Disorders of Sex Development

Precision Panel

Overview

Disorders of Sex Development (DSD), formerly termed intersex conditions, occur when there is a discrepancy between the appearance of the genitalia and the genetic makeup of an individual. These disorders can present from birth to adolescence. DSD can be mild or significant depending on the appearance of the genitalia and associated symptoms. DSD can be caused by changes at a chromosomal level and gene level thus the inheritance pattern of DSDs can be dominant, recessive or sex-linked. Additionally, DSDs can occur due to de novo changes in the DNA (for the first time in the affected individual).

The Igenomix Disorders of Sex Development Precision Panel can be used to make a directed and accurate differential diagnosis of ambiguous genitalia ultimately leading to a better management and prognosis of the disease. It provides a comprehensive analysis of the genes involved in this disease using next-generation sequencing (NGS) to fully understand the spectrum of relevant genes involved.

Indications

The Igenomix Disorders of Sex Development Precision Panel is indicated for those patients with clinical suspicion of an intersex condition presenting with the following manifestations:

- Family history of genital ambiguity
- History of early death of infants
- Maternal drug ingestion
- Ambiguous genitalia
- Abnormal size and degree of differentiation of phallus
- Abnormal position of urethral meatus
- Separated labioscrotal folds
- Labioscrotal folds with increased pigmentation

Clinical Utility

The clinical utility of this panel is:

- The genetic and molecular confirmation for an accurate clinical diagnosis of a symptomatic patient.

- Early initiation of treatment with a multidisciplinary team for early surgical reconstruction, psychosocial aids and pharmacologic treatment.
- Risk assessment of asymptomatic family members according to the mode of inheritance.

