Table S1. Primer sequences

Figure S1. *VTRNA2-1* methylation and expression in hematopoetic cell lines
Most of the lymphoid cell lines (Granta, JEKO, RL, REC, JVM) carry a *VTRNA2-1* methylation level close to the normal cells, while the myeloid cell lines (NB4, F36P, HL60, KG1, KG1a, and U937) are either fully methylated or unmethylated (<10% methylation by pyrosequencing). Expression of vtRNA2-1 was only detected in the cell lines with a hypomethylated or intermediate methylated promoter.

Figure S2. miR886-3p or 5p/svRNAs are not detected in HL60 cells after treatment with demethylating drugs
Northern blot showing that treatment with demethylating drugs upregulate the vtRNA2-1, the mature miRs/svRNAa are not detected.

Figure S3. The level of vtRNA2-1 expression corresponds to the level of methylation in PBL MNC of healthy individuals
Individuals with hypomethylated *VTRNA 2-1* show significant higher expression of vtRNA2-1 than individuals with intermediate methylation levels.

Figure S4. Correlation between methylation and expression in 4 lenalidomide treated MDS/AML patients
Expression in $CD34^+$ cells from 4 lenalidomide treated patients. vtRNA2-1 is induced by lenalidomide in the 2 patients (case 23 and 28) with an intermediate methylated or hypomethylated promoter. By contrast, expression is not detected and not inducible by lenalidomide from the cases with a hypermethylated promoter. Reactions were done in technical duplicates. Methylation levels were determined in BM MNC by pyrosequencing.

Figure S5. Over-all survival of AML patients corresponds to *VTRNA2-1* methylation status
Patients are divided into 2 groups depending on *VTRNA2-1* methylation status (<10% methylation, >10% methylation). Patients with <10% methylation of *VTRNA2-1* have a significant better survival.

Figure S5. No significant difference in the level of *LINE1* methylation in AML patients with or without methylation of *VTRNA2-1* promoter
BM MNC from 16 AML cases with methylation of the *VTRNA2-1* promoter (>10 % by pyrosequencing) and 16 AML cases without *VTRNA2-1* methylation (<10%) were examined for *LINE1* methylation by pyrosequencing. There was no significant difference between the two groups (t-test, P=0.662).

Table S1

Sequence	Assay		Primer/probe sequence (5´-3´)	Annealing/ number of cycles
vtRNA2-1	Expression	F R P	5´-CGGAGTTAGCTCAAGCGGTTA-3´ 5´-TCTCGAACCCCAGCACAGA-3´ 5´-6FAM-CTCCTCATGCCGGACTTTCTATCTGTCCAT–TAMRA-3´	60°C /40
	Ms-MCA	F1 R1 F2 R2	5´-GTTTTTTTAGGATAGGTTAGT-3´ 5´-AAAAAACCAACTACATATACTCCC-3´ 5´-TTTTTTTATGGTTTGAAGTTTTAGT-3´ 5´-TTACATAAAAAAATCAATAAACACC-3´	56°C /45 60°C /45
	Pyrosequencing	F R S	5´-TTATTTTTTTATGGTTTAGAAGTTTT-3´ 5´-BioTin-TTACATAAAAAAATCAATAAACACC-3´ 5´-TTTTTTTATGGTTTGAAGTTTTAGT-3´	56°C /45
	DGGE	F R	5´-[40CG][5AT]AGTTTCAGTCGCACACTCCT-3´ 5´- CAGATTATACCGAATTTATTGCATA-3´	56°C /38
	Bisulfite sequencing	F R	5´-GGAAGGGGGTAAAATTTATTTATTG-3 5´-ACCACAAAACCCCTACCTTTAAC-3	58°C /45
	RACE	5´-outer 5´-inner 3-outer	5’-TTATTGCATAAAAGGGTCAGTAAGCACC -3’ 5’- TCGAACCCCAGCACAGAGATG -3’ 5’-GTCGGAGTTAGCTCAAGCGGT-3’	
	Northern	P	5’- AAG GGT CAG TAA GCA CCC GCG -3’	
miR886-3p	Expression		TaqMan® MicroRNA Assays, ID 002194	60°C /40
miR886-5p	Expression		TaqMan MicroRNA Assays, ID 002195	60°C /40
miR377	Northern	P	5’-ACA AAA GTT GCC TTT GTG TGA T-3’	
RNU6B	Expression		TaqMan MicroRNA Assays, ID 001093	60°C /40
RNU6B	Northen	P	5’-GCA GGG GCC ATG CTA ATC TTC TCT GTA TCG-3’	
GAPDH	Expression		TaqMan Gene Expression Assays, ID Hs02758991_g1	60°C /40
LINE-1	Pyrosequencing		Qiagen PyroMark Q24 CpG LINE-1, cat. no. 970012	50°C /45
CTNNA1	Ms-MCA	F R	5´-GATTGGAGGGAGATAAAGTAG-3´ 5´-CCcACCCAAAAACCCTCT-3´	62°C /45

