Supplemental table 1: All detected mutations in HSD17B3 gene in patients with 46,XY DSD

No.	Mutant Exon	Mutation	Mutation type/Effect	Ethnicity	Phenotype/Clinical presentation	References
1	Exon 1	p.Trp50Stop	Nonsense/Truncated protein	Egyptian	46,XY DSD; well-developed breasts (B5), pubic hair (P5) and axillary hair (A3), moderate hirsutism mainly affecting the lower limbs, failure to menstruate, and clitoris-like phallus with normal female external genitalia (Sinnecker type 5)	Hassan et al., 2013
2		p. Ala51Val	Missense (Found in compound heterozygosity with p.Gln176Pro)	Egyptian	46,XY DSD; ambiguous genitalia, bilateral palpable gonads, labioscrotal folds with single opening, and penis-like phallus	The current study
3	Exon 2	p.Ser65Leu	Missense/Inactivates enzyme	Iranian	46,XY DSD; evaluated for hirsutism, clitoromegaly and failure to menstruate.	

4		p.Thr54Ala	Missense	Egyptian	46,XY DSD; hirsutism in body and face, and well developed breasts (B5), pubic hair (P5) and axillary hair (A2). No palpable gonads, and penis like phallus	The current study
5		p.Ala56Thr	Missense/Severe impairment of enzyme	South Asian	46,XY DSD; female prepubertal external genitalia, pubertal virilization, severe hair growth, voice changes and clitoral enlargement (6 months, child diagnosed because of family history).	
6		p.Asn74Thr	Missense	Dutch	46,XY DSD; ambiguous genitalia, pubertal virilization.	
7	Exon 3	p.Arg80Gln	Missense/Impaired enzyme activity (NADPH binding site)	Palestinian, Dutch, Brazilian, Portuguese, Turkish	46,XY DSD; ambiguous genitalia at birth to mild clitoromegaly, pubertal virilization, male gender role, and many reassigned as males if raised as girls.	Demir et al., 2015

8		Duplication that spans exons 3-10 of the HSD17B3 gene and extends from intron 2 to intron 10	Duplication (Found in compound heterozygosity with p.R80Q)	Cypriot	46,XY DSD; ambiguous genetalia, small penis, perineal blind vaginal pouch and posterior labioscrotal fusion.	Neocleous et al., 2012
9		p.Arg80Trp	Missense/Complete loss of enzyme activity (NADPH binding site)	Spanish, Italian, Lebanese, Iranian	46,XY DSD; female external genitalia, palpable gonads, clitoral enlargement and virilization at puberty.	George et al., 2011; Omrani et al., 2011
10	Intron 3	c.325+2T>G	Splice junction/Disrupts splice donor site (found in compound heterozygosity with c.325+4A>T)	Brazilian	46,XY DSD; pubic hair was Tanner stage 4, the vagina ended in a 3-cm pouch, and no gonads were palpable, also presented with acne, hirsutism, voice deepening, phallus enlargement, and the skin of labioscrotal folds were pigmented and rugged.	Castro et al., 2012
11		c.325+4A>T	Splice junction/Disrupts splice acceptor site	Dutch, Brazilian, German, American, Italian	46,XY DSD; normal female to ambiguous genitalia, palpable inguinal gonads.	

12		c.326–1G>C	Splice junction	Dutch, Brazilian	46,XY DSD; inguinal hernia, failure of breast development, facial and body hair growth, voice changes, clitoral enlargement.	
13	Exon 5	p.Asn130Ser	Missense/Severe impairment of enzyme activity	English, German	46,XY DSD; pubertal virilization, mild clitoromegaly, voice changes.	
14	Exon 6	p.H155P	Missense	Turkish	46,XY DSD; normal clitoral size and vaginal and urethral openings, palpable gonads in the inguinal region	Demir et al., 2015
15	Intron 6	c.538–1G>A	Splice junction	Unknown	46,XY DSD.	
16	Even 7	p.Met164Thr	Missense	Egyptian	46,XY DSD, ambiguous genitalia, two palpable gonads, single opening, and penis like phallus	The current study
17	Exon 7	c.585delG	Deletion/ Truncated protein	Egyptian	46,XY DSD, ambiguous genitalia, two palpable gonads, single opening, and clitoris like phallus	The current study