Genes & Diseases

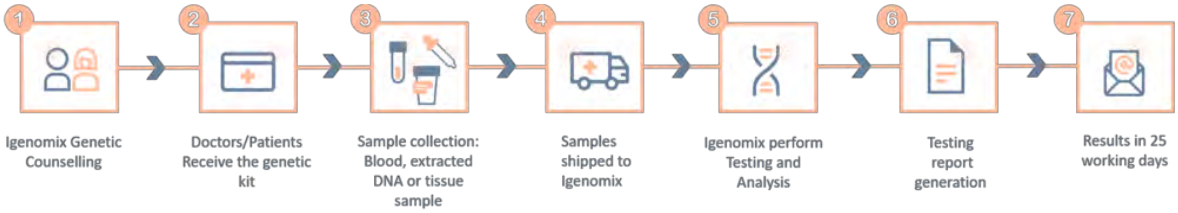
GENE	OMIM DISEASES	INHERITANCE*	% GENE COVERAGE (20X)	HGMD**
AKR1C2	46,XY Sex Reversal 8	AR	91.52%	5 of 7
AKR1C3	Prostate Cancer, Endometrial Cancer, Breast Cancer, Skin Squamous Cell Carcinoma	-	96.97%	2 of 2
AMH	Persistent Mullerian Duct Syndrome Types 1 and 2	AR	98.17%	76 of 96
AMHR2	Persistent Mullerian Duct Syndrome Types 1 and 2	AR	100%	87 of 95
ANOS1	Hypogonadotropic Hypogonadism 1 With Or Without Anosmia, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism,	X,XR,G	96.86%	NA of NA
AR	Androgen Insensitivity Syndrome, X-linked Hypospadias, Kennedy Disease, Partial Androgen Insensitivity Syndrome, Prostate Cancer, Reifenstein Syndrome, X-linked Spinal And Bulbar Muscular Atrophy	AD,X,XR,G	97.96%	NA of NA
ARX	Corpus Callosum Agenesis-Abnormal Genitalia Syndrome, Early Infantile Epileptic Encephalopathy, X-linked Lissencephaly With Abnormal Genitalia, X-linked Mental Retardation, Partington Syndrome, West Syndrome, X-linked Non-Syndromic Intellectual Disability, X-linked Spasticity-Intellectual Disability-Epilepsy Syndrome	X,XR,G	81.92%	NA of NA
ATRX	Alpha-Thalassemia Myelodysplasia Syndrome, Carpenter-Waziri Syndrome, Chudley-Lowry-Hoar Syndrome, Holmes-Gang Syndrome, Juberg-Marsidi Syndrome, X-Linked Mental Retardation-Hypotonic Facies Syndrome, Neuroendocrine Tumor Of Stomach, Smith-Fineman-Myers Syndrome	X,XR,XD,G	98.50%	NA of NA
BCOR	Acute Promyelocytic Leukemia, Lenz Type Microphthalmia, Oculofaciocardiodental Syndrome	X,XD,G	99.87%	NA of NA
CBX2	46,XY Complete Gonadal Dysgenesis,46XY Sex Reversal	AR	100%	6 of 6
CDK9	Primary Immunodeficiency, Multiple Myeloma, NUT Midline Carcinoma		82.69%	2 of 2
CDKN1C	Beckwith-Wiedemann Syndrome, IMAGE Syndrome, Intrauterine Growth Restriction-Short Stature-Early Adult-Onset Diabetes Syndrome, Intrauterine Growth Retardation, Metaphyseal Dysplasia, Adrenal Hypoplasia Congenita, And Genital Anomalies	AD	73.58%	55 of 76
CEP41	Joubert Syndrome	AR	100%	17 of 17
CHD7	CHARGE Syndrome, Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism, Omenn Syndrome	AD	96.25%	823 of 896
CITED4	Adult Oligodendroglioma, Breast Cancer		65.14%	NA of NA
CREBBP	Menke-Hennekam Syndrome, Rubinstein-Taybi Syndrome	AD	100%	318 of 318
CYB5A	46,XY Disorder Of Sex Development Due To Isolated 17,20-Lyase Deficiency, Hereditary Methemoglobinemia And Ambiguous Genitalia	AR	100%	5 of 5
CYP11A1	46,XY Disorder Of Sex Development-Adrenal Insufficiency Due To Cyp11a1 Deficiency		100%	39 of 39
CYP11B1	Congenital Adrenal Hyperplasia Due To Steroid 11-Beta-Hydroxylase Deficiency, Familial Hyperaldosteronism Type I, Glucocorticoid-Remediable Aldosteronism	AD,AR	100%	144 of 144
CYP17A1	46,XY Disorder Of Sex Development Due To Isolated 17,20-Lyase Deficiency, Congenital Adrenal Hyperplasia Due To 17-Alpha-Hydroxylase Deficiency	AR	100%	127 of 127
CYP19A1	Aromatase Deficiency, Aromatase Excess Syndrome	AD,AR	100%	33 of 35
CYP21A2	Congenital Adrenal Hyperplasia Due To 21-Hydroxylase Deficiency	AR	99.98%	278 of 280
DHCR7	Smith-Lemli-Opitz Syndrome	AR	100%	217 of 217
DHH	46,XY Complete Gonadal Dysgenesis	AR	99.85%	21 of 21
DYNC2H1	Jeune Syndrome, Short Rib-Polydactyly Syndrome, X,Short-Rib Thoracic Dysplasia With Or Without Polydactyly	AR,MU,D	99.78%	214 of 221
EMX2	Schizencephaly		100%	5 of 5
ERCC3	Trichothiodystrophy, Xeroderma Pigmentosum-Cockayne Syndrome Complex	AR	99.98%	24 of 24
FEZF1	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome	AR	99.95%	3 of 3

