ALOX15B	FALSE	17
cg21279955	SLC27A3	TRUE	1
cg06836849	SLC17A8	FALSE	12
cg10001720	LAPTM5	FALSE	1
cg04582938	UAP1L1	TRUE	9
cg11283860	SLC45A1	TRUE	1
cg19601035	COL2A1	FALSE	12
cg19728223	KCNQ1	TRUE	11
cg00974864	FCGR3B	FALSE	1
cg02732509	CTDSP2	TRUE	12
cg22396755	RAP1GA1	TRUE	1
cg20345446	OSBPL5	TRUE	11
cg20550118	CRABP1	TRUE	15
cg01683883	CMTM2	TRUE	16
cg26954174	CARD15	FALSE	16
cg11939496	CD244	FALSE	1
cg09039163	LOC339768	TRUE	2
cg23818978	AMICA1	FALSE	11
cg04925864	FAM65A	TRUE	16
cg12788313	MST1	FALSE	3
cg24697184	TTC22	TRUE	1

cg03887787	CTSW	FALSE	11
cg13471990	ENTPD1	FALSE	10
cg20059151	SLC44A3	TRUE	1
cg00269932	LAIR2	FALSE	19
cg22016649	PNPLA2	TRUE	11
cg27337148	CAMK1G	FALSE	1
cg19717326	MYADM	FALSE	19
cg19876444	CA2	TRUE	8
cg16509045	TRPM6	FALSE	9
cg07512517	NA	FALSE	7
cg05000446	MGC41945	FALSE	9
cg05252264	FCAR	TRUE	19
cg16139316	S100A9	FALSE	1
cg12832565	CD160	FALSE	1
cg11334469	GTF2I	TRUE	7
cg17527798	LTF	TRUE	3
cg01155039	AMN	TRUE	14
cg06092815	SKIP	TRUE	2
cg18390025	ELOVL3	TRUE	10
cg03165378	S100A9	FALSE	1
cg16516400	FAM89A	FALSE	1
cg15052901	SLC24A4	FALSE	14
cg10591174	MYL2	FALSE	12
cg21152671	TRAF1	TRUE	9
cg01625242	GRP	FALSE	18
cg07409200	FLJ40919	FALSE	13
cg24292612	DEFB1	FALSE	8
cg05697976	MLSTD1	FALSE	12
cg07423149	CHI3L1	FALSE	1
cg12478185	SCO1	FALSE	17
cg05556717	CCL26	FALSE	7
cg00399483	DCC	TRUE	18
cg23889010	SLPI	FALSE	20
cg07425555	FLJ23447	FALSE	19
cg15379858	ChGn	FALSE	8
cg11594137	EDG3	TRUE	9
cg21283680	SH3BP5	FALSE	3
cg08598221	SNTB1	FALSE	8
cg11027330	METRN	TRUE	16
cg27067618	CYP4F3	FALSE	19
cg18765542	DGKZ	TRUE	11
cg01820374	LAG3	FALSE	12
cg15361750	GPR77	FALSE	19
cg09997082	GIPR	FALSE	19
cg19103704	FCGBP	FALSE	19
cg20283107	FAM91A1	FALSE	8
cg15779716	CDCP1	TRUE	3
cg20720686	POR	FALSE	7
cg21846903	VTN	FALSE	17
cg23668631	CAMKK1	FALSE	17
cg13652336	DEPDC2	TRUE	8
cg23653187	ADPN	TRUE	22
cg21991396	CIAS1	FALSE	1

cg18361093	PAOX	TRUE	10
cg11254522	FGR	FALSE	1
cg11507178	BCL9L	TRUE	11
cg24237439	FLJ25422	FALSE	5
cg09948350	FLJ25084	FALSE	2
cg26928972	CSTA	FALSE	3
cg06911084	DLX5	TRUE	7
cg23813257	IL32	FALSE	16
cg11846968	PLUNC	FALSE	20
cg23082877	RASIP1	FALSE	19
cg12845808	PCDH12	FALSE	5
cg03118854	PNPLA5	TRUE	22
cg11935638	EHHADH	FALSE	3
cg13265003	SLC37A1	FALSE	21
cg22705929	YPEL4	FALSE	11
cg17468997	NCF1	FALSE	7
cg21842274	CRHBP	FALSE	5
cg02173484	GJA5	FALSE	1
cg08793459	PTRH2	TRUE	17
cg27019278	EMCN	FALSE	4
cg02806777	PGLYRP1	TRUE	19
cg15361231	GLRX2	FALSE	1
cg12600197	NEIL1	TRUE	15
cg03852570	C10orf33	FALSE	10
cg11009736	MARCO	FALSE	2
cg07958192	TIGD2	FALSE	4
cg23776012	KA21	TRUE	17
cg12640109	ASRGL1	TRUE	11
cg20789824	OLFML2A	FALSE	9
cg12865837	SIM1	TRUE	6
cg11787522	STRA6	FALSE	15
cg23637791	ODF3L1	FALSE	15
cg24399529	TMEM84	FALSE	15
cg12022621	LAX1	FALSE	1
cg20483374	C1QTNF5	TRUE	11
cg06776256	GPRC5A	TRUE	12
cg03764585	FMOD	FALSE	1
cg22680204	CRMP1	TRUE	4
cg15043057	CTPS	TRUE	1
cg11860203	CCL2	FALSE	17
cg25101936	ZBTB16	TRUE	11
cg08858521	WFIKKN1	FALSE	16
cg10201668	NIP	TRUE	15
cg17142183	IL1R2	TRUE	2
cg17786776	FKBP9	TRUE	7
cg16719404	CD2	FALSE	1
cg03330678	SEPT_9	TRUE	17
cg26490372	TATDN1	FALSE	8
cg18084554	ARID3A	FALSE	19
cg23713742	SPAG4	FALSE	20
cg20506783	ARHGAP22	TRUE	10
cg18087477	SYCP1	TRUE	1
cg22064129	SLC14A2	FALSE	18

cg23540745	HIST1H4G	TRUE	6
cg23154064	C3orf63	FALSE	3
cg08046471	CXCL11	FALSE	4
cg17338258	SHBG	FALSE	17
cg17348429	ENPP7	TRUE	17
cg01169778	GBGT1	TRUE	9
cg07879977	OR1F1	FALSE	16
cg08585897	TERF2IP	TRUE	16
cg14074641	ABCC12	FALSE	16
cg01795161	MCFP	FALSE	7

Table S11: Genes differentially methylated in transformed ET patients vs ET samples in the chronic phase. Red: Genes hypermetylated in transformed ET. Green: Genes hypometylated in transformed ET.

UniqueID	GEN NAME	CpG ISLAND	CHROMOSOME
cg01860753	RASSF5	TRUE	1
cg22187630	CACNA1A	TRUE	19
cg07460665	CALCOCO2	TRUE	17
cg23219570	FGF23	FALSE	12
cg01222684	TTC1	TRUE	5
cg11908570	KIAA0040	TRUE	1
cg00415993	F2RL2	FALSE	5
cg02983451	KLF11	TRUE	2
cg05270634	RND2	TRUE	17
cg16168311	APOA1BP	TRUE	1
cg19450025	SULT1A3	TRUE	16
cg07211259	PDCD1LG2	FALSE	9
cg06196379	TREM1	FALSE	6
cg25266232	DCC	TRUE	18
cg09769679	NUFIP1	TRUE	13
cg05157725	COL21A1	TRUE	6
cg12966875	SLPI	FALSE	20
cg15447486	GPR109B	FALSE	12
cg20541456	CYFIP2	FALSE	5
cg09047884	TTLL1	TRUE	22
cg23328404	ChGn	FALSE	8
cg01602416	GCSH	TRUE	16
cg16307860	C1orf80	TRUE	1
cg08713365	C20orf98	TRUE	20
cg04451770	ENTPD1	FALSE	10
cg23179321	RPP38	TRUE	10
cg25944100	MS4A3	FALSE	11
cg03600318	SFTPD	FALSE	10
cg13471990	ENTPD1	FALSE	10
cg25799986	WFDC2	TRUE	20
cg02860543	IGF2BP3	TRUE	7
cg10210238	CDKN2B	TRUE	9
cg26366091	CHI3L2	FALSE	1
cg07690018	CPNE7	TRUE	16
cg11098259	AQP9	FALSE	15
cg08241785	F2RL2	FALSE	5
cg26898336	TEKT3	TRUE	17
cg22933847	MRGPRF	FALSE	11
cg16604516	FBLN2	TRUE	3
cg07369274	DNASE1L3	FALSE	3
cg09076077	FLJ33860	TRUE	20
cg08858521	WFIKKN1	FALSE	16
cg25094569	WT1	TRUE	11
cg24641737	DENND2D	FALSE	1
cg10218646	ZBTB11	TRUE	3

cg26701826	MGC26963	FALSE	4
cg20070090	S100A8	FALSE	1
cg02332073	TSGA13	FALSE	7
cg07525077	RNASE3	FALSE	14
cg12865837	SIM1	TRUE	6
cg01982833	SURB7	FALSE	12
cg06645778	HSPC159	TRUE	2
cg18463686	CLEC5A	FALSE	7
cg24092914	VHL	TRUE	3
cg20748065	POR	TRUE	7
cg05000446	MGC41945	FALSE	9
cg21969640	GPR84	FALSE	12
cg09997082	GIPR	FALSE	19
cg19690214	PIP3-E	FALSE	6
cg25500444	FLJ23514	TRUE	11
cg08458487	SFTPD	FALSE	10
cg16708281	FOXD4L1	TRUE	2
cg12125117	GPR97	FALSE	16
cg27546682	STK40	TRUE	1
cg13064571	C8orf44	FALSE	8
cg06263495	ASCL2	TRUE	11
cg16097772	LYZ	FALSE	12
cg01081263	SCUBE2	TRUE	11
cg05252264	FCAR	TRUE	19
cg21126943	CEACAM6	FALSE	19
cg16139316	S100A9	FALSE	1
cg12836863	BRCA2	TRUE	13
cg26755715	FEZ2	TRUE	2
cg19319069	UBE2H	TRUE	7
cg12640109	ASRGL1	TRUE	11
cg15551881	TRAF1	FALSE	9
cg09418321	DYRK4	FALSE	12
cg22892110	MAPK15	TRUE	8
cg12949760	KCNQ1	TRUE	11
cg01980222	TREM2	FALSE	6
cg21492378	CEP1	FALSE	9
cg07384961	CLDN6	TRUE	16
cg09001777	FUT3	FALSE	19
cg04790129	ITGB2	FALSE	21
cg24059075	PRPH	FALSE	12
cg19963522	PIP3-E	FALSE	6
cg24642523	HSPA2	TRUE	14
cg03763616	SPIB	FALSE	19
cg09076123	NCF2	FALSE	1
cg04164824	SIGLEC9	FALSE	19
cg15958424	ACPP	FALSE	3
cg21402071	CHRNB4	FALSE	15
cg25341726	IL27	FALSE	16
cg07409200	FLJ40919	FALSE	13
cg13311440	CD48	FALSE	1
cg20720686	POR	FALSE	7
cg22016649	PNPLA2	TRUE	11
cg18611122	LASS2	TRUE	1

