Figure S1

Mimosine treatment synchronizes MEFs by G1-S arrest

MEFs were infected with different retroviruses encoding *Flag+sh-Luc* (Control), *Flag+sh-p53*, *sh-p53+Dnmt1*, or *sh-p53+sh-Dnmt1* on Hour -48. Two days after the infection (Hour 0), 0.5 μM mimosine was used to treat cells for addition 24 hours.

(A) Cell cycle stages of MEFs infected with retroviruses encoding *Flag+sh-Luc* (Control) were determined at different time points by FACS .

(B) Cell cycle stages of the four groups of infected cells were also determined after mimosine treatment (Hour 24).

Figure S1

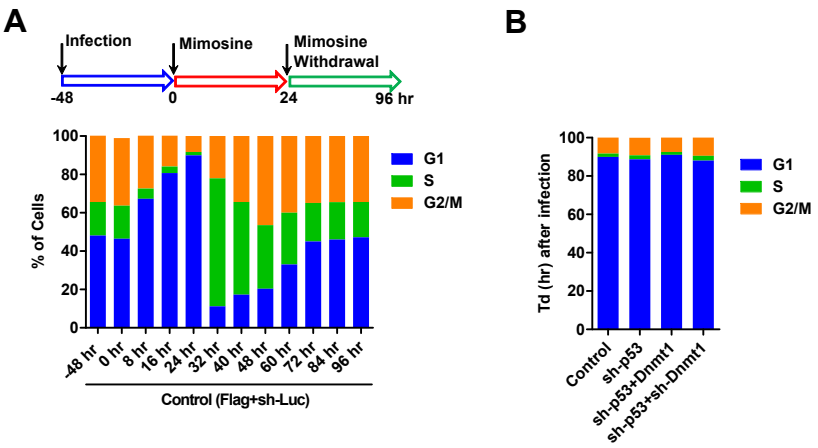
A
Infection
Mimosine
Mimosine Withdrawal
-48
0
24
96 hr
100
80
60
40
20
0
% of Cells
G1
S
G2/M
-48 hr
0 hr
8 hr
16 hr
24 hr
32 hr
40 hr
48 hr
60 hr
72 hr
84 hr
96 hr
Control (Flag+sh-Luc)
B
Td (hr) after infection
Control
sh-p53
sh-p53+Dnmt1
sh-p53+sh-Dnmt1

Figure S2

WGBS has no preferences to specific regions in genome

WGBS was performed in MEFs in G1 and G2/M phases.

The distribution and cumulative distribution of cytosines sequenced by WGBS as a function of sequencing depth are summarized in (A-B). The percentages of different forms of methylated cytosine are summarized in (C-D). The coverage and average methylation levels of different genomic elements are shown in (E-H).