18	Intron 7	c.572+2T>A	Splice junction	Sudanese	46,XY DSD, primary amenorrhea, undeveloped breasts, male pattern secondary characteristics, and external genitalia showed type IV genital circumcision.	Ellaithi et al., 2014
19		p.Gln176Pro	Missense	American (Italian, German- Irish), Egyptian	46,XY DSD; clitoromegaly and coarsening of voice, scrotalization of labia majora and inguinal masses. 46,XY DSD; ambiguous genitalia, Quigley score was 3	The current study
20	Exon 8	c.608delT	Deletion/Downstream premature Stop codon	German	46,XY DSD; female prepubertal development, clitoral enlargement at 12 years of age, testes in inguinal canal.	
21		p.Ala188Val	Missense/Inactivates enzyme	Turkish	46,XY DSD; prepubertal female external genitalia, inguinal mass.	
22		p.Trp192Stop	Nonsense/Truncated protein	Omani	46,XY DSD; ambiguous genitalia	Al-Sinani et al., 2015

23		p.Leu194Pro	Missense (Found in compound heterozygousity with silent mutation c.588C>T)	Egyptian	46,XY DSD; virilization after puberty and chest hair, two openings, and penis like phallus	The current study
24		p.Met197Lys	Missense/Alters secondary protein structure	Afghan	46,XY DSD; pubertal virilization, facial hair, 4–8 cm phallus and labioscrotal folds.	
25	Intron 8	c.655–1G>A	Splice junction/Disrupts splice acceptance site	Syrian, Turkish, Dutch, Greek- American	46,XY DSD; prepubertal female external genitalia, pubertal virilization, male gender role.	
26		p.Ala203Val	Missense/Inactivates enzyme	African- Brazilian, Italian	46,XY DSD; absence of menses, failure of breast development, facial and chest hair and clitoral enlargement, male and female gender identity in siblings.	
27	Exon 9	p.Ala203Glu	Missense	Southern Italian	46,XY DSD; pubertal virilization.	
28		p.Val205Glu	Missense/Inactivates enzyme	White American, English	46,XY DSD; prepubertal female external genitalia to perineoscrotal hypospadias, primary amenorrhea, mild clitoromegaly.	

29		p.Phe208Ile	Missense/Inactivates enzyme	German	46,XY DSD; born with ambiguous genitalia, clitoromegaly (1.5 cm) and posterior fusion and scrotalization of the labia majora which contained palpable masses.	
30		p.Leu212Gln	Missense/Inactivates enzyme	Italian	46,XY DSD; inguinal mass, mild clitoromegaly compound hetrozygous with M235V.	
31		c.461_467delGCACCCG	Deletion (Found in compound heterozygosity with c.761_762delAG)	Turkish	46,XY DSD; female external genitalia, 2 palpable gonads	Sagsak et al., 2015
32		p.Glu215Asp	Missense/Inactivates enzyme	White Brazilian, English	46,XY DSD; female or ambiguous genitalia at birth, male behaviors in childhood, pubertal virilization, absence of menses, male gender role.	
33		p.Cys206Stop	Nonsense/Truncated protein	Tunisian	46,XY DSD; female Prader IV.	Ben Rhouma et al., 2012
34	Exon 10	p.Ser232Leu	Missense/Inactivates enzyme	African- American, South Asian	46,XY DSD; clitoromegaly, primary amenorrhea, absent labia minora, severe hypospadias with undermasculinization – raised as males and females.	

35		p.Met235Val	Missense/Inactivates enzyme	African- American, Italian	46,XY DSD; clitoromegaly, primary amenorrhea, inguinal masses.	
36		c.777–783delGATAACC	Deletion/Frame shift truncates protein	Polish, Turkish, Egyptian	46,XY DSD; testis in herniorrhaphy sac, failure to menstruate. 46,XY DSD; ambiguous genitalia with two openings, and clitoromegaly	Alikasifoglu et al., 2012; The current study
37		c.761_762delAG	Deletion (Found in compound heterozygosity with c.461_467delGCACCCG)	Turkish	46,XY DSD; female external genitalia, 2 palpable gonads	Sagsak et al., 2015
38		p.Cys268Tyr	Missense/Inactivates enzyme	Pakistani	46,XY DSD; prominent clitoris, palpable inguinal gonads.	
39		p.His271Arg	Missense/Inactivates enzyme	French	46,XY DSD	
40		p.Pro282Leu	Missense/Inactivates enzyme	White American, Dutch	46,XY DSD; clitoromegaly, failure of breast development and deepening of voice.	
41	Exon 11	p.Tyr287Stop	Nonsense/Truncated protein	Turkish	Tanner stage 5. The patient had hirsutism and deepening voice change with normal female external genitalia except for a cliteromegaly (sinnecker type 5).	Tuhan et al., 2015

42		p.Gly289Ser	Polymorphism/Unknown	Italian, West Indian, Brazilian, Egyptians	46,XY DSD; normal female prepubertal genitalia, bilateral inguinal hernia at sonography. 46,XY DSD; ambiguous genitalia, single opening and penis-like phallus	Castro et al., 2012; The current study
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^{*} A modified table of *George et al.*, 2010 with the references of the added cases in *Bold Italic* style.