



**Supplementary Figure S1.** Odds ratios of risk factors for hypertension.

**Supplementary Table S1.** The pyrosequencing primer sequence

Gene	Primer	Sequence
<i>MT-COX1</i>	Forward primer	TATTAATTGGTTTTTAGGGTTTAT
	Reverse biotin primer (5' to 3')	CAACAAATCATTTTCATATTACTTCC
	Sequencing primer (5' to 3')	TATTATAGTAGGAAT
<i>MT-COX2</i>	Forward primer (5' to 3')	TTTATGAGTTGTTTTATATTAGGTTTAAA
	Reverse biotin primer (5' to 3')	ACTCCACAAATTTCAAACATTAAC
	Sequencing primer (5' to 3')	TAAAAATAGATGTAAT
<i>MT-COX3</i>	Forward primer (5' to 3')	TATATTATTTGTTTAAAAAGGTTTT
	Reverse biotin primer (5' to 3')	AATAAAAACTCAAAAAATCCTAC
	Sequencing primer (5' to 3')	TATATTATTTGTTTAAAAAGGTTTT
<i>MT-ATP6</i>	Forward primer (5' to 3')	TTATAAATTTAGTTATGGTTATTTTTTTAT
	Reverse biotin primer (5' to 3')	AAACTAAAACATTTTTAATCTTAAAAC
	Sequencing primer (5' to 3')	TTATAAATTTAGTTATGGTTATTTTTTTAT
<i>MT-ATP8</i>	Forward primer (5' to 3')	AAATTATAATAAATTTTGAGAATTAATAATG
	Reverse biotin primer (5' to 3')	AATAAACCTAAAATTATAAAAAACAATAAAT
	Sequencing primer (5' to 3')	AAATTATAATAAATTTTGAGAATTAATAATG

**Supplementary Table S2.** Comparison of methylation levels between male and female hypertensive patients

Loci	Male group (N = 25)	Female group (N = 312)	Z value	P value
<i>MT-COX1Pos.1</i>	9.38 (4.25)	10.24 (4.12)	-0.85	0.39
<i>MT-COX1Pos.2</i>	8.43 (3.52)	7.75 (2.84)	-0.62	0.53
<i>MT-COX1</i>	9.09 (3.70)	8.72 (3.31)	-0.28	0.78
<i>MT-COX2</i>	5.46 (2.60)	5.61 (2.60)	-0.05	0.96
<i>MT-COX3Pos.1</i>	4.43 (1.42)	4.85 (1.54)	-1.09	0.27
<i>MT-COX3Pos.2</i>	3.66 (1.38)	3.81 (1.18)	-0.75	0.45
<i>MT-COX3</i>	4.10 (1.32)	4.34 (1.16)	-1.14	0.25
<i>MT-ATP6Pos.1</i>	18.12 (3.44)	17.53 (5.33)	-0.44	0.66
<i>MT-ATP6Pos.2</i>	10.34 (4.39)	10.68 (3.97)	-1.22	0.22
<i>MT-ATP6Pos.3</i>	13.85 (6.71)	13.04 (5.56)	-0.38	0.70
<i>MT-ATP6</i>	14.26 (4.77)	13.58 (4.09)	-0.07	0.94
<i>MT-ATP8Pos.1</i>	7.32 (5.24)	6.35 (4.07)	-1.46	0.14
<i>MT-ATP8Pos.2</i>	7.10 (4.77)	6.04 (3.59)	-1.18	0.24
<i>MT-ATP8</i>	6.77 (5.03)	6.20 (3.76)	-1.31	0.19

**Note.** Continuous variables that do not conform to the normal distribution are described by median and interquartile range, and the differences both two groups are compared by Mann-Whitney U test. The categorical variables were presented using frequency and percentage, and the differences both two groups were compared by chi-square test. *MT-COX1* is the average methylation level of *MT-COX1Pos.1* and *MT-COX1Pos.2*; *MT-COX3* is the mean methylation level of *MT-COX3Pos.1* and *MT-COX3Pos.2*; *MT-ATP6* is the average methylation level of *MT-ATP6 Pos.1*, *MT-ATP6 Pos.2* and *MT-ATP6 Pos.3*; *MT-ATP8* is the mean methylation level of *MT-ATP8 Pos.1* and *MT-ATP8 Pos.2*.