Figure S1

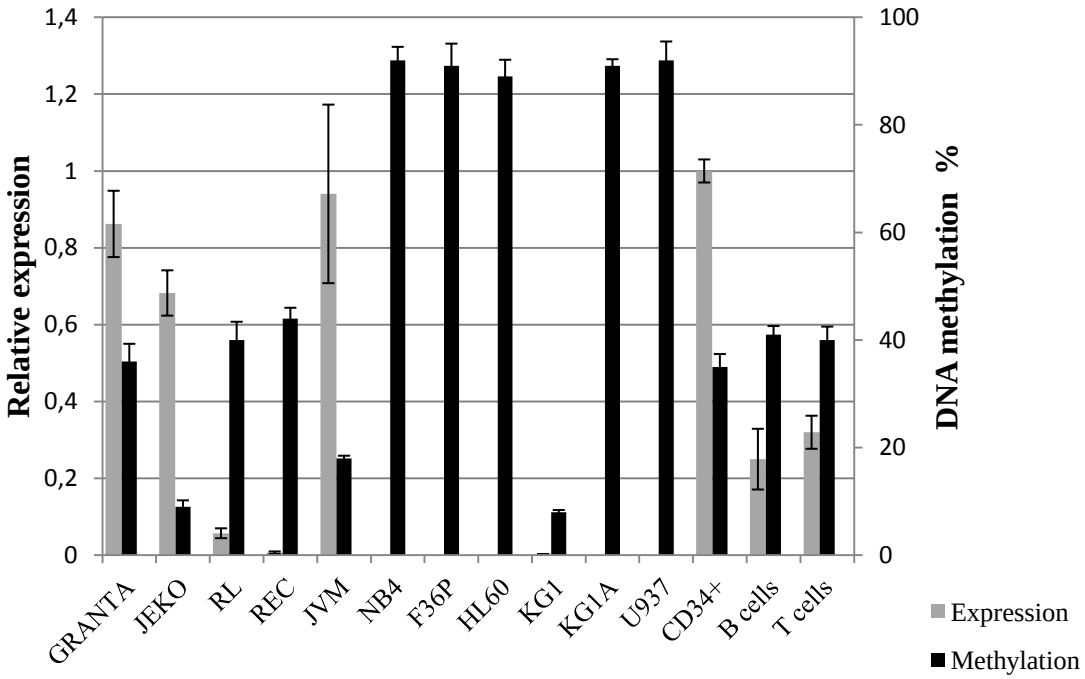

Relative expression
DNA methylation %
1,4
1,2
1
0,8
0,6
0,4
0,2
0
100
80
60
40
20
0
GRANTA
JEKO
RL
REC
JVM
NB4
F36P
HL60
KG1
KG1A
U937
CD34+
B cells
T cells
Expression
Methylation

