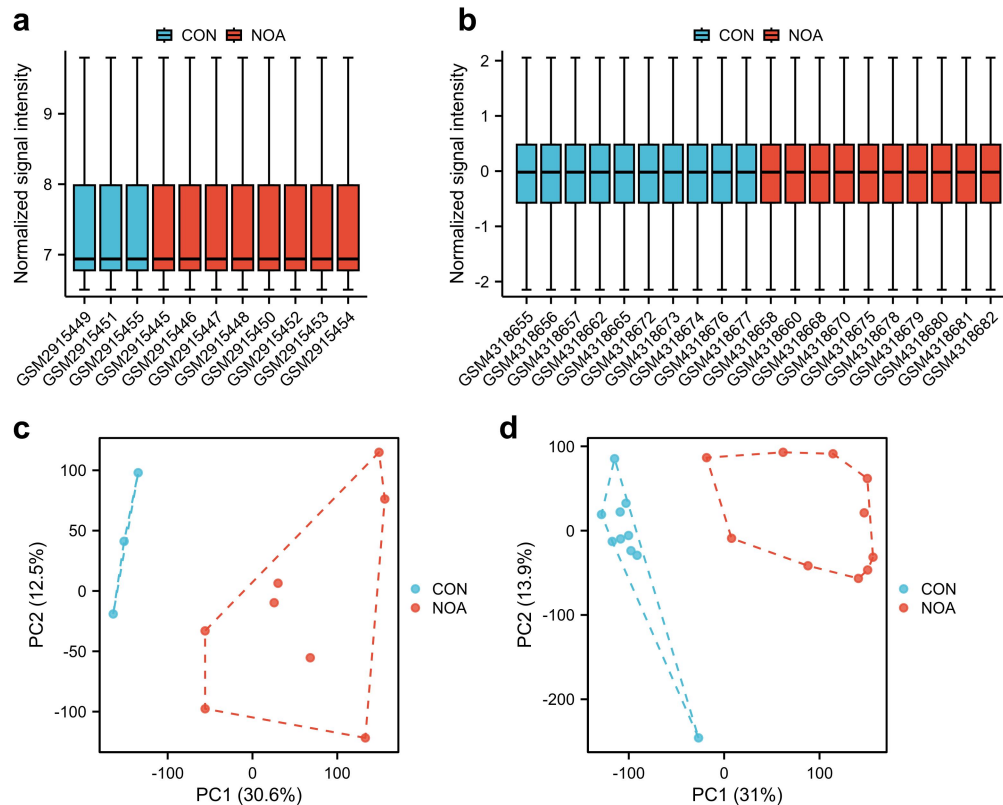
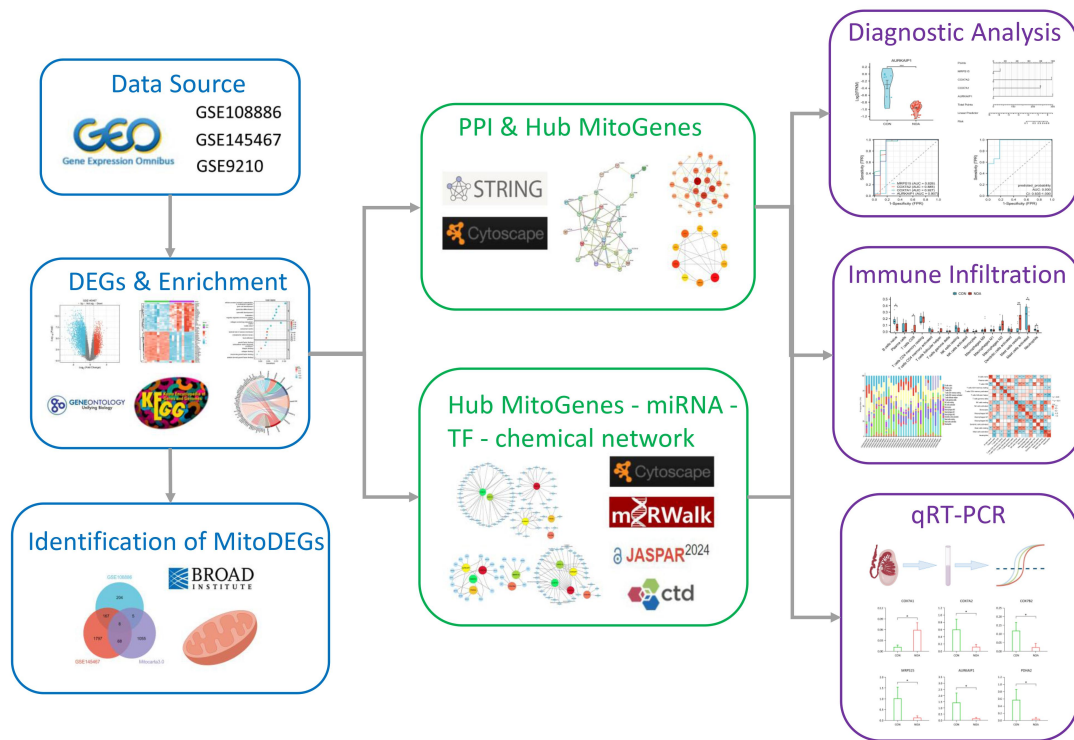


Integrative bioinformatics analyses of mitochondrial dysfunction-related genes in human non-obstructive azoospermia



Supplementary Fig. S1. Box plots and Principal Component Analysis of samples in GSE108886 and GSE145467. In the box plots for GSE 108886 (a) and GSE145467 (b), the x-axis represented the sample symbol and the y-axis represented the normalized gene expression value. In the Principal Component Analysis for GSE108886 (c) and GSE145467 (d), the x-axis and y-axis represented Principal Component 1 and Principal Component 2, respectively. And the distances between the points reflected the differences among samples. CON, control; NOA, non-obstructive azoospermia.