**Supplementary Table S3.** Comparison of methylation levels between BMI  $\geq 24$  and  $< 24$  hypertensive patients

Loci	BMI < 24 (N = 101)	BMI $\geq 24$ (N = 236)	Z value	P value
<i>MT-COX1Pos.1</i>	9.48 (4.06)	9.46 (4.22)	-0.41	0.68
<i>MT-COX1Pos.2</i>	8.22 (2.90)	7.73 (2.78)	-1.06	0.29
<i>MT-COX1</i>	8.99 (3.39)	8.56 (3.23)	-0.80	0.43
<i>MT-COX2</i>	5.53 (2.61)	5.68 (2.63)	-1.54	0.12
<i>MT-COX3Pos.1</i>	4.74 (1.60)	4.91 (1.52)	-1.00	0.32
<i>MT-COX3Pos.2</i>	3.81 (1.04)	3.80 (1.19)	-0.06	0.95
<i>MT-COX3</i>	4.22 (1.11)	4.35 (1.22)	-0.34	0.74
<i>MT-ATP6Pos.1</i>	17.41 (4.90)	17.65 (5.32)	-0.27	0.78
<i>MT-ATP6Pos.2</i>	10.58 (3.99)	10.68 (3.97)	-0.18	0.86
<i>MT-ATP6Pos.3</i>	13.08 (6.05)	13.12 (5.56)	-0.14	0.89
<i>MT-ATP6</i>	13.73 (3.93)	13.70 (4.19)	-0.10	0.92
<i>MT-ATP8Pos.1</i>	6.26 (4.27)	6.46 (4.05)	-0.02	0.98
<i>MT-ATP8Pos.2</i>	6.07 (3.40)	6.03 (3.59)	-0.30	0.77
<i>MT-ATP8</i>	6.15 (3.89)	6.26 (3.92)	-0.13	0.90

**Note.** Continuous variables that do not conform to the normal distribution are described by median and interquartile range, and the differences both two groups are compared by Mann-Whitney U test. The categorical variables were presented using frequency and percentage, and the differences both two groups were compared by chi-square test. *MT-COX1* is the average methylation level of *MT-COX1Pos.1* and *MT-COX1Pos.2*; *MT-COX3* is the mean methylation level of *MT-COX3Pos.1* and *MT-COX3Pos.2*; *MT-ATP6* is the average methylation level of *MT-ATP6 Pos.1*, *MT-ATP6 Pos.2* and *MT-ATP6 Pos.3*; *MT-ATP8* is the mean methylation level of *MT-ATP8 Pos.1* and *MT-ATP8 Pos.2*.

**Supplementary Table S4.** Comparison of methylation levels between age  $\geq 60$  and  $< 60$  hypertensive patients

Loci	Age $< 60$ (N = 139)	Age $\geq 60$ (N = 198)	Z value	P value
<i>MT-COX1Pos.1</i>	9.18 (4.57)	9.64 (3.98)	-0.78	0.43
<i>MT-COX1Pos.2</i>	7.27 (2.68)	8.22 (3.18)	-3.58	$< 0.001$
<i>MT-COX1</i>	8.41 (3.22)	8.93 (3.42)	-2.06	0.04
<i>MT-COX2</i>	5.38 (2.63)	5.71 (2.45)	-1.91	0.056
<i>MT-COX3Pos.1</i>	4.01 (1.55)	5.23 (1.15)	-8.93	$< 0.001$
<i>MT-COX3Pos.2</i>	3.68 (1.42)	3.86 (1.08)	-1.66	0.10
<i>MT-COX3</i>	3.91 (1.35)	4.61 (0.99)	-6.48	$< 0.001$
<i>MT-ATP6Pos.1</i>	18.40 (4.74)	17.09 (4.82)	-2.92	0.004
<i>MT-ATP6Pos.2</i>	9.57 (4.04)	10.92 (3.64)	-3.27	0.001
<i>MT-ATP6Pos.3</i>	12.95 (5.17)	13.20 (6.16)	-0.49	0.62
<i>MT-ATP6</i>	13.80 (4.06)	13.46 (4.11)	-0.64	0.52
<i>MT-ATP8Pos.1</i>	7.86 (3.78)	5.35 (3.24)	-7.17	$< 0.001$
<i>MT-ATP8Pos.2</i>	7.41 (3.66)	5.19 (2.97)	-6.66	$< 0.001$
<i>MT-ATP8</i>	7.70 (3.23)	5.40 (3.17)	-7.14	$< 0.001$

