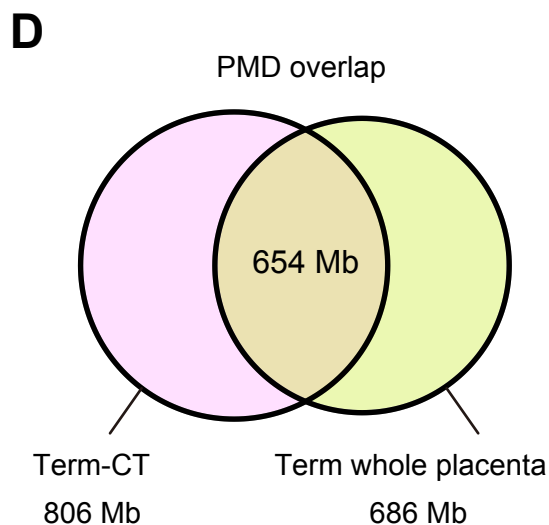
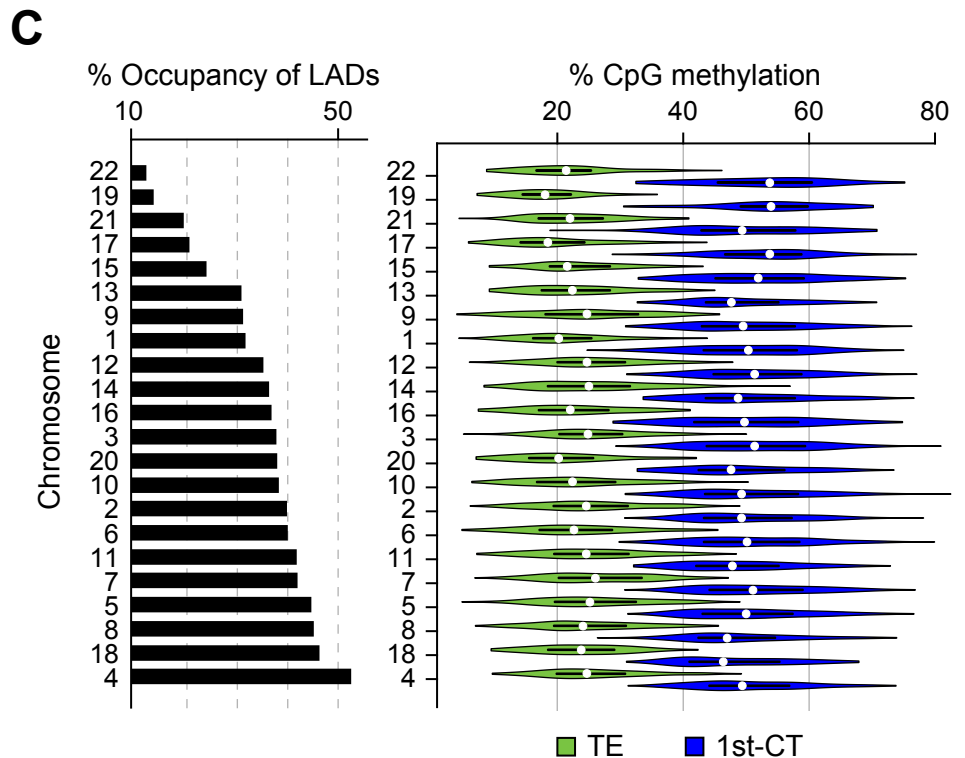
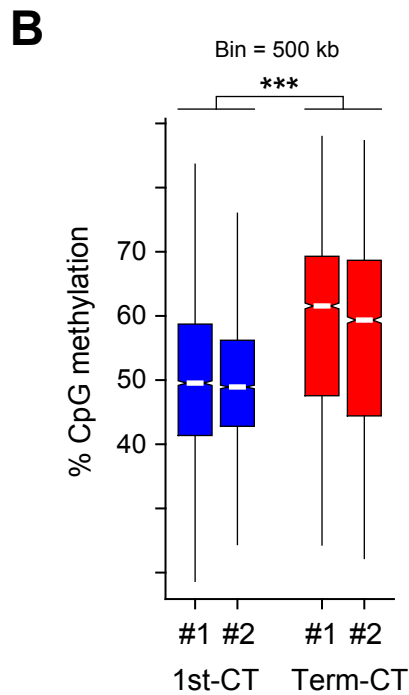
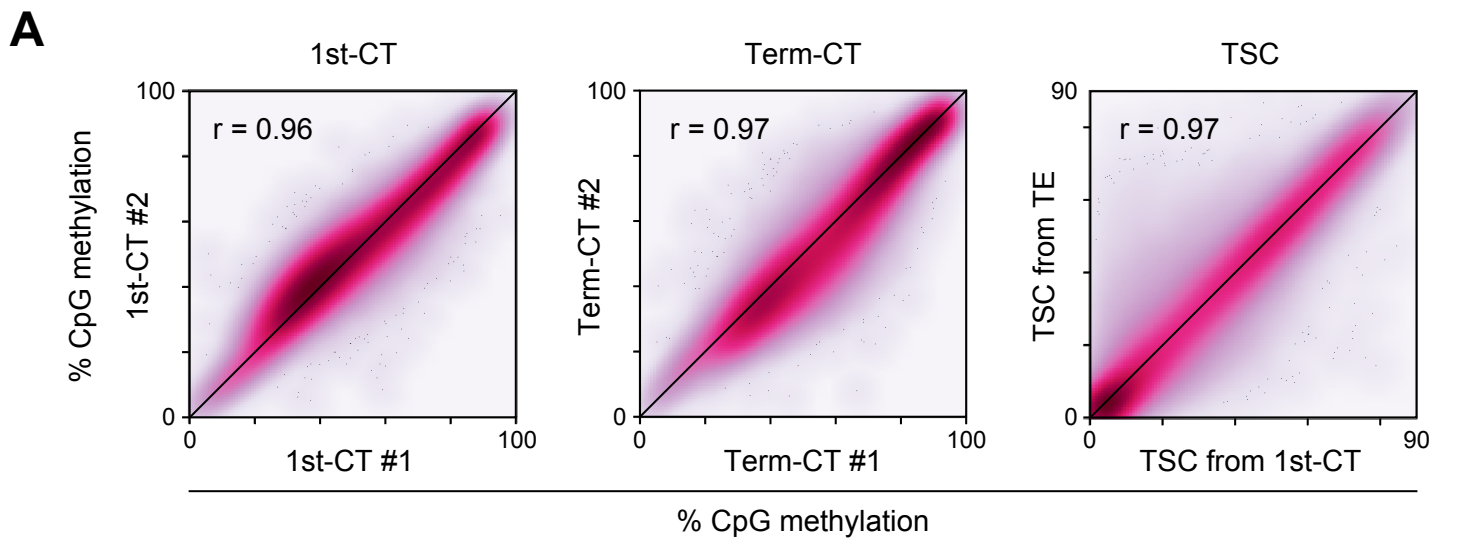


