SUPPLEMENT 1 – SEARCH TERMS

Search terms relating to "Mitochondrial Genetics"

Association analysis
Candidate gene
Circular DNA
Coding region
Copy number
Copy number variation
D-loop
Deep sequencing
Deletion
Displacement loop
DNA
DNA polymerase-gamma
DNA sequence
Electron transport chain
ETC
Gen* linkage
Gen* mapping
Gen* mutation
Gene expression
Gene expression profiling
Gene expression regulation
Gene frequency
Gene* profile
Gene regulatory network
Gene sequencing
Gene* variant
Genes
Genetic analysis
Genetic association
Genetic association study
Genetic background
Genetic defect
Genetic epidemiology
Genetic factor
Genetic influence
Genetic linkage
Genetic marker
Genetic polymorphism
Genetic predisposition to disease
Genetic stud*
Genetic susceptibility
Genetic techniqu*
Genetic test*
Genetic variation
Genetic*
Genome
Genome analysis
Genome-wide
Genome-wide association
Genomics
Haplotype
Heavy strand
HVR-1
HVR-2
Hypervariable
Hypervariable region
Hypervariable region-1
Hypervariable region-2
Insertion
Light strand
Messenger RNA
Microsatellite repeat
Mitochondrial DNA
Mitochondrial genome
Mitochondrial-encoded
Mitoribosome
mtDNA
Multifactorial inheritance
Mutation
Next generation sequencing
NGS
Non-coding region
Nucleotide sequencing
Organelle
Oxidative stress
PCR
Phenotype
Polygenic
Polymerase chain reaction
Polymorphism
Promoter region
Reactive oxygen species
Respiratory chain
Respiratory chain complex
ROS
Single nucleotide polymorphism
SNP
Southern blot
Tandem repeat
Transcript*
Transcription factor
Translation
Trinucleotide repeat
Western blot
Whole exome sequencing

Search terms relating to PCOS

Multicystic ovary
Polycystic ovary
PCO
PCOS
Polycystic disease of the ovary
Polycystic Ovarian Disease
Polycystic Ovarian Syndrome
Polycystic ovaries
Polycystic ovary disease
Polycystic ovary morphology
Polycystic Ovary Syndrome
POS
Stein-Leventhal Syndrome
Stein Leventhal Syndrome

SUPPLEMENT 2 – STUDIES INCLUDED IN SYSTEMATIC REVIEW

Table showing studies included in systematic review

	Study ID	Title of Publication	Location	Patient characteristics	Available at
INCLUDED IN META-ANALYSIS	**Hu et al. (2011)[14]**	Single Nucleotide Polymorphisms (SNPs) And Variable Number Tandem Repeats (VNTRs) In MtDNA D-Loop and CO II- tRNA Lys Intergenic Region With PCOS	China	Women aged 19-37 diagnosed with PCOS according to the revised 2003 Rotterdam Criteria and control group matched for age	http://dx.doi.org/10.1016/S1001-7844%2812%2960008-X
	Zhuo et al. (2012)[15]	Analysis of Mitochondrial DNA Sequence Variants in Patients with Polycystic Ovary Syndrome	China	Women 22-34 diagnosed with PCOS according to the revised 2003 Rotterdam Criteria and control group matched for age and BMI	https://dx.doi.org/10.1007/s00404-012-2358-7
	Ding et al. (2017)[18]	Mutations in Mitochondrial tRNA Genes May Be Related to Insulin Resistance in Women with Polycystic Ovary Syndrome	China	Women aged 18-37 diagnosed with insulin-resistant subtype PCOS according to the revised 2003 Rotterdam Criteria and control group matched for age and BMI	http://www.ajtr.org/files/ajtr0048638.pdf
	Reddy et al. (2019)[6]	Impact of Mitochondrial DNA Copy Number and Displacement Loop Alterations on Polycystic Ovary Syndrome Risk in South Indian Women	India	Women aged 22-36 diagnosed with PCOS according to the revised 2003 Rotterdam Criteria and control group matched for age and BMI	https://dx.doi.org/10.1016/j.mito.2017.12.010
	Saeed et al. (2019)[20]	Polycystic Ovary Syndrome Dependency on MtDNA Mutation; Copy Number and Its Association with Insulin Resistance	Iraq	Women aged 20-30 diagnosed with both diabetes and PCOS according to the revised 2003 Rotterdam Criteria and diabetic control group matched for age	https://dx.doi.org/10.1186/s13104-019-4453-3
	Shukla et al. (2020)[22]	Identification of Variants in Mitochondrial D-Loop and OriL Region and Analysis of Mitochondrial DNA Copy Number	India	Women aged 15-40 diagnosed with PCOS according to the	https://dx.doi.org/10.1

