Figure S1. Important transcription factors in the differentiation of Th1 and Th2 lymphocytes. Modified from O'Shea *et al* (58) and Wong *et al* (47) and created with Biorender. GATA3, GATA binding protein 3; p, phosphorylated; T-BET, T-Box transcription factor 21.
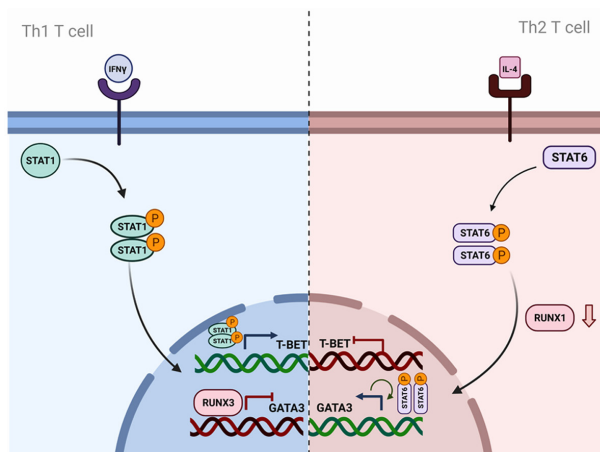
Figure S2. Analysis of the relative expression of IL-4 at the mRNA level in the placenta. Levels of expression of *IL-4* in samples in placentas from non-smoking women and women smokers. The horizontal bar represents the median of relative expression. A Mann-Whitney U statistical test was applied. *P<0.05.
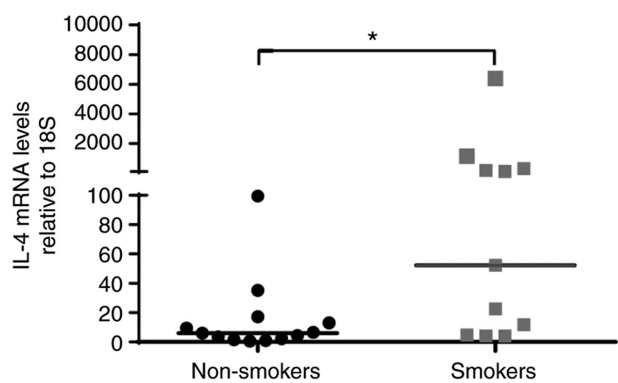
Figure S3. Analysis of the relative expression and specific methylation of T-BET at the mRNA level in the placenta. (A) Levels of expression of *T-BET* relative to *18S* in samples of placentas from non-smoking women compared with placentas from women smokers. (B) *T-BET* expression levels relative to *18S* levels in samples selected for endpoint MSP analysis. (C) Endpoint MSP analysis of placental samples from non-smoking women (upper bands) and women smokers (lower bands). β-actin, T-BET U-Met (oligos that recognize the non-methylated sequence), T-BET Met (oligos that recognize the methylated sequence), C+ and C-. Different gels were merged, as indicated by the vertical lines. Each vertical lane corresponds to the same type of sample. (D) MSP statistical bars demonstrate that 0 was assigned to the unmethylated state and 1 to the methylated state, according to the