**Table S1. Summary in WGBS and ChIP-seq of hCTs and hTSCs**

Cells and tissues		Sequenced reads (R1+R2)	Uniquely mapped reads
<b>WGBS</b>			
first trimester hCTs (#1, male, 7 weeks)		1,918,276,290	690,113,287
first trimester hCTs (#2, female, 7 weeks)		1,875,092,806	689,288,381
term hCTs (#1, male)		2,132,672,758	775,610,961
term hCTs (#2, female)		2,158,260,826	715,503,957
hTSCs from hCTs (female, 6 weeks)		725,797,809	444,323,973
hTSCs from trophectoderm (male)		636,290,805	383,680,848
<b>ChIP-seq</b>			
	<b>Histone H3</b>		
first trimester hCTs (#1, male, 7 weeks)	K27ac	84,077,366	79,730,691
	K27me3	147,326,520	143,727,948
	K36me3	159,773,014	155,499,908
	K4me1	157,721,306	153,961,380
	K4me3	81,528,852	77,860,906
	K9me3	170,035,518	151,234,202
	Input	186,476,942	176,868,917
	first trimester hCTs (#2, female, 7 weeks)	K27ac	63,754,920
K27me3		130,509,670	127,050,805
K36me3		128,867,216	125,242,822
K4me1		149,500,800	146,207,565
K4me3		58,845,628	56,539,971
K9me3		130,293,024	117,751,657
Input		149,933,526	142,787,111
term hCTs (#1, male)		K27ac	90,112,742
	K27me3	164,382,230	159,547,231
	K36me3	150,295,704	147,032,015
	K4me1	177,610,694	146,854,476
	K4me3	80,125,580	77,341,038
	K9me3	162,018,466	147,088,040
	Input	194,166,736	183,080,427
	term hCTs (#2, female)	K27ac	52,882,106
K27me3		126,340,992	123,885,838
K36me3		146,845,708	144,431,285
K4me1		131,385,032	121,109,407
K4me3		62,918,006	61,180,265
K9me3		127,136,754	118,740,568
Input		196,869,810	187,566,857
hTSCs from hCTs (female, 6 weeks)		K27ac	54,498,970
	K27me3	169,668,834	165,411,683
	K36me3	131,465,600	129,211,190
	K4me1	85,934,898	84,628,407
	K4me3	23,372,186	22,922,831
	K9me3	123,325,624	110,853,331
	Input	92,826,976	90,448,128
	hTSCs from trophectoderm (male)	K27ac	81,058,968
K27me3		156,416,844	153,113,354
K36me3		118,461,142	116,872,586
K4me1		126,647,556	124,712,619
K4me3		36,625,228	35,832,861
K9me3		132,055,826	117,839,884
Input		136,953,104	132,844,046