		in Women with Polycystic Ovary Syndrome		revised 2003 Rotterdam Criteria and control group matched for age	089/dna.2019.5323
	Wang et al. (2020)[23]	The Effects of Mitochondrial Dysfunction on Energy Metabolism Switch By HIF-1α Signaling in Granulosa Cells of Polycystic Ovary Syndrome	China	Women aged 21-33 diagnosed with PCOS according to the revised 2003 Rotterdam Criteria and control group matched for age	http://dx.doi.org/10.5603/EP.a2020.0002
	Deng et al. (2021)[33]	Polymorphisms and Haplotype of Mitochondrial DNA D-Loop Region Are Associated with Polycystic Ovary Syndrome in A Chinese Population	China	Women aged 24-31 diagnosed with PCOS according to the revised 2003 Rotterdam Criteria and control group matched for age	http://dx.doi.org/10.1016/j.mito.2020.12.006
INSUFFICIENT DATA FOR META-ANALYSIS	**Zhuo et al. (2010)[16]**	A 9-Bp Deletion Homoplasmy In Women with Polycystic Ovary Syndrome Revealed by Mitochondrial Genome-Mutation Screen	China	Women diagnosed with PCOS according to the revised 2003 Rotterdam Criteria and control group matched for age and BMI	https://dx.doi.org/10.1007/s10528-009-9308-5
	Lee et al. (2011)[43]	Mitochondrial DNA Copy Number in Peripheral Blood in Polycystic Ovary Syndrome	Korea	Women aged 24-33 diagnosed with PCOS according to the revised 2003 Rotterdam Criteria and control group matched for age and BMI	https://dx.doi.org/10.1016/j.metabol.2011.04.010
	Rabol et al. (2011)[49]	Skeletal Muscle Mitochondrial Function in Polycystic Ovarian Syndrome	Denmark	Lean and obese women aged 26-33 diagnosed with PCOS according to the revised 2003 Rotterdam Criteria and lean and obese control groups matched for age and BMI	https://dx.doi.org/10.1530/EJE-11-0419
	Ding et al. (2016a)[21]	The Mitochondrial tRNALeu (UUR) A3302G Mutation May Be Associated with Insulin Resistance in Women with Polycystic Ovary Syndrome	China	First and second generation family members of a Han	https://dx.doi.org/10.1177/19337191156027

				Chinese family with maternally inherited insulin resistance	77
	Ding et al. (2016b)[19]	Point Mutation in Mitochondrial tRNA Gene Is Associated with Polycystic Ovary Syndrome and Insulin Resistance	China	A female patient (age, 31 years) diagnosed with PCOS according to the revised 2003 Rotterdam Criteria and control group matched for age	https://dx.doi.org/10.3892/mmr.2016.4916
	Ding et al. (2018)[17]	Mitochondrial TRNALeu (UUR) C3275T, TRNAGln T4363C And TRNALys A8343G Mutations May Be Associated with PCOS And Metabolic Syndrome	China	Three-generation pedigree with maternally transmitted Metabolic syndrome, including a case of PCOS diagnosed according to the revised 2003 Rotterdam Criteria and control group matched for age and BMI	https://dx.doi.org/10.1016/j.gene.2017.11.049
	Yang et al. (2020)[50]	Changes in Peripheral Mitochondrial DNA Copy Number in Women with Polycystic Ovary Syndrome: A Longitudinal Study	Taiwan	Women aged 20-28 diagnosed with PCOS according to the revised 2003 Rotterdam Criteria treated with Metformin for 1 year	http://dx.doi.org/10.1186/s12958-020-00629-5