interpretation from the gel as the presence of band or not, respectively. A Mann-Whitney U statistical test was applied. *P<0.05, ***P<0.001. T-BET, T-Box transcription factor 21; MSP, methylation-specific PCR; U-Met, unmethylated; Met, methylated; C+, methylated genomic DNA control; C-, nonmethylated genomic DNA; NS, not significant.
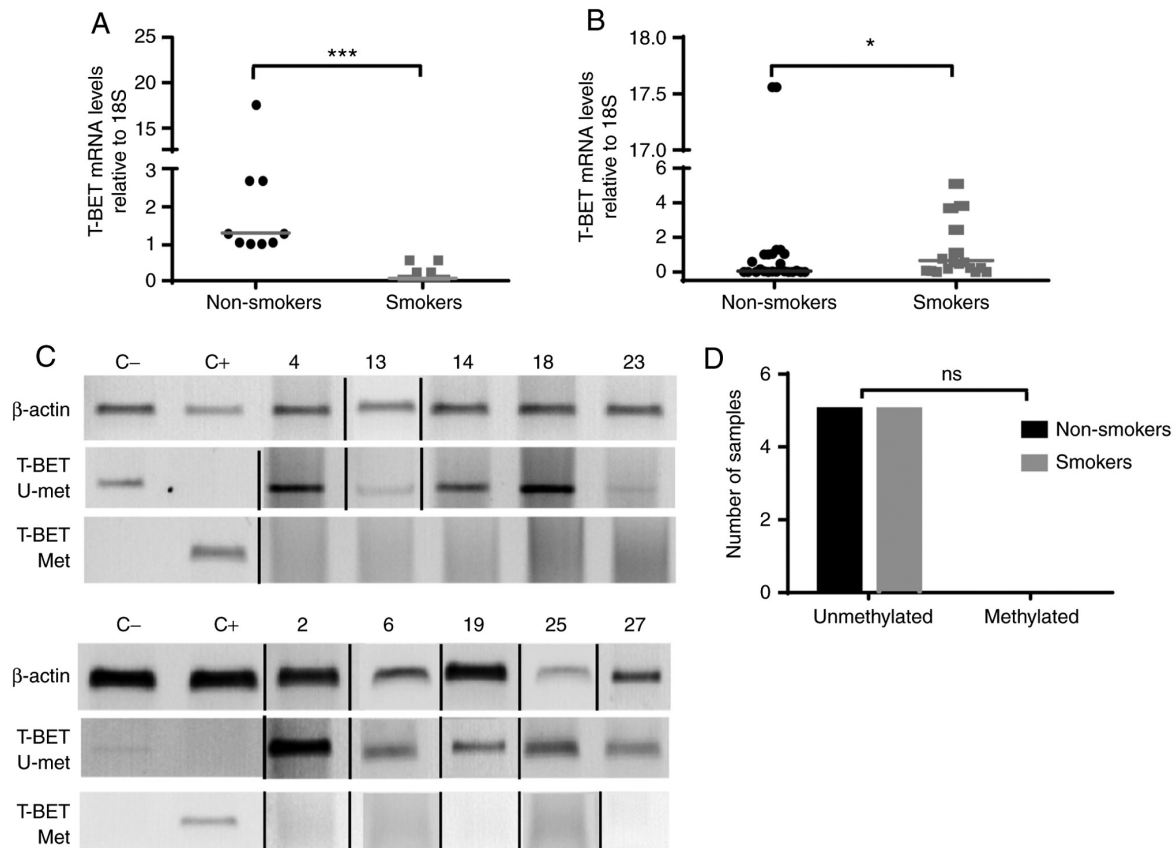
Figure S4. Analysis of RUNX1 protein expression in the placenta. (A) Number of placental samples classified according to the intensity of RUNX1 labeling by immunohistochemistry of chorion stromal cells. (B) Number of placental samples classified according to the ratio of RUNX1 labeling by immunohistochemistry of chorion stromal cells.
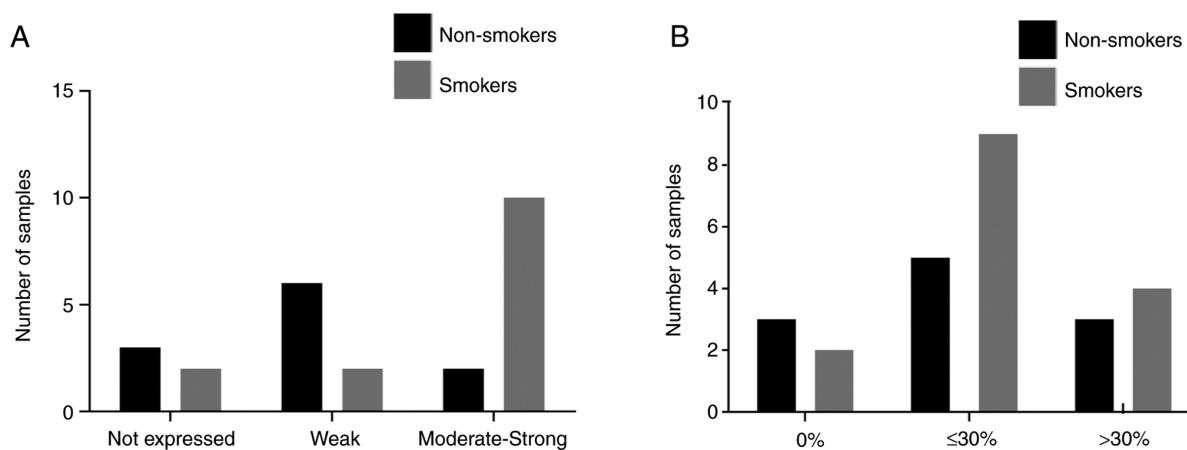
Table SI. Histological findings of patient samples included in the study.

A, Gross findings

Histologic findings	Women smokers (n=14)	Non-smoking women (n=20)	P-value
Placental weight, n (%)			0.29
Normal	13 (92.8)	20 (100.0)	
Abnormal (P<10)	1 (7.2)	0 (0.0)	
Umbilical cord site of insertion, n (%)			0.74
Normal	13 (92.8)	18 (90.0)	
Abnormal	1 (7.1)	2 (10.0)	
Umbilical cord coiling, n (%)			0.21
Normal	5 (35.7)	9 (45.0)	
Hypercoiled	7 (50.0)	3 (15.0)	
Hypocoiled	2 (14.3)	0 (0.0)	
Undetermined	0 (0.0)	8 (40.0)	

B, Maternal vascular malperfusion

Histologic findings	Smoking women (n=14)	Non-smoking women (n=20)	P-value
Infarction, n (%)			-
Present	3 (21.5)	Absent	
Absent	11 (78.5)	Absent	
Retroplacental hematoma, n (%)			-
Present	2 (14.3)	Absent	
Absent	12 (85.7)	Absent	