Appendix 1

Table 1: The 84 KMT2A variants observed in the individuals in my cohort with Wiedemann-Steiner syndrome.

Mutations refer to transcript: ENST00000534358.1 and Genome Reference Consortium human genome build 37 (GRCh37).

HGVSc (Transcript ENST00000534358.1)	HGVSp (ENSP00000436786.1)	Genomic co-ordinates	Consequence
c.152_186del35	p.Pro51ArgfsTer84	11:118307378-118307413	frameshift_variant
c.553C>T	p.Arg185Ter	11:118342427-118342427	stop_gained
c.1474_1493dup20	p.Pro500LeufsTer74	11:118343367-118343367	frameshift_variant
c.1660delC	p.Gln554SerfsTer13	11:118343533-118343534	frameshift_variant
c.2126_2127delCT	p.Ser709Ter	11:118343999-118344001	frameshift_variant
c.2262delC	p.Met755Ter	11:118344135-118344136	frameshift_variant
c.2318dupC	p.Ser774ValfsTer12	11:118344192-118344192	frameshift_variant
c.2318dupC	p.Ser774ValfsTer12	11:118344192-118344192	frameshift_variant
c.2318dupC	p.Ser774ValfsTer12	11:118344192-118344192	frameshift_variant
c.2452A>T	p.Lys818Ter	11:118344326-118344326	stop_gained
c.2461dupA	p.Ser821LysfsTer11	11:118344335-118344335	frameshift_variant
c.2659delG	p.Glu887SerfsTer62	11:118344532-118344533	frameshift_variant
c.2659G>T	p.Glu887Ter	11:118344533-118344533	stop_gained
c.3034C>T	p.Gln1012Ter	11:118344908-118344908	stop_gained
c.3460C>T	p.Arg1154Trp	11:118348807-118348807	missense_variant
c.3460C>T	p.Arg1154Trp	11:118348807-118348807	missense_variant
c.3482G>C	p.Cys1161Ser	11:118348829-118348829	missense_variant
c.3500G>A	p.Cys1167Tyr	11:118348847-118348847	missense_variant
c.3518_3521delGCTT	p.Cys1173Ter	11:118348864-118348868	frameshift_variant
c.3521T>G	p.Leu1174Ter	11:118348868-118348868	stop_gained
c.3556A>G	p.Lys1186Glu	11:118348903-118348903	missense_variant
c.3570-2A>G	-	11:118350887-118350887	splice_acceptor_variant
c.3613dupT	p.Tyr1205LeufsTer7	11:118350932-	frameshift_variant

		118350932	
c.3635-2A>C	-	11:118352428-118352428	splice_acceptor_variant
c.3647_3650delAAGA	p.Lys1216ArgfsTer18	11:118352441-118352445	frameshift_variant
c.3649G>T	p.Glu1217Ter	11:118352444-118352444	stop_gained
c.3651dupG	p.Lys1218GlufsTer4	11:118352446-118352446	frameshift_variant
c.3697delG	p.Val1233LeufsTer2	11:118352491-118352492	frameshift_variant
c.3697delG	p.Val1233LeufsTer2	11:118352491-118352492	frameshift_variant
c.3790C>T	p.Arg1264Ter	11:118352585-118352585	stop_gained
c.3790C>T	p.Arg1264Ter	11:118352585-118352585	stop_gained
c.3790C>T	p.Arg1264Ter	11:118352585-118352585	stop_gained
c.3790C>T	p.Arg1264Ter	11:118352585-118352585	stop_gained
c.3809delA	p.Lys1270ArgfsTer86	11:118352600-118352601	frameshift_variant
c.4012+1G>C	-	11:118352808-118352808	splice_donor_variant
c.4030C>T	p.Gln1344Ter	11:118353154-118353154	stop_gained
c.4054delA	p.Ser1352ValfsTer4	11:118353177-118353178	frameshift_variant
c.4090A>T	p.Lys1364Ter	11:118354901-118354901	stop_gained
c.4218+1delG	-	11:118355029-118355030	splice_donor_variant
c.4333-2A>C	-	11:118359327-118359327	splice_acceptor_variant
c.4503C>A	p.Cys1501Ter	11:118360530-118360530	stop_gained
c.4576-1G>A	-	11:118360843-118360843	splice_acceptor_variant
c.4599dupT	p.Lys1534Ter	11:118360867-118360867	frameshift_variant
c.4635G>A	p.Trp1545Ter	11:118360903-118360903	stop_gained
c.4635G>A	p.Trp1545Ter	11:118360903-118360903	stop_gained
c.4713_4714delCT	p.Cys1572Ter	11:118361926-118361928	frameshift_variant
c.5167delT	p.Tyr1723ThrfsTer12	11:118363933-118363934	frameshift_variant
c.5431C>T	p.Arg1811Ter	11:118366482-118366482	stop_gained
c.5646T>G	p.Tyr1882Ter	11:118367064-118367064	stop_gained
c.5664+1G>T	-	11:118367083-118367083	splice_donor_variant
c.5672G>T	p.Gly1891Val	11:118368658-118368658	missense_variant
c.5708A>G	p.His1903Arg	11:118368694-	missense_variant