SUPPLEMENT 3 – POLYMORPHISMS IN CODING REGIONS OF THE MITOCHONDRIAL GENOME

Study ID	Gene	Position
Zhuo 2010	A6	8584
Zhuo 2010	A6	8701
Zhuo 2010	A6	8745
Zhuo 2010	A6	8794
Zhuo 2010	A6	9053
Zhuo 2010	A6	9101
Zhuo 2010	A6	9128
Zhuo 2010	A6	9180
Zhuo 2012	A6	8584
Zhuo 2012	A6	8684
Zhuo 2012	A6	8745
Zhuo 2012	A6	8793
Zhuo 2012	A6	8860
Zhuo 2012	A6	9053
Zhuo 2012	A6	9126
Zhuo 2012	A6	9128
Ding 2016	A6	8585
Ding 2016	A6	8860
Ding 2017	A6	8584
Ding 2017	A6	8684
Zhuo 2010	A8	8392
Zhuo 2010	A8	8414
Zhuo 2010	A8	8459
Zhuo 2010	A8	8473
Zhuo 2012	A8	8392
Zhuo 2012	A8	8414
Zhuo 2012	A8	8459
Zhuo 2012	A8	8473
Ding 2016	A8	8414
Zhuo 2010	COX1	6392
Zhuo 2010	COX1	6962
Ding 2016	COX1	6392
Ding 2016	COX1	7028
Ding 2018	COX1	7028
Zhuo 2012	COX2	6221
Zhuo 2012	COX2	6272
Zhuo 2012	COX2	6338
Zhuo 2012	COX2	6392
Zhuo 2012	COX2	6455
Zhuo 2012	COX2	6962
Zhuo 2012	COX2	7028
Zhuo 2012	COX2	7142
Zhuo 2010	COX2	7853
Ding 2016	COX2	8020

Study ID	Gene	Position
Zhuo 2010	COX3	9536
Zhuo 2010	COX3	9540
Zhuo 2010	COX3	9548
Zhuo 2010	COX3	9824
Zhuo 2012	COX3	9242
Zhuo 2012	COX3	9336
Zhuo 2012	COX3	9377
Zhuo 2012	COX3	9540
Zhuo 2012	COX3	9559
Zhuo 2012	COX3	9824
Ding 2016	COX3	9540
Ding 2016	COX3	9824
Zhuo 2010	CYTB	14783
Zhuo 2010	CYTB	15038
Zhuo 2010	CYTB	15043
Zhuo 2010	CYTB	15244
Zhuo 2010	CYTB	15346
Zhuo 2010	CYTB	15301
Zhuo 2012	CYTB	14783
Zhuo 2012	CYTB	15043
Zhuo 2012	CYTB	15244
Zhuo 2012	CYTB	15301
Zhuo 2012	CYTB	15326
Zhuo 2012	CYTB	15460
Zhuo 2012	CYTB	15724
Ding 2016	CYTB	14766
Ding 2016	CYTB	15301
Ding 2016	CYTB	15326
Ding 2018	CYTB	14766
Ding 2018	CYTB	15326
Ding 2018	CYTB	15535
Zhuo 2010	ND1	3316
Zhuo 2010	ND1	3394
Zhuo 2010	ND1	3497
Zhuo 2010	ND1	3970
Zhuo 2010	ND1	4086
Zhuo 2010	ND1	4248
Zhuo 2012	ND1	3316
Zhuo 2012	ND1	3394
Zhuo 2012	ND1	3423
Zhuo 2012	ND1	3497
Zhuo 2012	ND1	3552
Zhuo 2012	ND1	3834
Zhuo 2012	ND1	3970