Figure S2

WGBS Information

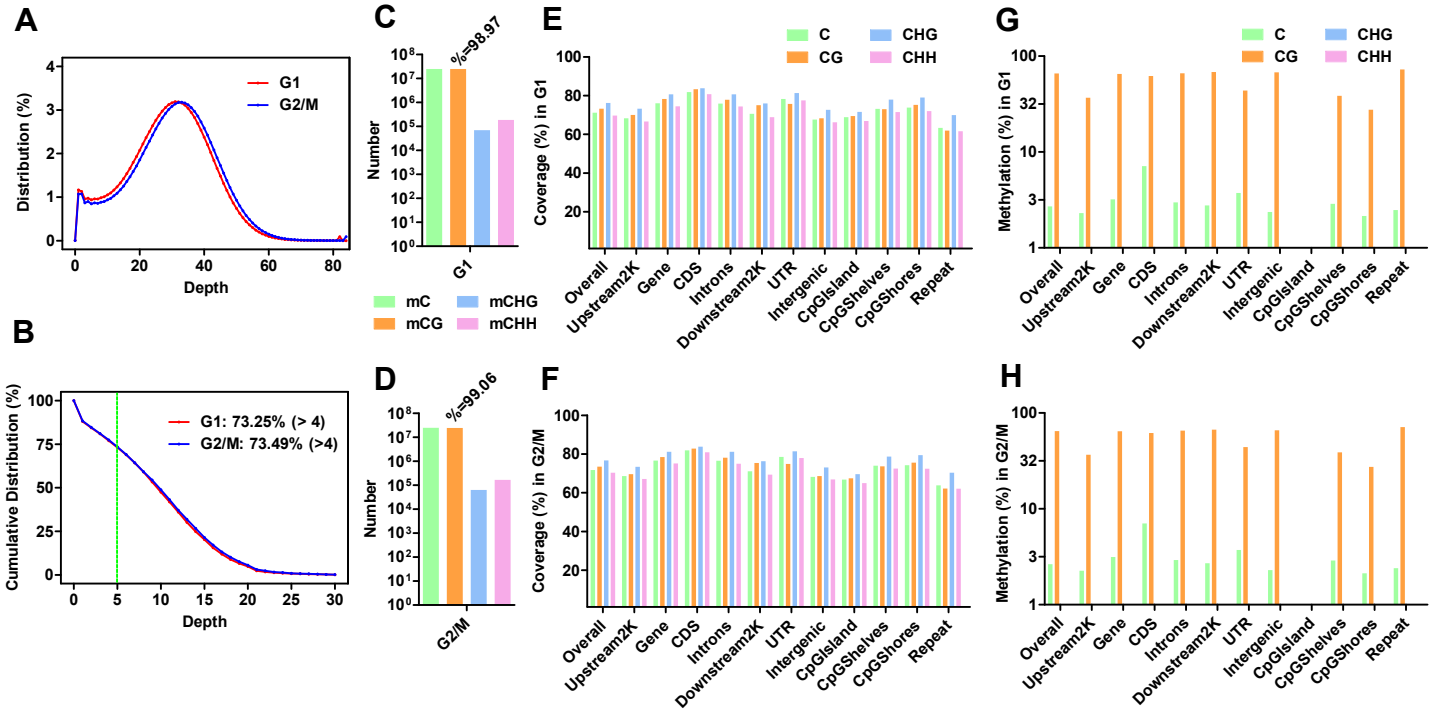

Figure S3

WGBS provides methylation information at various levels of resolution

(A-B) Distribution and methylation levels of surrounding CpGs as a function of the average distance (Dis(2)).

(C-E) The distributions of three groups of CpGs, all CpGs in the genome, CpGs within -1.5 kb to +2.0 kb around TSS, CpGs within -1.0 kb to +1.0 kb around TSS, were analyed as a function of methylation and of average distance (Dis(2)) (C-D). The Ave(2) of these three groups of CpGs as a function of core methylation is shown in (E).

(F-G) Distribution of genes as a function of pG1 methylation and CpG density of three different regions around the TSS, -10 kb to -1.5 kb (Up-8.5kb), -1.5 kb to +2.0 kb (Mid-3.5kb), +2.0 kb to +10 kb (Down-8kb).

(H) Retrovirus was used to introduce *Flag+sh-Luc* (Control), *Dnmt1*, *sh-Dnmt1*, and *sh-Dnmt1+sh-p53* into MEFs and into MEFs during OKMS-induced reprogramming without Vc (Vc-) or with Vc (Vc+). Global DNA methylation were determined 5 days after infection by RRBS. The methylation levels of protein-coding genes in G1 MEFs (WGBS) and in three control groups in RRBS were compared.