cg13870866	TBX20	TRUE	7
cg20542800	LTB4R	FALSE	14
cg22262140	FLJ36046	TRUE	22
cg24898863	S100A8	FALSE	1
cg16967583	AGXT	FALSE	2
cg13615963	CCR6	FALSE	6
cg10217449	GNPDA2	TRUE	4
cg08510456	BSN	TRUE	3
cg01402255	GATAD2B	FALSE	1
cg18951427	ACYP2	FALSE	2
cg22082462	CPNE6	TRUE	14
cg08872742	CDH5	FALSE	16
cg12014417	GPR109A	TRUE	12
cg21932814	CSTA	FALSE	3
cg04786857	SPDY1	TRUE	2
cg15522957	ALX4	TRUE	11
cg03630088	CPXM2	TRUE	10
cg05697976	MLSTD1	FALSE	12
cg00983520	CPT1B	TRUE	22
cg17607231	SP140	FALSE	2
cg11507178	BCL9L	TRUE	11
cg08145590	C3orf15	TRUE	3
cg16509045	TRPM6	FALSE	9
cg06270401	DYRK4	FALSE	12
cg22381196	DHODH	TRUE	16
cg02266731	CPM	FALSE	12
cg11921829	FCRL2	FALSE	1
cg17173423	MS4A3	FALSE	11
cg22511262	WT1	TRUE	11
cg21991396	CIAS1	FALSE	1
cg26207503	MYF5	TRUE	12
cg14178895	C6orf105	FALSE	6
cg27485921	ATP6V1E2	FALSE	2
cg21042619	EED	TRUE	11
cg04545708	C11orf1	FALSE	11
cg11283860	SLC45A1	TRUE	1
cg17527798	LTF	TRUE	3
cg23696618	SERPINB10	FALSE	18
cg00974864	FCGR3B	FALSE	1
cg22266967	S100P	FALSE	4
cg20449692	CLDN11	TRUE	3
cg02491012	SPIN1	TRUE	16
cg04182865	RNF14	FALSE	5
cg06575572	C22orf8	TRUE	22
cg03085377	RB1	TRUE	13
cg22276571	DSTN	TRUE	20
cg21578541	TLR9	FALSE	3
cg04353769	MS4A6A	FALSE	11
cg10636246	AIM2	FALSE	1
cg23326689	STMN2	TRUE	8
cg13830624	COL21A1	TRUE	6
cg13650156	PILRA	FALSE	7
cg17496921	TSPAN16	FALSE	19

cg12638745	C21orf13	FALSE	21
cg23213217	DEGS1	TRUE	1
cg15361231	GLRX2	FALSE	1
cg26928972	CSTA	FALSE	3
cg03491478	MAPK8IP1	TRUE	11
cg18084554	ARID3A	FALSE	19
cg02806777	PGLYRP1	TRUE	19
cg04988978	MPO	FALSE	17
cg22705225	PDZK3	TRUE	5
cg23181133	CEACAM3	FALSE	19
cg18390025	ELOVL3	TRUE	10
cg01820374	LAG3	FALSE	12
cg26227005	ELAVL4	FALSE	1
cg25559243	AAMP	TRUE	2
cg06516124	WT1	TRUE	11
cg18934187	STARD6	FALSE	18
cg14974772	FBLN5	TRUE	14
cg02863947	NR1I2	FALSE	3
cg03801286	KCNE1	FALSE	21
cg03064067	SLC6A15	TRUE	12
cg25418748	RUFY1	TRUE	5
cg06572160	KCNC3	TRUE	19
cg11009736	MARCO	FALSE	2
cg22825487	VNN3	FALSE	6
cg05674199	AHCY	TRUE	20
cg24427660	PNPLA2	TRUE	11
cg05222924	WT1	TRUE	11
cg25509184	CFTR	TRUE	7
cg12457773	VMP	TRUE	6
cg24489015	LPO	FALSE	17
cg26415655	IL31RA	FALSE	5
cg06908778	SPAG6	TRUE	10
cg11885098	EFNA2	TRUE	19
cg26861460	PARVG	FALSE	22
cg08840010	TNFRSF9	FALSE	1
cg22533573	WT1	TRUE	11
cg08368934	GPR97	FALSE	16
cg10095719	NRP1	TRUE	10
cg27016494	DLX5	TRUE	7
cg04431054	LOC133619	TRUE	5
cg12380764	IL19	FALSE	1
cg14189571	ZFP42	TRUE	4
cg13152535	CLEC11A	TRUE	19
cg02628202	LGMN	TRUE	14
cg05093686	MAB21L1	TRUE	13
cg04425624	TNF	FALSE	6
cg17586860	SSTR4	TRUE	20
cg21410991	ISL1	TRUE	5
cg07220939	SLC22A12	TRUE	11
cg24399529	TMEM84	FALSE	15
cg04481779	IL20RA	TRUE	6
cg05856931	MSI2	TRUE	17
cg13894021	RAB36	TRUE	22

cg00615241	PRTN3	FALSE	19
cg08810065	KIAA1333	TRUE	14
cg10731149	CYBRD1	TRUE	2
cg17356733	IFNGR2	TRUE	21
cg22947000	BCMO1	FALSE	16
cg20264732	RBM35B	TRUE	16
cg03826976	CYB5R2	TRUE	11
cg20287234	GPR55	TRUE	2
cg24777950	CTSG	FALSE	14
cg03991512	LDHD	FALSE	16
cg09646392	TNFSF13B	FALSE	13
cg26538116	LRPPRC	TRUE	2
cg17468997	NCF1	FALSE	7
cg10307548	SOD3	FALSE	4
cg21283680	SH3BP5	FALSE	3
cg21794225	PRKD1	TRUE	14
cg02870945	REEP1	TRUE	2
cg01333011	PTHLH	FALSE	12
cg15310873	C20orf85	TRUE	20
cg06812844	TRPM2	FALSE	21
cg05681757	FGD4	FALSE	12
cg08223235	BCL2	TRUE	18
cg23058901	ALX4	TRUE	11
cg21771250	FAM83F	TRUE	22
cg14173969	CD300C	FALSE	17
cg03958979	NR2E1	TRUE	6
cg25634666	FOLR3	FALSE	11
cg20377955	SP8	FALSE	7
cg24237439	FLJ25422	FALSE	5
cg25651505	VAMP5	TRUE	2
cg03469082	GABRG1	FALSE	4
cg20786074	EFEMP1	TRUE	2
cg26525091	MADCAM1	TRUE	19
cg24625388	NEBL	TRUE	10
cg15739581	GALNT3	FALSE	2
cg18536148	TBX4	TRUE	17
cg07007400	KRT7	TRUE	12
cg09134726	PRTN3	FALSE	19
cg15957394	AFAP	TRUE	4
cg20119051	R3HDM1	TRUE	2
cg11612345	SMOC2	TRUE	6
cg26252167	GPR6	TRUE	6
cg21432842	CSF3	FALSE	17
cg12324144	LRRC34	TRUE	3
cg01293647	NEUROD2	TRUE	17
cg24495017	PITX1	TRUE	5
cg05675373	KCNC4	TRUE	1
cg09381003	SHKBP1	TRUE	19
cg15248035	CCIN	TRUE	9
cg04675937	CDKN2B	TRUE	9
cg19564367	AFAP	TRUE	4
cg03000846	RAC3	TRUE	17
cg06317209	AVIL	FALSE	12

cg26789453	TMEM116	FALSE	12
cg16797831	KIAA1324	TRUE	1
cg25228126	FZD2	TRUE	17
cg01870826	LOC389458	TRUE	7
cg22268231	SPIB	TRUE	19
cg24182328	VMO1	TRUE	17
cg12629325	PCDHAC1	TRUE	5
cg02154186	PNMA2	TRUE	8
cg17279839	RARRES2	TRUE	7
cg17783509	PHOX2B	FALSE	4
cg08097657	SEMA3B	TRUE	3
cg24768561	CENTG2	TRUE	2
cg20760063	NBR2	TRUE	17
cg24164563	FOXJ1	TRUE	17
cg11334469	GTF2I	TRUE	7
cg20329958	CRH	TRUE	8
cg22242539	SERPINF1	TRUE	17
cg26465611	MEGF10	TRUE	5
cg17214107	FGF2	TRUE	4
cg13749822	HHIP	TRUE	4
cg00174901	PALM	FALSE	19
cg07935568	MLNR	TRUE	13
cg23347958	DHX8	TRUE	17
cg17923358	RELN	TRUE	7
cg24474182	P2RY13	FALSE	3
cg19731122	MYO1C	FALSE	17
cg21842274	CRHBP	FALSE	5
cg25484904	FLJ21511	TRUE	4
cg08301503	FLJ43752	TRUE	6
cg07084163	UGT3A2	TRUE	5
cg15779716	CDCP1	TRUE	3
cg12029639	MAB21L1	TRUE	13
cg00201234	FBLN2	TRUE	3
cg04743872	FLJ20701	TRUE	2
cg21126707	MYF5	TRUE	12
cg18979223	CDKN2B	TRUE	9
cg11935638	EHHADH	FALSE	3
cg15052901	SLC24A4	FALSE	14
cg20979799	RFXDC1	TRUE	6
cg14056644	PITX2	TRUE	4
cg23047271	PRICKLE2	FALSE	3
cg16464322	HNRPL	TRUE	19
cg19764555	AHNAK	TRUE	11
cg03699904	SLC2A2	TRUE	3
cg06911084	DLX5	TRUE	7
cg04398978	CBX4	TRUE	17
cg21152671	TRAF1	TRUE	9
cg05026186	ABLIM3	TRUE	5
cg09971646	DLK1	TRUE	14
cg15831515	ANXA3	FALSE	4
cg17272843	KCTD14	TRUE	11
cg12343777	ALOX15B	FALSE	17
cg13547644	ACTA1	TRUE	1