Study ID	Gene	Position
Zhuo 2012	ND1	4086
Ding 2016	ND1	3553
Ding 2016	ND1	4047
Ding 2017	ND1	3394
Zhuo 2010	ND2	5147
Zhuo 2010	ND2	5178
Zhuo 2010	ND2	5301
Zhuo 2010	ND2	5417
Zhuo 2010	ND2	5460
Zhuo 2012	ND2	4688
Zhuo 2012	ND2	4769
Zhuo 2012	ND2	4883
Zhuo 2012	ND2	5046
Zhuo 2012	ND2	5108
Zhuo 2012	ND2	5147
Zhuo 2012	ND2	5178
Zhuo 2012	ND2	5231
Zhuo 2012	ND2	5263
Zhuo 2012	ND2	5301
Zhuo 2012	ND2	5417
Zhuo 2012	ND2	5460
Ding 2018	ND2	4715
Ding 2018	ND2	4820
Zhuo 2010	ND3	10310
Zhuo 2010	ND3	10397
Zhuo 2010	ND3	10398
Zhuo 2010	ND3	10400
Zhuo 2012	ND3	10097
Zhuo 2012	ND3	10238
Zhuo 2012	ND3	10310
Zhuo 2012	ND3	10398
Zhuo 2012	ND3	10400
Ding 2016	ND3	10398
Ding 2016	ND3	10400
Zhuo 2012	ND4	10873
Zhuo 2012	ND4	10915
Zhuo 2012	ND4	11084
Zhuo 2012	ND4	11335
Zhuo 2012	ND4	11440
Zhuo 2012	ND4	11719
Zhuo 2012	ND4	11944
Zhuo 2012	ND4	12026

Study ID	Gene	Position
Zhuo 2010	ND4	10609
Zhuo 2010	ND4	10873
Zhuo 2010	ND4	11084
Zhuo 2010	ND4	11914
Zhuo 2010	ND4	11944
Zhuo 2010	ND4	12026
Ding 2016	ND4	10873
Ding 2016	ND4	11719
Ding 2018	ND4	11719
Zhuo 2010	ND5	12406
Zhuo 2010	ND5	12705
Zhuo 2010	ND5	12882
Zhuo 2010	ND5	13759
Zhuo 2010	ND5	13824
Zhuo 2010	ND5	13928
Zhuo 2010	ND5	13942
Zhuo 2010	ND5	14067
Zhuo 2012	ND5	12406
Zhuo 2012	ND5	12705
Zhuo 2012	ND5	12811
Zhuo 2012	ND5	13145
Zhuo 2012	ND5	13263
Zhuo 2012	ND5	13434
Zhuo 2012	ND5	13708
Zhuo 2012	ND5	13759
Zhuo 2012	ND5	13928
Ding 2016	ND5	12705
Ding 2016	ND5	13928
Ding 2018	ND5	13928
Ding 2017	ND5	12811
Ding 2016	ND5	12338
Zhuo 2010	ND6	14668
Zhuo 2012	ND6	14199
Zhuo 2012	ND6	14272
Zhuo 2012	ND6	14365
Zhuo 2012	ND6	14569
Zhuo 2012	ND6	14668
Ding 2018	ND6	14470

