NIMGenetics
New Integrated Medical Genetics

ReproNIM®

ReproNIM® is the study of carriers (or genetic risk test) by NIMGenetics, which analyses genes associated with diseases linked to the X chromosome and with a recessive autosomal inheritance pattern, by combining massive sequencing and other molecular diagnostic techniques.

Massive sequencing enables studying the entire coding sequence of the gene, as well as its splicing regions, with coverage rates in the panels of about 99 %, which increases its diagnostic efficacy.

The studied genes are associated with a set of diseases that have been selected based on their clinical relevance, incidence and recommendations from scientific societies.

NIMGenetics offers the following approaches:

ReproNIM® Focus-LX

ReproNIM® Focus-LX is the study approach aimed at a total of 38 diseases of recessive inheritance and/or linked to the X chromosome, selected for their severity, higher frequency of carriers in the general population, and early onset.

Among all genes analysed, those associated with recessive diseases present a prevalence of carriers greater than 1/100. By including 23 genes located in the X chromosome, this panel increases the safety compared to the minimum 7-gene panel recommended by the Spanish Fertility Society (SEF) for gamete donors.

Sample type: 3-5 mL of blood in EDTA.
Documents to be enclosed with the sample: Informed consent and request form.
Response time: 20 business days from the reception of the sample.
Reference: REP1004

Autosomal Recessive Disorder	Gene	Coverage (%)	Prevalence of carriers [a]
Acetyl-CoA dehydrogenase deficiency (medium chain)	*ACADM*	99	1:62
Canavan disease	*ASPA*	99	1:71
Cystic fibrosis	*CFTR*	99	1:28
Riley-Day syndrome (Familial Dysautonomia)	*IKBKAP*	99	1:76
Familial Mediterranean fever	*MEFV*	92.1	1:64
Gaucher disease	*GBA*	99	1:76
DFNB1 Nonsyndromic hereditary deafness	*GJB2*	99	1:42
Beta thalassemia	*HBB*	99	1:69
Sickle cell anaemia	*HBB*	99	1:69
Tay Sachs	*HEXA*	99	1:90
Spinal muscular atrophy [c]	*SMN1*	NA	1:57
Smith-Lemli-Opitz syndrome	*DHCR7*	99	1:68
Alpha Thalassemia [e]	*HBA1/HBA2*	90	1:50
Phenylalanine hydroxylase deficiency (Phenylketonuria)	*PAH*	99	1:75
Pompe disease	*GAA*	91.5	1:82

X chromosome-linked disease	Gene	Coverage (%)	Disease prevalence
X-linked adrenoleukodystrophy	*ABCD1*	89	1/42000
Androgen insensitivity	*AR*	84	1/20,000;1/50,000
Menkes disease	*ATP7A*	>99	1/99,000

Choroideremia	*CHM*	98.3	1/50,000
Alport syndrome, X-linked	*COL4A5*	98.5	1/50,000
Chronic granulomatous disease	*CYBB*	>99	1/130,000;1/1,000,000
X-linked hypohidrotic ectodermal dysplasia	*EDA*	99	1/5,000;1/10,000
X-linked Emery-Dreifuss muscular dystrophy	*EMD*	96	1/99,000
Haemophilia A	*F8*	98.1	1/10,000
Haemophilia B	*F9*	99	1/10,000
Glucose-6-phosphate dehydrogenase deficiency	*G6PD*	90	1/200
X-linked Charcot-Marie-Tooth type 1	*GJB1*	99	1/6,700
Fabry disease	*GLA*	99	1/50,000;1/117,000
Mucopolysaccharidosis type 2	*IDS*	89	1/99,000-1/170,000
Severe combined immunodeficiency T-B+	*IL2RG*	99	1/50,000-1/99,000
X-linked centronuclear myopathy	*MTM1*	99	1/50,000
Lowe Syndrome	*OCRL*	98.1	1/500,000
Ornithine transcarbamylase deficiency	*OTC*	99	1/70,000
X-linked Leigh syndrome	*PDHA1*	99	1/40,000
X-linked Charcot-Marie-Tooth type 5	*PRPS1*	99	<1/1,000,000
X-linked retinoschisis	*RS1*	99	1-9/99,000
Wiskott-Aldrich syndrome	*WAS*	93	1-10/1,000,000
Fragile X syndrome [b]	*FMR1*	N/A	1:170 (Premutation carriers)[d]

[a] Pan-ethnic population data. Lazarín *et al, Genetics in Medicine*, 2013.
[b] Detection of CGG expansion in 5'UTR region by fragment analysis.
[c] Detection of exon 7 deletion by q-PCR.
[d] Urbano *et al, Genetic Alterations in Oocyte Donors*, 2014.
[e] Detection of the most common deletions/duplications by MLPA.

