

**Supplemental Table 1: Genes linked to idiopathic hypogonadotropic hypogonadism\***

ADRB2	FLT2	NROB1	SIM1
ADRB3	FSHB	NROB2	SIN3A
AGRP	GHRL	NR5A1	SNRPN
ANK1	GLCE	NSMF	SOX10
AR	GLI3	NSMF(NELF)	SOX2
ARL6	GNAS	NTN1	SPRY4
AXL	GNRH1	OTUD4	STUB1
BBS1	GNRHR	PCSK1	TAC2
BMP2	HFE	PGM2	TAC3
CARTPT	HFE2	PHIP	TACR3
CCDC141	HS6ST1	PNPLA6	TBCE
CCDC28B	IL17RD	POLR1C	TCF12
CHD4	INSR	POLR3A	TFR2
CHD7	KAL1	POLR3B	TRIM37
CYP19A1	KISS1	POMC	Trp63
DCAF17	KISS1R	PPARG	TSHZ1
DCC	KL	PPARGC1B	TUBB3
DMXL1	KLB	PROK2	TYRO3
DUSP6	LEP	PROKR2	UCP1
ENPP1	LEPR	RAB3GAP2	UCP3
FEZF1	LHB	RBM28	WDR11
FGF17	LHCGR	RNF216	ZIC1
FGF8	MAGEL2	SDC3	
FGFR1	MC4R	SEMA3A	
FLRT3	NDN	SEMA3E	

\* List assembled from literature and those reported in Online Mendelian Inheritance in Man database ([www.omim.org](http://www.omim.org))

**Supplemental Table 2: Marsolf syndrome cases with previously reported reproductive phenotypes**

Cases	Martsolf et al. 1978 <sup>9</sup>		Hennekam et al. 1988 <sup>5</sup>	
	Case 1	Case 2	Case 1	Case 2
Sex	Male	Male	Male	Female
Last-reported age (yr)	28 years	25 years	12 years	17 years
Consanguinity	+	+	-	-
Genetic Characterization	-	-	-	-
Primary DX (Age)	Martsolf	Martsolf	Martsolf	Martsolf
Initial Treatment	Not reported	Not reported	Not reported	Not reported
Olfaction	Not reported	Not reported	Not reported	Not reported
Birth weight	-	2800 g	1980 g	2250 g
Postnatal growth retardation	+	+	+	+
Postnatal Microcephaly	+	+	+	+
Developmental delay/ mental retardation	Severe	Severe	Moderate	Moderate
Speech delayed	4 years	7 years	+	+
Walking delayed	4 years	4 years	+	+
Seizures	-	-	-	-
Microphthalmia	-	-	-	-
Bilateral congenital Cataracts	Bilateral lacy lenticular cataracts	Bilateral lacy lenticular cataracts	Bilateral posterior cortical cataracts	Bilateral posterior cortical cataracts
Optic nerve atrophy	-	-	-	-
Vision	-	-	Decreased	Decreased
Hypotonia	-	-	-	-
Limb spasticity	-	-	+	+
Hypogonadism	compensated hypergonadotropism	compensated hypergonadotropism	Pre-pubertal subject	Likely Hypogonadotropic Hypogonadism (since <18 years)
Reproductive phenotypes	Small testis	Small testis	Bilateral cryptorchidism, micropenis	No menstruation at 17 years
Other Non-reproductive phenotypes	Clinodactyly; Large ears	Short metacarpal and phalangeal bones;	Short metacarpal and phalangeal bones; Lax finger joints; Posteriorly rotated ears	Short metacarpal and phalangeal bones; Lax finger joints;
Lab investigations	FSH 113 pg/dl (N 2.5-6.0 pg/dl), LH 20 pg/dl (N 2.5-6.0 pg/dl)	FSH > 150 pg/dl, LH 31 pg/dl	FSH < 2.0 mU/ml (N 5.0-50 mU/ml)	FSH 5.7mU/ml; LH < 2.0 mU/ml
	T 361-429 ng/dl	T 413-566 ng/dl	T 2.9 nmol/l (N 0.7-19nmol/l)	E2 0.14 nmol/l (N < 0.11 nmol/l)
			PRL 6.8ng/ml (N 1.0-25.0 ng/ml)	PRL 6.3 ng/ml
Imaging (Brain/Pituitary etc)	Moderate cerebral atrophy	-	-	MRI normal

T: Testosterone; LH: Leutinizing hormone; FSH: Follicle stimulating hormone; E2: Estadiol; PRL: prolactin