SUPPLEMENT 4 - POLYMORPHISMS IN GENES CODING FOR MITOCHONDRIAL tRNAs

All polymorphisms detected in genes coding for mt-tRNAs

Study ID	Gene	Position	PCOS sample size	PCOS with SNP	PCOS without SNP	Frequency in PCOS (%)	Control sample size	Controls with SNP	Controls without SNP	Frequency in Controls (%)
Zhuo 2012	tRNA Arg	10454	57	1	56	1.7	38	0	38	0
Ding 2017	tRNA Arg	10454	80	2	78	2.5	50	0	50	0
Zhuo 2012	tRNA Asp	7543	57	1	56	1.7	38	0	38	0
Ding 2017	tRNA Asp	7543	80	1	79	1.25	50	0	50	0
Zhuo 2012	tRNA Cys	5821	57	1	56	1.7	38	0	38	0
Ding 2017	tRNA Cys	5821	80	3	77	3.75	50	1	49	2
Zhuo 2010	tRNA Gln	14693	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Ding 2018	tRNA Gln	4363	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Ding 2017	tRNA Gln	4363	80	4	76	5	50	0	50	0
Ding 2017	tRNA Gln	4395	80	1	79	1.25	50	0	50	0
Zhuo 2012	tRNA Glu	4395	57	17	40	29.8	38	0	38	0
Ding 2017	tRNA Glu	14693	80	1	79	1.25	50	0	50	0
Ding 2017	tRNA Met	4454	80	0	80	0	50	2	48	4
Ding 2016	tRNA Leu	3302	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Ding 2018	tRNA Leu	3275	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Ding 2017	tRNA Leu	3302	80	1	79	1.25	50	0	50	0
Ding 2017	tRNA Leu	3275	80	2	78	2.5	50	0	50	0
Saeed 2019	tRNA Leu	3157	70	2	68	2.86	59	0	59	0
Saeed 2019	tRNA Leu	3162	70	0	70	0	59	0	59	0
Saeed 2019	tRNA Leu	3203	70	3	67	4.29	59	1	58	1.69
Saeed 2019	tRNA Leu	3282	70	2	68	2.86	59	0	59	0
Saeed 2019	tRNA Leu	3285	70	2	68	2.86	59	0	59	0
Saeed 2019	tRNA Leu	3302	70	2	68	2.86	59	0	59	0
Saeed 2019	tRNA Leu	3275	70	4	66	5.71	59	0	59	0

Saeed 2019	tRNA Leu	4225	70	1	69	1.43	59	0	59	0
Saeed 2019	tRNA Leu	5206	70	3	67	4.29	59	0	59	0
Saeed 2019	tRNA Leu	8434	70	1	69	1.43	59	3	56	5.08
Zhuo 2012	tRNA Lys	8343	57	1	56	1.7	38	0	38	0
Ding 2018	tRNA Lys	8343	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Ding 2017	tRNA Lys	8343	80	2	78	2.5	50	0	50	0
Ding 2017	tRNA Ser	7492	80	1	79	1.25	50	0	50	0
Ding 2016	tRNA Ser	7492	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Ding 2017	tRNA Thr	15900	80	0	80	0	50	1	49	2

Dataset used in meta-analysis

Mitochondrial-encoded tRNA	Frequency of SNP in PCOS (%)	Frequency of SNP in Control (%)
Cys	2.9	1.1
Leu	2.7	0.6
Glu	13.1	0.0
Gln	3.1	0.0
Lys	2.2	0.0
Arg	1.9	0.0
Asp	1.5	0.0

SUPPLEMENT 5 – POLYMORPHISMS IN GENES CODING FOR MITOCHONDRIAL rRNAs

Study ID	Gene	Position
Zhuo 2010	12S rRNA	663
Zhuo 2010	12S rRNA	709
Zhuo 2010	12S rRNA	752
Zhuo 2010	12S rRNA	827
Zhuo 2010	12S rRNA	1438
Zhuo 2012	12S rRNA	663
Zhuo 2012	12S rRNA	709
Zhuo 2012	12S rRNA	750
Zhuo 2012	12S rRNA	752
Zhuo 2012	12S rRNA	827
Zhuo 2012	12S rRNA	1382
Zhuo 2012	12S rRNA	1438
Ding 2016	12S rRNA	750
Ding 2016	12S rRNA	1438
Ding 2018	12S rRNA	750
Ding 2018	12S rRNA	827
Ding 2018	12S rRNA	1438
Zhuo 2010	16S rRNA	1736
Zhuo 2010	16S rRNA	3010
Zhuo 2012	16S rRNA	1736
Zhuo 2012	16S rRNA	2706
Zhuo 2012	16S rRNA	3010
Ding 2016	16S rRNA	1734
Ding 2016	16S rRNA	2706
Ding 2018	16S rRNA	2706
Ding 2018	16S rRNA	3109