cg23696949	LAMC2	FALSE	1
cg14789259	FAM84A	TRUE	2
cg26833169	CALCA	TRUE	11
cg17347634	CYP7B1	TRUE	8
cg09522147	KRT7	TRUE	12
cg22631938	GPR27	TRUE	3
cg26306976	ITGB1BP1	FALSE	2
cg15787039	SGNE1	TRUE	15
cg23815491	HP	FALSE	16
cg09147222	CPNE4	TRUE	3
cg03311899	GPR109A	TRUE	12
cg04336379	LOC389458	TRUE	7
cg16232126	SLC5A7	TRUE	2
cg17965019	HIST1H3J	TRUE	6
cg25947945	LAD1	TRUE	1
cg16744741	PRKG2	FALSE	4
cg16421285	SAE1	TRUE	19
cg04456238	WT1	TRUE	11
cg25782229	WT1	TRUE	11
cg21935083	RAD50	TRUE	5
cg02564523	C7orf19	TRUE	7
cg16306115	DCDC2	TRUE	6
cg17950095	HOXA11	TRUE	7
cg05337441	APOB	TRUE	2
cg11511443	LMO3	FALSE	12
cg06295856	CALCA	TRUE	11
cg20588069	MSX1	TRUE	4
cg23242898	DCC	TRUE	18
cg25044651	FLJ90650	TRUE	5
cg14882700	OTOP1	TRUE	4
cg01580888	RHPN2	TRUE	19
cg27114120	PROKR2	TRUE	20
cg15799267	ALOX15B	FALSE	17
cg11241627	FERD3L	TRUE	7
cg01615704	MALL	TRUE	2
cg09851465	C1orf87	TRUE	1
cg09697795	SCRL	TRUE	19
cg01718139	UNQ3033	TRUE	19
cg08578734	GRIA1	FALSE	5
cg01643580	KCNK3	TRUE	2
cg05600717	FLJ13639	TRUE	13
cg22183706	CALCA	TRUE	11
cg01530101	KCNQ1DN	TRUE	11
cg02849695	CCDC19	TRUE	1
cg07036530	GPR26	TRUE	10
cg07260592	LPA	TRUE	6
cg08529529	ALOX5AP	FALSE	13
cg10660256	BHMT	TRUE	5
cg12782180	LEP	TRUE	7
cg13928306	ZNF205	FALSE	16
cg14166009	HKR1	TRUE	19
cg16842214	KBTBD5	TRUE	3
cg26976437	LY6K	TRUE	8

cg27337148	CAMK1G	FALSE	1
cg06098051	LOC400986	FALSE	2
cg07918509	ICAM2	FALSE	17
cg12754854	PHYHD1	FALSE	9
cg07974891	ITGB1BP1	FALSE	2
cg19730092	ADAMTS14	TRUE	10
cg22037121	C2orf21	FALSE	2
cg24949488	DNTT	TRUE	10
cg09841009	GYPA	FALSE	4
cg00819310	VANGL1	FALSE	1
cg02989940	ERAF	FALSE	16
cg26777475	PCOLCE	FALSE	7
cg16998872	GYPE	FALSE	4
cg27214365	GYPB	FALSE	4
cg18117847	ZNFN1A1	FALSE	7
cg08367223	SNRPA	FALSE	19
cg24928687	EPHX1	FALSE	1
cg02451670	DTL	FALSE	1
cg21478437	CTSE	FALSE	1
cg04228042	ART4	FALSE	12
cg00466436	DEFB126	FALSE	20
cg06641366	LRRC8C	FALSE	1
cg19306866	KRTAP6-2	TRUE	21
cg08585897	TERF2IP	TRUE	16
cg03938043	DTL	FALSE	1
cg12869058	ABCA4	FALSE	1
cg19216731	CSRP3	FALSE	11
cg22264436	SOST	TRUE	17
cg09447105	PDE6H	FALSE	12
cg07136421	GPR89A	TRUE	1
cg02797569	PCOLCE	FALSE	7
cg11161417	SPACA3	FALSE	17
cg17784922	KEL	FALSE	7
cg11380128	PRLH	FALSE	2
cg21065959	LCE1E	FALSE	1
cg22680812	EPB42	FALSE	15
cg26457013	TMEM86B	FALSE	19
cg11783497	IL1RN	FALSE	2
cg26136776	KLF1	FALSE	19
cg21063899	SCEL	FALSE	13
cg26424956	GRM4	FALSE	6
cg23696712	KRT6L	FALSE	12
cg11653858	SLC13A2	TRUE	17
cg23154272	LENEP	FALSE	1
cg23349242	SUSD2	FALSE	22
cg23464269	UGT1A3	FALSE	2
cg25501446	CDC2	FALSE	10
cg16779976	BLNK	FALSE	10
cg09801065	FAT2	FALSE	5
cg26309498	EDAR	TRUE	2
cg14074641	ABCC12	FALSE	16
cg26062856	ATP10A	TRUE	15
cg23154064	C3orf63	FALSE	3

cg03843951	DDC	FALSE	7
cg17452257	KIAA0753	FALSE	17
cg08046471	CXCL11	FALSE	4

Table S12: Differentially methylathed genes between transformated PMF patients vs PMF samples in chronic phase. Red: Genes hypermethylated in transformated PMF; Green: Genes hypomethylated in transformated PMF.

UniqueID	GEN NAME	CpG ISLAND	CHROMOSOME
cg01860753	RASSF5	TRUE	1
cg26538116	LRPPRC	TRUE	2
cg12789833	FBXO22	TRUE	15
cg03775422	MGC33530	TRUE	7
cg14191109	SLC25A16	TRUE	10
cg16826718	HRK	TRUE	12
cg03476195	ANK2	TRUE	4
cg10095719	NRP1	TRUE	10
cg23347958	DHX8	TRUE	17
cg21410991	ISL1	TRUE	5
cg06196379	TREM1	FALSE	6
cg21561173	C21orf81	TRUE	21
cg02388150	SFRP1	TRUE	8
cg04545708	C11orf1	FALSE	11
cg06933965	CMKLR1	FALSE	12
cg24641737	DENND2D	FALSE	1
cg07369274	DNASE1L3	FALSE	3
cg12819826	PPAN	TRUE	19
cg10218646	ZBTB11	TRUE	3
cg22381196	DHODH	TRUE	16
cg07271264	MYOD1	TRUE	11
cg09134726	PRTN3	FALSE	19
cg11916609	IL1RL1	FALSE	2
cg00754253	HRASLS5	FALSE	11
cg00468146	ID4	TRUE	6
cg12535715	HTRA4	TRUE	8
cg25944100	MS4A3	FALSE	11
cg23696618	SERPINB10	FALSE	18
cg04747322	SNCAIP	TRUE	5
cg25141674	C6orf155	TRUE	6
cg14348532	CALCA	TRUE	11
cg12836863	BRCA2	TRUE	13
cg19014419	ZNF300	TRUE	5
cg03506489	KCNA4	TRUE	11
cg15043057	CTPS	TRUE	1
cg01781266	PARVA	TRUE	11
cg08046471	CXCL11	FALSE	4
cg10846410	HSPA2	FALSE	14
cg22427279	NHLH2	FALSE	1
cg20576002	FAM112B	FALSE	12
cg04450876	FAM112B	FALSE	12
cg23154064	C3orf63	FALSE	3
cg00698688	SULT2B1	FALSE	19
cg14074641	ABCC12	FALSE	16
cg26946769	MAPK4	FALSE	18

cg04727522	C18orf22	TRUE	18
cg01795161	MCFP	FALSE	7
cg26200585	PRX	FALSE	19
cg08585897	TERF2IP	TRUE	16
cg03364781	ALPK1	FALSE	4
cg10990993	MLH1	FALSE	3
cg24607398	MLH1	FALSE	3
cg00626466	GNS	TRUE	12
cg03938043	DTL	FALSE	1
cg14290291	FLJ14346	FALSE	2
cg06194808	MGC9712	FALSE	7
cg00687674	TMEM84	FALSE	15
cg22724153	SPAM1	FALSE	7

Table S13. Common differentially methylated genes between the three transformed MPNs when compared to their chronic phases. Red: Genes hypermetylated in transformed MPNs. Green: Genes hypometylated in transformed MPNs.

UniqueID	GEN NAME	CpG ISLAND	CHROMOSOME
cg07369274	DNASE1L3	FALSE	3
cg25944100	MS4A3	FALSE	11
cg26538116	LRPPRC	TRUE	2
cg24641737	DENND2D	FALSE	1
cg04545708	C11orf1	FALSE	11
cg12836863	BRCA2	TRUE	13
cg06196379	TREM1	FALSE	6
cg23696618	SERPINB10	FALSE	18
cg22381196	DHODH	TRUE	16
cg10095719	NRP1	TRUE	10
cg23347958	DHX8	TRUE	17
cg10218646	ZBTB11	TRUE	3
cg09134726	PRTN3	FALSE	19
cg24399529	TMEM84	FALSE	15
cg14074641	ABCC12	FALSE	16
cg23154064	C3orf63	FALSE	3
cg08046471	CXCL11	FALSE	4
cg08585897	TERF2IP	TRUE	16

Table S14: Uncommon genes differentially methylated between the three transformed MPNs when compared to their chronic phases. Red: Genes hypermetylated in transformed MPNs. Green: Genes hypometylated in transformed MPNs.

UniqueID	GEN NAME	CpG ISLAND	CHROMOSOME
cg09744051	A4GALT	TRUE	22
cg00400028	ACPL2	TRUE	3
cg13619990	ACSM1	FALSE	16
cg23653187	ADPN	TRUE	22
cg14519515	ADRBK1	TRUE	11
cg09533063	ALDH8A1	FALSE	6
cg23818978	AMICA1	FALSE	11
cg01155039	AMN	TRUE	14
cg19342782	ANKRD13C	FALSE	1
cg19317715	AOC2	FALSE	17
cg20506783	ARHGAP22	TRUE	10
cg22252999	ART3	FALSE	4
cg22791453	ASS	TRUE	9
cg23771661	B3GNT3	TRUE	19
cg08044694	BRD4	TRUE	19
cg05886367	BTNL9	FALSE	5
cg09405083	C10orf26	FALSE	10
cg03852570	C10orf33	FALSE	10
cg03565081	C14orf93	FALSE	14
cg08130265	C15orf5	FALSE	15
cg08623383	C1orf38	FALSE	1
cg18752880	C1QTNF3	FALSE	5
cg20483374	C1QTNF5	TRUE	11
cg03169527	C3orf31	TRUE	3
cg12662162	C6orf106	TRUE	6
cg21197871	C8orf38	TRUE	8
cg19876444	CA2	TRUE	8
cg23668631	CAMKK1	FALSE	17
cg26954174	CARD15	FALSE	16
cg25346576	CCDC55	TRUE	17
cg11860203	CCL2	FALSE	17
cg05556717	CCL26	FALSE	7
cg11207564	CCL3L3	FALSE	17
cg12832565	CD160	FALSE	1
cg13765621	CD1D	FALSE	1

