Table S1. Sequence of primers used in RT-qPCR

Primer Name	Primer Sequence
P16Ink4a-F	G A AC T C T T T C G G T C G T A C C C
P16Ink4a-R	C G A A T C T G C A C C G T A G T T G A
P15Ink4b-F	C C A C C C T T A C C A G A C C T G T G
P15Ink4b-R	A G G C G T C A C A C A C A T C C A G
P19Arf-F	G C T C T G G C T T T C G T G A A C A T
P19Arf-R	G C A G A A G A G C T G C T A C G T G A
P53-F	T G G A A G A C T C C A G T G G G A A
P53-R	T C T T C T G T A C G G C G G T C T C T
P21cip1-F	T T G C A C T C T G G T G T C T G A G C
P21cip1-R	T G C G C T T G G A G T G A T A G A A A
P27kip1-F	A A C T A A C C C G G G A C T T G G A G
P27kip1-R	C C A G G G G C T T A T G A T T C T G A
P18Ink4c-F	T G G A A C T G G T T T T G C T G T C A
P18Ink4c-R	G G G C A G G T T C C C T T C A T T A T
P19Ink4d-F	G C A G G T C A T G A T G T T T G G A A
P19Ink4d-R	T A G T A C C G G A G G C A T C T T G G
P57Kip2-F	G G A G C A G G A C G A G A A T C A A G
P57kip2-R	G A A G A A G T C G T T C G C A T T G G
Kdm2b-F	T A A A G G A T G C C C A G A T G A G G
Kdm2b-R	A G G C G C A G C T C T A C A A T G T T
GAPDH-F	G C A G T G G C A A A G T G G A G A T T
GAPDH-R	G A A T T T G C C G T G A G T G G A G T

Table S2. Sequence of primers used in p15^{Ink4b} ChIP assay

Primer Name	Primer Sequence
Ink4bAmp1-F	C C G C C T A G A G A T G A A C T A G C C
Ink4bAmp1-R	C G C T T T T G C A A T T G A C T G A C
Ink4bAmp2-F	C A C C G A A G C T A C T G G G T C T C
Ink4bAmp2-R	C T G T G G C A G A A A T G G T C C T T
Ink4bAmp3-F	A T G T T C T A A G A G G C T T T G T T T C C A
Ink4bAmp3-R	C A T T T G T G C A T A G G A G A T C A G G

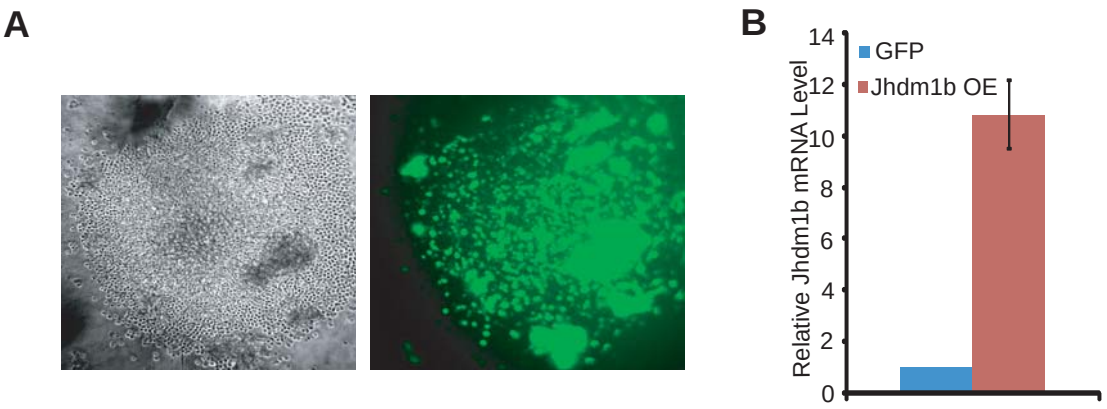

Figure S1. Over-expression of Kdm2b/Jhdm1b in hematopoietic progenitors

(A) Efficient transduction of hematopoietic progenitor cells by lentiviral vectors.Shown are the photographs of bright (left panel) and GFP flurorescent (right panel) fields of hematopoietic progenitor cells at 48 hours after lenti-GFP transduction.

