Supplementary Materials

Genetic defects in programmed meiotic DNA double-strand break formation and repair in human infertility

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Table S1. Reported human variants in genes involved in programmed meiotic DSB formation and repair and their associated reproductive phenotypes

Gene	Nucleotide change	Protein change	Variant type	Zygosity / genotype	Sex	Clinical phenotype	Reference
SPO11	c.556G>A	p.Glu186Lys	Missense	Homozygous	Male	NOA	Fakhro et al., 2018[1]
(NM_012444.3)	c.539G>A	p.Gly180Asp	Missense	Homozygous	Female	Recurrent blastulation failure	Chen et al., 2026[2]
	c.885delT	p.Met296CysfsTer26	Frameshift	Homozygous	Female	Recurrent blastulation failure	Chen et al., 2026[2]
TOP6BL	c.1501T>C	p.Ser501Pro	Missense	Homozygous	Female	RHM	Nguyen et al., 2018[3]
(NM_024650.3)	c.783dup	p.Glu262Ter	Nonsense	Homozygous	Male;	NOA;	Jiao et al., 2020[4] ;
					Female	RHM	Nguyen et al., 2018[3]
	c.1067C>G	p.Pro356Arg	Missense	Homozygous	Male	NOA	Wang et al., 2025[5]
	c.1543C>T	p.Arg515Ter	Nonsense	Homozygous	Male	NOA	Wang et al., 2025[5]
	c.523+1G>C	p.?	Splicing	Homozygous	Male	NOA	Okutman et al., 2026[6]
MEI1	c.3307C>T	p.Arg1103Trp	Missense	Homozygous;	Male;	NOA;	Ben Khelifa et al., 2018[7]; Chen
(NM_152513.4)				compound heterozygous with c.2548C>T	Female	Recurrent blastulation failure	et al., 2026[2]
	c.1196+1G>A	p.?	Splicing	Compound heterozygous with c.2206del	Male;	NOA;	Nguyen et al., 2018[3];
					Female	RHM	
	c.2206del	p.Val736SerfsTer31	Frameshift	Compound heterozygous with c.1196+1G>A	Male;	NOA;	Nguyen et al., 2018[3]
					Female	RHM	
	c.3452G>A	p.Trp1151Ter	Nonsense	Homozygous	Female	RHM; RPL	Nguyen et al., 2018[3];
	c.1088C>T	p.Thr363Met	Missense	Compound heterozygous with c.925C>T	Male	NOA	Krausz et al., 2020[8]
	c.925C>T	p.Leu309Phe	Missense	Compound heterozygous with c.1088C>T	Male	NOA	Krausz et al., 2020[8]
	c.1585T>A	p.Phe529Ile	Missense	Homozygous or compound heterozygous	Male;	NOA;	Dong et al., 2021[9]; Zhang et al.,
					Female	RHM; PREMBA; RIF; blastulation failure	2023[10];
							Chen et al., 2026[2]
	c.745C>T	p.Gln249Ter	Nonsense	Compound heterozygous with c.1585T>A	Female	PREMBA; RIF	Dong et al., 2021[9];
	c.251delT	p.Val84GlyfsTer11	Frameshift	Compound heterozygous with c.1585T>A	Male	NOA	Zhang et al., 2023[10]
	c.186G>C	p.Lys62Asn	Missense	Compound heterozygous with c.1585T>A or	Male;	NOA;	Dong et al., 2021[9]; Zhang et al.,
				c.734-2A>C	Female	RHM; PREMBA; RIF	2023[10]
	c.734-2A>C	p.?	Splicing	Compound heterozygous with c.186G>C	Male;	NOA;	Dong et al., 2021[9]
					Female	PREMBA; RIF	
	c.1792+1G>T	p.?	Splicing	Homozygous	Female	PREMBA; RIF	Dong et al., 2021[9]
	c.2071C>G	p.Gln691Glu	Missense	Compound heterozygous with c.529+5G>A	Male	Cryptozoospermia / spermatogenic failure	Chen et al., 2023 [11]
	c.529+5G>A	p.?	Splicing	Compound heterozygous with c.2071C>G	Male	Cryptozoospermia / spermatogenic failure	Chen et al., 2023 [11]
	c.2264_2268+11delGTGA	p.?	Splicing	Compound heterozygous with c.3002delC	Female	PREMBA; RIF	Wu et al., 2024[12]
	GGTATGGACCAC						
	c.3002delC	p.Pro1001LeufsTer27	Frameshift	Compound heterozygous with	Female	PREMBA; RIF	Wu et al., 2024[12]
				c.2264_2268+11del			
	c.131G>T	p.Cys44Phe	Missense	Homozygous	Male	NOA	Huang et al., 2024[13]
	c.2647C>T	p.Arg883Ter	Nonsense	Compound heterozygous with c.622T>C	Female	Abnormal fertilization; PREMBA	Jiao et al., 2025[14]