cg16719404	CD2	FALSE	1
cg11939496	CD244	FALSE	1
cg07423149	CHI3L1	FALSE	1
cg15775914	CHML	FALSE	1
cg11905488	CLEC12A	FALSE	12
cg20098659	CLEC9A	TRUE	12
cg08020808	CMA1	FALSE	14
cg01683883	CMTM2	TRUE	16
cg19601035	COL2A1	FALSE	12
cg20550118	CRABP1	TRUE	15
cg22680204	CRMP1	TRUE	4
cg12205591	CRYAA	TRUE	21
cg02732509	CTDSP2	TRUE	12
cg03887787	CTSW	FALSE	11
cg27067618	CYP4F3	FALSE	19
cg06785429	DCUN1D1	FALSE	3
cg24292612	DEFB1	FALSE	8
cg13652336	DEPDC2	TRUE	8
cg18765542	DGKZ	TRUE	11
cg14448145	DNAJC5	TRUE	20
cg12696750	DNALI1	TRUE	1
cg11024597	ECRG4	FALSE	2
cg11594137	EDG3	TRUE	9
cg27019278	EMCN	FALSE	4
cg04925864	FAM65A	TRUE	16
cg16516400	FAM89A	FALSE	1
cg20283107	FAM91A1	FALSE	8
cg19103704	FCGBP	FALSE	19
cg21624359	FFAR3	FALSE	19
cg11254522	FGR	FALSE	1
cg17786776	FKBP9	TRUE	7
cg07425555	FLJ23447	FALSE	19
cg09948350	FLJ25084	FALSE	2
cg12968903	FLJ32028	FALSE	4
cg09848074	FLJ44186	FALSE	7
cg03764585	FMOD	FALSE	1
cg00333528	GABRR1	FALSE	6
cg17518962	GAL3ST4	FALSE	7
cg03547797	GAS2	FALSE	11
cg02990612	GATA4	TRUE	8
cg19560287	GEMIN5	TRUE	5
cg02173484	GJA5	FALSE	1

cg11752275	GNLY	FALSE	2
cg00145118	GNPDA1	FALSE	5
cg20867633	GOLT1A	TRUE	1
cg15361750	GPR77	FALSE	19
cg06776256	GPRC5A	TRUE	12
cg10849854	GREB1	FALSE	2
cg01625242	GRP	FALSE	18
cg17071957	GSN	TRUE	9
cg04340502	GSTA3	FALSE	6
cg03875678	GZMB	FALSE	14
cg06521852	HRIHFB2122	TRUE	22
cg14145194	ICAM3	FALSE	19
cg21504624	IL11RA	FALSE	9
cg21282997	IL18RAP	FALSE	2
cg17142183	IL1R2	TRUE	2
cg00294382	IL23A	FALSE	12
cg07979357	IL27RA	TRUE	19
cg26105232	IL2RA	FALSE	10
cg23813257	IL32	FALSE	16
cg21004129	IL8RA	FALSE	2
cg23776012	KA21	TRUE	17
cg24471894	KIAA0020	FALSE	9
cg27236973	KRT17	TRUE	17
cg20320468	LAIR1	FALSE	19
cg00269932	LAIR2	FALSE	19
cg10001720	LAPTM5	FALSE	1
cg12022621	LAX1	FALSE	1
cg01525376	LCK	FALSE	1
cg22438810	LCN2	FALSE	9
cg14611112	LCN6	FALSE	9
cg13053608	LGP1	FALSE	17
cg09358725	LMO2	FALSE	11
cg05461841	LOC124220	FALSE	16
cg03627896	LOC283932	TRUE	16
cg09039163	LOC339768	TRUE	2
cg24926276	LRG1	FALSE	19
cg12167564	LYST	FALSE	1
cg02490034	MEST	TRUE	7
cg11027330	METRN	TRUE	16
cg14117297	MGC23244	FALSE	19
cg10261191	MGC39545	TRUE	11
cg04845628	MINA	TRUE	3

cg12788313	MST1	FALSE	3
cg19717326	MYADM	FALSE	19
cg10591174	MYL2	FALSE	12
cg07512517	NA	FALSE	7
cg17166812	NDUFS2	FALSE	1
cg12600197	NEIL1	TRUE	15
cg02836529	NEUROD1	TRUE	2
cg10201668	NIP	TRUE	15
cg10126923	NKG7	FALSE	19
cg14700707	NOTCH4	FALSE	6
cg01377911	NTF5	TRUE	19
cg23637791	ODF3L1	FALSE	15
cg20789824	OLFML2A	FALSE	9
cg14262937	OPRM1	FALSE	6
cg20345446	OSBPL5	TRUE	11
cg11919271	P2RY12	FALSE	3
cg09571369	P2RY14	FALSE	3
cg23043245	PACSIN1	TRUE	6
cg18361093	PAOX	TRUE	10
cg02626929	PAQR4	FALSE	16
cg16046376	PC	FALSE	11
cg12845808	PCDH12	FALSE	5
cg27217148	PCGF6	TRUE	10
cg07713493	PCTK3	FALSE	1
cg21198021	PHC2	FALSE	1
cg08176694	PITPNM2	TRUE	12
cg11846968	PLUNC	FALSE	20
cg03118854	PNPLA5	TRUE	22
cg04036898	POMGNT1	TRUE	1
cg13035743	PRRT1	TRUE	6
cg07073964	PRSSL1	TRUE	19
cg18675600	PTP4A3	TRUE	8
cg14859417	PTPRE	TRUE	10
cg08793459	PTRH2	TRUE	17
cg18943195	RAB11FIP5	TRUE	2
cg22396755	RAP1GA1	TRUE	1
cg23082877	RASIP1	FALSE	19
cg07300408	RNASE11	FALSE	14
cg11320084	RNF2	TRUE	1
cg01031251	RPS6KA1	TRUE	1
cg01946401	RUNX2	FALSE	6
cg19836808	S100A7	FALSE	1

cg26215727	SCNN1A	FALSE	12
cg22421766	SCNN1D	FALSE	1
cg12478185	SCO1	FALSE	17
cg03330678	SEPT_9	TRUE	17
cg14740251	SIGLEC5	FALSE	19
cg06092815	SKIP	TRUE	2
cg18468842	SLC13A3	TRUE	20
cg06836849	SLC17A8	FALSE	12
cg21279955	SLC27A3	TRUE	1
cg13265003	SLC37A1	FALSE	21
cg23547429	SLC43A3	FALSE	11
cg20059151	SLC44A3	TRUE	1
cg13473336	SLC5A2	FALSE	16
cg20938359	SLC6A12	FALSE	12
cg08598221	SNTB1	FALSE	8
cg16415058	SORCS1	TRUE	10
cg23713742	SPAG4	FALSE	20
cg11787522	STRA6	FALSE	15
cg18087477	SYCP1	TRUE	1
cg00666746	SYDE1	TRUE	19
cg26490372	TATDN1	FALSE	8
cg20018806	TCN1	FALSE	11
cg07958192	TIGD2	FALSE	4
cg04355435	TMEM125	FALSE	1
cg26912636	TMEPAI	FALSE	20
cg19504245	TNNT1	FALSE	19
cg03025569	TRIM16	FALSE	17
cg09983885	TRIM21	TRUE	11
cg09298484	TSGA10	FALSE	2
cg24697184	TTC22	TRUE	1
cg04582938	UAP1L1	TRUE	9
cg10044101	VNN2	FALSE	6
cg21846903	VTN	FALSE	17
cg22705929	YPEL4	FALSE	11
cg25101936	ZBTB16	TRUE	11
cg08209724	ZNF207	TRUE	17
cg16708981	ZNF677	TRUE	19
cg05026186	ABLIM3	TRUE	5
cg13547644	ACTA1	TRUE	1
cg15957394	AFAP	TRUE	4
cg05674199	AHCY	TRUE	20
cg15799267	ALOX15B	FALSE	17

cg16168311	APOA1BP	TRUE	1
cg05337441	APOB	TRUE	2
cg06263495	ASCL2	TRUE	11
cg08223235	BCL2	TRUE	18
cg22947000	BCMO1	FALSE	16
cg10660256	BHMT	TRUE	5
cg16307860	C1orf80	TRUE	1
cg09851465	C1orf87	TRUE	1
cg15310873	C20orf85	TRUE	20
cg12638745	C21orf13	FALSE	21
cg06575572	C22orf8	TRUE	22
cg08145590	C3orf15	TRUE	3
cg02564523	C7orf19	TRUE	7
cg22187630	CACNA1A	TRUE	19
cg26833169	CALCA	TRUE	11
cg04398978	CBX4	TRUE	17
cg02849695	CCDC19	TRUE	1
cg14173969	CD300C	FALSE	17
cg10210238	CDKN2B	TRUE	9
cg24768561	CENTG2	TRUE	2
cg25509184	CFTR	TRUE	7
cg21402071	CHRNB4	FALSE	15
cg20449692	CLDN11	TRUE	3
cg13152535	CLEC11A	TRUE	19
cg05157725	COL21A1	TRUE	6
cg02266731	CPM	FALSE	12
cg07690018	CPNE7	TRUE	16
cg00983520	CPT1B	TRUE	22
cg03630088	CPXM2	TRUE	10
cg20329958	CRH	TRUE	8
cg21432842	CSF3	FALSE	17
cg24777950	CTSG	FALSE	14
cg03826976	CYB5R2	TRUE	11
cg10731149	CYBRD1	TRUE	2
cg17347634	CYP7B1	TRUE	8
cg16306115	DCDC2	TRUE	6
cg09971646	DLK1	TRUE	14
cg22276571	DSTN	TRUE	20
cg20786074	EFEMP1	TRUE	2
cg11885098	EFNA2	TRUE	19
cg26227005	ELAVL4	FALSE	1
cg14789259	FAM84A	TRUE	2

cg16604516	FBLN2	TRUE	3
cg14974772	FBLN5	TRUE	14
cg11241627	FERD3L	TRUE	7
cg26755715	FEZ2	TRUE	2
cg05681757	FGD4	FALSE	12
cg17214107	FGF2	TRUE	4
cg05600717	FLJ13639	TRUE	13
cg04743872	FLJ20701	TRUE	2
cg25484904	FLJ21511	TRUE	4
cg25500444	FLJ23514	TRUE	11
cg08301503	FLJ43752	TRUE	6
cg25044651	FLJ90650	TRUE	5
cg25634666	FOLR3	FALSE	11
cg16708281	FOXD4L1	TRUE	2
cg24164563	FOXJ1	TRUE	17
cg25228126	FZD2	TRUE	17
cg03469082	GABRG1	FALSE	4
cg10217449	GNPDA2	TRUE	4
cg12014417	GPR109A	TRUE	12
cg07036530	GPR26	TRUE	10
cg22631938	GPR27	TRUE	3
cg26252167	GPR6	TRUE	6
cg08578734	GRIA1	FALSE	5
cg13749822	HHIP	TRUE	4
cg17965019	HIST1H3J	TRUE	6
cg14166009	HKR1	TRUE	19
cg16464322	HNRPL	TRUE	19
cg17950095	HOXA11	TRUE	7
cg23815491	HP	FALSE	16
cg02860543	IGF2BP3	TRUE	7
cg04481779	IL20RA	TRUE	6
cg26415655	IL31RA	FALSE	5
cg26306976	ITGB1BP1	FALSE	2
cg16842214	KBTBD5	TRUE	3
cg06572160	KCNC3	TRUE	19
cg05675373	KCNC4	TRUE	1
cg03801286	KCNE1	FALSE	21
cg01643580	KCNK3	TRUE	2
cg01530101	KCNQ1DN	TRUE	11
cg17272843	KCTD14	TRUE	11
cg11908570	KIAA0040	TRUE	1
cg16797831	KIAA1324	TRUE	1