ReproNIM® Carrier

ReproNIM® Carrier is the approach by which a total of 427 genes are analysed, resulting in a study that analyses >4,000 variants. Among all genes analysed, 357 are associated with recessive diseases and 70 are related to diseases linked to the X chromosome.

This study is aimed at highly-severe and early-onset diseases caused by pathogenic variants in DNA-coding regions and exon-intron binding spots. This study is especially indicated to establish the genetic risk in a couple with the utmost level of information. The genes incorporated in the panel are considered actionable at different levels:

- **Pre-implantation:** Couples at reproductive risk could have a Pre-implantation Genetic Test to detect monogenic diseases.
- **Prenatal and/or neonatal:** The genetic status of the foetus can be known before birth.

The scope of ReproNIM® Carrier enables the assessment of genetic compatibility with most studies available on the market today. Also, when required, ReproNIM® Carrier extends the information previously obtained with other studies of carriers (which requires sending the previous report for evaluation).

Sample type: 3-5 mL of blood in EDTA.
Documents to be enclosed with the sample: Informed consent and request form
Response time: 30 business days from the reception of the sample.
Reference: REP1001

Disease	Gene	Refseq
Congenital ichthyosiform erythroderma	*ABCA12*	NM_173076.3
Cone-rod dystrophy 3	*ABCA4*	NM_000350.2
Cholestasis, benign recurrent intrahepatic, 2	*ABCB11*	NM_003742.2
ABCC8-Related Familial Hyperinsulinism	*ABCC8*	NM_000352.4
Adrenoleukodystrophy	*ABCD1*[x]	NM_000033.3
Methylmalonic aciduria and homocystinuria, cblJ type	*ABCD4*	NM_005050.3
Acyl-CoA dehydrogenase, medium chain, deficiency of	*ACADM*	NM_000016.5
Acyl-CoA dehydrogenase, short-chain, deficiency of	*ACADS*	NM_000017.3
2-methylbutyrylglycinuria	*ACADSB*	NM_001609.3
VLCAD deficiency	*ACADVL*	NM_000018.3
Alpha-methylacetoacetic aciduria	*ACAT1*	NM_000019.3
Peroxisomal acyl-CoA oxidase deficiency	*ACOX1*	NM_004035.6
Combined malonic and methylmalonic acidemia	*ACSF3*	NM_174917.4
Mental retardation, X-linked 63	*ACSL4*[x]	NM_004458.2
Severe combined immunodeficiency due to ADA deficiency	*ADA*	NM_000022.3
Ehlers-Danlos syndrome,type vii,autosomal recessive	*ADAMTS2*	NM_014244.4
Hypermethioninemia due to adenosine kinase deficiency	*ADK*	NM_001123.3
Mental retardation, X-linked, FRAXE type	*AFF2*[x]	NM_002025.3
Aspartylglucosaminuria	*AGA*	NM_000027.3
Glycogen storage disease IIIa	*AGL*	NM_000642.2
Rhizomelic chondrodysplasia punctata, type 3	*AGPS*	NM_003659.3
Hyperoxaluria, primary, type 1	*AGXT*	NM_000030.2
Hypermethioninemia with deficiency of S-adenosylhomocysteine hydrolase	*AHCY*	NM_000687.3
Joubert syndrome 3	*AHI1*	NM_017651.4
Cone-rod dystrophy, 604393 (Congenital Leber Amaurosis, 4)	*AIPL1*	NM_014336.4
Autoimmune polyendocrinopathy syndrome , type I	*AIRE*	NM_000383.3
Âgren-Larsson syndrome	*ALDH3A2*	NM_000382.2
Hyperprolinemia, type II	*ALDH4A1*	NM_003748.3
Fructose intolerance	*ALDOB*	NM_000035.3
Congenital disorder of glycosylation	*ALG6*	NM_013339.3
Alstrom syndrome	*ALMS1*	NM_015120.4
Infantile hypophosphatasia,Skeletal dysplasia	*ALPL*	NM_000478.5
Persistent Mullerian duct syndrome	*AMH*	NM_000479.4
Persistent mullerian duct syndrome,type II	*AMHR2*	NM_020547.3
Glycine encephalopathy	*AMT*	NM_000481.3
Mental retardation, X-linked syndromic 5	*AP1S2*[x]	NM_003916.4
Androgen insensitivity	*AR*[x]	NM_000044.3
Argininemia	*ARG1*	NM_000045.3
Joubert syndrome 8	*ARL13B*	NM_182896.2
Metachromatic leukodystrophy	*ARSA*	NM_000487.5
Mucopolysaccharidosis type VI (Maroteaux-Lamy)	*ARSB*	NM_000046.3
Chondrodysplasia punctata, X-linked recessive	*ARSE*[x]	NM_000047.2
Chondrodysplasia punctata, X-linked recessive	*ARSF*[x]	NM_004042.4
Epileptic encephalopathy, early infantile, 1	*ARX*[x]	NM_139058.2
Argininosuccinic aciduria	*ASL*	NM_000048.3
Asparagine synthetase deficiency	*ASNS*	NM_133436.3
Canavan disease	*ASPA*	NM_000049.2
Citrullinemia	*ASS1*	NM_000050.4
Ataxia-telangiectasia	*ATM*	NM_000051.3
Renal tubular acidosis with progressive nerve deafness	*ATP6V1B1*	NM_001692.3
Menkes kinky-hair syndrome	*ATP7A*[x]	NM_000052.6
Wilson disease	*ATP7B*	NM_000053.3
Alpha-thalassemia/mental retardation syndrome	*ATRX*[x]	NM_000489.4