	c.622T>C	p.Ser208Pro	Missense	Compound heterozygous with c.2647C>T	Female	Abnormal fertilization; PREMBA	Jiao et al., 2025[14]
	c.3037T>G	p.Trp1013Gly	Missense	Compound heterozygous with Exon21_31del	Female	PREMBA	Jiao et al., 2025[14]
	Exon21_31del	p.?	Exon deletion	Compound heterozygous with c.3037T>G	Female	PREMBA	Jiao et al., 2025[14]
	Exon19del	p.?	Exon deletion	Homozygous	Male; Female	NOA; PREMBA	Liu et al., 2025[15]
	c.2503C>T	p.Gln835Ter	Nonsense	Presumed compound heterozygous with c.3428-2A>G	Female	Recurrent blastulation failure	Chen et al., 2026[2]
	c.3428-2A>G	p.?	Splicing	Presumed compound heterozygous with c.2503C>T	Female	Recurrent blastulation failure	Chen et al., 2026[2]
	c.2548C>T	p.Leu850Phe	Missense	Compound heterozygous with c.3307C>T	Female	Recurrent blastulation failure	Chen et al., 2026[2]
	c.2668_2669del	p.Leu890AlafsTer60	Frameshift	Homozygous	Female	Recurrent blastulation failure	Chen et al., 2026[2]
	c.2864A>C	p.Gln955Pro	Missense	Presumed compound heterozygous with c.1585T>A	Female	Recurrent blastulation failure	Chen et al., 2026[2]
	c.2885A>G	p.Tyr962Cys	Missense	Presumed compound heterozygous with c.131G>C	Female	Recurrent blastulation failure	Chen et al., 2026[2]
	c.131G>C	p.Cys44Ser	Missense	Presumed compound heterozygous with c.2885A>G	Female	Recurrent blastulation failure	Chen et al., 2026[2]
REC114	c.334-1G>A	p.?	Splicing	Homozygous	Female	RHM	Nguyen et al., 2018[3]
(NM_00104236	c.397T>G	p.Cys133Gly	Missense	Homozygous	Female	Multiple pronuclei; PREMBA	Wang et al., 2020[16]
7.2)	c.546+5G>A	p.?	Splicing	Homozygous	Female	Abnormal fertilization; PREMBA	Wang et al., 2020[16]
	c.568C>T	p.Gln190Ter	Nonsense	Homozygous	Male; Female	NOA; POI/DOR	Xu et al., 2024[17]; Xu et al., 2025[18]
	c.123C>A	p.Cys41Ter	Nonsense	Compound heterozygous with c.659_706dup	Male	NOA	Liu et al., 2025[19]
	c.659_706dup	p.Leu220_Gly235dup	In-frame duplication	Compound heterozygous with c.123C>A	Male	NOA	Liu et al., 2025[19]
	c.523_524del	p.Lys175GlufsTer50	Frameshift	Compound heterozygous with c.640_641del	Male	NOA	Ni et al., 2025[20]
	c.640_641del	p.Leu214SerfsTer11	Frameshift	Compound heterozygous with c.523_524del	Male	NOA	Ni et al., 2025[20]
	c.731A>G	p.Asp244Gly	Missense	Homozygous	Female	Recurrent blastulation failure	Chen et al., 2026[2]
MEI4	c.293C>T	p.Ser98Leu	Missense	Compound heterozygous with c.401C>G	Female	PREMBA	Pan et al., 2024[21]
(NM_00132224	c.391C>G	p.Pro131Ala	Missense	Compound heterozygous with c.914A>T	Female	PREMBA	Pan et al., 2024[21]
7.2)	c.401C>G	p.Pro134Arg	Missense	Homozygous or compound heterozygous; partner variants include c.908C>G, c.293C>T, or c.992G>A	Female	PREMBA; RPL	Pan et al., 2024[21]; Kong et al., 2026[22]
	c.899A>T	p.Gln300Leu	Missense	Homozygous	Female	Oocyte maturation arrest	Pan et al., 2024[21]
	c.908C>G	p.Ala303Gly	Missense	Compound heterozygous with c.401C>G	Female	PREMBA	Pan et al., 2024[21]
	c.914A>T	p.Tyr305Phe	Missense	Compound heterozygous with c.391C>G	Female	PREMBA	Pan et al., 2024[21]
	c.992G>A	p.Gly331Asp	Missense	Compound heterozygous with c.401C>G	Female	RPL	Kong et al., 2026[22]
	c.15delA	p.Lys5AsnfsTer4	Frameshift	Heterozygous	Female	POI	Wang et al., 2026[23]