(B) Kdm2b/Jhdm1b-transduced hematopoietic progenitor cells express much higher levels of Kdm2b/Jhdm1b compared to GFP control. Relative mRNA levels are measured by RT-qPCR and normalized to the Gapdh. The mRNA level of GFP control cells is set as 1.

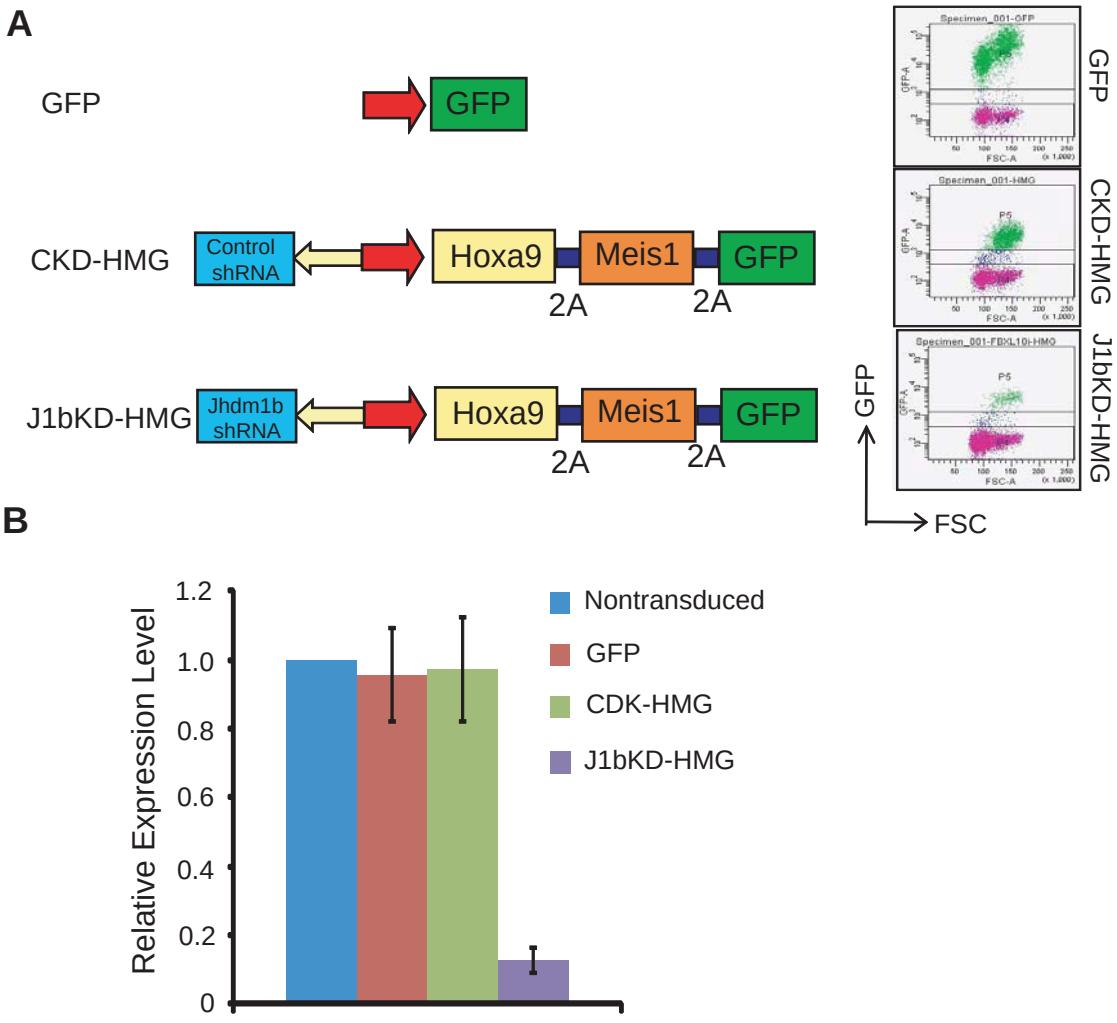

Figure S2. Genetic modifications of hematopoietic progenitor cells

(A) Schematic representation of lentiviral vectors used in the experiments. Shown are diagrams of polycistronic lentiviral vectors that express GFP alone, or Hoxa9, Meis1 and GFP coupled with control shRNA (CKD-HMG) or shRNA targeting Kdm2b/Jhdm1b (J1bKD-HMG). Transgenes are linked by P2A sequence of foot-to-mouth disease virus. shRNA driven by the U6 promoter is used for Kdm2b/Jhdm1b knocking down (Left panel). Transduced GFP+ cells are sorted by FACS and used for functional analysis (right panel).

(B) RT-qPCR analysis demonstrating that Kdm2b/Jhdm1b is efficiently knocked down after transducing with a lentiviral vector expressing Kdm1b/Jhdm1b shRNA (J1bKD-HMG). Relative mRNA levels are normalized to the Gapdh. The mRNA level of Kdm2b/Jhdm2b in non-trasduced cells is set as 1.