cg08810065	KIAA1333	TRUE	14
cg02983451	KLF11	TRUE	2
cg07007400	KRT7	TRUE	12
cg25947945	LAD1	TRUE	1
cg23696949	LAMC2	FALSE	1
cg18611122	LASS2	TRUE	1
cg03991512	LDHD	FALSE	16
cg12782180	LEP	TRUE	7
cg02628202	LGMN	TRUE	14
cg11511443	LMO3	FALSE	12
cg04431054	LOC133619	TRUE	5
cg01870826	LOC389458	TRUE	7
cg07260592	LPA	TRUE	6
cg12324144	LRRC34	TRUE	3
cg26976437	LY6K	TRUE	8
cg16097772	LYZ	FALSE	12
cg05093686	MAB21L1	TRUE	13
cg26525091	MADCAM1	TRUE	19
cg01615704	MALL	TRUE	2
cg22892110	MAPK15	TRUE	8
cg03491478	MAPK8IP1	TRUE	11
cg26465611	MEGF10	TRUE	5
cg07935568	MLNR	TRUE	13
cg04353769	MS4A6A	FALSE	11
cg05856931	MSI2	TRUE	17
cg20588069	MSX1	TRUE	4
cg26207503	MYF5	TRUE	12
cg19731122	MYO1C	FALSE	17
cg09076123	NCF2	FALSE	1
cg24625388	NEBL	TRUE	10
cg01293647	NEUROD2	TRUE	17
cg03958979	NR2E1	TRUE	6
cg09769679	NUFIP1	TRUE	13
cg14882700	OTOP1	TRUE	4
cg24474182	P2RY13	FALSE	3
cg00174901	PALM	FALSE	19
cg12629325	PCDHAC1	TRUE	5
cg22705225	PDZK3	TRUE	5
cg17783509	PHOX2B	FALSE	4
cg24495017	PITX1	TRUE	5
cg14056644	PITX2	TRUE	4
cg02154186	PNMA2	TRUE	8

cg23047271	PRICKLE2	FALSE	3
cg21794225	PRKD1	TRUE	14
cg16744741	PRKG2	FALSE	4
cg27114120	PROKR2	TRUE	20
cg01333011	PTHLH	FALSE	12
cg13894021	RAB36	TRUE	22
cg03000846	RAC3	TRUE	17
cg17279839	RARRES2	TRUE	7
cg03085377	RB1	TRUE	13
cg20264732	RBM35B	TRUE	16
cg02870945	REEP1	TRUE	2
cg17923358	RELN	TRUE	7
cg20979799	RFXDC1	TRUE	6
cg01580888	RHPN2	TRUE	19
cg05270634	RND2	TRUE	17
cg25418748	RUFY1	TRUE	5
cg22266967	S100P	FALSE	4
cg16421285	SAE1	TRUE	19
cg09697795	SCRL	TRUE	19
cg01081263	SCUBE2	TRUE	11
cg08097657	SEMA3B	TRUE	3
cg15787039	SGNE1	TRUE	15
cg09381003	SHKBP1	TRUE	19
cg04164824	SIGLEC9	FALSE	19
cg03699904	SLC2A2	TRUE	3
cg16232126	SLC5A7	TRUE	2
cg03064067	SLC6A15	TRUE	12
cg11612345	SMOC2	TRUE	6
cg10307548	SOD3	FALSE	4
cg20377955	SP8	FALSE	7
cg06908778	SPAG6	TRUE	10
cg04786857	SPDY1	TRUE	2
cg03763616	SPIB	FALSE	19
cg17586860	SSTR4	TRUE	20
cg27546682	STK40	TRUE	1
cg23326689	STMN2	TRUE	8
cg19450025	SULT1A3	TRUE	16
cg13870866	TBX20	TRUE	7
cg18536148	TBX4	TRUE	17
cg26898336	TEKT3	TRUE	17
cg26789453	TMEM116	FALSE	12
cg02332073	TSGA13	FALSE	7

cg01222684	TTC1	TRUE	5
cg19319069	UBE2H	TRUE	7
cg07084163	UGT3A2	TRUE	5
cg24182328	VMO1	TRUE	17
cg12457773	VMP	TRUE	6
cg25799986	WFDC2	TRUE	20
cg25094569	WT1	TRUE	11
cg14189571	ZFP42	TRUE	4
cg13928306	ZNF205	FALSE	16
cg03476195	ANK2	TRUE	4
cg21561173	C21orf81	TRUE	21
cg25141674	C6orf155	TRUE	6
cg06933965	CMKLR1	FALSE	12
cg12789833	FBXO22	TRUE	15
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cg03506489	KCNA4	TRUE	11
cg03775422	MGC33530	TRUE	7
cg07271264	MYOD1	TRUE	11
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cg14191109	SLC25A16	TRUE	10
cg04747322	SNCAIP	TRUE	5
cg19014419	ZNF300	TRUE	5
cg17348429	ENPP7	TRUE	17
cg01169778	GBGT1	TRUE	9
cg23540745	HIST1H4G	TRUE	6
cg07879977	OR1F1	FALSE	16
cg17338258	SHBG	FALSE	17
cg22064129	SLC14A2	FALSE	18
cg12869058	ABCA4	FALSE	1
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cg04228042	ART4	FALSE	12
cg26062856	ATP10A	TRUE	15
cg16779976	BLNK	FALSE	10
cg22037121	C2orf21	FALSE	2
cg25501446	CDC2	FALSE	10
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cg21478437	CTSE	FALSE	1

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cg09801065	FAT2	FALSE	5
cg07136421	GPR89A	TRUE	1
cg26424956	GRM4	FALSE	6
cg09841009	GYPA	FALSE	4
cg27214365	GYPB	FALSE	4
cg16998872	GYPE	FALSE	4
cg07918509	ICAM2	FALSE	17
cg11783497	IL1RN	FALSE	2
cg17784922	KEL	FALSE	7
cg17452257	KIAA0753	FALSE	17
cg26136776	KLF1	FALSE	19
cg23696712	KRT6L	FALSE	12
cg19306866	KRTAP6-2	TRUE	21
cg21065959	LCE1E	FALSE	1
cg23154272	LENEP	FALSE	1
cg06098051	LOC400986	FALSE	2
cg06641366	LRRC8C	FALSE	1
cg26777475	PCOLCE	FALSE	7
cg09447105	PDE6H	FALSE	12
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cg22264436	SOST	TRUE	17
cg11161417	SPACA3	FALSE	17
cg23349242	SUSD2	FALSE	22
cg26457013	TMEM86B	FALSE	19
cg23464269	UGT1A3	FALSE	2
cg00819310	VANGL1	FALSE	1
cg18117847	ZNFN1A1	FALSE	7
cg03364781	ALPK1	FALSE	4
cg04727522	C18orf22	TRUE	18
cg20576002	FAM112B	FALSE	12
cg14290291	FLJ14346	FALSE	2

cg00626466	GNS	TRUE	12
cg26946769	MAPK4	FALSE	18
cg06194808	MGC9712	FALSE	7
cg10990993	MLH1	FALSE	3
cg22427279	NHLH2	FALSE	1
cg26200585	PRX	FALSE	19
cg22724153	SPAM1	FALSE	7
cg00698688	SULT2B1	FALSE	19

Table S15: Specific primers and probes corresponding to pyrosequencing analysis

GENE	PRIMERS	SEQUENCE	AMPLIF.	Tª	CYCLES	INTERMEDIATE PYROSEQUENCING PRIMERS	
GAS2	GAS2-F	TGTGGATATTGATTAATTGTAGTTG	132bp	50ºC	45	GAS2-PYRO	AAGGAATGTTTTTTTTTAATT
	GAS2-R	TTAAAAAAAACCACCAAAACC					
BHMT	BHMT-F	TTTGGGTGAATAATTTGGATTATTT	134bp	58ºC	45	BHMT-PYRO	GGTTTGATGAAGGGTTGGTGGG
	BHMT-R	TAAAAAAAACCTCCCAACCAC					

SUPPLEMENTAL FILE

Figure S1. Unsupervised hierarchical correlation clustering analysis of MPNs and controls samples. This cluster was performed using all probes included on the array except those probes located on sexual chromosomes. The top bar beneath the dendrogram indicates either control healthy donor samples, PV, ET or PMF sample type in a specific color-code. Second bar indicates MPNs and control healthy donor samples.

Figure S2. DNA methylation analysis. Pyrosequencing results of analyzed CpG loci on the array, corresponding to *BHMT* and *GAS2* genes. The values are expressed as percentage of methylation.

Figure S3. Analysis of differentially methylated genes in MPNs samples in comparison with healthy donor samples. A. Venn Diagram. Each circle in this representation contains the genes differentially methylated between each neoplasia and the control healthy donor samples. The intersections between circles correspond to common genes differentially methylated between comparisons. **B**. Cluster analysis of genes commonly deregulated in the three neoplasias when compared with the control healthy donor samples group. The top bar beneath the dendrogram indicates control healthy donor, PV, ET or PMF samples in a specific colour-code. Second bar indicates MPNs and control healthy donor samples. **C.** Cluster analysis of no-overlapping genes in the three comparisons. The top bar beneath the dendrogram indicates control healthy donor, PV, ET or PMF samples in a specific colour-code. Second bar indicates MPNs and control healthy donor samples.

Figure S4. Hierarchical cluster analysis based on differentially methylated genes between the three MPN disease entities. β values are depicted using a pseudocolour scale. Red: Genes hypermethylated; Green: Unmethylated genes. The top bar beneath the dendrogram indicates PV, ET, PMF sample type in a specific colour-code.

Figure S5. Network of genes obtained using Ingenuity Pathway Analysis software containing differentially methylated genes between MPNs patient samples and control healthy donor samples.