Supplementary Fig. S2. The workflow chart of data processing, analysis and validation.

18 **Supplementary Table S1.** Summary of hub genes, their enriched signaling pathways,
19 and predicted regulators.

Hub genes	Targeting miRNAs	Bingding TFs	Enrichment pathways
COX7A1	hsa-miR-6848-3p hsa-miR-650 hsa-miR-6789-5p hsa-miR-5008-5p hsa-miR-431-3p hsa-miR-657 hsa-miR-6769a-3p hsa-miR-6824-3p hsa-miR-3677-3p hsa-miR-7703, et al	FOXC1, YY1, MEF2A, FOXA1	• Regulation of ATP metabolic process • Regulation of oxidative phosphorylation • Regulation of aerobic respiration • Regulation of generation of precursor metabolites and energy
COX7A2	hsa-miR-4494 hsa-miR-6803-5p hsa-miR-4721 hsa-miR-3059-3p hsa-miR-4632-5p hsa-miR-6718-5p hsa-miR-4658 hsa-miR-6884-5p hsa-miR-769-3p hsa-miR-664b-5p, et al	ARID3A, FOXC1, GATA2, YY1, POU2F2, NFYA, SRF, GATA3	• Regulation of ATP metabolic process • Regulation of oxidative phosphorylation • Regulation of aerobic respiration • Regulation of generation of precursor metabolites and energy • Amyotrophic lateral sclerosis
COX7B2	hsa-miR-17-5p hsa-miR-106a-5p	SRY, FOXL1, HOXA5, NFIC	• Amyotrophic lateral sclerosis • Regulation of ATP metabolic process
MRPS15	hsa-miR-1286 hsa-miR-4664-3p hsa-miR-4726-5p hsa-miR-296-5p hsa-miR-659-3p hsa-miR-1296-5p hsa-miR-1972 hsa-miR-4269 hsa-miR-6846-3p hsa-miR-6834-3p, et al	NFIC, HNF4A, E2F1, SREBF1, EN1	• Regulation of oxidative phosphorylation
AURKAIP1	hsa-miR-4787-5p hsa-miR-4433b-3p hsa-miR-1908-5p hsa-miR-4701-3p hsa-miR-6769b-5p hsa-miR-6088 hsa-miR-7162-3p hsa-miR-6883-5p hsa-miR-21-3p hsa-miR-424-5p	SPIB, FOXC1, GATA2, PPARG, TP53, STAT1, ELK4, FOXA1	• Regulation of mitotic cell cycle • Regulation of oxidative phosphorylation
PDHA2	hsa-miR-5571-5p hsa-miR-216a-3p hsa-miR-3175 hsa-miR-448	BRCA1, GATA2, MEF2A, SRF, FOXA1	• Carbon metabolism • Glycolysis / Gluconeogenesis • Central carbon metabolism in cancer • Pyruvate metabolism • HIF-1 signaling pathway • Glucose metabolic process • Monosaccharide metabolic process • Hexose metabolic process

21 **Supplementary Table S2.** Demographic and clinical characteristics between NOA
 22 and OA patients.

Characteristics	NOA (n=3)	OA (n=3)	<i>P</i> value
Age (year)	31.67±2.40	33.33±6.01	0.809
BMI (Kg/m ²)	23.35±1.66	23.89±1.11	0.798
FSH (mIU/ml)	27.34±0.90	6.82±3.10	0.003
INB (pg/ml)	37.88±5.22	87.77±5.96	0.003
Testosterone (ng/ml)	3.45±0.33	4.52±0.95	0.038
Mean testicular volume (ml)	8.83±0.72	17.5±1.44	0.006
NAG (mU/ejaculate)	31.50±1.36	4.84±2.58	<0.001
Fructose (μmol/ejaculate)	32.83±6.16	37.43±7.64	0.664

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 24 Data are presented as mean ± standard error. NOA: non-obstructive azoospermia; OA:
 25 obstructive azoospermia; FSH: follicle-stimulating hormone; INH-B: inhibin B; NAG:
 26 neural α-glucosidase.

27 **Supplementary Table S3.** Summary of key information of datasets used in the study.

GSE Accession	Platform	Organism	Sample	Type	Sample size	
					Control	NOA
GSE108886	GPL10558	Homo sapiens	Testis tissue	mRNA	3	8
GSE145467	GPL4133	Homo sapiens	Testis tissue	mRNA	10	10
GSE9210	GPL887	Homo sapiens	Testis tissue	mRNA	20	20

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