		118368694	
c.5749G>T	p.Asp1917Tyr	11:118368735-118368735	missense_variant
c.5873A>G	p.His1958Arg	11:118369155-118369155	missense_variant
c.5902_5903delGT	p.Val1968LeufsTer4	11:118369183-118369185	frameshift_variant
c.5935C>T	p.Arg1979Ter	11:118369217-118369217	stop_gained
c.6002_6005delTTGT	p.Phe2001TrpfsTer8	11:118370057-118370061	frameshift_variant
c.6079+1G>A	-	11:118370136-118370136	splice_donor_variant
c.6379C>T	p.Arg2127Ter	11:118372446-118372446	stop_gained
c.6379C>T	p.Arg2127Ter	11:118372446-118372446	stop_gained
c.6571C>T	p.Arg2191Ter	11:118373178-118373178	stop_gained
c.6712delG	p.Asp2238IlefsTer8	11:118373318-118373319	frameshift_variant
c.6811delA	p.Arg2271GlyfsTer6	11:118373417-118373418	frameshift_variant
c.6913delT	p.Ser2305LeufsTer2	11:118373519-118373520	frameshift_variant
c.7144C>T	p.Arg2382Ter	11:118373751-118373751	stop_gained
c.7264G>T	p.Gly2422Ter	11:118373871-118373871	stop_gained
c.7419delT	p.Pro2474LeufsTer35	11:118374025-118374026	frameshift_variant
c.7485_7488delTTCT	p.Ser2496CysfsTer12	11:118374091-118374095	frameshift_variant
c.7567_7570delGTCA	p.Val2523LysfsTer2	11:118374173-118374177	frameshift_variant
c.7753delG	p.Asp2585IlefsTer17	11:118374359-118374360	frameshift_variant
c.8095C>T	p.Arg2699Ter	11:118374702-118374702	stop_gained
c.8099_8106delTGGCATCC	p.Leu2700ProfsTer2	11:118374705-118374713	frameshift_variant
c.8267delT	p.Leu2756Ter	11:118374873-118374874	frameshift_variant
c.8577T>A	p.Asn2859Lys	11:118375184-118375184	missense_variant
c.8806_8809delGTCT	p.Val2936Ter	11:118375412-118375416	frameshift_variant
c.8874_8875delAG	p.Lys2961GlufsTer13	11:118375480-118375482	frameshift_variant
c.9495dupA	p.His3166ThrfsTer10	11:118376102-118376102	frameshift_variant
c.9661delC	p.Leu3221SerfsTer35	11:118376267-118376268	frameshift_variant
c.9857_9858delCC	p.Pro3286GlnfsTer7	11:118376463-118376465	frameshift_variant
c.9983dupA	p.His3328GlnfsTer31	11:118376590-118376590	frameshift_variant
c.10353delA	p.Glu3451AspfsTer8	11:118376959-	frameshift_variant

		118376960	
c.10457_10458delTT	p.Phe3486TyrfsTer8	11:118377063-118377065	frameshift_variant
c.11374_11376delCCT	p.Pro3792del	11:118390723-118390726	inframe_deletion
Chr11:118354782-118362888del		11:118354782-118362888	Exonic_deletion

Figure 1. Wiedemann-Steiner syndrome and Hypertrichosis (WiSH) Study phenotype questionnaire

On the next three pages follows the phenotype questionnaire.

Wiedemann-Steiner syndrome and Hypertrichosis (WiSH) Study phenotype questionnaire

Study Number:…….. Genetics Centre…….. Clinician……..
Male / female Date of birth…….. Age at last assessment……..Yrs……..months……..