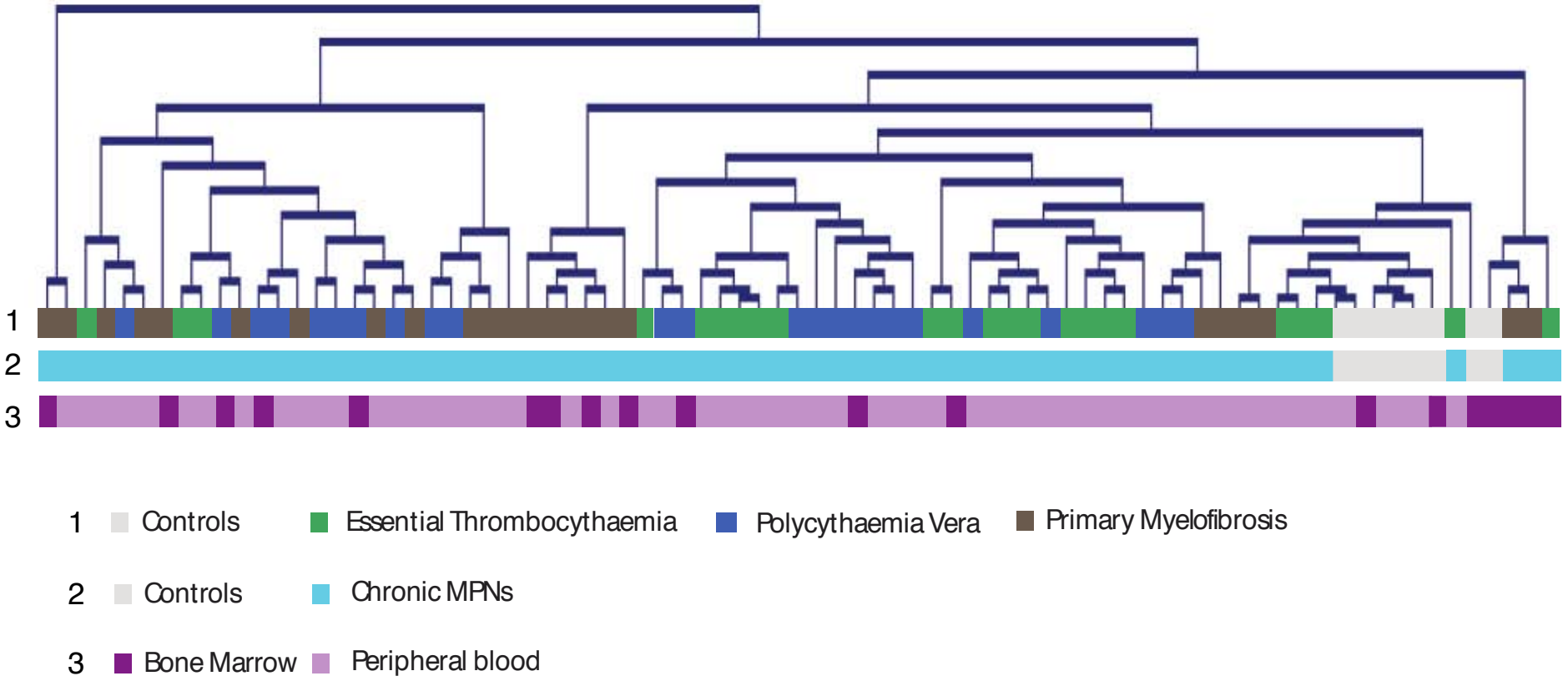
Figure S6. Unsupervised hierarchical correlation clustering analysis of transformed MPNs and controls healthy donor samples. This cluster was performed using all probes included on the array except those probes located on sexual chromosomes. The top bar beneath the dendrogram indicates either control healthy donor samples, PV, ET, PMF, or MPNs transformed to acute leukaemia in a specific colour-code. Second bar indicates control healthy donor samples, chronic MPNs and transformed MPN samples.

Figure S7. Bioinformatic studies of differentially methylated genes using GSEA. A. This GSEA analysis determined a statistically significant ($p>0.001$) positive enrichment of genes differentially methylated in chronic MPNs in a gene set of differentially methylated genes in transformed MPNs. **B.** This GSEA analysis showed a statistically significant ($p>0.001$) positive enrichment of genes differentially methylated in transformed MPNs in a gene set of differentially methylated genes in primary acute myeloid leukaemia samples.

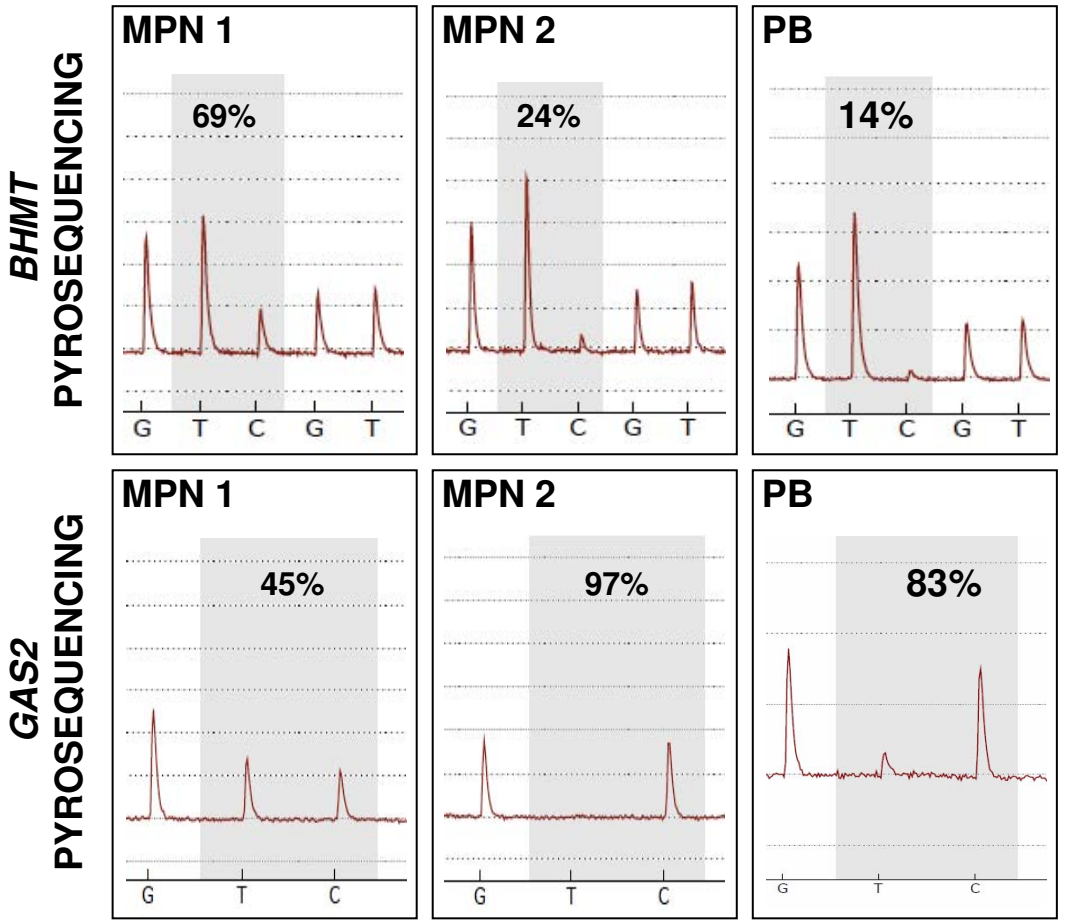
Figure S8. Analysis of differentially methylated genes in MPNs samples transformed to acute leukemia in comparison with MPNs in chronic phase. A. Venn Diagram. Each circle in this representation contains the genes differentially methylated between each transformed MPN and its chronic phase MPN. The intersections between circles correspond to common genes differentially methylated between comparisons. **B**. Cluster analysis of genes commonly deregulated in the three transformed MPNs when compared with its chronic MPNs. The top bar beneath the dendrogram indicates either control healthy donor samples, chronic PV, chronic ET, chronic PMF, transformed PV, transformed ET and transformed PMF samples in a specific colour-code. Second bar indicates control healthy donor samples, chronic MPNs and transformed MPN samples. **C.** Cluster analysis of no-overlapping genes in the three comparisons. The top bar beneath the dendrogram indicates either control healthy donor samples, chronic PV, chronic ET, chronic PMF, transformed PV, transformed ET and transformed PMF samples in a specific colour-code. Second bar indicates control healthy donor samples, chronic MPNs and transformed MPN samples.

Figure S9. Network of genes obtained using Ingenuity Pathway Analysis software containing differentially methylated genes between transformed MPNs patient samples and MPNs in chronic phase