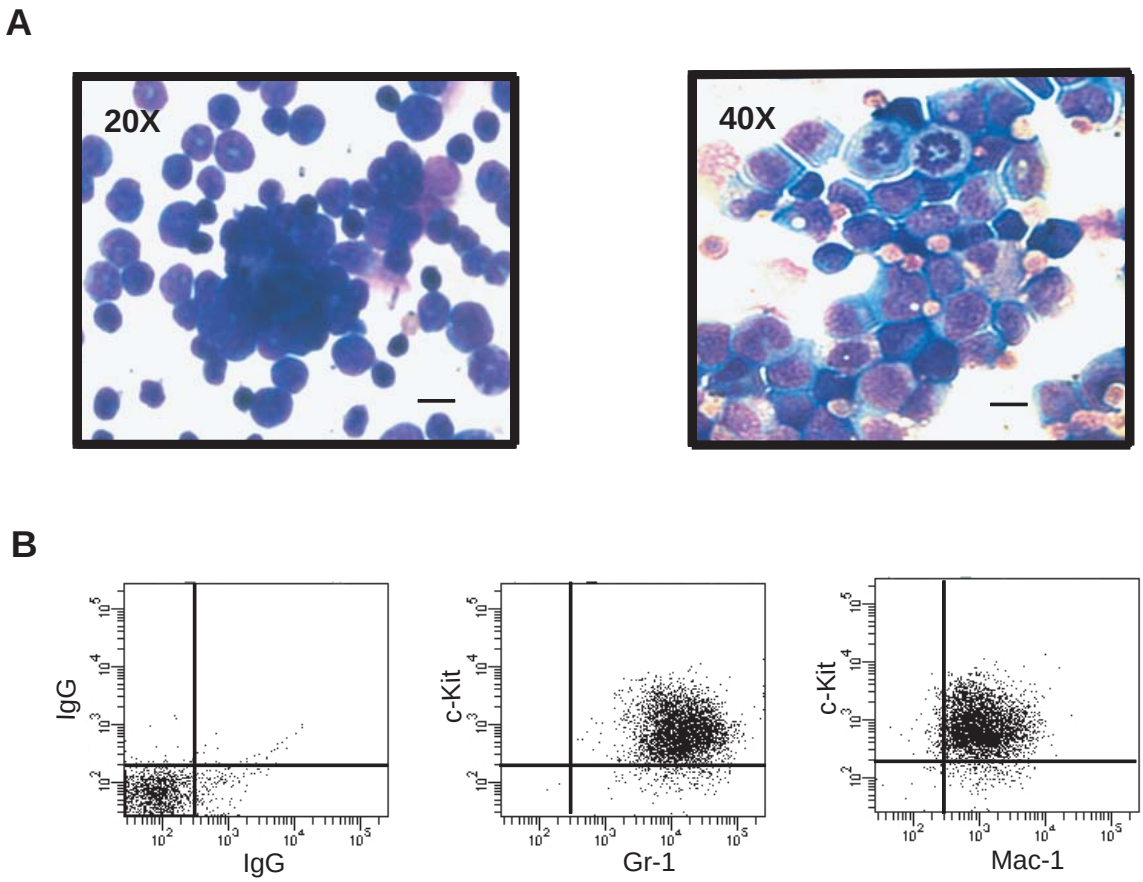

Figure S3. Characterization of Hoxa9/Meis1 induced murine AML

(A) May-Grunwald/Giemsa staining showing typical leukoblasts in the bone marrow of recipient mice transplanted with CKD-HMG cells (left, 20x magnification, Bar =20μm; right, 40x magnification, Bar = 10μm).

(B) Flow cytometry analysis demonstrates that Hoxa9/Meis1 induced leukemic cells expressing both c-kit and myeloid lineage markers Gr-1/Mac-1.