SUPPLEMENT 6 – POLYMORPHISMS IN THE D-LOOP OF THE MITOCHONDRIAL GENOME

All polymorphisms detected in the D-Loop of the mitochondrial genome

Study ID	Polymorphism	PCOS sample size	PCOS with SNP	PCOS without SNP	Frequency in PCOS (%)	Control sample size	Control with SNP	Control without SNP	Frequency in controls (%)
Zhuo 2012	A73G	57	10	47	17.5	38	8	30	21.6
Zhuo 2012	T146C	57	1	56	1.7	38	1	37	2.7
Zhuo 2012	C150T	57	6	51	10.5	38	3	35	8.1
Zhuo 2012	A153G	57	4	53	7.0	38	2	36	5.4
Zhuo 2012	T195A	57	5	52	8.7	38	2	36	5.4
Zhuo 2012	A235G	57	3	54	5.3	38	2	36	5.4
Zhuo 2012	A263G	57	8	49	14.0	38	7	31	18.9
Zhuo 2012	G316A	57	1	56	1.7	38	0	38	0
Zhuo 2012	T489A	57	4	53	7.0	38	3	35	8.1
Zhuo 2012	G16129A	57	2	55	3.5	38	2	36	5.4
Zhuo 2012	T16140C	57	3	54	5.3	38	0	38	0
Zhuo 2012	T16189C	57	6	51	10.5	38	4	34	10.8
Zhuo 2012	C16223T	57	9	48	15.8	38	2	36	5.4
Zhuo 2012	A16316G	57	6	51	10.5	38	5	33	13.5
Zhuo 2012	T16357C	57	1	56	1.7	38	0	38	0
Zhuo 2012	T16519C	57	2	55	3.5	38	1	37	2.7
Reddy 2019	A73G	118	75	43	63.6	114	75	39	65.8
Reddy 2019	A93G	118	7	111	5.9	114	4	110	3.5
Reddy 2019	T146C	118	8	110	6.8	114	12	102	10.5
Reddy 2019	T152C	118	23	95	19.5	114	23	91	20.2
Reddy 2019	A189G	118	31	87	26.3	114	15	99	13.2
Reddy 2019	T195A	118	8	110	6.8	114	7	107	6.1
Reddy 2019	A263G	118	72	46	61.0	114	76	38	66.7
Reddy 2019	316C	118	71	47	60.1	114	68	46	59.6
Reddy 2019	T489C	118	25	93	21.2	114	14	100	12.3
Reddy 2019	522CA	118	15	103	12.7	114	7	107	6.1

Reddy 2019	G16129A	118	9	109	7.6	114	11	103	9.6
Reddy 2019	T16172C	118	10	108	8.5	114	11	103	9.6
Reddy 2019	T16189C	118	14	104	11.9	114	15	99	13.2
Reddy 2019	C16223T	118	44	74	37.3	114	52	62	45.6
Reddy 2019	T16311C	118	13	105	11.0	114	16	98	14.0
Reddy 2019	G16319A	118	12	106	10.2	114	5	109	4.4
Reddy 2019	T16362C	118	14	104	11.9	114	8	106	7.0
Reddy 2019	T16519C	118	63	55	53.4	114	54	60	47.4
Reddy 2019	D310	118	64	54	54.2	114	33	81	28.9
Deng 2021	C150T	421	79	342	18.76	409	103	306	25.18
Deng 2021	G207A	421	11	410	2.61	409	28	381	6.85
Deng 2021	A263G	421	418	3	99.29	409	399	10	97.56
Deng 2021	16036G	421	24	397	5.70	409	42	367	10.27
Deng 2021	16036GG	421	2	419	0.48	409	22	387	5.38
Deng 2021	16049G	421	2	419	0.48	409	36	373	8.80
Deng 2021	C16234T	421	17	404	4.04	409	30	379	7.33
Deng 2021	T16362C	421	169	252	40.14	409	196	213	47.92
Hu 2011	16094T/C	77	7	70	9.09	45	4	41	8.89
Hu 2011	C16173T	77	67	10	87.01	45	38	7	84.40
Hu 2011	16181 – 16195	77	76	1	98.70	45	44	1	97.78
Hu 2011	A2C12	77	6	71	7.89	45	1	44	2.27
Hu 2011	A3C11	77	9	68	11.84	45	8	37	18.18
Hu 2011	A4C9T	77	48	29	63.16	45	31	14	70.45
Hu 2011	A4C8T2	77	13	64	17.11	45	4	41	9.09
Hu 2011	T16225C	77	24	53	31.17	45	14	31	31.11
Hu 2011	T16300C	77	9	68	11.69	45	8	37	17.78
Hu 2011	T16306C	77	10	67	12.99	45	4	41	8.89
Hu 2011	T16313C	77	10	67	12.99	45	7	38	15.56
Hu 2011	G16321A	77	9	68	11.69	45	8	37	17.78
Hu 2011	T16364C	77	28	49	36.36	45	18	27	40.00