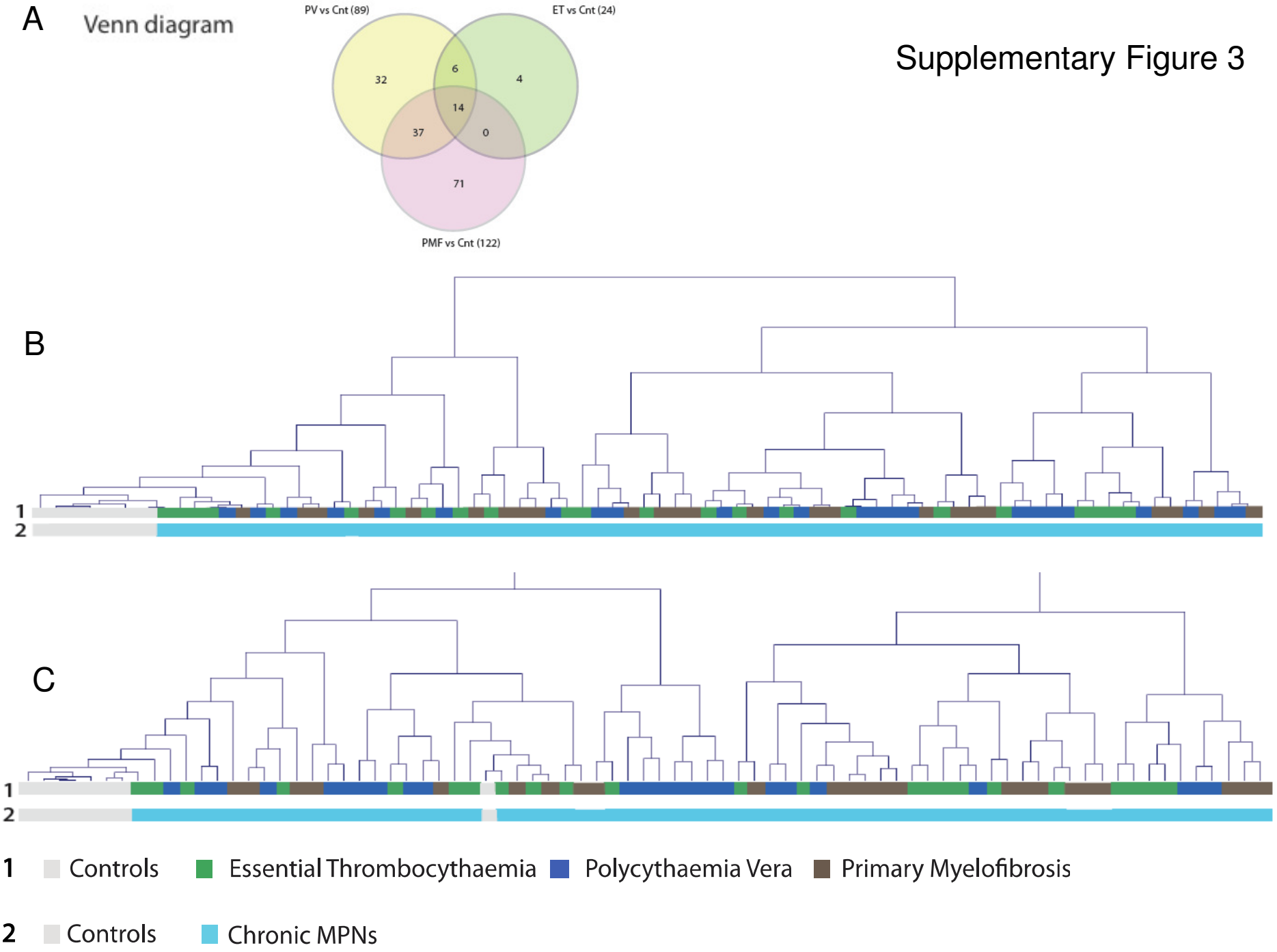
Supplementary Figure 1

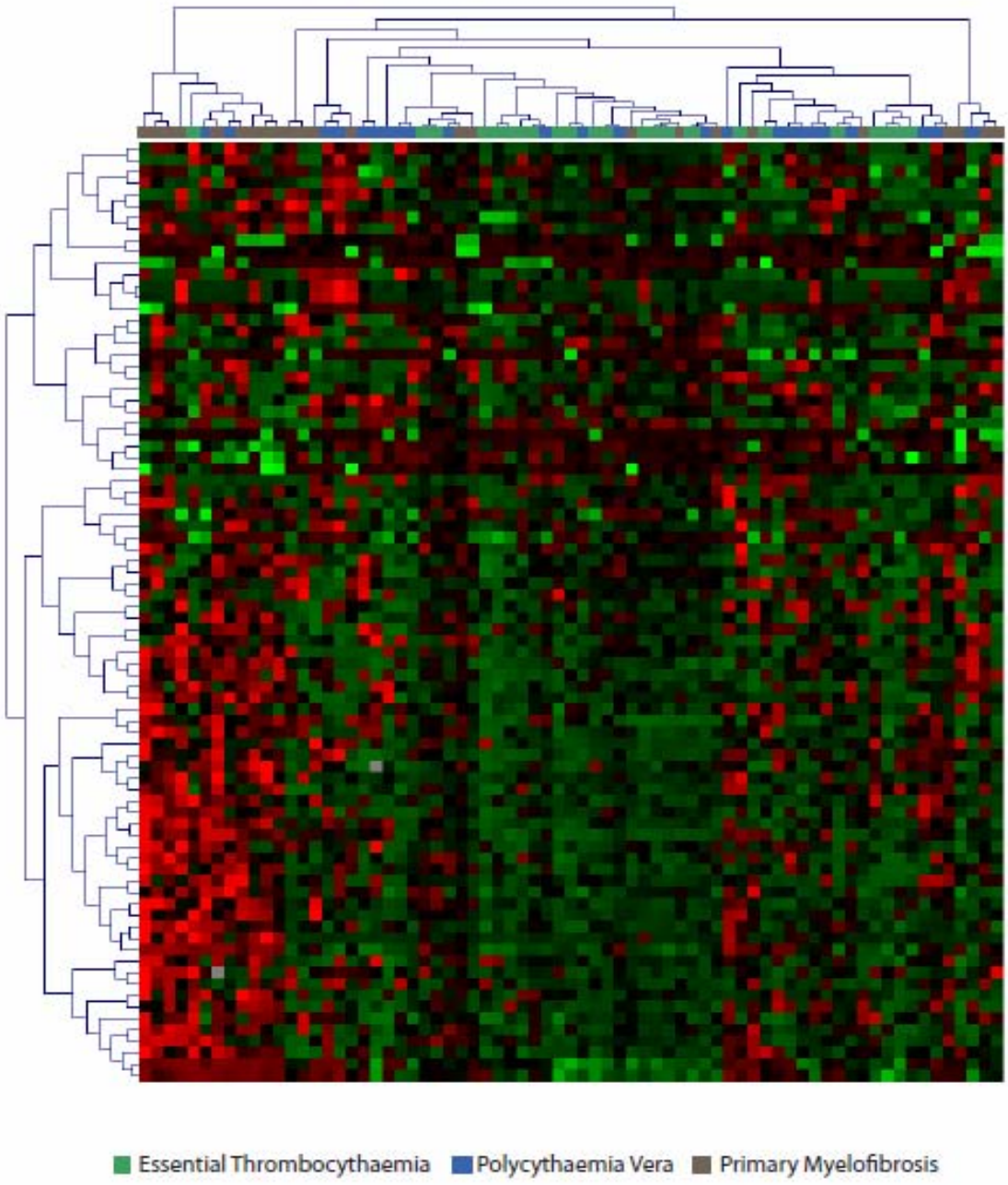


Supplementary Figure 2

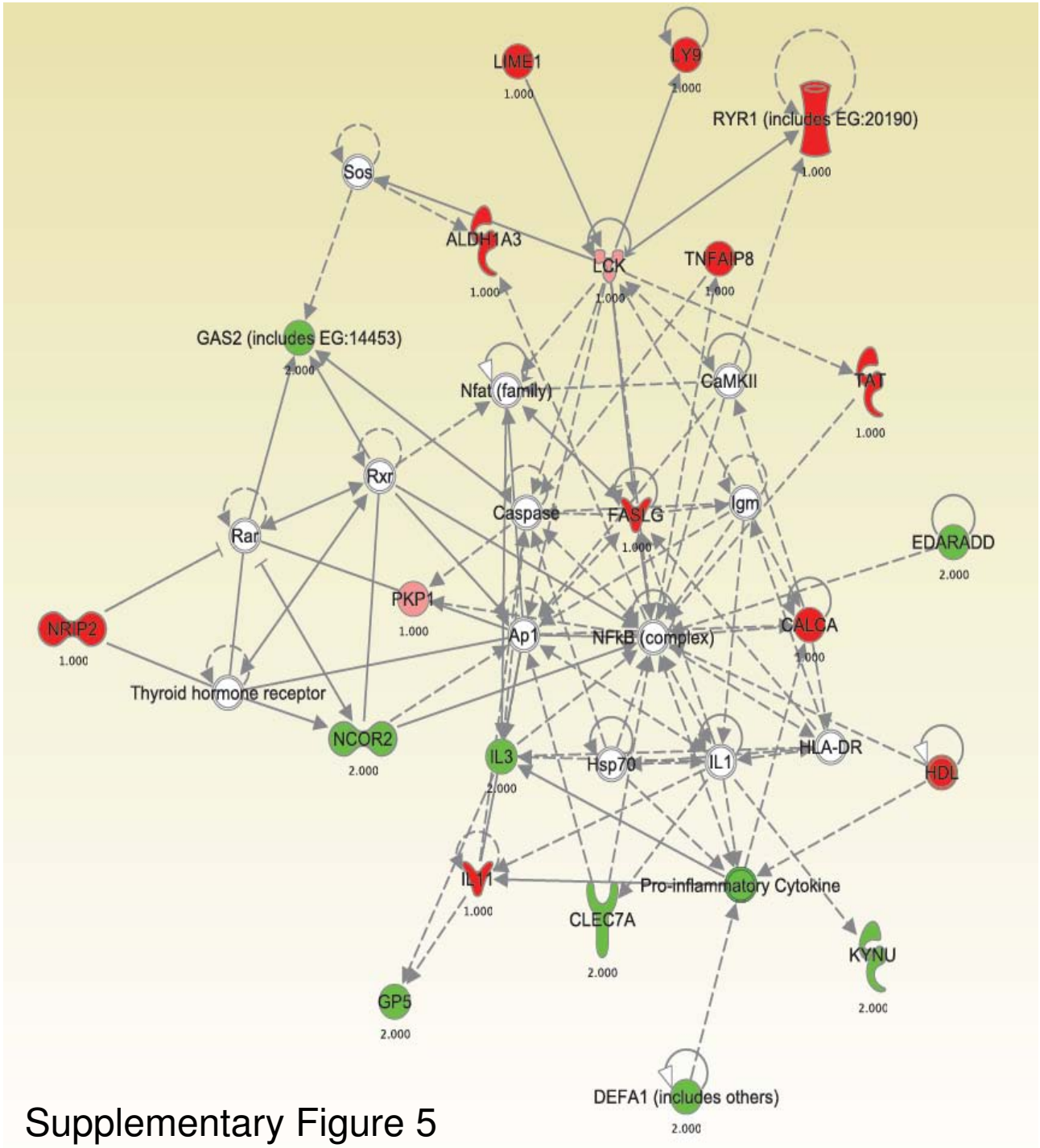


Supplementary Figure 3



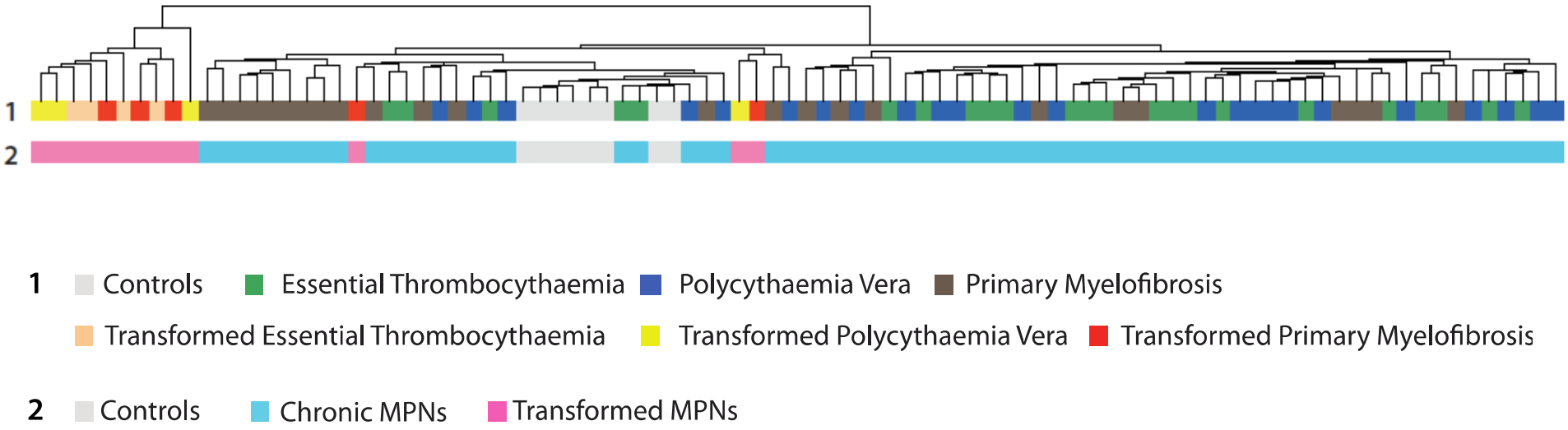


Supplementary Figure 4



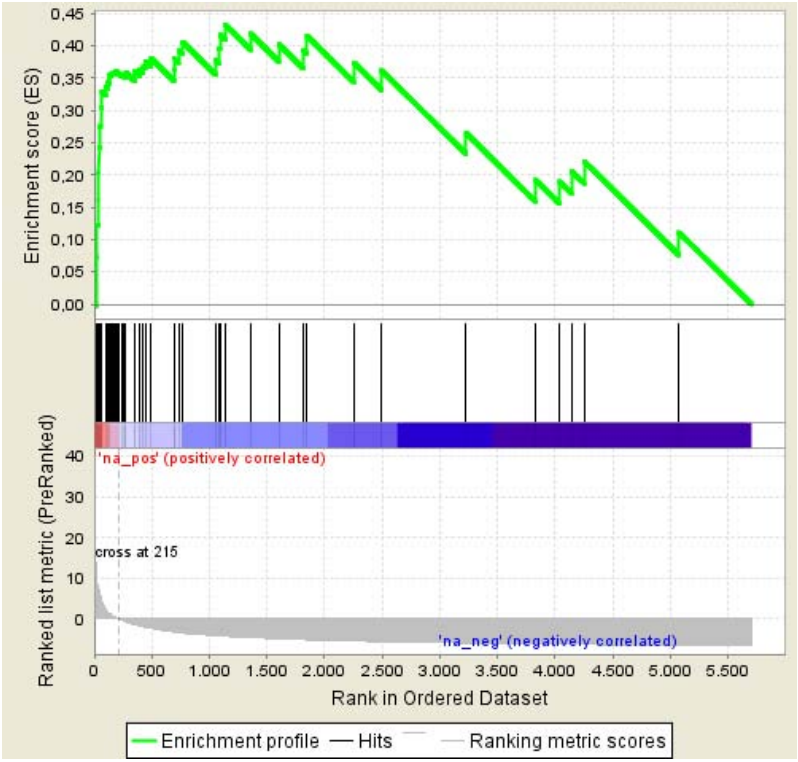
