Supplementary Table SIV **Details of all prioritized and validated variants identified in this study.**

Patient	Gene	gDNA	cDNA	Protein	Zygosity	In-homozygosity region	GnomAD variant frequency (population with highest frequency)*	Align GVGD** (Tavtigian *et al.*, 2006)	SIFT (Vaser *et al.*, 2016)	Mutation Taster (Schwarz *et al.*, 2010)	PolyPhen2 (Adzhubei *et al.*, 2010)	Variant classification according to the ACMG/AMP 2015 guideline	Mouse model	Link to acrosome biology	Conclusion
GL-1 GL-2	*GGN*	Chr19(GRCh37): g.38876631del	NM_152657.3 (GGN):c.1271del	p.(Gly424 Alafs*65)	Homozygous	Yes	0.00% (SAS: 0.01%)	N/A	N/A	N/A	N/A	Likely pathogenic	Yes, meiotic arrest (Jamsai *et al.*, 2013)	No	Possibly causative
GL-3	*DNAH17*	Chr17(GRCh37): g.76533410G > A Chr17(GRCh37): g.76475687A > T	NM_173628.3 (DNAH17): c.2830C > T NM_173628.3 (DNAH17): c.7780 T > A	p.(Arg944Trp) p.(Phe2594Ile)	Heterozygous Heterozygous	No No	0.15% (NFE: 0.24%) Absent	C0 C0	Deleterious Tolerated	Disease-causing Disease-causing	N/A N/A	Uncertain significance Uncertain significance	Yes, male infertility (Dickinson *et al.*, 2016)	No	Possibly causative
GL-3	*MAGEA3*	ChrX (GRCh37): g.151935566G > A	NM_005362.3 (MAGEA3): c.601C > T	p.(Leu201Phe)	Hemizygous	N/A	0.00% (SAS: 0.01%)	C0	Tolerated	Polymorphism	Possibly damaging	Uncertain significance	No	No	Unlikely causative
GL-4	*C2CD6 (ALS2CR11)*	Chr2(GRCh37): g.202467979 T > C	NM_001168221.1 (C2CD6): c.338A > G	p.(His113Arg)	Homozygous	Yes	Absent	C0	Deleterious	Polymorphism	Benign	Uncertain significance	No	Yes (Wang *et al.*, 2015)	Possibly causative
GL-11	*ZPBP*	Chr7(GRCh37): g.50022968G > A	NM_007009.2 (ZPBP): c.931C > T	p.(Gln311*)	Homozygous	Yes	Absent	N/A	N/A	N/A	N/A	Likely pathogenic	Yes, globozoospermia (Lin *et al.*, 2007)	Yes (Lin *et al.*, 2007)	Likely causative
GL-11	*TM4SF19*	Chr3(GRCh37): g.196053903C > A	NM_001204897.1 (TM4SF19): c.202G > T	p.(Val68Leu)	Homozygous	No	0.02% (OTH: 0.15%)	C0	Deleterious	Disease-causing	Probably damaging	Uncertain significance	No	No	Unlikely causative
GL-12	*CCIN*	Chr9(GRCh37): g.36170352G > A	NM_005893.2 (CCIN):c.853G > A	p.(Gly285Ser)	Homozygous	Yes	0.00% (NFE: 0.01%)	C55	Deleterious	Disease-causing	Probably damaging	Uncertain significance	No	Yes (Lecuyer *et al.*, 2000)	Possibly causative
GL-13	*CCDC62*	Chr12(GRCh37): g.123270311C > T Chr12(GRCh37): g.123281928C > T	NM_201435.4 (CCDC62): c.442C > T NM_201435.4 (CCDC62): c.847C > T	p.(Gln148*) p.(His283Tyr)	Homozygous Homozygous	Yes Yes	Absent 0.01% (NFE: 0.01%)	N/A C0	N/A Deleterious	N/A Polymorphism	N/A Probably damaging	Likely pathogenic Uncertain significance	Yes, globozoospermia (Li *et al.*, 2017)	Yes (Li *et al.*, 2017)	Likely causative
GL-13	*CCDC73*	Chr11(GRCh37): g.32676493dup	NM_001008391.2 (CCDC73): c.671dup	p.(Leu224 Phefs*11)	Homozygous	Yes	0.00% (NFE: 0.00%)	N/A	N/A	N/A	N/A	Uncertain significance	Yes, no infertility (Khan *et al.*, 2018)	No	Unlikely causative

Continued

Supplementary Table SIV Continued.

Patient	Gene	gDNA	cDNA	Protein	Zygosity	In-homozygosity region	GnomAD variant frequency (population with highest frequency)*	Align GVGD** (Tavtigian *et al.*, 2006)	SIFT (Vaser *et al.*, 2016)	Mutation Taster (Schwarz *et al.*, 2010)	PolyPhen2 (Adzhubei *et al.*, 2010)	Variant classification according to the ACMG/AMP 2015 guideline	Mouse model	Link to acrosome biology	Conclusion
GL-13	*NRIP3*	Chr11(GRCh37): g.9009122A > T	NM_020645.2 (NRIP3): c.395 T > A	p.(Ile132Asn)	Homozygous	Yes	Absent	C65	Deleterious	Disease-causing	Possibly damaging	Uncertain significance	No	No	Unlikely causative
GL-13	*ATP8A2*	Chr13(GRCh37): g.26273432G > A	NM_016529.5 (ATP8A2): c.2333G > A	p.(Arg778Gln)	Homozygous	Yes	0.04% (ASJ: 0.10%)	C0	Deleterious	N/A	N/A	Uncertain significance	No	No	Unlikely causative
ARG13	*C7orf61*	Chr7(GRCh37): g.100061114del	NM_001004323.2 (C7orf61): c.259del	p.(Glu87 Argfs*46)	Homozygous	Yes	Absent	N/A	N/A	N/A	N/A	Likely pathogenic	No	Yes (Behrouzi *et al.*, 2013)	Possibly causative

*GnomAD variant frequency was downloaded from http://gnomad.broadinstitute.org/ (version 2.1). SAS: South Asian, NFE: Non-Finnish European, OTH: Other, ASJ: Ashkenazi Jewish.
**Align GVGD (http://agvgd.iarc.fr/) classified missense mutations in categories C0, C15, C25, C45, C55 and C65, of which C0 is least likely to be pathogenic and C65 is most likely to be pathogenic.