Family history

Ethnicity……. Consanguinity Yes ☐, No ☐
Family History of developmental disorders Yes ☐ No ☐ Unknown ☐
Details…….....
Mother's age at birth of child……..Yrs Father's age at birth of child……..Yrs

Pregnancy, birth and neonatal period

Conception: Natural ☐ Assisted ☐
Details.....
Were there any pregnancy or labour complications (inc. maternal illness, bleeding, abnormal scans, assisted delivery)? Yes ☐ No ☐ Unknown ☐
Details……....
Duration of pregnancy:.....weeks

Birth weight .....g (.....centile) Birth length.....cm (.....centile)
Birth OFC.....cm (.....centile)

Neonatal feeding problems? Yes ☐ No ☐ Unknown ☐
Details…….
Neonatal hypotonia? Yes ☐ No ☐ Unknown ☐
Details…….
Other neonatal problems? Yes ☐ No ☐ Unknown ☐
Details…….

Development, learning and behaviour:

Milestones (please write NYA if not yet achieved)
Sat …… ..months, Walked ……..….yrs…….. months, First words ……. Yrs…… months

Learning difficulties? No ☐ Mild ☐Moderate ☐Severe☐ Profound ☐
Behavioural problems (inc autism)? Yes ☐No ☐Unknown☐
Details…….
School type: Mainstream ☐ Special needs ☐
Details…….

Growth

Height.....cm (age .....yrs….....months) (..... centile)
Head circumference.....cm (age .....yrs.....months) (..... centile)
Weight.....kg (age….....yrs.....months) (.....centile)
Mother's height.....cm Father's height.....cm

Clinical features

Constipation? Yes ☐ No ☐ Unknown ☐
Details……...
Feeding difficulties Yes ☐ No ☐ Unknown ☐
Details…….

NG or PEG feeding Yes ☐ No ☐ Unknown ☐
Details……
Other GI problems Yes ☐ No ☐ Unknown ☐
Details……

Frequent infections? Yes ☐ No ☐ Unknown ☐
Details……...

Cardiac anomaly? Yes ☐ No ☐ if no, have they had an echo? Yes ☐ No ☐
Details of cardiac
anomaly……

Seizures? Yes ☐ No ☐ Unknown ☐
Details……
Autonomic dysfunction? Yes ☐ No ☐ Unknown ☐
Details…….....
Sleep disturbance? Yes ☐ No ☐ Unknown ☐
Details…….....
Reduced pain perception? Yes ☐ No ☐ Unknown ☐
Details……...
Other neurological abnormality? Yes ☐ No ☐ Unknown ☐
Details……...
Have they had a brain MRI? Yes ☐ No ☐ Unknown ☐
Result……...

Visual Abnormality? Yes ☐ No ☐ Unknown ☐
Details……...

Audiological Abnormality? Yes ☐ No ☐ Unknown ☐
Details……...

Premature eruption of dentition? Yes ☐ No ☐ Unknown ☐ Details……...
Other dental abnormality? Yes ☐ No ☐ Unknown ☐
Details……...

Hypertrichosis Arms Yes ☐ No ☐, Legs Yes ☐No ☐, Back Yes ☐No ☐, Face Yes ☐No ☐
Age hair growth first noted and distribution
……...
Swelling of hands or feet? Yes ☐ No ☐ Unknown ☐
Details……...
Other skin/bone/muscle abnormality Yes ☐ No ☐ Unknown ☐
Details……...

Urogenital Abnormalities? Yes ☐ No ☐ Unknown ☐
Details……...
Have they had a renal US? Yes ☐ No ☐ Unknown ☐
Result……...

Age entered puberty Normal ☐, Early ☐, Late ☐, Unknown ☐, Not reached ☐
Menstrual disturbance Yes ☐ No ☐ Unknown ☐ Details ……..
Other endocrine abnormality Yes ☐ No ☐ Unknown ☐ Details
……..