Supplementary Figure 5

Supplementary Figure 6



Supplementary Figure 7

A



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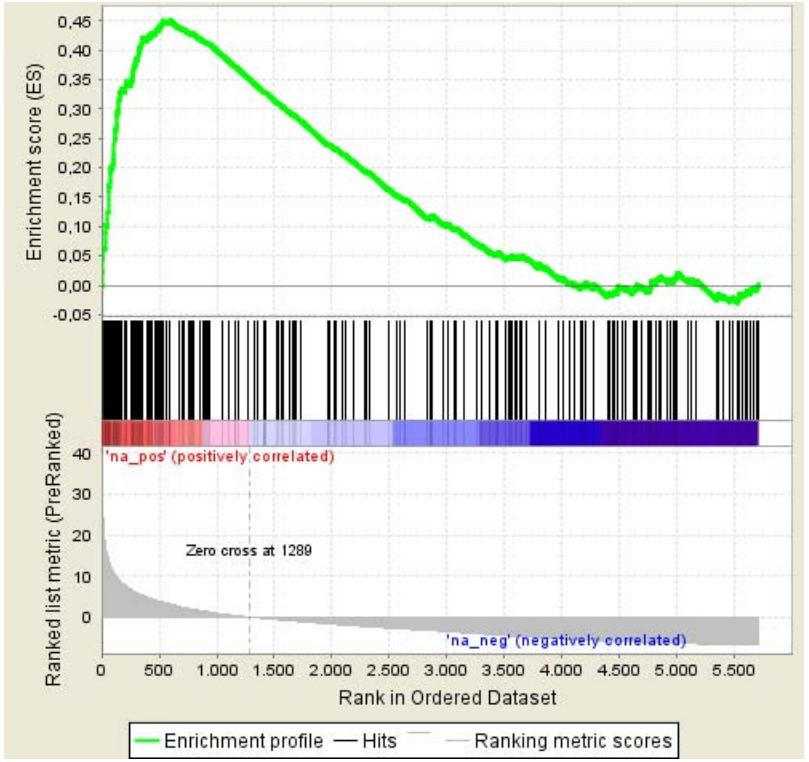
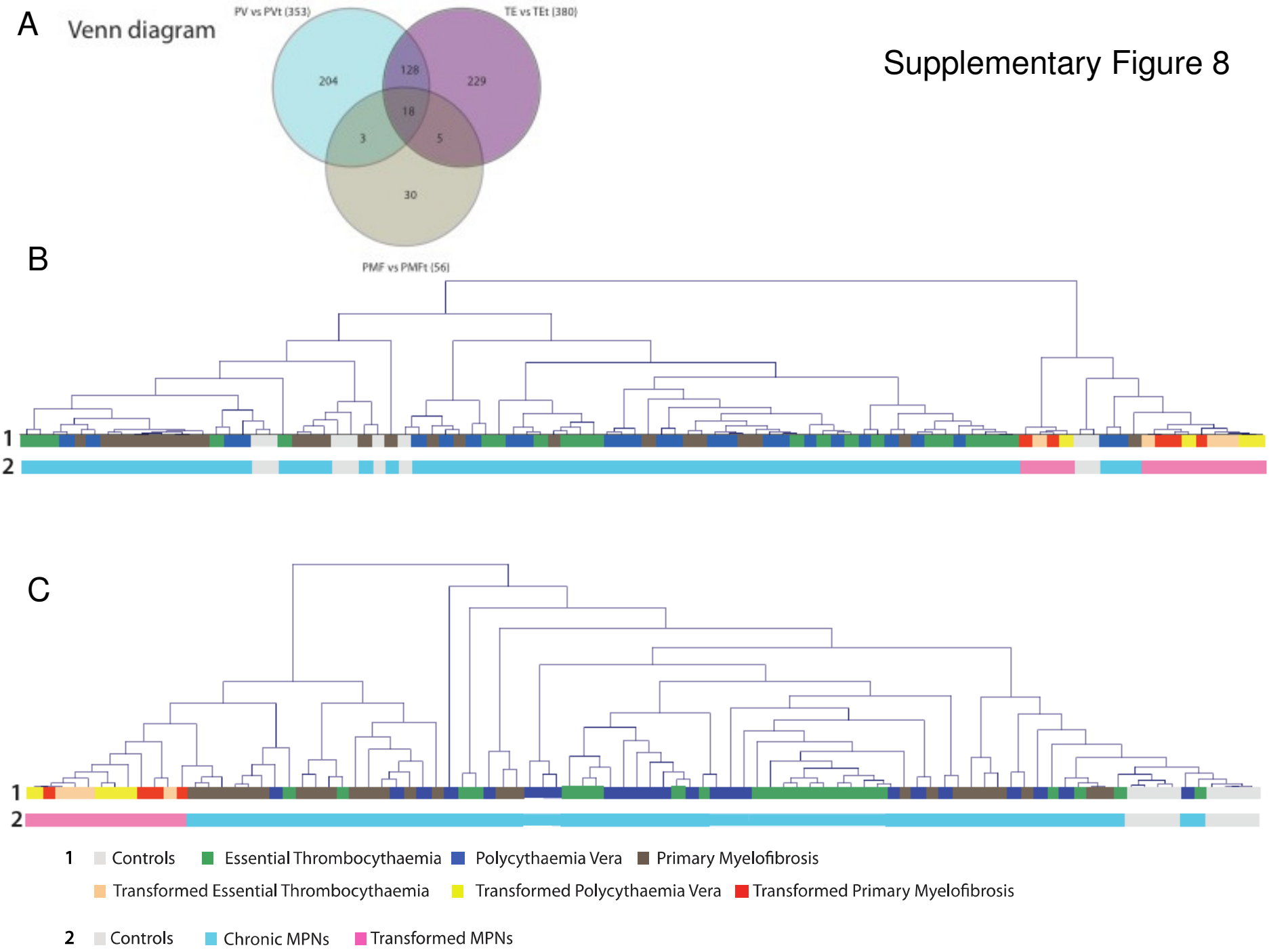
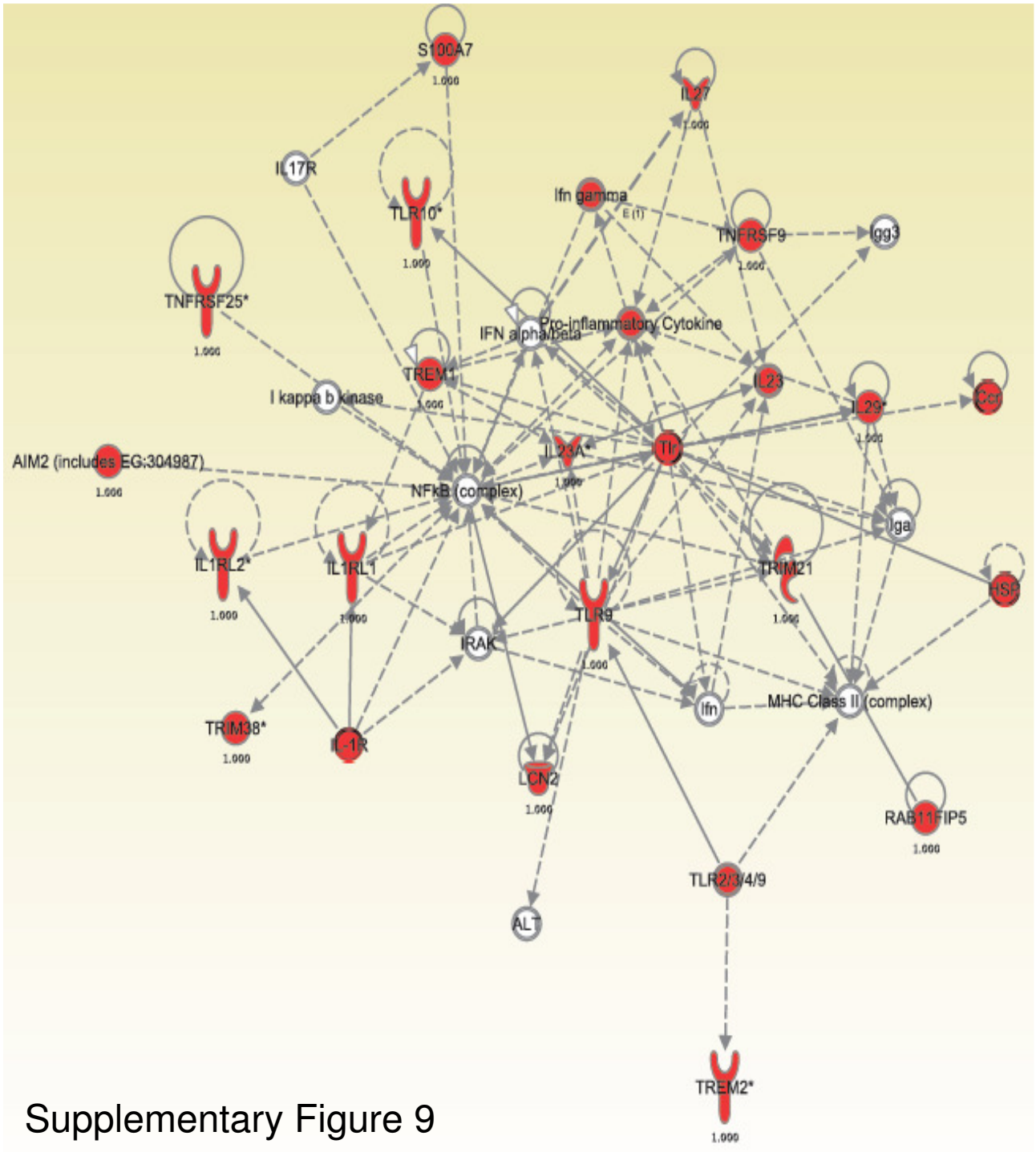


Supplementary Figure 8





Supplementary Figure 9