Whole Exome Sequencing
Gene package Disorders of Sex Development (DSD), version 5.1, 22-11-2017

Technical information
DNA was enriched using Agilent SureSelect Clinical Research Exome V2 capture and paired-end sequenced on the Illumina platform (outsourced). The aim is to obtain 8.1 Giga base pairs per exome with a mapped fraction of 0.99. The average coverage of the exome is ~50x. Duplicate reads are excluded. Data are demultiplexed with bcl2fastq Conversion Software from Illumina. Reads are mapped to the genome using the BWA-MEM algorithm (reference: http://bio-bwa.sourceforge.net/). Variant detection is performed by the Genome Analysis Toolkit HaplotypeCaller (reference: http://www.broadinstitute.org/gatk/). The detected variants are filtered and annotated with Cartagenia software and classified with Alamut Visual. It is not excluded that pathogenic mutations are being missed using this technology. At this moment, there is not enough information about the sensitivity of this technique with respect to the detection of deletions and duplications of more than 5 nucleotides and of somatic mosaic mutations (all types of sequence changes).

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HGNC approved gene symbol	Phenotype description including OMIM phenotype ID(s)	OMIM gene ID	median depth	% covered >10x	% covered >20x	% covered >30x
AKR1C1	No OMIM phenotype	600449	66	100	100	94
AKR1C4	{46XY sex reversal 8, modifier of}, 614279	600451	52	100	100	93
AMH	Persistent Mullerian duct syndrome, type I, 261550	600957	64	100	100	93
AMHR2	Persistent Mullerian duct syndrome, type II, 261550	600956	80	100	100	94
ANOS1	Hypogonadotropic hypogonadism 1 with or without anosmia (Kallmann syndrome 1), 308700	300836	44	100	93	75
AR	Androgen insensitivity, 300068 Androgen insensitivity, partial, with or without breast cancer, 312300 Hypospadias 1, 300633 {Prostate cancer, susceptibility to}, 176807 Spinal and bulbar muscular atrophy of Kennedy, 313200	313700	60	100	95	81
ARX	Epileptic encephalopathy, early infantile, 1, 308350 Hydranencephaly with abnormal genitalia, 300215 Lissencephaly 2, 300215 Mental retardation 29 and others, 300419 Partington syndrome, 309510 Proud syndrome, 300004	300382	42	89	80	65
ATRX	Alpha-thalassemia myelodysplasia syndrome, somatic, 300448 Alpha-thalassemia/mental retardation syndrome, 301040 Mental retardation-hypotonic facies syndrome, 309580	300032	40	100	91	76
BMP15	Ovarian dysgenesis 2, 300510 Premature ovarian failure 4, 300510	300247	52	100	100	86
CBX2	?46XY sex reversal 5, 613080	602770	89	100	98	94

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CDKN1C	Beckwith-Wiedemann syndrome, 130650 IMAGE syndrome, 614732	600856	56	91	83	74
CHD7	CHARGE syndrome, 214800 Hypogonadotropic hypogonadism 5 with or without anosmia, 612370	608892	60	100	99	93
CREBBP	Rubinstein-Taybi syndrome 1, 180849	600140	81	100	99	91
CYB5A	?Methemoglobinemia, type IV, 250790	613218	47	100	100	89
CYP11A1	Adrenal insufficiency, congenital, with 46XY sex reversal, partial or complete, 613743	118485	68	100	100	100
CYP17A1	17-alpha-hydroxylase/17,20-lyase deficiency, 202110 17,20-lyase deficiency, isolated, 202110	609300	80	100	100	98
CYP19A1	Aromatase deficiency, 613546 Aromatase excess syndrome, 139300	107910	49	100	97	79
DHCR7	Smith-Lemli-Opitz syndrome, 270400	602858	84	100	100	100
DHH	46XY partial gonadal dysgenesis, with minifascicular neuropathy, 607080 46XY sex reversal 7, 233420	605423	79	100	100	100
DMRT1	No OMIM phenotype	602424	80	100	100	100
DMRT2	No OMIM phenotype	604935	71	100	99	92
FAM58A	STAR syndrome, 300707	300708	50	81	81	80
FGF8	Hypogonadotropic hypogonadism 6 with or without anosmia, 612702	600483	94	99	94	94
FGFR1	Encephalocraniocutaneous lipomatosis, 613001 Hartsfield syndrome, 615465 Hypogonadotropic hypogonadism 2 with or without anosmia, 147950 Jackson-Weiss syndrome, 123150 Osteoglophonic dysplasia, 166250 Pfeiffer syndrome, 101600 Trigonocephaly 1, 190440	136350	70	100	100	96
FGFR2	Antley-Bixler syndrome without genital anomalies or disordered steroidogenesis, 207410 Apert syndrome, 101200 Beare-Stevenson cutis gyrata syndrome, 123790 Bent bone dysplasia syndrome, 614592 Craniofacial-skeletal-dermatologic dysplasia, 101600 Craniosynostosis, nonspecific Crouzon syndrome, 123500 Gastric cancer, somatic, 613659 Jackson-Weiss syndrome, 123150 LADD syndrome, 149730 Pfeiffer syndrome, 101600 Saethre-Chotzen syndrome, 101400 Scaphocephaly and Axenfeld-Rieger anomaly Scaphocephaly, maxillary retrusion, and mental retardation, 609579	176943	49	100	98	81