Figure S2

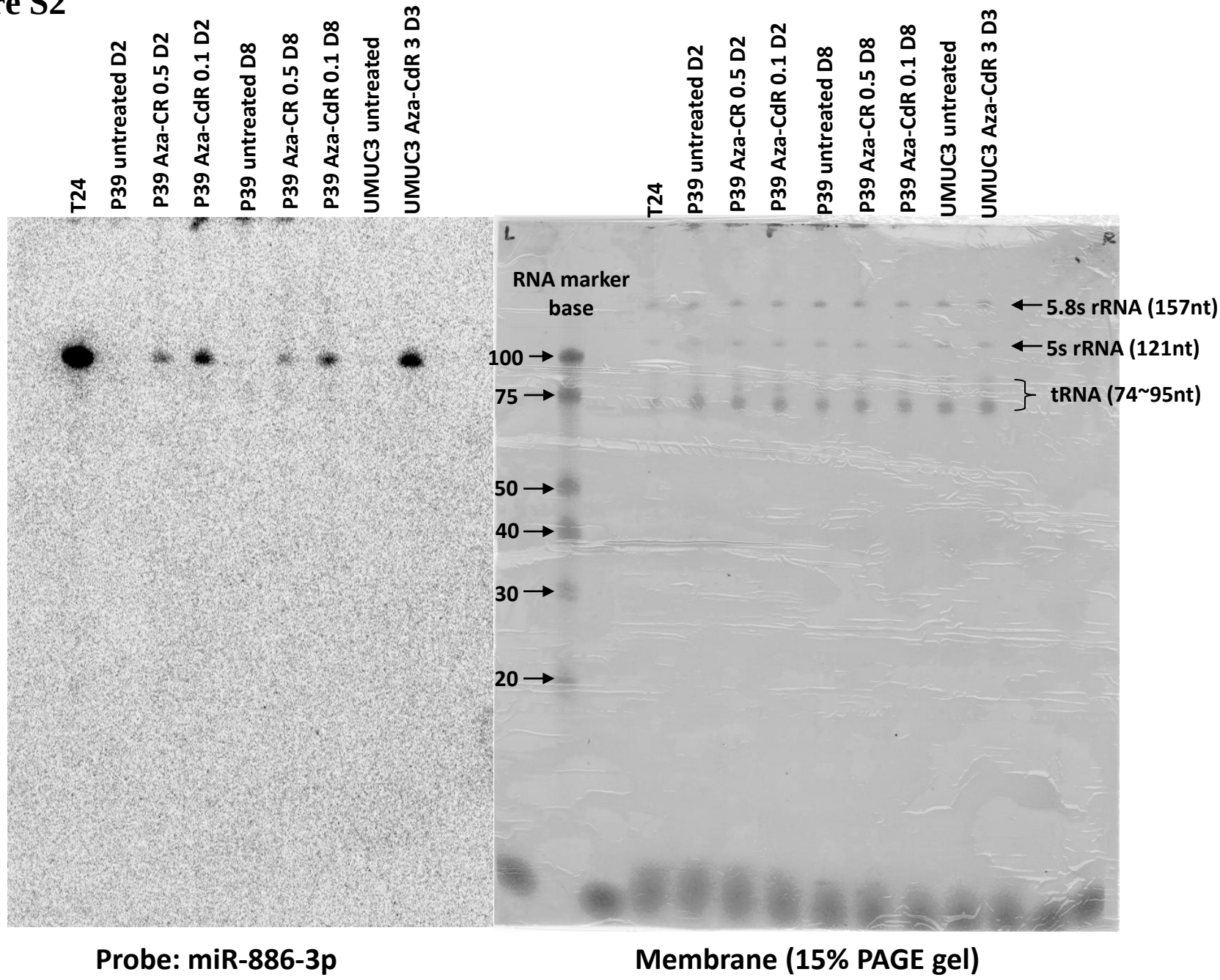

T24
P39 untreated D2
P39 Aza-CR 0.5 D2
P39 Aza-CdR 0.1 D2
P39 untreated D8
P39 Aza-CR 0.5 D8
P39 Aza-CdR 0.1 D8
UMUC3 untreated
UMUC3 Aza-CdR 3 D3
RNA marker base
100
75
50
40
30
20
5.8s rRNA (157nt)
5s rRNA (121nt)
tRNA (74~95nt)
Probe: miR-886-3p
Membrane (15% PAGE gel)