Please list any other problems / difficulties:……
……
……

On examination:

Joint hypermobility	Yes ☐	No ☐	Not Assessed ☐			
Fetal finger pads	Yes ☐	No ☐	Not Assessed ☐			
Deep palmar creases	Yes ☐	No ☐	Not Assessed ☐			
Sacral dimple	Yes ☐	No ☐	Not Assessed ☐			
Abnormal fat pads on feet	Yes ☐	No ☐	Not Assessed ☐			
Muscular Build	Yes ☐	No ☐	Not Assessed ☐			
Abnormal body fat distribution	Yes ☐	No ☐	Not Assessed ☐			

Other Examination findings:……
……

Do they take any medications? Yes ☐ No ☐ Unknown ☐, if yes please list:
……
……
……
Have they ever been admitted to hospital or attended the emergency department? Yes ☐ No ☐ Unknown ☐, if yes please list each occasion:
……
……
……
……

Please include relevant clinic letters, laboratory reports and growth data.

Do they take any medications? Yes ☐ No ☐ Unknown ☐, if yes please list:
……
……
……
Have they ever been admitted to hospital or attended the emergency department? Yes ☐ No ☐ Unknown ☐, if yes please list each occasion:
……
……
……
……

Please include relevant clinic letters, laboratory reports and growth data.

Appendix 2

Table 1: Pathogenic variants in *KMT2A*

KMT2A variants identified through Whole Exome Sequencing in 248 individuals with a phenotype consistent with Wiedemann-Steiner syndrome, related phenotypes or increased body hair plus other phenotypic features. Position refers to position on chromosome 11 and to transcript ENST00000534358. All variants are unique in the DDD dataset and WiSH dataset and not present in the eXac database [ref], The bottom two variants had previously present in ExAC but then had been subsequently removed. ** Patient is known to have an affected mother, all other individual have unaffected parents NB some trios we do not know about parents affected status. DN = de novo. PAT MOS = Paternal mosaicism.

ID	POSITION	CONSEQ	PolyPhen SIFT (Missense)	REF	ALT	HGVSc	HGVSp	INH
272567	118374704	Frameshift	-	ACTGGCATC	A	c.8098_8105delCTGGCATC	p.Leu2700ProfsTer2	*DN*
273060	118374171	Frameshift	-	ACAGT	A	c.7565_7568delCAGT	p.Val2523LysfsTer2	*DN*
267429	118353193	Stop gained	-	C	T	c.4069C>T	p.Gln1357Ter	U
259584	118375405	Frameshift	-	ATCTG	A	c.8799_8802delTCTG	p.Val2936Ter	U
260169	118367053	Frameshift	-	TG	T	c.5636delG	p.Cys1879PhefsTer2	U
260165	118352786	Stop gained	-	C	T	c.3991C>T	p.Gln1331Ter	U
258665	118374786	Frameshift	-	AC	A	c.8180delC	p.Thr2727LysfsTer30	U
265131	118372446	Stop gained	-	C	T	c.6379C>T	p.Arg2127Ter	*DN*
264841	118368658	Missense	PDamDel	G	T	c.5672G>T	p.Gly1891Val	*DN*
271611	118359327	Splice acceptor variant	-	A	C	c.4333-2A>C		*DN*
271660	118344530	Frameshift	-	CG	C	c.2657delG	p.Glu887SerfsTer62	*DN*
259227	118363932	Frameshift	-	AT	A	c.5166delT	p.Tyr1723ThrfsTer12	*DN*
273901	118375184	Missense	PDamDel	T	A	c.8577T>A	p.Asn2859Lys	*DN*
260868		Frameshift	-			c.1474_1493dup20	p.Pro500Leufs*74	*DN*
276248	118343528	Frameshift	-	GCCCCCC	GCCCCC	c.1654_1655delGCinsG	p.Gln554SerfsTer13	*DN*
270606	118390134-118392246	Multi-exonic deletion						*DN*
WW1	118348807	Missense	PDamDel	C	T	c.3460C>T	p.Arg1154Trp	*DN*
WW2	118348847	Missense	PDamDel	G	A	c.3500G>A	p.Cys1167Tyr	*DN*
WW3	118350931	Frameshift	-	C	CT	c.3612_3613insT	p.Tyr1205LeufsTer7	*DN*
WW4	118352436	Frameshift	-	AAAAG	A	c.3642_3645delAAAG	p.Lys1216ArgfsTer18	*DN*
WW5	118352491	Frameshift	-	TG	T	c.3697delG	p.Val1233LeufsTer2	PATMOS
WW6	118369155	Missense	PDamDel	A	G	c.5873A>G	p.His1958Arg	NOTMAT
WW7	118370136	Splice donor	-	G	A	c.6079+1G>A		*DN*
WW8	118374358	Frameshift	-	AG	A	c.7752delG	p.Asp2585IlefsTer17	*DN*
WW9	118376461	Frameshift	-	TCC	T	*DN*	:p.Pro3286GlnfsTer7	NOTMAT
WW10	118377062	Frameshift	-	CTT	C	c.10456_10457delTT	p.Phe3486TyrfsTer8	*DN*
WW11	118344185	Frameshift	-	A	AC	c.2311_2312insC	p.Ser774ValfsTer12	*DN*
WW12	118344185	Frameshift	-	A	AC	c.2311_2312insC	p.Ser774ValfsTer12	