**Note.** Continuous variables that do not conform to the normal distribution are described by median and interquartile range, and the differences both two groups are compared by Mann-Whitney U test. The categorical variables were presented using frequency and percentage, and the differences both two groups were compared by chi-square test. *MT-COX1* is the average methylation level of *MT-COX1Pos.1* and *MT-COX1Pos.2*; *MT-COX3* is the mean methylation level of *MT-COX3Pos.1* and *MT-COX3Pos.2*; *MT-ATP6* is the average methylation level of *MT-ATP6 Pos.1*, *MT-ATP6 Pos.2* and *MT-ATP6 Pos.3*; *MT-ATP8* is the mean methylation level of *MT-ATP8 Pos.1* and *MT-ATP8 Pos.2*.

**Supplementary Table S5.** Comparison of methylation levels between smoking and non-smoking hypertensive patients

Loci	Non-smoking (N = 177)	Smoking (N = 158)	Z value	P value
<i>MT-COX1Pos.1</i>	10.20 $\pm$ 4.26	10.22 (4.34)	-0.24	0.81
<i>MT-COX1Pos.2</i>	7.85 (3.09)	7.75 (2.82)	-0.21	0.83
<i>MT-COX1</i>	8.72 (3.20)	8.74 (3.46)	-0.04	0.97
<i>MT-COX2</i>	5.45 (2.47)	5.76 (2.79)	-0.27	0.79
<i>MT-COX3Pos.1</i>	4.77 (1.57)	4.94 (1.49)	-1.27	0.21
<i>MT-COX3Pos.2</i>	3.66 (1.12)	3.92 (1.01)	-2.66	$< 0.01$
<i>MT-COX3</i>	4.19 (1.17)	4.43 (1.05)	-2.38	0.02
<i>MT-ATP6Pos.1</i>	16.55 (5.66)	17.80 (4.15)	-3.03	$< 0.01$
<i>MT-ATP6Pos.2</i>	10.43 (3.67)	10.88 (4.01)	-1.22	0.22
<i>MT-ATP6Pos.3</i>	12.79 (5.72)	13.37 (5.76)	-1.45	0.15
<i>MT-ATP6</i>	12.97 (4.56)	14.18 (3.65)	-2.01	0.04
<i>MT-ATP8Pos.1</i>	6.35 (4.58)	6.49 (4.10)	-0.56	0.58
<i>MT-ATP8Pos.2</i>	5.94 (3.86)	6.09 (3.46)	-0.20	0.85
<i>MT-ATP8</i>	6.15 (4.37)	6.32 (3.57)	-0.42	0.68

**Note.** Continuous variables that do not conform to the normal distribution are described by median and interquartile range, and the differences both two groups are compared by Mann-Whitney U test. The categorical variables were presented using frequency and percentage, and the differences both two groups were compared by chi-square test. *MT-COX1* is the average methylation level of *MT-COX1Pos.1* and *MT-COX1Pos.2*; *MT-COX3* is the mean methylation level of *MT-COX3Pos.1* and *MT-COX3Pos.2*; *MT-ATP6* is the average methylation level of *MT-ATP6 Pos.1*, *MT-ATP6 Pos.2* and *MT-ATP6 Pos.3*; *MT-ATP8* is the mean methylation level of *MT-ATP8 Pos.1* and *MT-ATP8 Pos.2*.