Figure S3

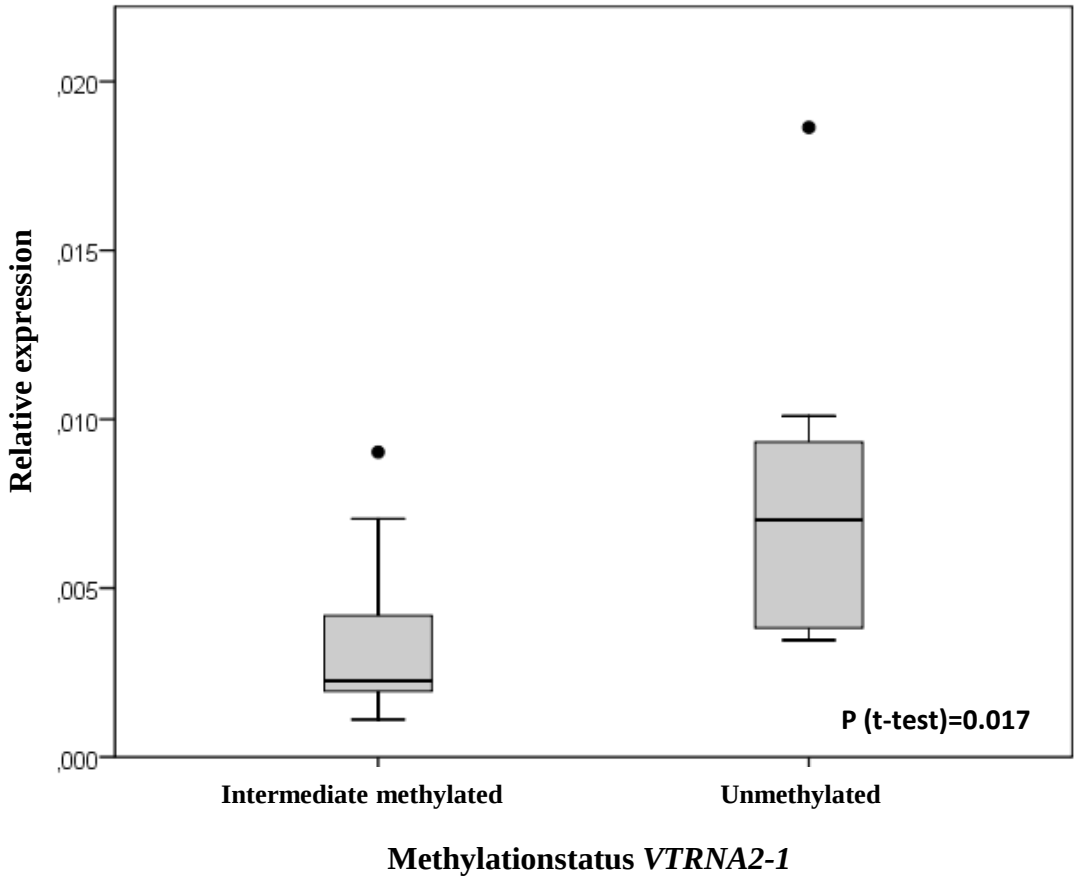

Relative expression
,020
,015
,010
,005
,000
P (t-test)=0.017
Intermediate methylated
Unmethylated
Methylationstatus *VTRNA2-1*