	c.1066C>T	p.Gln356Ter	Nonsense	Heterozygous	Female	POI	Wang et al., 2026[23]
	c.695delA	p.Lys232SerfsTer18	Frameshift	Heterozygous	Female	POI	Wang et al., 2026[23]
ANKRD31	c.1565-2A>G	p.?	Splicing	Heterozygous	Female	POI	Wang et al., 2021[24]
(NM_001164443.1)	c.985C>T	p.Gln329Ter	Nonsense	Heterozygous	Female	POI	Wang et al., 2021[24]
HORMAD1 (NM_032132.5)	c.1021C>T	p.Gln341Ter	Nonsense	Homozygous	Male	NOA	Okutman et al., 2023[25]
DMC1 (NM_007068.4)	c.106G>A	p.Asp36Asn	Missense	Homozygous	Male; Female	NOA; POI	He et al., 2018[26]
	c.28delG	p.Glu10AsnfsTer31	Frameshift	Homozygous	Male; Female	NOA; DOR	Chen et al., 2020[27]; Cao et al., 2021[28]
	c.860C>A	p.Pro287His	Missense	Homozygous	Male	NOA	Kherraf et al., 2022[29]
	c.364A>G	p.Thr122Ala	Missense	Homozygous	Male	NOA	Kherraf et al., 2022[29]
	c.164C>T	p.Thr55Ile	Missense	Homozygous	Male	NOA	Ullah et al., 2025[30]
	c.490A>G	p.Thr164Ala	Missense	Homozygous	Male	NOA	Ullah et al., 2025[30]
	c.581A>G	p.Tyr194Cys	Missense	Homozygous	Male	NOA	Ullah et al., 2025[30]
	c.494+4A>G	p.?	Splicing	Compound heterozygous with c.597G>C	Male	NOA	Wang et al., 2025[31]
	c.597G>C	p.Gln199His	Missense	Compound heterozygous with c.494+4A>G	Male	NOA	Wang et al., 2025[31]
	c.724C>T	p.Arg242Trp	Missense	Homozygous	Female	Recurrent blastulation failure	Chen et al., 2026[2]
TEX15	c.3279T>G	p.Tyr1093Ter	Nonsense	Homozygous	Male	NOA	Okutman et al., 2015[32]
(NM_001350162.2)	c.3568A>T	p.Lys1190Ter	Nonsense	Compound heterozygous with c.4189del	Male	NOA	Colombo et al., 2017[33]
	c.4189del	p.Ser1397LeufsTer5	Frameshift	Compound heterozygous with c.3568A>T	Male	NOA	Colombo et al., 2017[33]
	c.5170G>A	p.Ala1724Thr	Missense	Compound heterozygous with c.8197_8198del	Male	NOA	Wyrwoll et al., 2023[34]
	c.8197_8198del	p.Glu2733LysfsTer26	Frameshift	Compound heterozygous with c.5170G>A	Male	NOA	Wyrwoll et al., 2023[34]
	c.2549G>T	p.Trp850Leu	Missense	Compound heterozygous with c.4119C>A	Male	NOA	Qureshi et al., 2023[35]
	c.4119C>A	p.Ser1373Arg	Missense	Compound heterozygous with c.2549G>T	Male	NOA	Qureshi et al., 2023[35]
	c.5590G>C	p.Glu1864Gln	Missense	Compound heterozygous with c.6874_6877del	Male	NOA	Qureshi et al., 2023[35]
	c.6874_6877del	p.Ser2292LysfsTer11	Frameshift	Compound heterozygous with c.5590G>C	Male	NOA	Qureshi et al., 2023[35]
	c.7414C>T	p.Arg2472Ter	Nonsense	Compound heterozygous with c.8164-17G>A	Male	NOA	Qureshi et al., 2023[35]
	c.8164-17G>A	p.?	Splicing	Compound heterozygous with c.7414C>T	Male	NOA	Qureshi et al., 2023[35]
	c.6823G>A	p.Ala2275Thr	Missense	Homozygous	Male	Cryptozoospermia	Qureshi et al., 2023[35]
	c.688-6T>C	p.?	Splicing	Compound heterozygous with c.6848_6849delGA	Male	NOA	Qureshi et al., 2023[35]
	c.6848_6849delGA	p.Arg2283AsnfsTer22	Frameshift	Compound heterozygous with c.688-6T>C or c.6271dupA	Male	NOA	Qureshi et al., 2023[35]