**Supplementary Table S6.** Comparison of methylation levels between drinking and non-drinking hypertensive patients

Loci	Non-drinking (N = 198)	Drinking (N =137)	Z value	P value
<i>MT-COX1Pos.1</i>	9.42 (4.31)	9.58 (4.39)	-0.75	0.46
<i>MT-COX1Pos.2</i>	7.76 (2.83)	7.85 (3.04)	-0.71	0.48
<i>MT-COX1</i>	8.72 (3.12)	9.37 (3.94)	-0.63	0.53
<i>MT-COX2</i>	5.47 (2.52)	5.68 (2.70)	-0.04	0.97
<i>MT-COX3Pos.1</i>	4.78 (1.52)	4.98 (1.48)	-1.23	0.22
<i>MT-COX3Pos.2</i>	3.68 (1.11)	3.92 (1.03)	-2.32	0.02
<i>MT-COX3</i>	4.19 (1.18)	4.44 (1.01)	-2.20	0.03
<i>MT-ATP6Pos.1</i>	16.78 (5.32)	18.13 (4.31)	-2.42	0.02
<i>MT-ATP6Pos.2</i>	10.52 (3.59)	10.78 (4.23)	-1.28	0.20
<i>MT-ATP6Pos.3</i>	12.78 (5.62)	13.66 (5.86)	-1.29	0.20
<i>MT-ATP6</i>	13.20 (4.28)	14.37 (3.99)	-1.86	0.06
<i>MT-ATP8Pos.1</i>	6.16 (4.39)	6.59 (3.91)	-0.20	0.85
<i>MT-ATP8Pos.2</i>	5.86 (3.59)	6.51 (3.69)	-1.00	0.32
<i>MT-ATP8</i>	6.01 (4.10)	6.50 (3.47)	-0.60	0.55

**Note.** Continuous variables that do not conform to the normal distribution are described by median and interquartile range, and the differences both two groups are compared by Mann-Whitney U test. The categorical variables were presented using frequency and percentage, and the differences both two groups were compared by chi-square test. *MT-COX1* is the average methylation level of *MT-COX1Pos.1* and *MT-COX1Pos.2*; *MT-COX3* is the mean methylation level of *MT-COX3Pos.1* and *MT-COX3Pos.2*; *MT-ATP6* is the average methylation level of *MT-ATP6 Pos.1*, *MT-ATP6 Pos.2* and *MT-ATP6 Pos.3*; *MT-ATP8* is the mean methylation level of *MT-ATP8 Pos.1* and *MT-ATP8 Pos.2*.

**Supplementary Table S7.** Comparison of methylation levels between with anti-hypertensive treatment and without anti-hypertensive treatment patients

Loci	Hypertension group		Z value	P value
	Anti-hypertensive treatment (56)	Without anti-hypertensive treatment (281)		
<i>MT-COX1Pos.1</i>	8.77 (3.47)	9.62 (4.12)	-1.62	0.11
<i>MT-COX1Pos.2</i>	8.13 (2.47)	7.76 (3.06)	-0.27	0.79
<i>MT-COX1</i>	8.53 (2.61)	8.83 (3.42)	-0.93	0.35
<i>MT-COX2</i>	5.75 (2.68)	5.50 (2.62)	-1.14	0.26
<i>MT-COX3Pos.1</i>	5.06 (1.51)	4.82 (1.57)	-1.48	0.14
<i>MT-COX3Pos.2</i>	3.68 (1.45)	3.83 (1.07)	-0.21	0.83
<i>MT-COX3</i>	4.39 (1.09)	4.30 (1.20)	-0.72	0.47
<i>MT-ATP6Pos.1</i>	15.80 (4.75)	17.97 (4.90)	-2.70	<b>0.01</b>
<i>MT-ATP6Pos.2</i>	9.99 (3.80)	10.68 (3.96)	-1.14	0.25
<i>MT-ATP6Pos.3</i>	12.79 (6.16)	13.12 (5.71)	-1.41	0.16
<i>MT-ATP6</i>	12.93 (4.33)	14.01 (4.08)	-1.89	0.06
<i>MT-ATP8Pos.1</i>	6.81 (3.97)	6.35 (4.13)	-0.23	0.82
<i>MT-ATP8Pos.2</i>	5.87 (3.40)	6.07 (3.65)	-0.01	0.99
<i>MT-ATP8</i>	6.28 (3.66)	6.24 (3.89)	-0.13	0.90

