Supplementary Table 1. Polymorhpic sites analyzed to assign Caucasic and American mtDNA haplogroups

Haplogroup	Polymorhpic sites												
	Caucasic						American						
	t7028c	a10398g	a12308g	t4216c	t14766c	g4580a	a663g	t12705c	a13263g	c10400t	c5178a	c6371t	del8281:8289 a(CCCCCTCTA)g
A	T	A	A	-	T	G	G	T	A	C	C	C	-
B	T	-	A	T	-	G	A	C	A	C	C	C	YES
C	T	A	A	T	T	G	A	T	G	T	C	C	NO
D	T	A	A	-	T	G	A	T	A	T	A	C	-
X	T	A	A	-	T	G	A	T	A	C	C	T	NO
H	C	A	A	T	C	G	A	C	A	C	C	C	NO
V	T	A	A	T	C	A	A	C	A	C	C	C	NO
HV*	T	A	A	T	C	G	A	C	A	C	C	C	NO
U	T	A	G	T	T	G	-	C	A	C	C	C	-
K	T	G	G	T	T	G	A	C	A	C	C	C	-
T	T	A	A	C	T	G	A	C	A	C	C	C	-
J	T	G	A	C	T	G	A	C	A	C	C	C	NO

Diagnostic SNP for each haplogroup

Supplementary Table 2. Primer sequences for polymerase chain reaction (PCR) and single base extension (SBE) reaction

Polymorphic site	PCR primer	SBE primer
mt663a>g	F: 5´- ACCAAACCCCAAAGACACCC -3´ R: 5´- GTGTGGCTAGGCTAAGCGTT -3´	5´- CCCATAAACAAATAGGTTTGGTCCT -3´
mt12705t>c	F: 5´- ACTGAGCCACAACCCAAACA -3´ R: 5´- CATCTGCTCGGGCGTATCAT -3´	5'- TGTTAGCGGTAACTAAGATTAGTATGGTAATTAGGAA -3'
mt13263a>g	F: 5´- GCTTAGGCGCTATCACCACT -3´ R: 5´- TCCTGCTAATGCTAGGCTGC -3´	5'- aaagactgactgactgactgactcccccCGTAGCCTTCTCCACTTCAAGTCA -3'
mt10400c>t	F: 5´- GCCCTACAAACAACTAACCTGC -3´ R: 5´- TGTAAATGAGGGGCATTTGGT -3´	5'- CTATGAGTGACTACAAAAAGGATTAGACTGAAC -3'
mt5178c>a	F: 5´- ACCAAACCCAGCTACGCAAA -3´ R: 5´- AGGAGGGTGATGGTGGCTAT -3´	5'- gactgactgactgactgactCCTACTACTATCTCGCACCTGAAACAAG -3'
mt6371c>t	F: 5´- CGTTTCCCCGCATAAACAAC -3´ R: 5´- GAAGGTGGTGTTGAGGTTGC -3´	5´- ttgactgactgactgactgactgactgaTTCTCCTTACACCTAGCAGGTGTCTC -3´
del8281:8289 a(ccccctcta)g	F: 5´- CCACTTTCACCGCTACACGA -3´ R: 5´- AGGATTGTGGGGGCAATGAA -3´	

PCR: polymerase chain reaction; F: forward; R: reverse; del: deletion; SBE: single base extension

Supplementary Table 3. Analysis of the interaction between obesity and mtDNA haplogroup A in patients with knee OA

Categories	Healthy (N=364)	OA (N=353)	Total (N=717)	B	OR	Interaction parameters		
							95% CI *	
No-obese + no-A (Ref)	170 (46.7)	138 (39.1)	308 (43.0)		1			
Obese + no-A	46 (12.6)	62 (17.6)	108 (15.1)	0.507	1.66	RERI 2.23	0.37	4.09
No-obese + Haplo A	124 (34.1)	81 (22.9)	205 (28.6)	-0.217	0.80	AP 0.60	0.34	0.87
Obese + Haplo A	24 (6.6)	72 (20.4)	96 (13.4)	1.307	3.70	S 5.80	0.95	35.35

Values are number of patients with percentage in parentheses; OR: odds ratio; B: regression coefficient; CI: confidence interval; (*) 95% CI calculated using Delta method by Hosmer & Lemeshow (1992); Ref: reference category; RERI: relative excess risk due to interaction; AP: attributable proportion due to interaction; S: synergy index

Supplementary Table 4. Frequency distribution of American mtDNA haplogroups between osteoarthritic patients and healthy controls stratified by obesity status excluding subjects from Mexico city

Obesity status	mtDNA haplogroup	Healthy (N=285)	OA (N=223)	p-value*	OR	95% CI
Obese (BMI≥30 Kg/m^2)	A	21 (35.0)	44 (57.1)	**0.010**	2.48	1.23 – 4.97
	B	11 (18.3)	8 (10.4)	0.182	0.51	0.19 – 1.38
	C	12 (20.0)	11 (14.3)	0.375	0.67	0.27 – 1.64
	D	7 (11.7)	1 (1.3)	**0.010**	0.10	0.01 – 0.83
	Others	9 (15.0)	13 (16.9)	0.766	1.15	0.46 – 2.91
Total		60	77			
No-obese (BMI<30 Kg/m^2)	A	95 (42.2)	49 (33.6)	0.094	0.69	0.45 – 1.07
	B	47 (20.9)	38 (26.0)	0.250	1.33	0.82 – 2.17
	C	36 (16.0)	24 (16.4)	0.911	1.03	0.59 – 1.82
	D	18 (8.0)	10 (6.8)	0.682	0.85	0.38 – 1.89
	Others	29 (12.9)	25 (17.1)	0.259	1.40	0.78 – 2.50
Total		225	146			

Values are number of patients with percentage in parentheses; BMI: body mass index; OR: odds ratio; CI: confidence interval; (*) statistical significance declared at p ≤0.01 (in bold) after Bonferroni correction

Supplementary Table 5. Multivariate logistic regression model to explore the effect of the interaction between obesity and mtDNA haplogroup A on the risk of knee OA excluding subjects from Mexico city

Variable	B	Adjusted OR	95% CI	p-value
Age	0.081	1.08	1.07 – 1.10	**<0.001**
Gender (female)	0.400	1.49	0.97 – 2.29	0.068
Obesity	0.433	1.54	0.84 – 2.83	0.161
mtDNA haplogroup A	-0.143	0.87	0.52 – 1.43	0.577
Obesity*mtDNA haplogroup A	1.265	3.54	1.42 – 8.86	**0.007**

BMI: body mass index; B: regression coefficient; OR: odds ratio; CI: confidence interval; statistical significance declared at p<0.05 (in bold)