	c.6271dupA	p.Arg2091LysfsTer6	Frameshift	Compound heterozygous with c.6848_6849delGA	Male	NOA	Podgrajsek et al., 2025[36]
XRCC2 (NM_005431.2)	c.41T>C	p.Leu14Pro	Missense	Homozygous	Male; Female	NOA; POI	Yang et al., 2018[37] Zhang et al., 2019[38]
	c.643C>T	p.Arg215Ter	Nonsense	Homozygous	Male	Male infertility / spermatogenic failure	Alhathal et al., 2020[39]
ZSWIM7 (NM_001042697.2)	c.201+1G>T	p.?	Splicing	Homozygous	Male	NOA	Alhathal et al., 2020[39]
	c.38T>C	p.Leu13Pro	Missense	Homozygous	Female	POI	Yatsenko et al., 2022[40]
	c.173C>G	p.Ser58Ter	Nonsense	Homozygous	Female	POI	McGlacken-Byrne et al., 2022[41]
	c.176C>T	p.Ser59Leu	Missense	Homozygous	Male; Female	NOA; POI	Hussain et al., 2022[42]; Lokchine et al., 2025[43]
	c.231_232del	p.Cys78PhefsTer21	Frameshift	Homozygous; compound heterozygous with c.151C>T or c.22del	Male; Female	NOA; POI	Li et al., 2021[44]; Yatsenko et al., 2022[40]; Lokchine et al., 2025[43]; Christofolini et al., 2025[45]
	c.151C>T	p.Arg51Ter	Nonsense	Compound heterozygous with c.231_232del	Female	POI	Lokchine et al., 2025[43]
	c.22del	p.Val8LeufsTer6	Frameshift	Compound heterozygous with c.231_232del	Female	POI	Lokchine et al., 2025[43]
MEIOB (NM_001163560.3)	c.191A>T	p.Asn64Ile	Missense	Homozygous	Male	NOA	Gershoni et al., 2017[46]
	c.1098del	p.Ser366fsTer12	Frameshift	Homozygous	Male	NOA	Gershoni et al., 2019[47]
	c.1218G>A	p.Thr406= (exon 12 skipping → p.Cys345TrpfsTer8)	Synonymous (Splicing-altering)	Homozygous	Female	POI	Caburet et al., 2019[48]
	c.897_1431del	p.(219del178aa)	Inframe deletion	Homozygous	Male	NOA	Krausz et al., 2020[8]
	c.1140_1143del	p.Asp381Ter	Frameshift	Homozygous	Male	NOA	Krausz et al., 2020[8]
	c.683-1G>A	p.?	Splicing	Homozygous	Male; Female	NOA; Female infertility	Wu et al., 2021[49]
	c.1118_1121del	p.Phe373SerfsTer6	Frameshift	Homozygous	Male	NOA	Kherraf et al., 2022[29]
	c.258_259del	p.Val87AspfsTer3	Frameshift	Homozygous	Female	POI	Wang et al., 2022[50]
	c.1072_1073del	p.Met358ValfsTer12	Frameshift	Homozygous	Male; Female	NOA; POI	Wang et al., 2022[50]
	c.814C>T	p.Arg272Ter	Nonsense	Homozygous; Compound heterozygous with c.976G>A	Male	NOA	Wang et al., 2022[50]; Zhu et al., 2024[51]
	c.976G>A	p.Ala326Thr	Missense	Compound heterozygous with c.814C>T	Male	NOA	Zhu et al., 2024[51]
	c.528+3A>C	p.?	Splicing	Homozygous	Male	NOA	Zhu et al., 2024[51]
	c.673C>T	p.Arg225Ter	Nonsense	Homozygous	Male	NOA	Sharifi et al., 2025[52]
SPATA22 (NM_001170695.2)	c.203del	p.Leu68TrpfsTer4	Frameshift	Homozygous	Male	NOA	Wu et al., 2021[49]
	c.31C>T	p.Arg11Ter	Nonsense	Compound heterozygous with c.900+1G>A	Female	POI	Yao et al., 2022[53]; Xia et al., 2026[54]