Table 2: Pathogenic d*e novo* loss of function or missense mutations in DDG2P genes

De novo loss of function or missense variants assessed to be pathological in causing the individual's phenotype identified through whole Exome Sequencing in 228 individuals with a phenotype consistent with Wiedemann-Steiner syndrome, related phenotypes or increased body hair plus other phenotypic features.

ID	GENE	CHR	POS	TRANS	CONSEQ	PolyPhen/ SIFT	REF / ALT	MAF	GENO	EXAC
261629	ARID1B	6	157100465	ENST00000346085	Stop gained		C/T	***	1/0/0	NA
270826	ADNP	20	49507987	ENST00000396029	Frameshift		CA /C		1/0/0	NA
262888	CBL	11	119148874	ENST00000264033	Splice acceptor		A/T	NA	1/0/0	NA
263977	ARID1B	6	157150547	ENST00000346085	Stop gained		C/T	NA	1/0/0	NA
274225	MBD5	2	149226237	ENST00000407073	Frameshift		AC/ A	NA	1/0/0	NA
281166	SMARCA2	9	2086862	ENST00000382203	Missense	Benign DEL *	C/T	NA	1/0/0	NA
261706	SCN2A	2	166172031	ENST00000357398	Frameshift		TG/ T	NA	1/0/0	NA
273003	MED13L	12	116429567	ENST00000281928	Frameshift		G/G C	NA	1/0/0	NA
261065	MED13L	12	116452954	ENST00000281928	Stop gained		G/A	NA	1/0/0	NA
272674	CREBBP	16	3801726	ENST00000262367	Splice donor		C/A	NA	1/0/0	NA
260414	DNMT3A	2	25470582	ENST00000264709	Missense	ProbDam DEL	C/T	NA	1/0/0	NA
262471	BCL11A	2	60773352	ENST00000335712	Missense	ProbDam DEL	T/G	NA	1/0/0	NA
265865	HNRNPU	1	245022576	ENST00000283179	Splice donor		C/T	NA	1/0/0	NA
263116	ARID1B	6	157527664	ENST00000346085	Frameshift		CTG TT/ C	NA	1/0/0	NA
279294	SMAD4	18	48604664	ENST00000342988	Missense	ProbDam DEL	C/T	8.24 E-06	1/0/0	1
262215	SMARCB1	22	24175856	ENST00000263121	Inframe deletion		GA GA/ G	NA	1/0/0	NA
266748	EP300	22	41562653	ENST00000263253	Missense	PossDam DEL	A/G	NA	1/0/0	NA
257812	COL4A3BP	5	74722257	ENST00000380494	Missense	ProbDam DEL	G/A	NA	1/0/0	NA
260433	ARID1B	6	157150439	ENST00000346085	Stop gained		C/T	NA	1/0/0	NA
261034	ARID1B	6	157527539	ENST00000346085	Frameshift		CAG AA/ C	NA	1/0/0	NA
262754	SMARCA2	9	2060867	ENST00000382203	Missense	PossDam DEL	C/T	NA	1/0/0	NA
263882	ADNP	20	49508751	ENST00000396029	Frameshift		CTT TAT/ CT	NA	1/0/0	NA
267419	DYRK1A	21	38850576	ENST00000398960	Frameshift		AT/ A	NA	1/0/0	NA
272205	MED13L	12	116401227	ENST00000281928	Missense	ProbDam(0.999),DEL(0)	G/A	NA	1/0/0	NA
273042	ABCC9	12	21997785	ENST00000261200	Missense	PossDam DEL	G/T	NA	1/0/0	NA
273981	SYNGAP1	6	33411558	ENST00000418600	Frameshift		ACA GT/ A	NA	1/0/0	NA
276409	EP300	22	41543865	ENST00000263253	Frameshift		GCA TGG	NA	1/0/0	NA