Figure S3

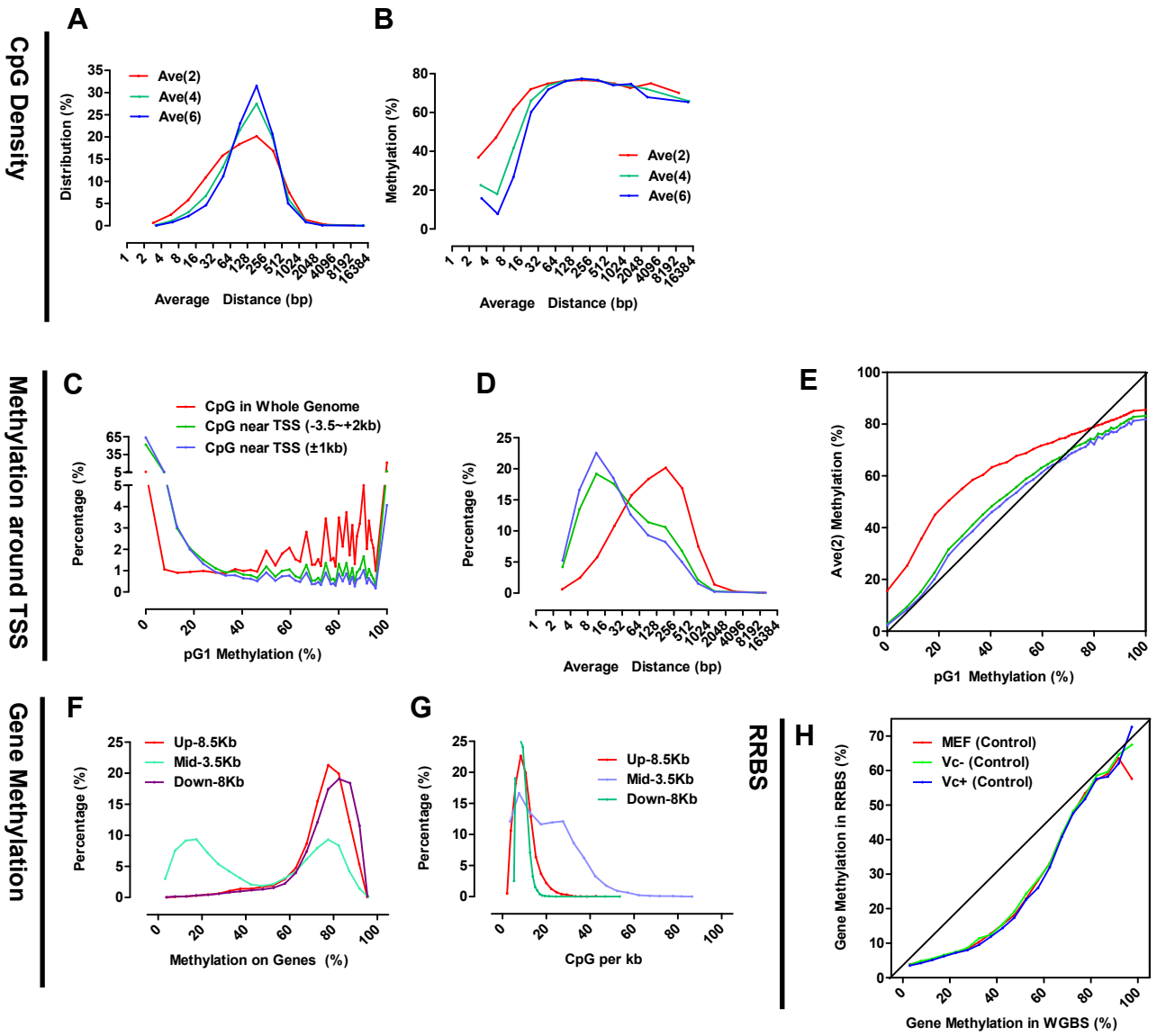
CpG Density
A
Ave(2)
Ave(4)
Ave(6)
Distribution (%)
Average Distance (bp)
B
Methylation (%)
Ave(2)
Ave(4)
Ave(6)
Average Distance (bp)
Methylation around TSS
C
CpG in Whole Genome
CpG near TSS (-3.5~+2kb)
CpG near TSS (±1kb)
Percentage (%)
pG1 Methylation (%)
D
Percentage (%)
Average Distance (bp)
E
Ave(2) Methylation (%)
pG1 Methylation (%)
Gene Methylation
F
Up-8.5Kb
Mid-3.5Kb
Down-8Kb
Percentage (%)
Methylation on Genes (%)
G
Up-8.5Kb
Mid-3.5Kb
Down-8Kb
Percentage (%)
CpG per kb
RRBS
H
MEF (Control)
Vc- (Control)
Vc+ (Control)
Gene Methylation in RRBS (%)
Gene Methylation in WGBS (%)

Table S1

qPCR results for epigenetic factors during cell cycle regulation

Regulating the expression of *p53*, *p21*, *Ccne1*, *Ccnd1* and *Cdk4* successfully modulated the proliferation rate, especially the length of the G1 phase (Figure 1A). The expression levels of 102 genes related to DNA methylation, histone methylation or other epigenetic modifications were determined by qPCR 4 days after infection. Doubling time (Td) was calculated by dividing the 96-hour $\log_2$ increase in cell number over a 4-day period. The correlation between cell proliferation (24/Td) and expression (normalized to the Control group) was calculated for each gene using a linear regression model in GraphPad Prism 5.0. The experiments were repeated at least 5 times. qPCR primers used for other genes studied in current manuscript were also listed.

Table S2

Materials used in current manuscript

As title

Table S3

Gene expression in MEFs as determined by WGBS, RRBS, and RNA-seq

Based on greater than 50% coverage of their TSS regions (-1.5 to +2.0 kb) by current qualified CpGs in WGBS, 11,783 protein-coding genes were selected. The expression levels of these genes in MEFs were obtained from GSE61694 and GSE68902 and are shown in the column labeled MEF1. The expression levels of these genes in MEFs, ESCs and iPSCs were obtained from GSE10871 and GSE14012 and are shown in the columns labeled MEF2, ESC/iPSC, and PSC vs MEF. RNA-seq and RRBS results are also provided. Gene expression under the

current detection limit of RNA-seq was considered as 1. Gene methylation not detected in RRBS is denoted by “na”.

Table S4

Statistics information for each figure and panel

As title