	c.900+1G>A	p.?	Splicing	Compound heterozygous with c.31C>T	Female	POI	Yao et al., 2022[53]; Xia et al., 2026[54]
	c.400C>T	p.Arg134Ter	Nonsense	Homozygous	Male; Female	NOA; POI	Yao et al., 2022[53]
MSH4	c.2355+1G>A	p.?	Splicing	Homozygous	Female	POI	Carlosama et al., 2017[55]
(NM_002440.4)	c.1913C>T	p.Pro638Leu	Missense	Homozygous	Male	NOA	Krausz et al., 2020[8]
	c.1552C>T	p.Gln518Ter	Nonsense	Homozygous	Male	NOA	Tang et al., 2020[56]
	c.1453C>T	p.Gln485Ter	Nonsense	Compound heterozygous with c.1686del	Male	NOA	Wyrwoll et al., 2021[57]
	c.1686del	p.Val563Ter	Nonsense	Compound heterozygous with c.1453C>T	Male	NOA	Wyrwoll et al., 2021[57]
	c.2198C>A	p.Ser733Ter	Nonsense	Homozygous	Male; Female	NOA; POI	Wyrwoll et al., 2021[57]
	c.2261C>T	p.Ser754Leu	Missense	Homozygous; Compound heterozygous with c.1392delG	Male; Female	NOA; POI	Akbari et al., 2021[58]; Wyrwoll et al., 2021[57]; Podgrajsek et al., 2025[59]
	c.244G>A	p.Gly82Ser	Missense	Compound heterozygous with c.670delT	Male	NOA	Li et al., 2022[60]
	c.670delT	p.Leu224CysfsTer3	Frameshift	Compound heterozygous with c.244G>A	Male	NOA	Li et al., 2022[60]
	c.805_812del	p.Val269GlnfsTer15	Frameshift	Homozygous	Male	NOA	Li et al., 2022[60]
	c.1950G>A	p.Trp650Ter	Nonsense	Compound heterozygous with c.2179delG	Male	NOA	Li et al., 2022[60]
	c.2179delG	p.Asp727MetfsTer11	Frameshift	Compound heterozygous with c.1950G>A	Male	NOA	Li et al., 2022[60]
	c.2222_2225del	p.Lys741ArgfsTer2	Frameshift	Homozygous in male; compound heterozygous in females	Male; Female	NOA; POI/DOR	Li et al., 2022[60]; Luo et al., 2023[61]; Wan et al., 2023[62]
	c.2728C>T	p.Arg910Ter	Nonsense	Compound heterozygous with c.2222_2225del	Female	POI	Luo et al., 2023[61]
	c.2374A>G	p.Thr792Ala	Missense	Compound heterozygous with c.2222_2225del	Female	POI/DOR	Luo et al., 2023[61]; Wan et al., 2023[62]
	c.1025C>T	p.Thr342Ile	Missense	Compound heterozygous with c.2222_2225del	Female	POI	Luo et al., 2023[61]
	c.1094T>A	p.Ile365Asn	Missense	Compound heterozygous with c.1345T>G	Female	POI	Ke et al., 2023[63]
	c.1345T>G	p.Tyr449Asp	Missense	Compound heterozygous with c.1094T>A	Female	POI	Ke et al., 2023[63]
	c.2531-1G>A	p.?	Splicing	Homozygous	Female	POI	Zeng et al., 2023[64]
	c.118C>T	p.Gln40Ter	Nonsense	Homozygous	Male; Female	NOA; POI	Hashemi Sheikhshabani et al., 2024[65]
	c.2107+5G>A	p.?	Splicing	Homozygous	Male	NOA	Zhou et al., 2024[66]
	c.1392delG	p.Ile465LeufsTer4	Frameshift	Compound heterozygous with c.2261C>T	Male	Azoospermia	Podgrajsek et al., 2025[59]
	c.2658_2659delAG	p.Arg886SerfsTer8	Frameshift	Homozygous	Female	POI	Xu et al., 2025[18]
MSH5	c.553G>C	p. Gly185Arg	Missense	Compound heterozygous with c.2009T>C	Female	POI	Shen et al., 2021[67]
(NM_172166.4)	c.2009T>C	p. le670Thr	Missense	Compound heterozygous with c.553G>C	Female	POI	Shen et al., 2021[67]
	c.75dup	p.Ser26GlnfsTer42	Frameshift	Homozygous	Male	NOA	Wyrwoll et al., 2021[57]