FGF8	Alobar Holoprosencephaly, Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome	AD	98.36%	38 of 38
FGFR1	Encephalocraniocutaneous Lipomatosis, Hartsfield Syndrome, Isolated Trigonocephaly, Jackson-Weiss Syndrome, Kallmann Syndrome, Lobar Holoprosencephaly,Microform Holoprosencephaly, Normosmic Congenital Hypogonadotropic Hypogonadism, Oligodontia, Osteoglophonic Dysplasia, Pfeiffer Syndrome, Septo-Optic Dysplasia Spectrum, Nonsyndromic Trigonocephaly	AD	100%	279 of 280
FIG4	Amyotrophic Lateral Sclerosis, Bilateral Parasagittal Parieto-Occipital Polymicrogyria, Charcot-Marie-Tooth Disease, Cleidocranial Dysplasia With Micrognathia, Absent Thumbs And Distal, Polymicrogyria, Bilateral Temporooccipital, Yunis-Varon Syndrome	AD,AR	99.92%	72 of 72
FOXL2	Blepharophimosis, Ptosis, And Epicanthus Inversus, Premature Ovarian Failure	AD	89.36%	136 of 201
FRAS1	Fraser Syndrome	AR	98.73%	57 of 58
GNRH1	Hypogonadotropic Hypogonadism With Or Without Anosmia, Normosmic Congenital Hypogonadotropic Hypogonadism	AR	100%	12 of 12
GNRHR	Hypogonadotropic Hypogonadism Without Anosmia, Normosmic Congenital Hypogonadotropic Hypogonadism	AR	100%	59 of 59
HSD17B3	46,XY Disorder Of Sex Development Due To 17-Beta-Hydroxysteroid Dehydrogenase Deficiency, Male Pseudohermaphroditism With Gynecomastia	AR	100%	61 of 61
HSD3B2	Congenital Adrenal Hyperplasia Due To 3-Beta-Hydroxysteroid Dehydrogenase Deficiency, Congenital Adrenal Hyperplasia Due To 3-Beta-Hydroxysteroid Dehydrogenase Deficiency	AR	100%	70 of 70
IL17RD	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome	AD,AR	99.95%	17 of 17
IRF6	Autosomal Dominant Popliteal Pterygium Syndrome, Cleft Lip And Alveolus, Cleft Lip/Palate, Isolated Cleft Lip, Oligodontia, Orofacial Cleft, Van Der Woude Syndrome	AD,MU,P	99.98%	325 of 335
KISS1	Hypogonadotropic Hypogonadism With Or Without Anosmia, Normosmic Congenital Hypogonadotropic Hypogonadism	AR	100%	9 of 10
KISS1R	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism, Central Precocious Puberty	AD,AR	99.41%	42 of 43
LHB	Hypogonadotropic Hypogonadism Without Anosmia	AR	100%	11 of 11
LHCGR	Familial Male-Limited Precocious Puberty, Hypergonadotropic Hypogonadism, Precocious Puberty, Male-limited	AD,AR	100%	75 of 75
LHX9	Gonadal Agenesis, 46 XY Sex Reversal		99.65%	1 of 1
MAMLD1	X-linked Hypospadias, X-linked Myotubular Myopathy-Abnormal Genitalia Syndrome	X,XR,G	99.87%	NA of NA
MAP3K1	46,XY Complete Gonadal Dysgenesis, 46 XY Partial Gonadal Dysgenesis, 46 XY Sex Reversal	AD	96.50%	31 of 32
MKRN3	Prader-Willi Syndrome, Central Precocious Puberty	AD,ADWMI	99.98%	39 of 41
MKS1	Bardet-Biedl Syndrome, Joubert Syndrome, Meckel Syndrome	AR	99.98%	49 of 49
NR0B1	46,XX Testicular Disorder Of Sex Development, 46XY Complete Gonadal Dysgenesis, 46XY Partial Gonadal Dysgenesis, Congenital Adrenal Hypoplasia, Dosage-Sensitive Sex Reversal	X,XR,G	99.87%	NA of NA
NR5A1	46,XX Gonadal Dysgenesis, 46 XX Ovotesticular Disorder Of Sex Development,46 XX Sex Reversal, 46 XX Testicular Disorder Of Sex Development,46 XY Complete Gonadal Dysgenesis, 46 XY Partial Gonadal Dysgenesis, 46 XY Sex Reversal, Male Infertility With Azoospermia Or Oligozoospermia Due To Single Gene Mutation, Premature Ovarian Failure, Spermatogenic Failure	AD	99.97%	222 of 224
POR	Antley-Bixler Syndrome With Genital Anomalies And Disordered Steroidogenesis, Congenital Adrenal Hyperplasia Due To Cytochrome P450 Oxidoreductase Deficiency, Disordered Steroidogenesis Due To Cytochrome P450 Oxidoreductase	AD,AR	99.98%	67 of 68
PROK2	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism	AD	100%	20 of 20
PROKR2	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism, Pituitary Stalk Interruption Syndrome, Septo-Optic Dysplasia Spectrum	AD	100%	64 of 64
RSPO1	Palmoplantar Hyperkeratosis With Squamous Cell Carcinoma Of Skin, 46 XX Sex Reversal, Palmoplantar Keratoderma	AR	100%	6 of 7
SAMD9	Mirage Syndrome, Familial Normophosphatemic Tumoral Calcinosis	AD,AR	99.72%	45 of 46
SGPL1	Nephrotic Syndrome	AR	98.96%	18 of 18