Figure S4

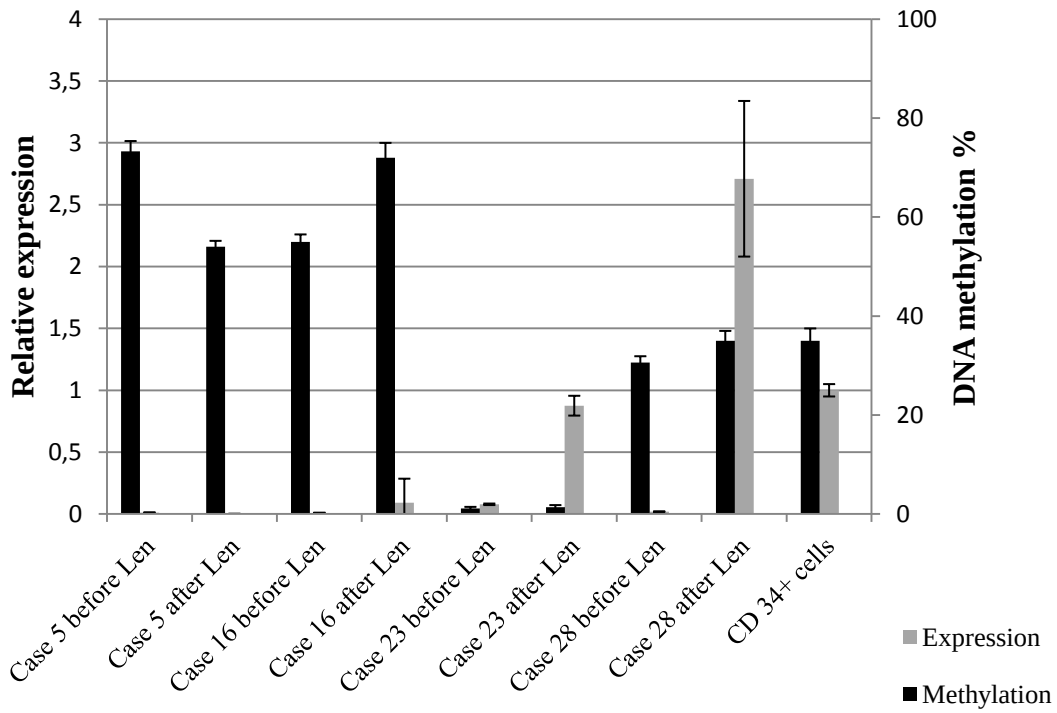

Relative expression
DNA methylation %
4
3,5
3
2,5
2
1,5
1
0,5
0
100
80
60
40
20
0
Case 5 before Len
Case 5 after Len
Case 16 before Len
Case 16 after Len
Case 23 before Len
Case 23 after Len
Case 28 before Len
Case 28 after Len
CD 34+ cells
Expression
Methylation