	c.1857del	p.Ala620GlnfsTer9	Frameshift	Homozygous	Male	NOA	Wyrwoll et al., 2021[57]
	c.964C>T	p.Arg322Cys	Missense	Homozygous in male; compound heterozygous with c.1914C>A in female	Male; Female	NOA; DOR	Wyrwoll et al., 2021[57]; Xu et al., 2025[18]
	c.537+1G>A	p.?	Splicing	Homozygous	Male	NOA	Kherraf et al., 2022[29]
	c.1126del	p.Ser376AlafsTer6	Frameshift	Homozygous	Male	NOA	Gong et al., 2022[68]
	c.678_681del	p.Tyr227ValfsTer21	Frameshift	Homozygous	Male	NOA	Chen et al., 2022[69]
	c.830C>T	p.Pro277Leu	Missense	Compound heterozygous with c.1459G>T	Male	NOA	Chen et al., 2022[69]
	c.1459G>T	p.Asp487Tyr	Missense	Compound heterozygous with c.830C>T or c.1914C>A in males; Homozygous in female	Male; Female	NOA; POI	Guo et al., 2017[70]; Chen et al., 2022[69]
	c.1914C>A	p.Cys638Ter	Nonsense	Compound heterozygous with c.1459G>T in male; Homozygous or compound heterozygous with c.964C>T in females	Male; Female	NOA; DOR	Chen et al., 2022[69]; Xu et al., 2025[18]
	c.1133T>C	p.Ile378Thr	Missense	Compound heterozygous with c.648-2A>G	Male	NOA	Liu et al., 2025[19]
	c.648-2A>G	p.?	Splicing	Compound heterozygous with c.1133T>C	Male	NOA	Liu et al., 2025[19]
	c.390_392delCAT	p.Ile131del	In-frame deletion	Homozygous	Male	NOA	Podgrajsek et al., 2025[59]
	c.271+1G>A	p.?	Splicing	Homozygous	Female	POI	Mao et al., 2026[71]
MLH3	c.615del	p.Asp206ThrfsTer18	Frameshift	Homozygous	Male	NOA	Chen et al., 2020[27]
(NM_001040108.2)	c.3632delA	p.Asn1211MetfsTer49	Frameshift	Homozygous	Male	Severe oligozoospermia	Nawaz et al., 2021[72]
	c.3570+1G>A	p.?	Splicing	Homozygous	Male	Infertility	Gu et al., 2026[73]
	c.980_999del	p.Leu327ArgfsTer27	Frameshift	Compound heterozygous with c.1798C>T	Female	PREMBA	Zhang et al., 2026[74]
	c.1798C>T	p.Arg600Ter	Nonsense	Compound heterozygous with c.980_999del	Female	PREMBA	Zhang et al., 2026[74]
	c.1882A>T	p.Lys628Ter	Nonsense	Compound heterozygous with c.3997C>T	Female	PREMBA	Zhang et al., 2026[74]
	c.1989_1993del	p.Ser663ArgfsTer22	Frameshift	Compound heterozygous with c.3997C>T	Female	PREMBA	Zhang et al., 2026[74]
	c.3997C>T	p.Arg1333Ter	Nonsense	Compound heterozygous with c.1989_1993del or c.1882A>T	Female	PREMBA	Zhang et al., 2026[74]
	c.3316del	p.Val1107PhefsTer14	Frameshift	Homozygous	Female	PREMBA	Zhang et al., 2026[74]
	c.2255G>A	p.Gly752Glu	Missense	Compound heterozygous with c.3905delG	Female	URPL	Wu et al., 2026[75]
	c.3905delG	p.Gly1302GlufsTer21	Frameshift	Compound heterozygous with c.2255G>A	Female	URPL	Wu et al., 2026[75]
	c.3658G>A	p.Val1220Met	Missense	Presumed compound heterozygous with c.4015C>T	Female	URPL	Wu et al., 2026[75]
	c.4015C>T	p.Leu1339Phe	Missense	Presumed compound heterozygous with c.3658G>A	Female	URPL	Wu et al., 2026[75]
	c.3689G>A	p.Arg1230His	Missense	Homozygous	Female	Recurrent blastulation failure	Chen et al., 2026[2]
HFM1 (NM_001017975.6)	c.2206G>A	p.Gly736Ser	Missense	Compound heterozygous with c.3929_3930delinsG	Female	POI	Wang et al., 2014[76]
	c.3929_3930delinsG	p.Pro1310ArgfsTer41	Frameshift	Compound heterozygous with c.2206G>A	Female	POI	Wang et al., 2014[76]

