Supplementary Table 2: Proteins involved in key functions that are underexpressed and may contribute to sperm dysfunction or in the development of varicocele as revealed by GO, STRAP, DAVID and reactome analysis

Function	*UniProt number*	*Accession number*	*Gene name*	*Protein name*	*Protein function*
Spermatogenesis	Q8NEB7	17999524	ACRBP	Acrosin binding protein	Expressed in testis. Phosphorylated in Involved in packaging and condensation of acrosin zymogen in the acrosomal matrix via its association with proacrosin
	Q96M32	148727333	AK7	Adenylate kinase 7	Involved in spermatogenesis
	Q13733	153946397	ATP1A4	Sodium/potassium-transporting ATPase subunit alpha-4	Specifically found in the testis. Expressed in mature sperm. Provides energy for active transport of nutrients. Involved in motility
	Q92526	58331173	CCT6B	T-complex protein 1 subunit zeta-2	Molecular chaperone. Involved in protein (actin and tubulin) folding
	P54652	13676857	HSPA2	Heat shock-related 70 kDa protein 2	Stabilizes preexistent proteins against aggregation and mediate folding of newly translated polypeptides in the cytosol as well as within the organelles. They bind with a net hydrophobic character during membrane translocation or following stress-induced damage
	O95757	31541941	HSPA4L	Heat shock 70 kDa protein 4L	Possesses chaperone activity. Protein involved in stress response (such as temperature)
	P56597	4505413	NMES	Nucleoside diphosphate kinase homolog 5	Confers protection from cell death and alters the cellular levels of several antioxidant enzymes. May play a role in spermiogenesis by increasing the ability of late-stage spermatids to eliminate reactive oxygen species
	Q9Y265	4506753	RUVBL1	RuvB-like 1	May participate in transcriptional regulation
	Q15506	8394343	SPA17	Sperm surface protein Sp17	Sperm surface zona pellucida binding protein. Helps bind spermatozoa to the zona pellucida with high affinity.
Sperm motility	Q13733	153946397	ATP1A4	Sodium/potassium-transporting ATPase subunit alpha-4	Catalyzes the hydrolysis of ATP. Plays a role in sperm motility
	P17612	46909584	PRKACA	cAMP-dependent protein kinase catalytic subunit alpha	Phosphorylates a large number of substrates in the cytoplasm and the nucleus. Activated by ATP and cAMP. Isoform 2 phosphorylates and activates ABL1 (abelson murine leukemia viral oncogene 1) in sperm flagellum to promote spermatozoa capacitation
	P10644	4506063	PRKAR1A	cAMP-dependent protein kinase type I-alpha regulatory subunit	Regulatory subunit of the cAMP-dependent protein kinases involved in cAMP signaling in cells
Mitochondrial dysfunction	Q99798	4501867	ACO2	Aconitate hydratase, mitochondrial	Catalyzes the isomerization of citrate to is-citrate
	P28331	33519475	NDUFS1	NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial	Core subunit of mitochondrial membrane respiratory chain NADH dehydrogenase
	Q02218	259013553	OGDH	2-oxoglutarate dehydrogenase, mitochondrial	The 2-oxoglutarate dehydrogenase complex catalyzes the overall conversion of 2-oxoglutarate to succinyl-CoA and CO_2. Involved in glycolysis
	P22695	50592988	UQCRC2	Cytochrome b-c1 complex subunit 2, mitochondrial	This is a component of the ubiquinol-cytochrome c reductase complex. It is part of the mitochondrial respiratory chain
Metabolism of nucleotides	Q96M32	148727333	AK7	Adenylate kinase 7	Nucleoside monophosphate kinase that catalyzes the reversible transfer of the terminal phosphate group between nucleoside triphosphates and monophosphates. Involved in maintaining ciliary structure and function
	P02647	4557321	APOA1	Apolipoprotein A-I	Participates in the reverse transport of cholesterol from tissues to liver. Activates sperm motility
	Q13733	153946397	ATP1A4	Sodium/potassium-transporting ATPase subunit alpha-4	It is the catalytic component of the active enzyme, which catalysis the hydrolysis of ARTP couples with exchange of sodium and potassium ions across the plasma membrane. Provides energy for active transport of various nutrients. Plays a role in sperm motility. Specifically expressed in the testis and mature sperm at protein level
	P36543	4502317	ATP6V1EJ	V-type proton ATPase subunit E 1	Subunit of the peripheral VI complex of vacuolar ATPase essential for assembly or catalytic function
	O43837	28178821	IDH3B	Isocitrate dehydrogenase (NAD) subunit beta, mitochondrial	Involved in the catalytic activity and conversion of isocitrate and NBAD+ to 2-oxoglutarate and NADH
	P28331	33519475	NDUFS1	NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial	Core subunit of the mitochondrial membrane respiratory chain NADH dehydrogenase (Complex I)
	Q02218	259013553	OGDH	2-oxoglutarate dehydrogenase, mitochondrial	The 2-oxoglutarate dehydrogenase complex catalyzes the overall conversion of 2-oxoglutarate to succinyl-CoA and CO_2
Fatty acid metabolism	P16219	4557233	ACADS	Short-chain specific acyl-CoA dehydrogenase, mitochondrial	Involved in lipid metabolism and mitochondrial fatty acid oxidation
	Q9UKUO	327412327	ACSL6	Short-chain specific acyl-CoA dehydrogenase, mitochondrial	Involved in lipid metabolism and fatty acid beta- oxidation
	Q13011	70995211	ECH1	Delta(3,5)-Delta(2,4)-dienoyl-CoA isomerase, mitochondrial	Involved in fatty beta-oxidation. Located in the mitochondrion, peroxisomes, and membranes
Muscle cell formation	Q9NY47	291290994	CACNA2D	Voltage-dependent calcium channel subunit alpha-2/delta-2	The alpha-2/delta subunit of voltage-dependent calcium channels regulates calcium current density. Highly expressed in the testis
	P10253	119393891	GAA	Lysosomal alpha-glucosidase	Essential for the degradation of glycogen to glucose in lysosomes. Present in lysosomes and
	P10644	4506063	PRKARIA	cAMP-dependent protein kinase type I-alpha regulatory subunit	Regulatory subunit of the cAMP-dependent protein kinases involved in cAMP signaling in cells

GO: gene ontology; STRAP: Software for Researching Annotations of Proteins; DAVID: Database for Annotation, Visualization and Integrated Discovery; NAD: isocitrate dehydrogenase