Figure S5

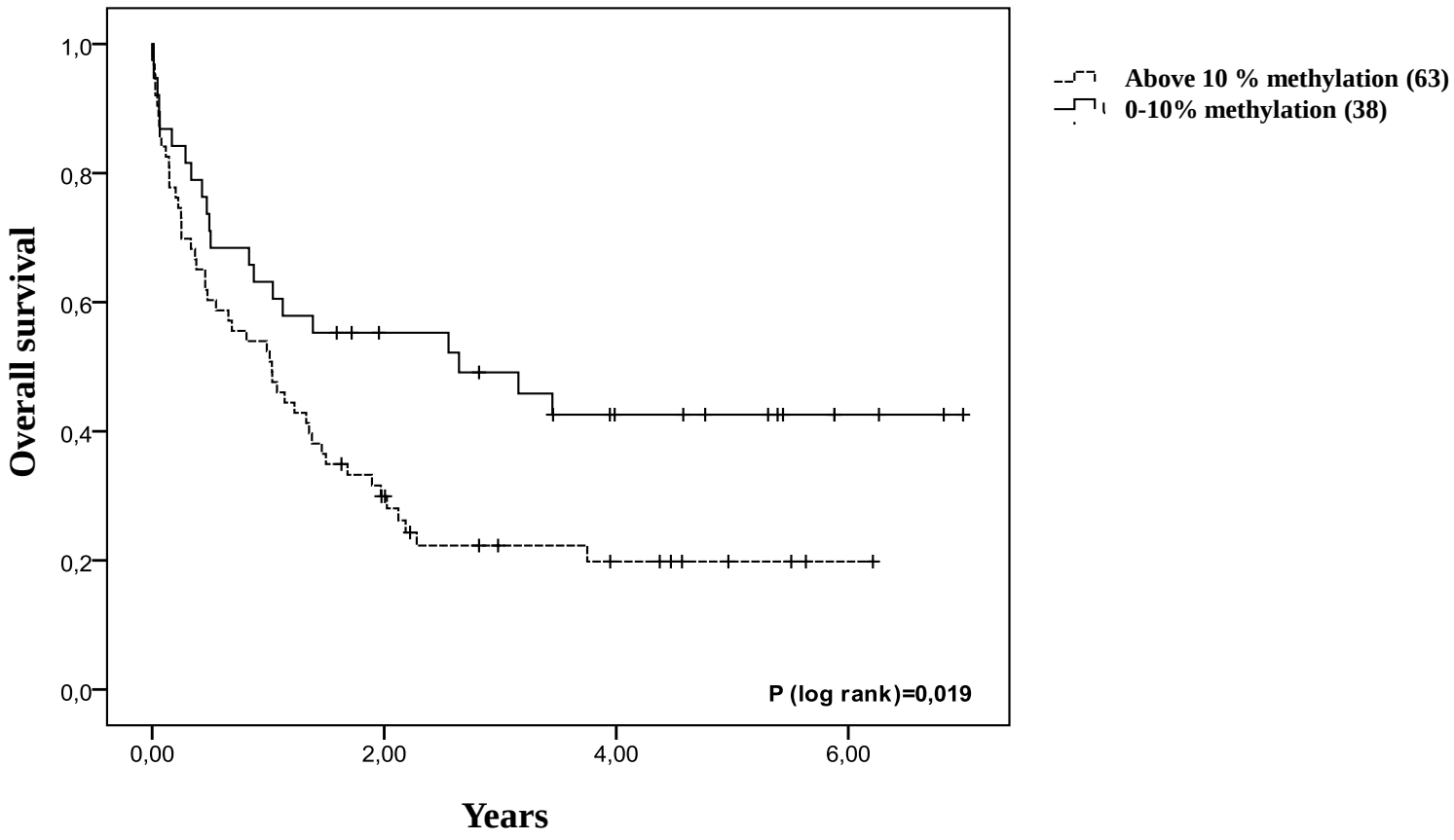
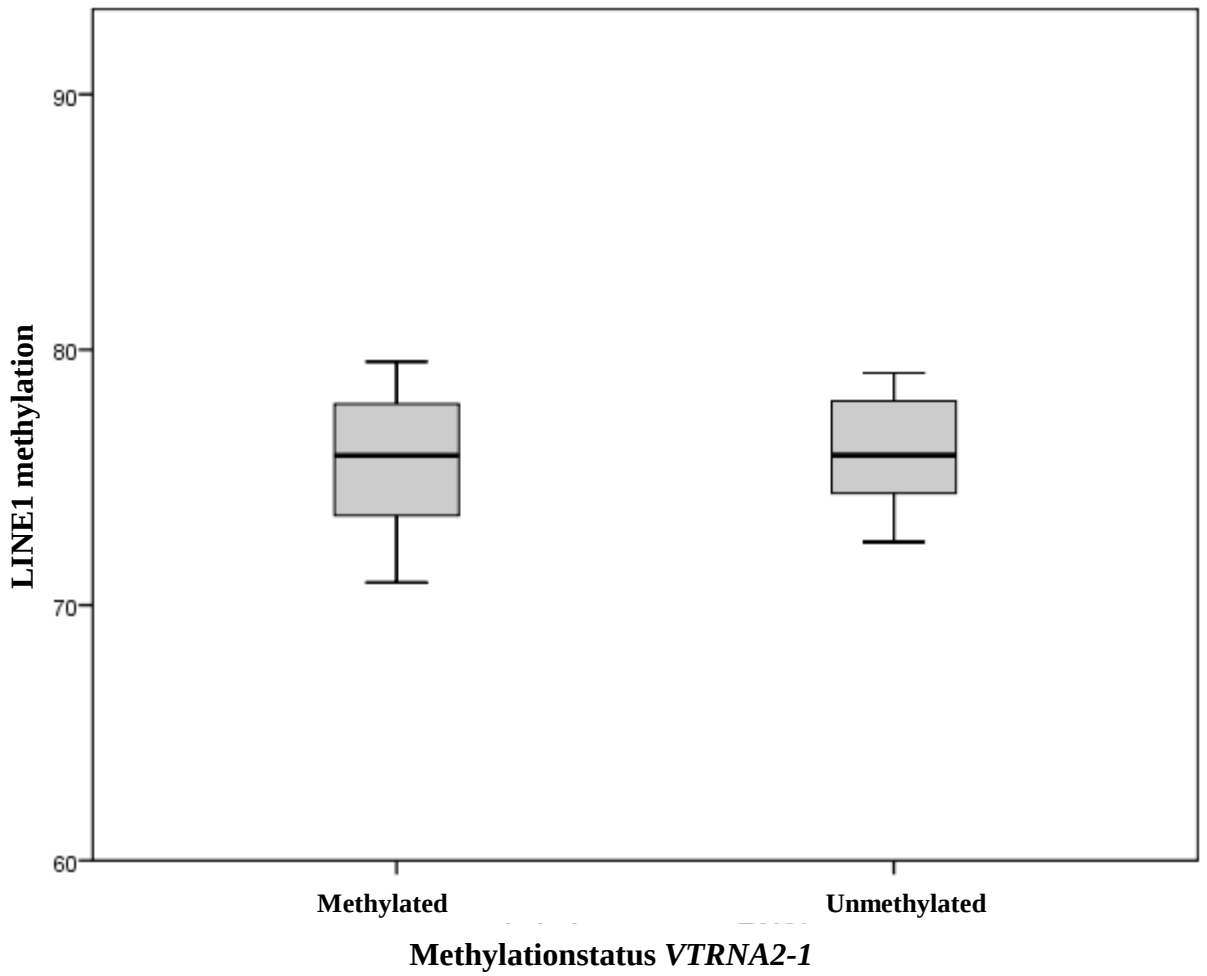

Overall survival
1,0
0,8
0,6
0,4
0,2
0,0
0,00
2,00
4,00
6,00
Years
P (log rank)=0,019
Above 10 % methylation (63)
0-10% methylation (38)

Figure S6


LINE1 methylation
90
80
70
60
Methylated
Unmethylated
Methylationstatus *VTRNA2-1*