	c.1686-1G>C	p.?	Splicing	Compound heterozygous with c.2651T>G	Female	POI	Wang et al., 2014[76]
	c.2651T>G	p.Ile884Ser	Missense	Compound heterozygous with c.1686-1G>C	Female	POI	Wang et al., 2014[76]
	c.1006+1G>T	p.?	Splicing	Compound heterozygous with c.3100G>A	Female	POI	Liu et al., 2020[77]
	c.3100G>A	p.Gly1034Ser	Missense	Compound heterozygous with c.1006+1G>T	Female	POI	Liu et al., 2020[77]
	c.1905T>A	p.Tyr635Ter	Nonsense	Homozygous	Female	POI	Okutman et al., 2021[78]
	c.3490C>T	p.Gln1164Ter	Nonsense	Homozygous	Male	NOA	Tang et al., 2021[79]
	c.3470G>A	p.Cys1157Tyr	Missense	Homozygous	Male	NOA	Tang et al., 2021[79]
	c.1355G>A	p.Arg452Gln	Missense	Homozygous	Male	NOA	Xie et al., 2022[80]
	c.1472T>C	p.Leu491Pro	Missense	Homozygous	Male	NOA	Xie et al., 2022[80]
	c.2487_2491del	p.Lys829AsnfsTer23	Frameshift	Compound heterozygous with c.3490C>T	Male	NOA	Xie et al., 2022[80]
	c.3490C>T	p.Gln1164Ter	Nonsense	Compound heterozygous with c.2487_2491del	Male	NOA	Xie et al., 2022[80]
	c.2562_2563del	p.Glu856AsnfsTer56	Frameshift	Compound heterozygous with c.4126del	Male	NOA	Xie et al., 2022[80]
	c.4126del	p.Glu1376ArgfsTer49	Frameshift	Compound heterozygous with c.2562_2563del	Male	NOA	Xie et al., 2022[80]
	c.1832-2A>T	p.?	Splicing	Homozygous	Male	NOA	Saebnia et al., 2022[81]
	c.2410G>T	p.Glu804Ter	Nonsense	Homozygous	Female	POI	Tucker et al., 2022[82]
	c.2680+3_2680+4delAT	p.?	Splicing	Homozygous; Compound heterozygous with c.1978-2A>C	Female	DOR; RPL	Yu et al., 2022[83]; Zhang et al., 2026[84]
	c.1978-2A>C	p.?	Splicing	Compound heterozygous with c.2680+3_2680+4delAT, or c.2681-3T>A, or c.1880T>C	Female	DOR; RPL; POI	Yu et al., 2022[83]; Luo et al., 2023[61]; Yuan et al., 2026[85]
	c.2681-3T>A	p.?	Splicing	Homozygous in males; Compound heterozygous with c.1978-2A>C in female	Male; Female	NOA; POI	Yao et al., 2023[86]; Yuan et al., 2026[85]
	c.1730-1G>T	p.?	Splicing	Homozygous	Male; Female	NOA; POR;RIF	Tang et al., 2023[87]
	c.1792G>C	p.Val598Leu	Missense	Compound heterozygous with c.3784G>A	Female	POI	Ke et al., 2023[63]
	c.3784G>A	p.Val1262Met	Missense	Compound heterozygous with c.1792G>C	Female	POI	Ke et al., 2023[63]
	c.3124dupT	p.Tyr1042LeufsTer18	Frameshift	Homozygous; Compound heterozygous with c.1159-1G>A	Female	RHM	Rezaei et al., 2024[88]
	c.1159-1G>A	p.?	Splicing	Compound heterozygous with c.3124dupT	Female	RHM	Rezaei et al., 2024[88]
	c.803C>T	p.Pro268Leu	Missense	Compound heterozygous with c.2011C>T	Male	NOA	Liu et al., 2025[89]
	c.2011C>T	p.Arg671Ter	Nonsense	Compound heterozygous with c.803C>T	Male	NOA	Liu et al., 2025[89]
RNF212 (NM_001131034.4)	c.111dup	p.Lys38Ter	Frameshift	Homozygous	Male	NOA	Riera-Escamilla et al., 2019[90]

SHOC1 (NM_173521.5)	c.1347T>A	p.Cys449Ter	Nonsense	In cis with c.1351del; compound heterozygous with c.945_948del	Male	NOA	Krausz et al., 2020[8]
	c.1351del	p.Ser451LeufsTer23	Frameshift	In cis with c.1347T>A; compound heterozygous with c.945_948del	Male	NOA	Krausz et al., 2020[8]
	c.945_948del	p.Glu315AspfsTer6	Frameshift	Compound heterozygous with allele carrying c.1347T>A and c.1351del	Male	NOA	Krausz et al., 2020[8]
	c.797delT	p.Leu266GlnfsTer6	Frameshift	Homozygous	Male	NOA	Krausz et al., 2020[8]
	c.1085_1086del	p.Glu362ValfsTer25	Frameshift	Homozygous	Male	NOA	Krausz et al., 2020[8]; Nagirnaja et al., 2022[91]; Rotte et al., 2025[92]
	c.231_232delAC	p.Leu78SerfsTer9	Frameshift	Compound heterozygous with c.1582C>T; also homozygous in independent families	Male	NOA	Yao et al., 2021[93]; Wang et al., 2022[94]
	c.1194delA	p.Leu400CysfsTer7	Frameshift	Homozygous	Male	NOA	Yao et al., 2021[93]
	c.1464delT	p.Asp489ThrfsTer13	Frameshift	Homozygous	Male	NOA	Yao et al., 2021[93]
	c.1582C>T	p.Arg528Ter	Nonsense	Compound heterozygous with c.231_232del	Male	NOA	Yao et al., 2021[93]
	c.1978G>A	p.Ala660Thr	Missense	Compound heterozygous with c.4274G>A	Male	NOA	Wang et al., 2022[94]
	c.4274G>A	p.Arg1425His	Missense	Compound heterozygous with c.1978G>A	Male	NOA	Wang et al., 2022[94]
	c.1939+2T>C	p.?	Splicing	Homozygous	Male	NOA	Rotte et al., 2025[92]
	c.38_39ins(121 bp)	p.Ser13ProfsTer31	Frameshift	Hemizygous	Male	NOA	Rotte et al., 2025[92]
	c.416_419del	p.Ser139PhefsTer9	Frameshift	Compound heterozygous with c.1769A>G	Male	NOA	Zhang et al., 2026[95]
	c.1769A>G	p.Gln590Arg	Missense	Compound heterozygous with c.416_419del	Male	NOA	Zhang et al., 2026[95]
	c.2738-1G>A	p.?	Splicing	Homozygous	Male	NOA	Zhang et al., 2026[95]
TEX11 (NM_031276.3)	c.349T>A	p.Trp117Arg	Missense	Hemizygous	Male	NOA	Yang et al., 2015[96]
	c.515A>G	p.Gln172Arg	Missense	Hemizygous	Male	NOA	Yang et al., 2015[96]
	c.747+1G>A	p.?	Splicing	Hemizygous	Male	NOA	Yatsenko et al., 2015[97]
	c.1792+1G>C	p.?	Splicing	Hemizygous	Male	NOA	Yatsenko et al., 2015[97]
	c.466A>G	p.Met156Val	Missense	Hemizygous	Male	NOA	Yatsenko et al., 2015[97]; An et al., 2021[98]
	c.2568G>T	p.Trp856Cys	Missense	Hemizygous	Male	NOA	Sha et al., 2018[99]
	c.39_606del	p.13del189aa	In-frame deletion	Hemizygous	Male	NOA	Krausz et al., 2020[8]
	c.1246C>T	p.Gln416Ter	Nonsense	Hemizygous	Male	NOA	An et al., 2021[98]
	c.1337G>T	p.Arg446Met	Missense	Hemizygous	Male	NOA	An et al., 2021[98]
	c.2240C>A	p.Ser747Ter	Nonsense	Hemizygous	Male	NOA	An et al., 2021[98]
	c.151_154del	p.Asp51PhefsTer8	Frameshift	Hemizygous	Male	NOA	Yu et al., 2021[100]
	c.253delG	p.Val85LeufsTer5	Frameshift	Hemizygous	Male	NOA	Ji et al., 2021[101]
	c.812delA	p.Lys271ArgfsTer5	Frameshift	Hemizygous	Male	NOA	Ji et al., 2021[101]
	c.1381-1G>A	p.?	Splicing	Hemizygous	Male	NOA	Ji et al., 2021[101]