Hu 2011	T146C	77	9	68	11.69	45	5	40	11.11
Hu 2011	C150T	77	62	15	80.52	45	39	6	80.00
Hu 2011	T152C	77	19	58	24.68	45	9	36	20.00
Hu 2011	C195T	77	66	11	85.71	45	42	3	93.33
Hu 2011	A248	77	17	60	22.08	45	9	36	20.00
Hu 2011	T491C	77	48	29	62.34	45	22	23	48.89
Hu 2011	303-317	77	76	1	98.70	45	44	1	97.78
Hu 2011	C8TC6	77	41	36	53.95	45	18	27	40.91
Hu 2011	C9TC6	77	11	66	14.47	45	5	40	11.36
Hu 2011	C7TC6	77	24	53	31.58	45	21	24	47.73
Zhuo 2010	T146C	-	-	-	-	-	-	-	-
Zhuo 2010	T150C	-	-	-	-	-	-	-	-
Zhuo 2010	T152C	-	-	-	-	-	-	-	-
Zhuo 2010	C195T	-	-	-	-	-	-	-	-
Zhuo 2010	A200G	-	-	-	-	-	-	-	-
Zhuo 2010	G207A	-	-	-	-	-	-	-	-
Zhuo 2010	A235G	-	-	-	-	-	-	-	-
Zhuo 2010	A263G	-	-	-	-	-	-	-	-
Zhuo 2010	T489C	-	-	-	-	-	-	-	-
Zhuo 2010	G16129A	-	-	-	-	-	-	-	-
Zhuo 2010	T16172C	-	-	-	-	-	-	-	-
Zhuo 2010	T16189C	-	-	-	-	-	-	-	-
Zhuo 2010	C16223T	-	-	-	-	-	-	-	-
Zhuo 2010	C16290T	-	-	-	-	-	-	-	-
Zhuo 2010	G16319A	-	-	-	-	-	-	-	-
Zhuo 2010	T16362C	-	-	-	-	-	-	-	-
Zhuo 2010	T16519C	-	-	-	-	-	-	-	-
Ding 2016	A73G	-	-	-	-	-	-	-	-
Ding 2016	T152C	-	-	-	-	-	-	-	-
Ding 2016	D310	-	-	-	-	-	-	-	-

Ding 2016	T16189C	-	-	-	-	-	-	-	-
Ding 2016	T16519C	-	-	-	-	-	-	-	-
Ding 2018	A73G	-	-	-	-	-	-	-	-
Ding 2018	C150T	-	-	-	-	-	-	-	-
Ding 2018	C328T	-	-	-	-	-	-	-	-
Ding 2018	T16142C	-	-	-	-	-	-	-	-
Ding 2018	T16189C	-	-	-	-	-	-	-	-
Ding 2018	T16224C	-	-	-	-	-	-	-	-