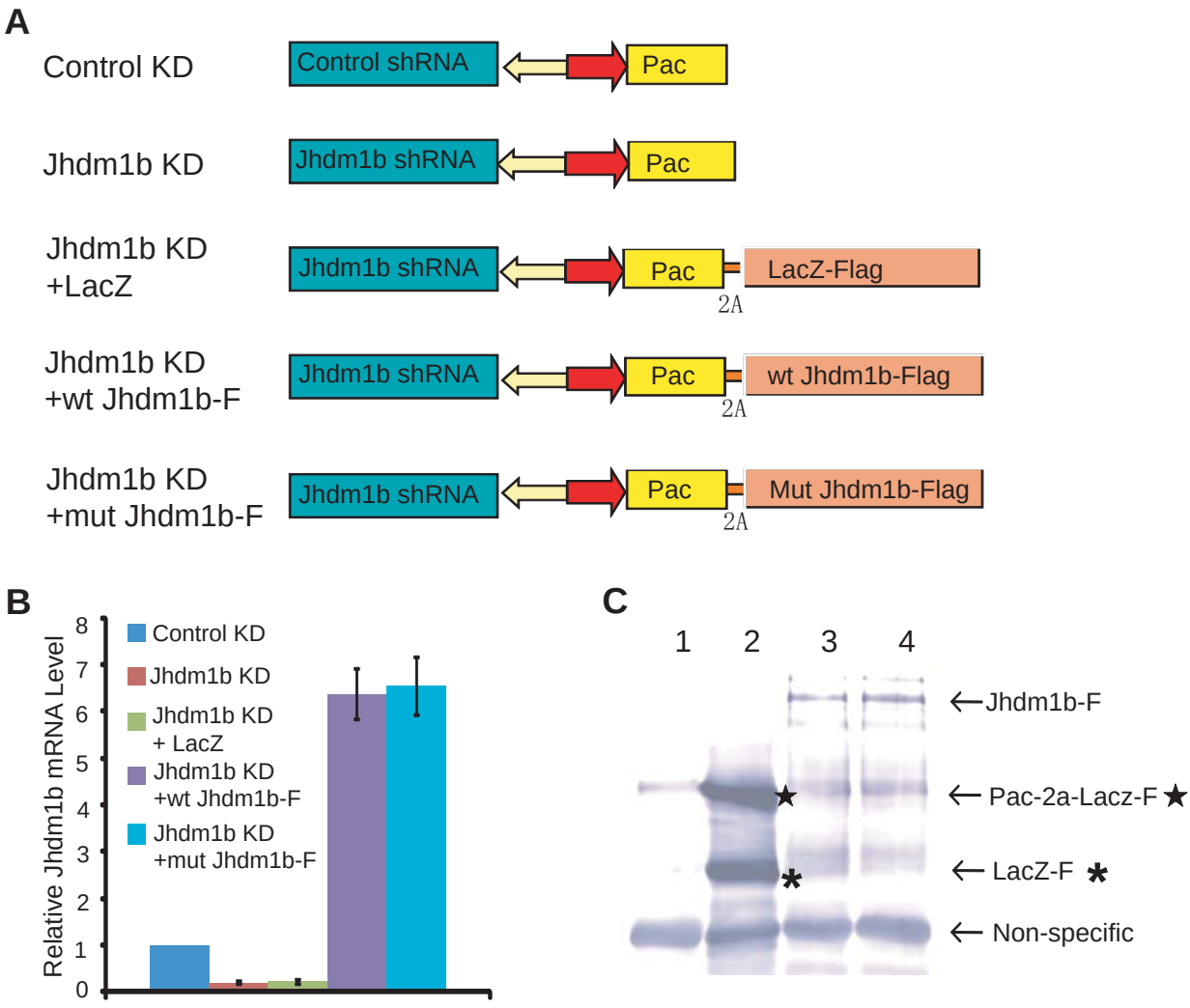

Figure S4. Genetic modifications of leukemia stem cells

(A) Schematic representation of lentiviral vectors used for genetic modification of leukemia stem cells isolated from primary AML mouse. The polycistronic lentiviral vectors express LacZ-Flag, shRNA-resistant wild type and mutant Kdm2b/Jhdm1b-Flag and a drug selection marker (Pac). Transgenes are linked by P2A sequence of foot-to-mouth disease virus. shRNA driven by U6 promoter is used for Kdm2b/Jhdm1b knockdown.

(B) RT-qPCR analysis shows the relative Kdm2b/Jhdm1b levels in the cells with control knockdown, Kdm2b/Jhdm1b knockdown, Kdm2b/Jhdm1b knockdown rescued with lacZ, wild-type or mutant Kdm2b/Jhdm1b. Relative mRNA levels are normalized to the Gapdh. The mRNA level of Kdm2b/Jhdm2b in control knockdown cells is set as 1.

(C) Western blot analysis using anti-Flag antibody demonstrates the expression of transgenes. Lane 1: Mock control; Lane 2: Kdm2b/Jdhm1bKD+LacZ-F, * denotes LacZ-Flag, ✱ denotes uncleaved Pac-2a-LacZ-Flag fusion protein;
Lane 3: Kdm2b/Jdhm1bKD+wild-type Kdm2b/Jdhm1b-F;
Lane 4: Kdm2b/Jdhm1bKD +wild-type Kdm2b/Jdhm1b-F.