**Note.** Continuous variables that do not conform to the normal distribution are described by median and interquartile range, and the differences both two groups are compared by Mann-Whitney U test. The categorical variables were presented using frequency and percentage, and the differences both two groups were compared by chi-square test. *MT-COX1* is the average methylation level of *MT-COX1Pos.1* and *MT-COX1Pos.2*; *MT-COX3* is the mean methylation level of *MT-COX3Pos.1* and *MT-COX3Pos.2*; *MT-ATP6* is the average methylation level of *MT-ATP6 Pos.1*, *MT-ATP6 Pos.2* and *MT-ATP6 Pos.3*; *MT-ATP8* is the mean methylation level of *MT-ATP8 Pos.1* and *MT-ATP8 Pos.2*.

**Supplementary Table S8.** Association between mtDNA methylation level and the risk of hypertension

Loci	Unadjusted model			Adjusted model		
	$\beta$ value	OR (95% CI)	P value	$\beta$ value	OR (95% CI)	P value
<i>MT-COX1Pos.1</i>	-0.06	0.95 (0.91–0.98)	< 0.001	-0.05	0.95 (0.92–0.99)	0.01
<i>MT-COX1Pos.2</i>	0.01	0.99 (0.94–1.03)	0.58	-0.04	0.96 (0.91–1.01)	0.12
<i>MT-COX1</i>	-0.05	0.95 (0.91–1.00)	0.03	-0.06	0.95 (0.90–0.99)	0.03
<i>MT-COX2</i>	-0.03	0.98 (0.93–1.03)	0.33	-0.04	0.96 (0.90–1.02)	0.17
<i>MT-COX3Pos.1</i>	0.13	1.14 (1.02–1.29)	0.03	-0.06	0.94 (0.82–1.08)	0.38
<i>MT-COX3Pos.2</i>	-0.06	0.95 (0.84–1.07)	0.37	-0.12	0.89 (0.77–1.03)	0.12
<i>MT-COX3</i>	0.06	1.06 (0.93–1.20)	0.39	-0.11	0.90 (0.76–1.05)	0.19
<i>MT-ATP6Pos.1</i>	-0.03	0.97 (0.94–1.01)	0.13	-0.01	0.99 (0.96–1.03)	0.72
<i>MT-ATP6Pos.2</i>	-0.03	0.97 (0.92–1.02)	0.25	-0.05	0.95 (0.90–1.01)	0.12
<i>MT-ATP6Pos.3</i>	-0.02	0.99 (0.96–1.01)	0.29	-0.01	0.99 (0.96–1.02)	0.62
<i>MT-ATP6</i>	-0.03	0.97 (0.93–1.01)	0.16	-0.02	0.98 (0.94–1.03)	0.44
<i>MT-ATP8Pos.1</i>	-0.06	0.94 (0.89–0.99)	0.01	-0.02	0.98 (0.93–1.03)	0.42
<i>MT-ATP8Pos.2</i>	-0.07	0.93 (0.89–0.98)	< 0.001	-0.04	0.96 (0.92–1.02)	0.16
<i>MT-ATP8</i>	-0.08	0.93 (0.88–0.98)	< 0.001	-0.04	0.97 (0.91–1.02)	0.22

**Note.** Adjusted model: adjusted for age, gender, BMI, smoking, drinking, exercise, hypertensive treatment, FBG, TC, and TG.