Dataset used in meta-analysis

Polymorphism	Study ID	PCOS sample size	PCOS with SNP	PCOS without SNP	Frequency in PCOS (%)	Control sample size	Control with SNP	Control without SNP	Frequency in controls (%)
C150T	Hu 2011	77	62	15	80.52	45	39	6	80.00
	Zhuo 2012	57	6	51	10.5	38	3	35	8.1
	Deng 2021	421	79	342	18.76	409	103	306	25.18
T146C	Hu 2011	77	9	68	11.69	45	5	40	11.11
	Zhuo 2012	57	1	56	1.7	38	1	37	2.7
	Reddy 2019	118	8	110	6.8	114	12	102	10.5
A263G	Zhuo 2012	57	8	49	14.0	38	7	31	18.9
	Reddy 2019	118	72	46	61.0	114	76	38	66.7
	Deng 2021	421	418	3	99.29	409	399	10	97.56

SUPPLEMENT 7 – MtDNA COPY NUMBERS

	Study ID	Cells	Total Sample Size (n)	PCOS Sample Size	Control Sample Size	PCOS Log (mean mt CN)	Control Log (mean mt CN)	PCOS SEM	Control SEM	PCOS SD	Control SD
Included in meta-analysis	Ding et al. 2017	Blood	130	80	50	0.29	0.84	0.31	0.88	0.44	0.79
	Reddy et al. 2019	Blood	232	118	114	1.36	1.50	0.44	0.56	4.78	5.98
	Shukla et al. 2020	Blood	60	30	30	1.22	1.64	0.33	0.35	1.81	1.92
	Wang et al. 2020	Granulosa	107	39	68	0.761	1.021	0.05	0.06	0.31	0.49
Insufficient data for meta-analysis	Lee et al. 2011	Blood	110	50	60	1.44	1.88	-	-	-	-
	Ding et al. 2016	Blood	-	-	-	-	-	-	-	-	-
	Ding et al. 2018	Blood	-	-	-	-	-	-	-	-	-
	Saeed et al. 2019	Blood	63	38	25	0.88	1.00	-	-	-	-
	Yang et al. 2020	Blood	88	0	-	-	-	-	-	-	-

SUPPLEMENT 8 – QUALITY ASSESSMENT SCORES

Study ID	Rationale for study	Selection and definition of outcome of interest	Selection and comparability of comparison group	Technical classification of the exposure	Non-technical classification of the exposure	Other sources of bias	Sample size and power	A priori planning of analyses	Statistical methods and control for confounding	Testing of assumptions and inferences for genetic analyses	Appropriateness of inferences drawn from results	Total score	Quality status
Zhuo 2010	5	4	4	3	1	1	2	2	1	3	3	29	Poor
Hu 2011	4	3	4	5	3	3	2	5	6	4	3	42	Moderate
Lee 2011	6	5	6	6	5	7	2	5	6	6	6	60	Good
Rabol 2011	7	4	5	3	2	1	1	5	3	4	5	40	Moderate
Zhuo 2012	6	5	5	3	3	2	2	3	5	5	4	43	Moderate
Ding 2016a	2	2	2	2	1	2	1	2	1	3	1	19	Poor
Ding 2016b	1	2	1	1	1	1	1	2	1	1	1	13	Poor
Ding 2017	6	6	6	6	6	2	3	6	4	7	6	58	Good
Ding 2018	3	2	2	3	1	2	1	3	2	4	2	25	Poor
Reddy 2019	7	6	7	7	7	3	3	7	7	6	3	63	Good
Saeed 2019	4	2	4	6	4	3	2	6	5	1	2	39	Moderate
Yang 2020	7	2	-	6	3	6	2	7	5	5	6	49	Good
Shukla 2020	6	3	6	6	3	1	2	5	2	5	5	44	Moderate
Wang 2020	5	4	4	7	3	1	1	4	3	5	5	42	Moderate
Deng 2021	7	3	5	3	3	1	4	7	7	6	4	50	Good
Median	6	3	4	5	3	2	2	5	4	5	4		
Q1	4	2	2	3	1	1	1	3	2	3	2		
Q3	7	5	6	6	4	3	2	6	6	6	5		
IQR	4-7	2-5	2-6	3-6	1-4	1-3	1-2	3-6	2-6	3-6	2-5		