Supplementary Methods

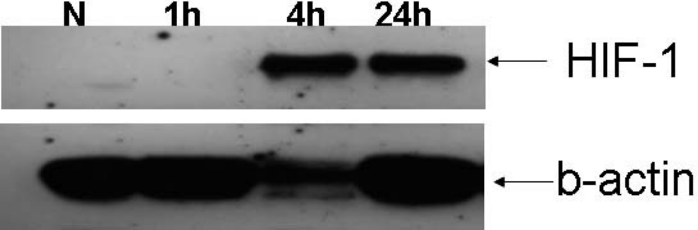
Cell-line and culture: The U87MG cells were maintained in DMEM (Dulbecco's Modified Eagle's Medium) supplemented with 10% (v/v) FCS (Fetal Calf Serum), 3.7g/l sodium bicarbonate and Ciprofloxacin 10µg/ml at 37° C, while SaOS2 cells were cultured in McCoy's 5A medium with similar supplementations. The cells were cultured in 75cm^2 and 25cm^2 angled neck tissue culture flasks with vented caps.

DNA methylation analysis by PCR sequencing: The software 'Bioedit' (http://www.mbio.ncsu.edu/ BioEdit/bioedit.html) was used for analyzing the change in methylation status of the CpG islands by comparing height of peaks of T (indicating unmethylated cytosine) and the peaks of C (indicating methylated cytosine) at a CpG island. The ratio of the heights for T and C at the original C in CpG gives the ratio of unmethylated to methylated C in that position in bisulphite treated DNA. Sequence chromatogram from 6 week hypoxia (H), 6 week normoxia (N) and 6 week hypoxia reverted to 4 week normoxia (HR) were compared.

Global Methylation: PCR products amplified from bisulfite treated DNA and LINE-COBRA primers were digested with restriction enzyme TaqI which recognizes TCGA and were subsequently separated by electrophoresis on a 2% agarose gels. Methylated C is protected from bisulfite treatment and is not converted to T and recognized by *Taq1*. The Integrated density values (IDV) ratio of the digested fragment (80 bp) derived from methylated DNA divided by the sum of the digested fragment and undigested fragment (160 bp) derived from unmethylated DNA represents the fractional methylation (expressed as a percentage) at the LINE *TaqI* site.

PAGE elution, cloning and sequencing: The excised PAGE bands were finely crushed and soaked in twice the volume of elution buffer containing 0.5M Ammonium Acetate,10mM Magnesium Acetate and 1mM EDTA (pH8.0) and incubated at 37°C with frequent shaking. DNA was precipitated with ice-cold Ethanol and dissolved in Tris-EDTA (pH 8.0) and 25µl of 3M Sodium Acetate (pH5.2) was added. The mixture was precipitated again with Ethanol. The pellet was finally dissolved in 10µl of water. After cloning and transformation, all colonies were screened by restriction digestion and the size checked by running on a 6-8% native PAGE.

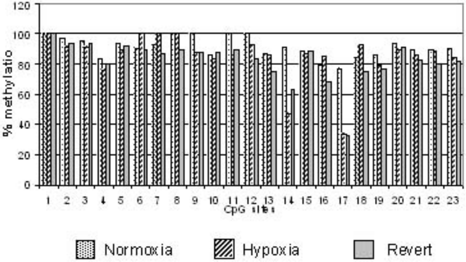
Supplementary Figure 1



Supplementary Figure 2

U87MG site specific CpG methylation at SINE locus on chromosome 16

CpG Site	N	H	R
1	100	100	100
2	97.07	92.14	94.16
3	95.31	92.02	93.54
4	84.34	76.43	80.1
5	93.83	89.98	92.18
6	91.02	100	90.06
7	93.33	100	87.19
8	100	100	89.73
9	100	87.98	88.24
10	86.21	84.05	87.88
11	100	86.23	90
12	100	92.59	84.18
13	87.5	86.79	75.61
14	91.67	47.88	62.82
15	88.89	87.02	88.84
16	78.95	85.71	69.11
17	77.14	34.24	33.33
18	85.11	92.97	75.61
19	86.21	79.45	77.12
20	93.94	90.16	91.55
21	90.17	86.86	83.92
22	90	89.05	80.29
23	90.99	84.84	81.69



▒ Major subgroup showing hypomethylation in H wrt N

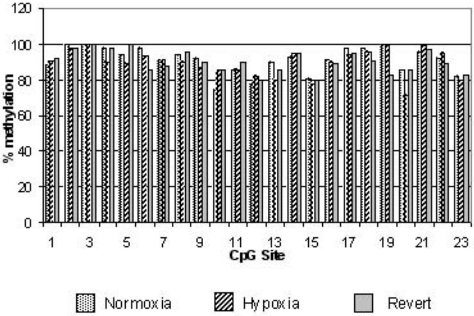
☐ Minor subgroup: sites showing hypermethylation in H wrt N

