Supplemental Material

Decreased mitochondrial D-loop region methylation mediates an increase in mitochondrial DNA copy number in CADASIL

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Table S1. The sequence of primer for mtDNAcn detection

Name	**Sequence (5'to3')**
SERPINA1 F	CAGTGAATAAATGAGGCGTACATCC
SERPINA1 R	GACTGTTTCTCATGCCTCTGGAAAG
SLCO2B1 F	CCTGATGCCTAGGTTTCTTTTCTTG
SLCO2B1 R	GGTCATCTGCCTACCCTAGAAC
MTND1 F	TACGGGCTACTACAACCCTTC
MTND1 R	ATGGTAGATGTGGCGGGTTT
MTND5 F	CATTACTAACAACATTTCCCCCGC
MTND5 R	GGCTGTGAGTTTTAGGTAGAGGG

Table S2. The associations between CADASIL and mtDNAcn in different adjusted models

	mtDNAcn	
	β(95%*CI*)	*P*
Total		
Model 1	-1.49(-2.08,-0.89)	<0.001
Model 2	-1.45(-2.04,-0.85	<0.001
Model 3	-1.45(-2.04,-0.85)	<0.001
Model 4	-1.48(-2.06,-0.90)	<0.001
Model 5	-1.48(-2.06,-0.90)	<0.001
Model 6	-1.46(-2.04,-0.87)	<0.001
Male		
Model 1	-0.90(-1.61,-0.18)	0.015
Model 2	-0.85(-1.57,-0.14)	0.019
Model 3	-0.88(-1.60,-0.16)	0.017
Female		
Model 1	-2.72(-3.70,-1.74)	<0.001
Model 2	-2.70(-3.68,-1.72)	<0.001
Model 3	-2.86(-3.88,-1.84)	<0.001

Model 1: adjust for age
Model 2: adjust for hypertension, diabetes mellitus, dyslipidemia
Model 3: adjust for age, hypertension, diabetes mellitus, dyslipidemia
Model 4: adjust for gender
Model 5: adjust for age, gender
Model 6: adjust for hypertension, diabetes mellitus, dyslipidemia

Table S3. The associations between CADASIL and D-loop methylation levels in different adjusted models

	D-loop methylation (%)	
	β(95%*CI*)	*P*
Total		
Model 1	38.44(31.48,45.39)	<0.001
Model 2	38.63(31.68,45.58)	<0.001
Model 3	38.61(31.66,45.57)	<0.001
Model 4	38.55(31.70,45.40)	<0.001
Model 5	38.57(31.73,45.41)	<0.001
Model 6	38.55(31.69,45.41)	<0.001
Male		
Model 1	33.92(25.20,42.63)	<0.001
Model 2	34.39(25.90,42.88)	<0.001
Model 3	34.41(25.80,43.02)	<0.001
Female		
Model 1	48.83(37.45,60.21)	<0.001
Model 2	46.44(35.09,57.78)	<0.001
Model 3	48.47(36.65,60.29)	<0.001

Model 1: adjust for age

Model 2: adjust for hypertension, diabetes mellitus, dyslipidemia

Model 3: adjust for age, hypertension, diabetes mellitus, dyslipidemia

Model 4: adjust for gender

Model 5: adjust for age, gender

Model 6: adjust for gender, hypertension, diabetes mellitus, dyslipidemia

Table S4. The associations between mtDNAcn and D-loop methylation levels in different adjusted models

	mtDNAcn	
	β(95%*CI*)	*P*
Total		
Model 1	-5.21(-7.30,-3.13)	<0.001
Model 2	-5.24(-7.31,-3.17)	<0.001
Model 3	-5.25(-7.32,-3.18)	<0.001
Model 4	-5.72(-7.79,-3.65)	<0.001
Model 5	-5.77(-7.84,-3.70)	<0.001
Model 6	-5.72(-7.78,-3.67)	<0.001
Male		
Model 1	-4.25(-6.99,-1.50)	0.002
Model 2	-4.31(-7.04,-1.58)	0.002
Model 3	-4.32(-7.04,-1.60)	0.002
Female		
Model 1	-7.64(-10.69,-4.58)	<0.001
Model 2	-7.74(-10.66,-4.83)	<0.001
Model 3	-7.65(-10.56,-4.74)	<0.001

Model 1: adjust for age;
Model 2: adjust for hypertension, diabetes mellitus, dyslipidemia;
Model 3: adjust for age, hypertension, diabetes mellitus, dyslipidemia;
Model 4: adjust for gender;
Model 5: adjust for age, gender;
Model 6: adjust for gender, hypertension, diabetes mellitus, dyslipidemia.