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FOXL2	Blepharophimosis, epicanthus inversus, and ptosis, type 1, 110100 Blepharophimosis, epicanthus inversus, and ptosis, type 2, 110100 Premature ovarian failure 3, 608996	605597	86	100	94	88
FSHB	Hypogonadotropic hypogonadism 24 without anosmia, 229070	136530	58	100	100	100
FSHR	Ovarian dysgenesis 1, 233300 Ovarian hyperstimulation syndrome, 608115 Ovarian response to FSH stimulation, 276400	136435	55	100	99	89
GATA4	Atrial septal defect 2, 607941 Atrioventricular septal defect 4, 614430 ?Testicular anomalies with or without congenital heart disease, 615542 Tetralogy of Fallot, 187500 Ventricular septal defect 1, 614429	600576	42	100	86	65
GNRHR	Hypogonadotropic hypogonadism 7 without anosmia, 146110	138850	74	100	100	98
HOXA13	Guttmacher syndrome, 176305 Hand-foot-uterus syndrome, 140000	142959	75	86	78	72
HSD17B3	Pseudohermaphroditism, male, with gynecomastia, 264300	605573	42	100	95	79
HSD3B2	Adrenal hyperplasia, congenital, due to 3-beta-hydroxysteroid dehydrogenase 2 deficiency, 201810	613890	108	100	100	100
LHCGR	Leydig cell adenoma, somatic, with precocious puberty, 176410 Leydig cell hypoplasia with hypergonadotropic hypogonadism, 238320 Leydig cell hypoplasia with pseudohermaphroditism, 238320 Luteinizing hormone resistance, female, 238320 Precocious puberty, male, 176410	152790	55	100	98	84
MAMLD1	Hypospadias 2, 300758	300120	65	100	97	93
MAP3K1	46XY sex reversal 6, 613762	600982	53	100	99	90
MCM8	?Premature ovarian failure 10, 612885	608187	40	100	95	73
MCM9	Ovarian dysgenesis 4, 616185	610098	60	100	99	89
NR0B1	Adrenal hypoplasia, congenital, 300200 46XY sex reversal 2, dosage-sensitive, 300018	300473	77	100	100	99
NR5A1	Adrenocortical insufficiency, 612964 Premature ovarian failure 7, 612964 Spermatogenic failure 8, 613957 46, XX sex reversal 4, 617480 46XY sex reversal 3, 612965	184757	72	100	98	95
NUP107	Nephrotic syndrome, type 11, 616730	607617	37	100	94	69
POR	Antley-Bixler syndrome with genital anomalies and disordered steroidogenesis, 201750 Disordered steroidogenesis due to cytochrome P450 oxidoreductase, 613571	124015	84	100	100	100
PROK2	Hypogonadotropic hypogonadism 4 with or without anosmia, 610628	607002	38	100	100	81
PROKR2	Hypogonadotropic hypogonadism 3 with or without anosmia, 244200	607123	138	100	100	100
PSMC3IP	Ovarian dysgenesis 3, 614324	608665	73	100	100	100

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RSPO1	Palmoplantar hyperkeratosis and true hermaphroditism, 610644 Palmoplantar hyperkeratosis with squamous cell carcinoma of skin and sex reversal, 610644	609595	50	100	100	94
SOX3	Mental retardation, with isolated growth hormone deficiency, 300123 Panhypopituitarism, 312000	313430	56	100	96	89
SOX9	Acampomelic campomelic dysplasia, 114290 Campomelic dysplasia, 114290 Campomelic dysplasia with autosomal sex reversal, 114290	608160	66	100	100	99
SRD5A2	Pseudovaginal perineoscrotal hypospadias, 264600	607306	44	100	94	76
SRY	46XX sex reversal 1, 400045 46XY sex reversal 1, 400044	480000	20	50	41	35
STAG3	Premature ovarian failure 8, 615723	608489	65	100	98	93
STAR	Lipoid adrenal hyperplasia, 201710	600617	75	100	100	100
SYCE1	?Premature ovarian failure 12, 616947 ?Spermatogenic failure 15, 616950	611486	55	100	100	93
TSPYL1	Sudden infant death with dysgenesis of the testes syndrome, 608800	604714	87	100	100	100
WDR11	Hypogonadotropic hypogonadism 14 with or without anosmia, 614858	606417	59	100	98	86
WNT4	Mullerian aplasia and hyperandrogenism, 158330 ?SERKAL syndrome, 611812	603490	115	92	92	92
WT1	Denys-Drash syndrome, 194080 Frasier syndrome, 136680 Meacham syndrome, 608978 Mesothelioma, somatic, 156240 Nephrotic syndrome, type 4, 256370 Wilms tumor, type 1, 194070	607102	80	100	98	96
ZFPM2	Diaphragmatic hernia 3, 610187 Tetralogy of Fallot, 187500 46XY sex reversal 9, 616067	603693	60	100	100	100

- Gene symbols according HGCN
- OMIM release used: 2-6-2017
- "No OMIM phenotypes" indicates a gene without a current OMIM association
- OMIM phenotypes between "[ ]", indicate "nondiseases," mainly genetic variations that lead to apparently abnormal laboratory test values
- OMIM phenotypes between "{}", indicate risk factors
- OMIM phenotypes with a question mark, "?", before the disease name indicates an unconfirmed or possibly spurious mapping
- The statistics above are based on a set of 96 samples
- Median depth is the median of the mean sequence depth over the protein coding exons (±10bp flanking introns) of the longest transcript
- % Covered 10x describes the percentage of a gene's coding sequence (±10bp flanking introns) that is covered at least 10x
- % Covered 20x describes the percentage of a gene's coding sequence (±10bp flanking introns) that is covered at least 20x