	c.1006G>T	p.Glu336Ter	Nonsense	Hemizygous	Male	NOA	Ji et al., 2021[101]
	c.1751+2T>G	p.?	Splicing	Hemizygous	Male	NOA	Ji et al., 2021[101]
	c.559_560del	p.Met187ValfsTer6	Frameshift	Hemizygous	Male	NOA	Tang et al., 2022[102]
	c.1483G>A	p.Ala495Thr	Missense	Hemizygous	Male	NOA	Ozturk, 2023[103]
	c.313C>T	p.Arg105Ter	Nonsense	Hemizygous	Male	NOA	Song et al., 2023[104]
	c.2575G>A	p.Gly859Arg	Missense	Hemizygous	Male	NOA	Song et al., 2023[104]
	c.925+1G>T	p.?	Splicing	Hemizygous	Male	NOA	Muranishi et al., 2024[105]
	c.686G>A	p.Trp229Ter	Nonsense	Hemizygous	Male	NOA	Rotte et al., 2025[92]
	c.1008dup	p.Ser337ValfsTer14	Frameshift	Hemizygous	Male	NOA	Rotte et al., 2025[92]
	c.1200G>A	p.Trp400Ter	Nonsense	Hemizygous	Male	NOA	Rotte et al., 2025[92]
	c.1683dup	p.Thr562TyrfsTer16	Frameshift	Hemizygous	Male	NOA	Ma et al., 2026[106]
SPO16	c.160+8A>G	p.?	Splicing	Homozygous	Female	POI	Qi et al., 2023[107]
(NM_001012425.2)	c.266del	p.Leu89TrpfsTer15	Frameshift	Homozygous	Male	NOA	Rotte et al., 2025[92]

IHO1 is not included because no human infertility-associated variants have been reported to date.

Abbreviations and symbols: DSB, DNA double-strand break; NOA, non-obstructive azoospermia; POI, premature ovarian insufficiency; DOR, diminished ovarian reserve; POR, poor ovarian response; RHM, recurrent hydatidiform mole; RIF, recurrent implantation failure; RPL, recurrent pregnancy loss; URPL, unexplained recurrent pregnancy loss; PREMBA, preimplantation embryonic arrest; aa, amino acid(s).

Variant nomenclature: NM_, NCBI RefSeq transcript accession; ENST, Ensembl transcript accession; c., coding DNA-level HGVS notation; p., protein-level HGVS notation; >, nucleotide substitution; del, deletion; dup, duplication; ins, insertion; delins, deletion–insertion; fs, frameshift; Ter, termination codon; =, synonymous protein consequence; _, a range between two positions; + and −, intronic positions downstream and upstream of an exon boundary, respectively.

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