							CC/G			
278805	EYA1	8	72211338	ENST00000340726	Frameshift		TG/T	NA	1/0/0	NA
279844	CTCF	16	67655480	ENST00000264010	Missense	ProbDam TOL	G/A	NA	1/0/0	NA
280914	DNMT3A	2	25467466	ENST00000264709	Missense	ProbDam DEL	C/T	NA	1/0/0	NA
265425	TUBA1A	12	49579605	ENST00000546918	stop_lost		C/A	NA	1/0/0	NA
258278	ABCC9	12	22061091	ENST00000261200	Missense	PossDam TOL	C/T	NA	1/0/0	NA
258975	ARID1B	6	157527679	ENST00000346085	Stop gained		C/T	NA	1/0/0	NA
258975	ARID1B	6	157527679	ENST00000346085	Stop gained		C/T	NA	1/0/0	NA
259221	ACTB	7	5567395	ENST00000331789	Missense	ProbDam DEL	T/C	NA	1/0/0	NA

Table 3: Pathogenic heterozygous variants in DDG2P genes inherited from an affected parent

Loss of function and functional variants in DDG2P genes inherited from an affected parent and assessed to be pathological in causing the individual's phenotype identified through whole Exome Sequencing in 228 individuals with a phenotype consistent with Wiedemann-Steiner syndrome, related phenotypes or increased body hair plus other phenotypic features.

ID	GENE	CHR	POS	TRANS	CONSEQ	Poly Phen /SIFT	REF / ALT	MAF	GENO	EXAC	PHENO
272901	RAD21	8	117866693	ENST00000297338	Frameshift		CT/C	NA	1/0/1	NA	FIT
260000	ARID1B	6	157517398	ENST00000346085	Missense	Poss Dam DEL	T/G	0.000122	1/0/1	NA	DP
263662	GRIN2A	16	10031815	ENST00000396573	Splice donor		C/A	NA	1/1/0	NA	CF
276420	ANKRD11	16	89350830	ENST00000301030	Frameshift		TC/T	NA	1/1/0	NA	FIT

Table 4: Pathogenic heterozygous variants in dominant DDG2P genes where inheritance information was not available

Loss of function and functional variants in dominant DDG2P genes where inheritance information was not available and assessed to be pathologenic in causing the individual's phenotype identified through whole Exome Sequencing in 228 individuals with a phenotype consistent with Wiedemann-Steiner syndrome, related phenotypes or increased body hair plus other phenotypic features.

ID	GENE	CHR	POS	TRANS	CONSEQ	PolyPhen/SIFT	REF/ALT	MAF	GENO	EXAC	Path
258284	ASXL3	18	31324288	ENST00000269197	Frameshift		AAGCTC/A	NA	1/NA/NA	NA	FIT
259668	HNRNPU	1	245022606	ENST00000283179	Stop gained		C/T	NA	1/NA/NA	NA	FIT
262336	NIPBL	5	37022374	ENST00000282516	Missense	ProbDamDEL	G/A	NA	1/NA/NA	NA	FIT
264183	ASXL3	18	31318772	ENST00000269197	Frameshift		A/AAATC	NA	1/NA/NA	NA	FIT
264262	EP300	22	41548351	ENST00000263253	Frameshift		AAG/A	NA	1/NA/NA	NA	FIT
264723	ARID1B	6	157527837	ENST00000346085	Frameshift		TAGAA/T	NA	1/NA/NA	NA	FIT
267485	WAC	10	28824686	ENST00000354911	Splice donor		GGTGA/GAACAGCAGTCCCCAAAGCCACTCTCAGCCCTTGCAGACGTCCCACCGCATGTGA	NA	1/NA/NA	NA	FIT
268440	ARID1B	6	157502271	ENST00000346085	Stop gained		C/T	NA	1/NA/NA	NA	FIT
270585	SETD5	3	9483320	ENST00000402198	Frameshift		TC/T	NA	1/NA/NA	NA	FIT
272241	ANKRD11	16	89351042	ENST00000301030	Frameshift		GTGTTT/G	NA	1/NA/NA	NA	FIT
259607	ANKRD11	16	89350783	ENST00000301030	Frameshift		CTT/C	NA	1/NA/NA	NA	FIT
259639	WAC	10	28878738	ENST00000354911	Frameshift		CA/C	NA	1/NA/NA	NA	FIT

Table 5: Pathogenic variants in X-linked DDG2P genes

Loss of function and functional variants in X-linked DDG2P genes assessed to be pathogenic in causing the individual's phenotype identified through whole Exome Sequencing in 228 individuals with a phenotype consistent with Wiedemann-Steiner syndrome, related phenotypes or increased body hair plus other phenotypic features.