░ Minor subgroup: sites which are unchanged in H wrt N

Supplementary Figure 3

SaOS2 site specific CpG methylation at SINE locus on chromosome 16

CpG site	N	H	R
1	87.94	90.14	91.48
2	100	98.15	98.05
3	100	100	99.81
4	98.5	89.69	97.28
5	93.58	89.55	100
6	98.08	92.98	85.74
7	91	91.19	87.36
8	93.81	89.96	95.48
9	91.94	87.04	90.07
10	74.29	85.67	85.58
11	85.79	85.91	90.03
12	77.34	82.31	79.08
13	89.64	80.06	86.08
14	92.55	94.1	94.19
15	80.5	77.57	79.44
16	90.78	90.03	88.97
17	96.94	93.74	94.92
18	97.38	95.35	90.45
19	100	100	83.16
20	85.71	71.28	85.95
21	95.3	99.27	96.72
22	91.92	94.62	88.48
23	82.22	78.98	82.61



■ Major subgroup showing hypomethylation in H wrt N

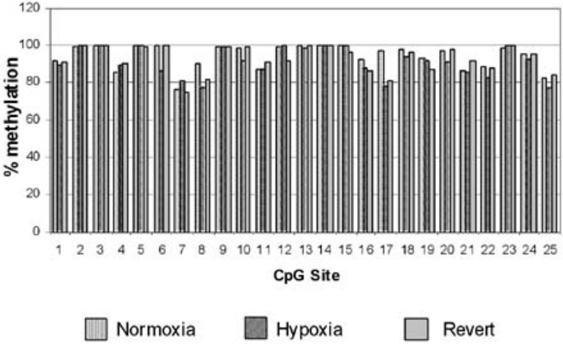
□ Minor subgroup: sites showing hypermethylation in H wrt N

░ Minor subgroup: sites which are unchanged in H wrt N

Supplementary Figure 4

U87MG site specific CpG methylation at SINE locus on chromosome 7

CpG Sites	N	H	R
1	91.98	89.63	91.32
2	99.35	100	100
3	100	99.79	99.81
4	85.7	89.14	90.22
5	99.79	99.88	98.84
6	99.46	86.27	100
7	76.46	80.96	74.9
8	89.77	77.92	82.44
9	99.35	99.06	99.07
10	98.55	92.26	98.81
11	87.39	87.7	90.89
12	99.26	100	91.75
13	100	98.58	99.75
14	100	100	99.65
15	100	100	96.32
16	92.56	88.25	87.01
17	97.18	77.95	80.81
18	97.54	93.87	96.35
19	93.18	92.19	87.63
20	96.88	91.07	97.59
21	86.95	85.71	91.94
22	89	82.87	88.28
23	98.36	99.79	99.77
24	95.52	92.78	95.79
25	82.95	77.05	84.26



▨ Major subgroup showing hypomethylation in H wrt N

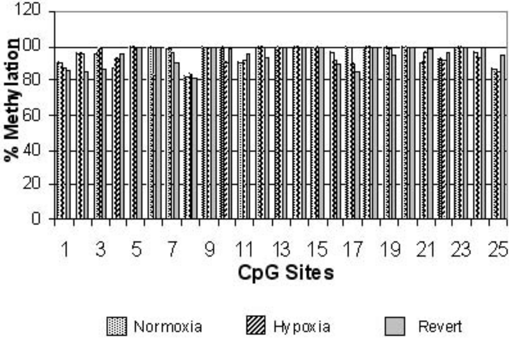
□ Minor subgroup: sites showing hypermethylation in H wrt N

░ Minor subgroup: sites which are unchanged in H wrt N

Supplementary Figure 5

SaOS2 site specific CpG methylation at SINE locus on chromosome 7

CpG sites	N	H	R
1	90.87	87.96	85.82
2	94.76	95.51	84.76
3	95.26	98.28	86.89
4	87.93	92.74	95.2
5	100	99.88	100
6	100	83.03	100
7	97.91	96.16	90.16
8	82.29	84.37	81.57
9	99.49	99.35	99.33
10	99.63	90.77	98.19
11	90.29	91.12	95.53
12	99.78	99.69	92.89
13	100	100	100
14	100	100	100
15	100	100	99.3
16	96.03	91.81	89.81
17	99.86	89.94	85.32
18	99.92	99.32	99.8
19	99.49	98.71	94.03
20	100	99.86	100
21	90.21	95.81	99.23
22	92.41	91.45	95.85
23	100	99.34	100
24	96.41	92.87	99.83
25	86.94	85.29	93.96



■ Major subgroup showing hypomethylation in H wrt N

□ Minor subgroup: sites showing hypermethylation in H wrt N

▒ Minor subgroup: sites which are unchanged in H wrt N