**Figure S1.**

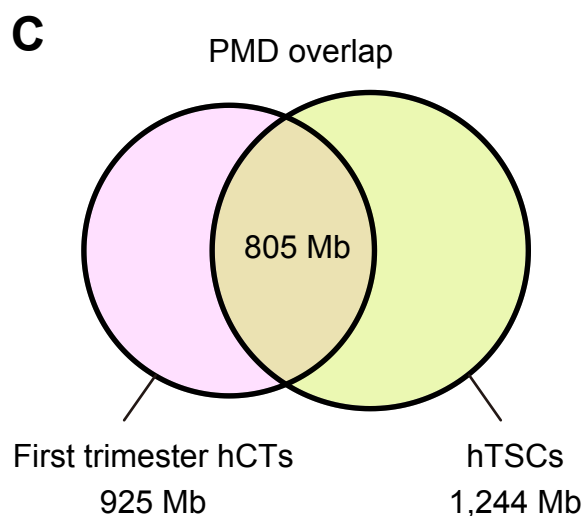
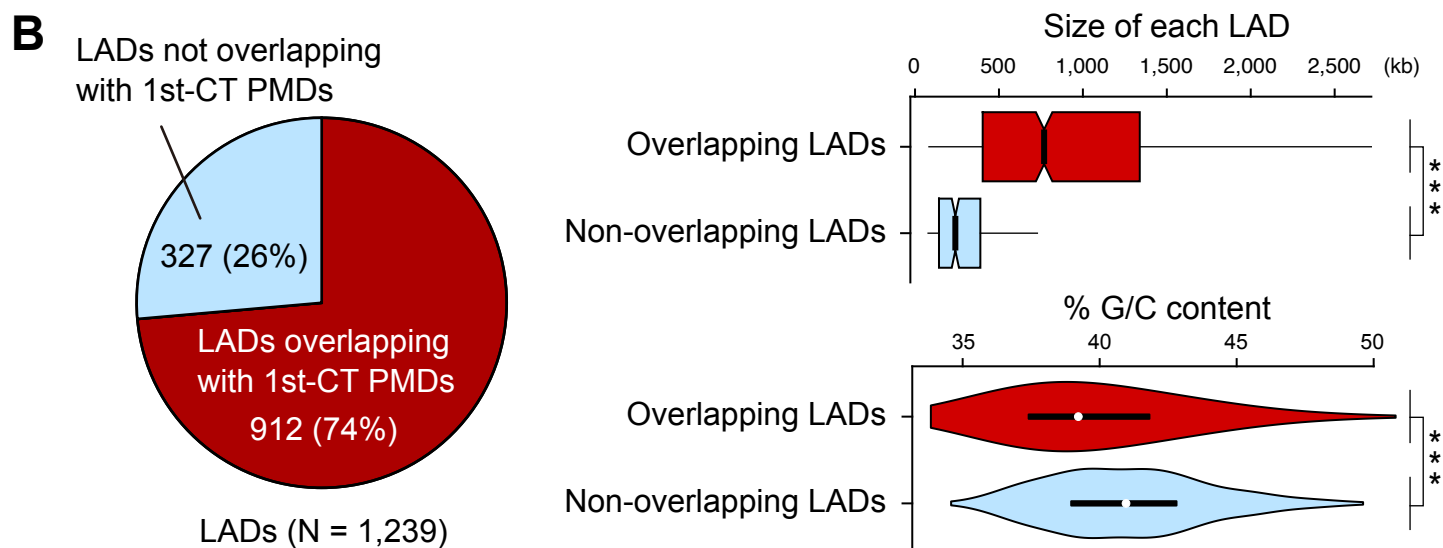
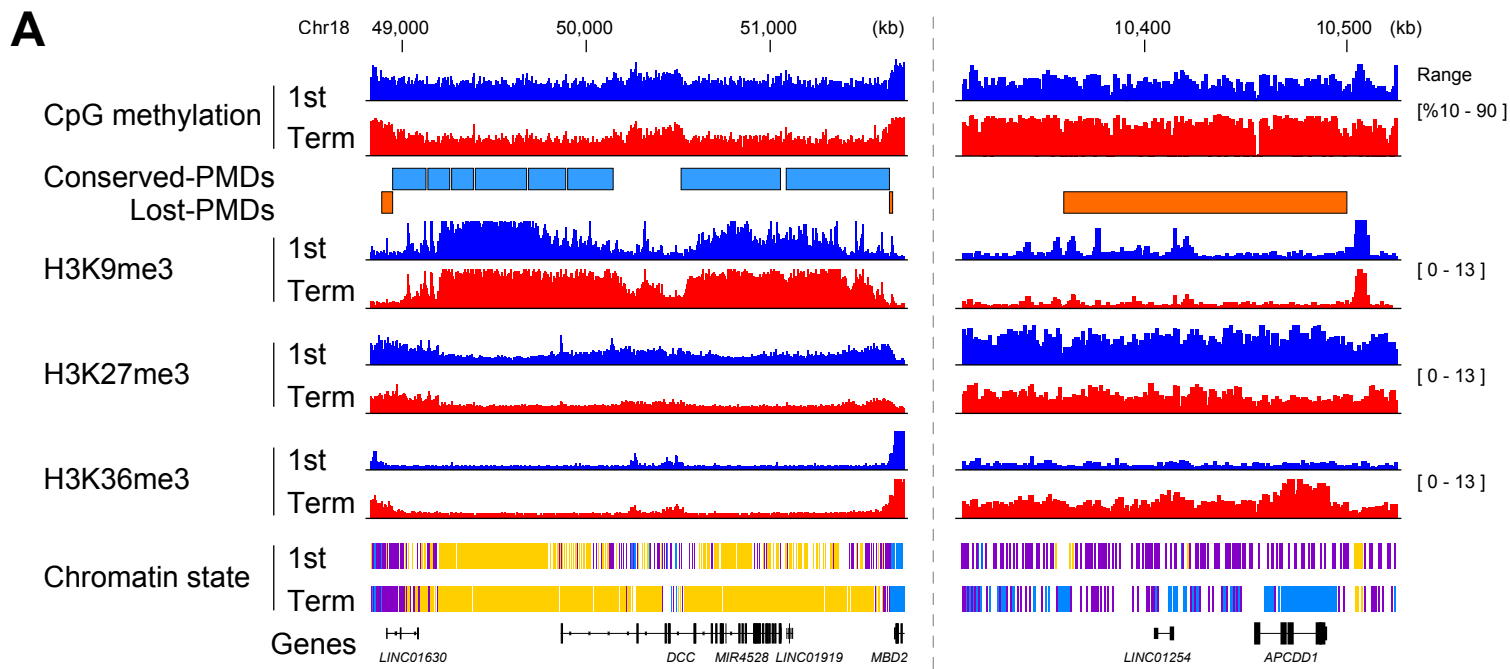
**Dynamics of PMDs during human placental development.**