ID	GENE	CHR	POS	TRANS	CONSEQ	PolyPhen/ SIFT	REF / ALT	MAF	GENO	EXAC
263763	PHF6	X	133527600	ENST00000332070	Missense	ProbDam DEL	C/T	NA	1/NA/ NA	NA
259485	HDAC8	X	71708853	ENST00000373561	Missense	Benign*	G/A		1/1/0	NA
260478	HDAC8	X	71715077	ENST00000373573	Missense	ProbDam DEL	A/G	NA	1/0/0	NA
258681	SMC1A	X	53432045	ENST00000322213	Missense	ProbDam DEL	G/A	0.00 012 2	1/0/0	NA
274689	DDX3X	X	41205589	ENST00000399959	Missense	PossDam DEL	C/T	NA	1/0/0	NA
269411	HDAC8	X	71571623	ENST00000373573	Missense	ProbDam DEL	A/T	NA	1/0/0	NA
267559	DDX3X	X	41205876	ENST00000399959	Splice donor		G/C	NA	1/0/0	NA
271331	HDAC8	X	71684432	ENST00000373573	Stop gained		A/T	NA	1/0/0	NA
271619	HDAC8	X	71684483	ENST00000373573	Missense	PossDam DEL	A/C	NA	1/0/0	NA
273139	DCX	X	110653435	ENST00000338081	Stop gained		G/C	NA	1/0/0	NA
277224	MECP2	X	153296516	ENST00000453960	Stop gained		G/A	NA	1/0/0	NA
278845	IQSEC2	X	53270970	ENST00000396435	Missense	ProbDam DEL	A/G	NA	2/0/0	NA
259137	DDX3X	X	41203558	ENST00000399959	Stop gained		C/T	NA	1/0/0	NA
270216	PHF8	X	54037639	ENST00000357988	Stop gained		G/A	0.00 013 8	2/1/0	NA

Table 6: Pathogenic biallelic variants in DDG2P genes

Loss of function and functional variants in biallelic DDG2P genes assessed to be pathogenic in causing the individual's phenotype identified through whole Exome Sequencing in 228 individuals with a phenotype consistent with Wiedemann-Steiner syndrome, related phenotypes or increased body hair plus other phenotypic features. *HACE1: Had recently been identified as a DD gene by the DDD analysis team. The publication documentation detailing this was under submission when this analysis was carried out.

ID	GENE	CHR	POS	TRANS	CONSEQ	REF/ ALT	MAF	GENO	EXAC
259339	TMCO1	1	165737436	ENST00000367881	Frameshift	ACT/A	0.000854	2/1/1	17
281381	HACE1* HACE1	6 6	105224626 105280997	ENST00000262903 ENST00000262903	Frameshift Stop gained	CTG/C G/A	0.000138 0.000138	1/1/0 1/0/1	NA NA

Table 7: Possible pathogenic variants in dominant DDG2P genes

Loss of function and functional variants in dominant DDG2P genes assessed to be possibly pathogenic in causing or contributing to the individual's phenotype identified through whole Exome Sequencing in 228 individuals with a phenotype consistent with Wiedemann-Steiner syndrome, related phenotypes or increased body hair plus other phenotypic features.