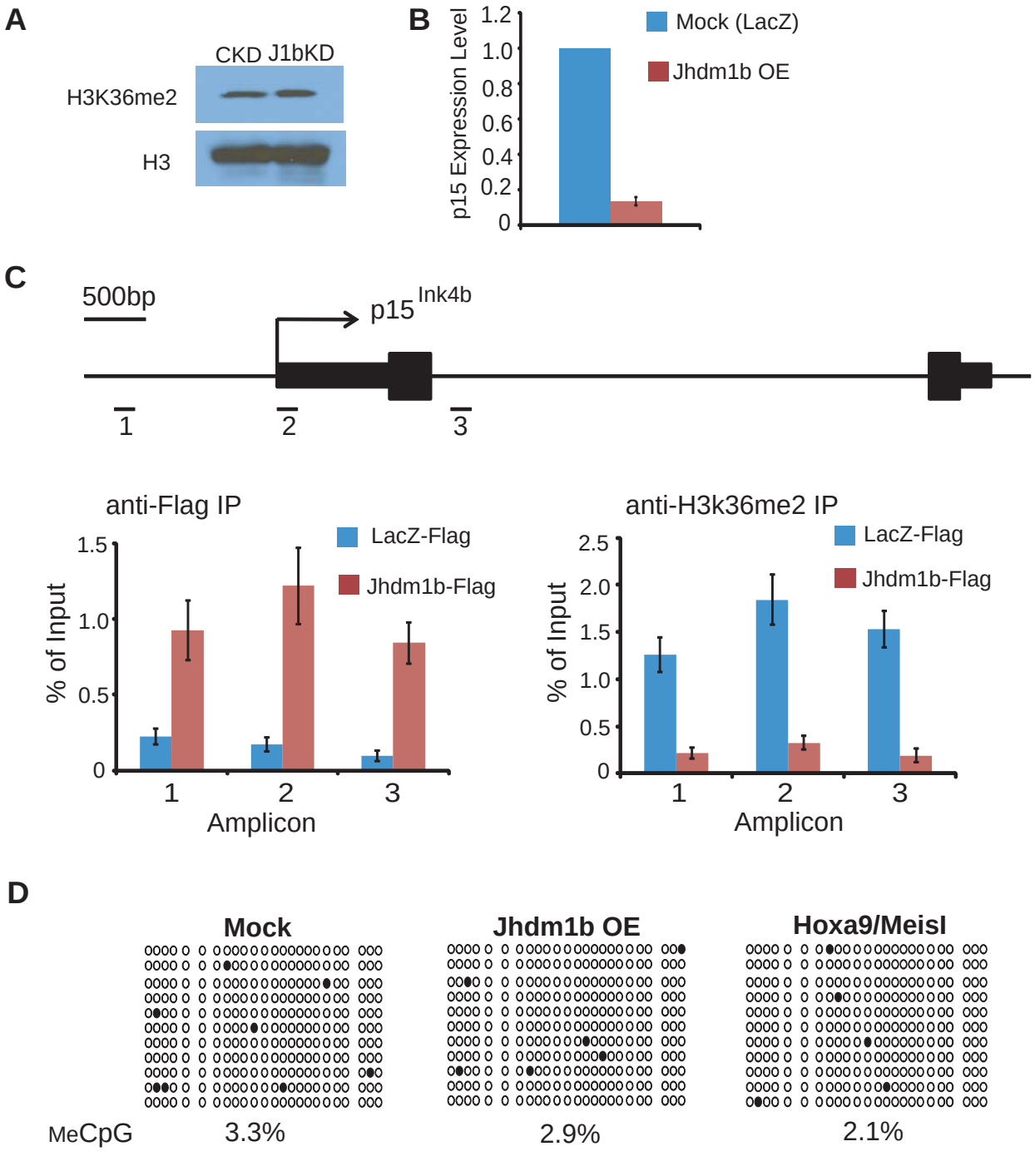

Figure S5. Epigenetic analysis of p15Ink4b locus in Kdm2b/Jhdm1b modified cells

(A) Western blot analysis using anti-H3K36me2 and anti-H3 antibodies demonstrates the global H3K36me2 expression level upon Kdm2b/Jhdm1b knockdown.

(B) RT-qPCR analysis shows the relative p15Ink4b levels in the mock and Kdm2b/Jhdm1b over-expressing cultured for 2 weeks. Relative mRNA levels are normalized to the Gapdh. The mRNA level of mock HPCs is set as 1.

(C) ChIP experiments using chromatin prepared from HPCs over-expressing LacZ-Flag and Kdm2b/Jhdm1b-Flag were carried out using anti-Flag and anti-H3K36me2 antibodies. Kdm2b/Jhdm1b-Flag binding and H3K36me2 level was assayed by qPCR at the three genomic regions depicted in upper panel.

(D) Bisulfite analysis demonstrates the DNA methylation levels in controlled HPCs, Kdm2b/Jhdm1b immortalized HPCs and Hoxa9/MeisI transformed cells. Empty circle represents unmethylated CpG dinucleotides and black circle represents methylated CpG dinucleotides. The percentage of methylated CpG dinucleotides = total methylated CpG dinucleotides/ total CpG dinucleotides x 100%.