SOX10	Kallmann Syndrome, Peripheral Demyelinating Neuropathy-Central Dysmyelinating Leukodystrophy, Waardenburg Syndrome, Hirschsprung Disease, Peripheral Demyelinating Neuropathy, Central Dysmyelination	AD	99.74%	139 of 147
SOX13	Metastatic Cancer Disease		100%	1 of 1
SOX3	46, XX Testicular Disorder Of Sex Development, X-linked Mental Retardation With Isolated Growth Hormone Deficiency, Non-Acquired Panhypopituitarism, X-linked Panhypopituitarism, Septo-Optic Dysplasia Spectrum	X,G	92.88%	NA of NA
SOX9	46,XX Ovotesticular Disorder Of Sex Development, 46 XX Testicular Disorder Of Sex Development, 46 XY Complete Gonadal Dysgenesis, 46XY Partial Gonadal Dysgenesis, Campomelic Dysplasia, Isolated Pierre Robin Syndrome	AD	97.28%	87 of 95
SRD5A2	46,XY Disorder Of Sex Development Due To 5-Alpha-Reductase Deficiency, Pseudovaginal Perineoscrotal Hypospadias	AR	na	na
SRY	45X/46 XY Mixed Gonadal Dysgenesis,46 XX Ovotesticular Disorder Of Sex Development, 46XX Testicular Disorder Of Sex Development, 46XY Complete Gonadal Dysgenesis, 46XY Partial Gonadal Dysgenesis, 46XX Sex Reversal, 46XY Sex Reversal	X,XD,Y,G	45%	NA of NA
STAR	Familial Glucocorticoid Deficiency, Lipoid Congenital Adrenal Hyperplasia	AR	100%	80 of 80
TAC3	Hypogonadotropic Hypogonadism With Or Without Anosmia, Normosmic Congenital Hypogonadotropic Hypogonadism	AR	100%	10 of 10
TACR3	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism	AR	99.97%	40 of 40
TOE1	Pontocerebellar Hypoplasia	AR	99.98%	12 of 12
TSPYL1	Sudden Infant Death With Dysgenesis Of The Testes Syndrome	AR	99.92%	8 of 8
WDR11	Hypogonadotropic Hypogonadism With Or Without Anosmia, Kallmann Syndrome, Normosmic Congenital Hypogonadotropic Hypogonadism, Pituitary Stalk Interruption Syndrome	AD,AR	100%	19 of 19
WT1	46 XY Complete Gonadal Dysgenesis, 46 XY Partial Gonadal Dysgenesis, Aniridia, Denys-Drash Syndrome, Desmoplastic Small Round Cell Tumor, Frasier Syndrome, Meacham Syndrome, Mesothelioma, Malignant, Nephroblastoma, Nephrotic Syndrome, WAGR Syndrome, Wilms Tumor, Aniridia, Genitourinary Anomalies, And Mental Retardation Syndrome Chromosome 11p13 Deletion Syndrome	AD	98.92%	178 of 185
ZFPM2	46 XY Partial Gonadal Dysgenesis, 46 XY Sex Reversal, Congenital Diaphragmatic Hernia, Tetralogy Of Fallot	AD	99.40%	44 of 46

*Inheritance: AD: Autosomal Dominant; AR: Autosomal Recessive; X: X linked; XLR: X linked Recessive; Mi: Mitochondrial; Mu: Multifactorial.
**Number of clinically relevant mutations according to HGMD

Methodology



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Call +34 963 905 310 or send an email to supportspain@igenomix.com for any of the following objectives:

- Get more information about the test.
- Request your kit.
- Request a pick up of the kit after collecting the sample.

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