ID	GENE	CHR	POS	TRANS	CONSEQ	PolyPhen/ SIFT	REF/ ALT	MAF	GENO	EX AC
267975	DYNC1H1	14	102467512	ENST00000360184	Missense	Prob Dam, DEL	G/A	NA	1/NA/ NA	**NA**
279847	CHAMP1	13	115091109	ENST00000361283	Missense	Poss Dam, TOL	G/A	0.001	1/0/1	**5**
258295	SCN1A	2	166908329	ENST00000303395	Missense	Poss Dam, TOL	C/A	NA	1/0/1	**NA**
266755	ZSWIM6	5	60790136	ENST00000252744	Missense	Poss Dam, TOL	C/A	3.57E-05	1/0/1	**1**
267298	ARID1A	1	27087348	ENST00000324856	Missense	Unknown	A/C	NA	1/NA/ NA	**NA**
269266	SCN2A	2	166166908	ENST00000357398	Missense	Prob Dam, DEL	G/C	NA	1/0/0	**NA**
270556	ARID1B	6	157431623	ENST00000346085	Missense	Prob Dam, DEL	C/G	NA	1/NA/ NA	**NA**
271218	ARID1A	1	27088789	ENST00000324856	Missense	Unknown	G/C	NA	1/0/1	**NA**
272732	FANCA	16	89877126	ENST00000389301	Missense	Poss Dam, TOL	A/G	0.000276	1/1/0	**NA**
272732	FANCA	16	89882881	ENST00000567943	Missense	Unknown	G/T	0.0038	1/0/1	**2**
273187	ARID1B	6	157527742	ENST00000346085	Missense	Prob Dam, DEL	G/A	NA	1/1/0	**NA**
273379	HDAC4	2	240003811	ENST00000345617	Missense	Prob Dam, DEL	C/T	NA	1/NA/ NA	**NA**
278746	CBL	11	119149311	ENST00000264033	Missense	Poss Dam	G/T	0.000138	1/1/0	**2**
279847	IGF1R	15	99192836	ENST00000268035	Missense	Poss Dam, TOL	C/G	8.24E-06	1/0/1	**1**

Table 8: Possible pathogenic variants in biallelic DDG2P genes

Loss of function and functional variants in biallelic DDG2P genes assessed to be possibly pathogenic in causing or contributing to the individual's phenotype identified through whole Exome Sequencing in 228 individuals with a phenotype consistent with Wiedemann-Steiner syndrome, related phenotypes or increased body hair plus other phenotypic features.

ID	GENE	CHR	POS	TRANS	CONSEQ	PolyPhen/ SIFT	REF/ ALT	MAF	GENO	EX AC
275918	PC	11	66617092	ENST00000393960	Missense	Poss Dam, DEL	T/C	0.000 276	2/1/1	**5**
267275	CPS1	2	211523345	ENST00000430249	Missense	Poss Dam, DEL	T/C	0.000 244	2/1/1	**NA**
264350	COG1	17	71196139	ENST00000299886	Missense	Prob Dam, DEL	C/T	0.008 8600 9	2/1/1	**642**
271585	FAT4	4	126336669	ENST00000394329	Missense	Prob Dam, DEL	G/A	0.000 244	2/1/1	**NA**
259262	FAR1	11	13729542	ENST00000354817	Missense	Prob Dam, DEL	C/T	0.000 276	2/1/1	**NA**
259262	COG1	17	71202934	ENST00000299886	Missense	Prob Dam, DEL	C/T	0.000 276	2/1/1	1

Table 9: Possible pathogenic variants in X-linked DDG2P genes

Loss of function and functional variants in X-linked DDG2P genes assessed to be possibly pathogenic in causing or contributing to the individual's phenotype identified through whole Exome Sequencing in 228 individuals with a phenotype consistent with Wiedemann-Steiner syndrome, related phenotypes or increased body hair plus other phenotypic features.

ID	GENE	CHR	POS	TRANS	CONSEQ	Poly Phen /SIFT	REF/ ALT	MAF	GENO	EX AC
266180	HUWE1	X	53634593	ENST00000342160	Missense	Prob Dam, TOL	T/A	0.00019	1/1/0	5
267975	OPHN1	X	67333062	ENST00000355520	Missense	Poss Dam, DEL	T/C	NA	1/NA/ NA	NA
258369	OCRL	X	128721053	ENST00000371113	Missense	Prob Dam, DEL	C/G	0.00012 2	2/1/0	NA

Table 10: ZMYD11 *de novo* missense variants in the wider DDD cohort

Loss of function and functional *de novo* mutations in ZMYD11 identified from the wider DDD study of 4293 individuals. This excludes the two individuals with *de novo* mutations in ZMYD11 detailed in Chapter 3.

ID	SEX	CHR	POS	TRANS	CONSEQ	ALT/ REF	GENO (P/M/F)	ExAC FREQ
272015	F	10	294310	ENST00000397962	Missense	G/A	1/0/0	0
265790	M	10	294525	ENST00000397962	Missense	G/A	1/0/0	0
264849	M	10	298321	ENST00000397962	Missense	T/C	1/0/0	0