(A) Scatter plots comparing CpG methylation levels in 10-kb bins across replicates of each sample. 1st-CT, first trimester hCTs; Term-CT, term hCTs; TSC, hTSCs; TE, trophoctoderm.

(B) Comparison of global CpG methylation levels between first trimester and term hCTs.

(C) Correlation between position in the nucleus and DNA methylation levels. Bar plots show the LAD occupancy for each chromosome, ordered from top to bottom by decreasing LAD occupancy, with LAD data taken from Guelen et al. (2008) [33]. Violin plots compare the absolute methylation levels in trophoctoderm and first trimester hCTs for each chromosome.

(D) A Venn diagram showing the overlap between PMDs in term hCTs and those previous reported in term whole placentas. Data for term whole placentas are from Schroeder et al. (2013) [19].



**Figure S2.**

**Characteristics of PMDs in human cytotrophoblasts.**

(A) A genome browser view of regions containing conserved-PMDs (left) and lost-PMDs (right). DNA methylation levels and histone H3 modification signals for first trimester hCTs and term hCTs are shown. Plots are provided for each histone H3 modification from one of the individual biological replicates, with PMDs marked as rectangles. Three chromatin states (H3K9me3, H3K27me3, H3K36me3) in ChromHMM were shown at the bottom. The color code for chromatin states is the same as in Figure 2A.

(B) Analysis of overlap of LADs with PMDs. The pie chart shows the proportion of LADs overlapping with PMDs in first trimester hCTs. Box plots show the size distribution of LADs that overlap and do not overlap with PMDs. Violin plots show the G/C content of LADs that overlap and do not overlap with PMDs. Statistical significance was assessed using the Wilcoxon rank sum test, with triple asterisks (\*\*\*) indicating  $P < 0.0001$ .

(C) A Venn diagram showing the overlap between PMDs in first trimester hCTs and those in hTSCs.