Disease	Gene	Refseq
Bardet-Biedl syndrome 1	*BBS1*	NM_024649.4
Bardet-Biedl syndrome 10	*BBS10*	NM_024685.3
Bardet-Biedl syndrome 12	*BBS12*	NM_152618.2
Bardet-Biedl syndrome 2	*BBS2*	NM_031885.3
Deficiency of butyrylcholine esterase	*BCHE*	NM_000055.3
Maple syrup urine disease, type Ia	*BCKDHA*	NM_000709.3
Maple syrup urine disease, type Ib	*BCKDHB*	NM_183050.3
Bjornstad syndrome	*BCS1L*	NM_004328.4
Bloom syndrome	*BLM*	NM_000057.3
Fanconi anemia	*BRIP1*	NM_032043.2
X-linked mental retardation (XLMR) associated with macrocephaly	*BRWD3*[x]	NM_153252.4
Bartter syndrome, type 4a	*BSND*	NM_057176.2
Biotinidase deficiency	*BTD*	NM_000060.4
Muscular dystrophy, limb-girdle, type 2A	*CAPN3*	NM_000070.2
Mental retardation and microcephaly with pontine and cerebellar hypoplasia	*CASK*[x]	NM_003688.3
Ventricular tachycardia, catecholaminergic polymorphic, 2	*CASQ2*	NM_001232.3
Homocystinuria, B6-responsive and nonresponsive types	*CBS*	NM_000071.2
Immunodeficiency, X-linked, with hyper-IgM	*CD40LG*[x]	NM_000074.2
Deafness, autosomal recessive 12	*CDH23*	NM_022124.5
Bardet-Biedl syndrome 14; Joubert syndrome 5; Meckel syndrome 4; Senior-Loken syndrome 6	*CEP290*	NM_025114.3
Retinitis pigmentosa 26	*CERKL*	NM_001030311.2
Cystic Fibrosis; Congenital bilateral absence of vas deferens	*CFTR*	NM_000492.3
Choroideremia	*CHM*[x]	NM_000390.3
Congenital myasthenic syndrome	*CHRNE*	NM_000080.3
Lethal multiple pterygium syndrome	*CHRNG*	NIM_005199.4
Macular corneal dystrophy	*CHST6*	NM_021615.4
Bare lymphocyte syndrome 2	*CIITA*	NM_000246.3
Myotonia congenita, recessive	*CLCN1*	NM_000083.2
Ceroid lipofuscinosis, neuronal, 3	*CLN3*	NM_001042432.1
Ceroid lipofuscinosis, neuronal, 5	*CLN5*	NM_006493.2
Ceroid lipofuscinosis, neuronal, 6	*CLN6*	NM_017882.2
Ceroid lipofuscinosis, neuronal, 8	*CLN8*	NM_018941.3
Usher syndrome, type 3A	*CLRN1*	NM_174878.2
Retinitis pigmentosa 49	*CNGA1*	NM_000087.3
Retinitis pigmentosa 45	*CNGB1*	NM_001297.4
Achromatopsia-3	*CNGB3*	NM_019098.4
Alport syndrome	*COL4A3*	NM_000091.4
Alport syndrome, autosomal recessive	*COL4A4*	NM_000092.4
Alport syndrome,X-linked recessive	*COL4A5*[x]	NM_000495.4
EBD inversa	*COL7A1*	NM_000094.3
Carbamoylphosphate synthetase I deficiency	*CPS1*	NM_001875.4
CPT deficiency, hepatic, type IA	*CPT1A*	NM_001876.3
CPT II deficiency, lethal neonatal	*CPT2*	NM_000098.2
Leber congenital amaurosis 8	*CRB1*	NM_201253.2
Cystathioninuria	*CTH*	NM_001902.5
Cystinosis, atypical nephropathic	*CTNS*	NM_004937.2
CTSC-Related Disorders	*CTSC*	NM_001814.5
Ceroid lipofuscinosis, neuronal, 10	*CTSD*	NM_001909.4
Pyknodysostosis	*CTSK*	NM_000396.3
Mental retardation, X-linked, syndromic 15	*CUL4B*[x]	NM_003588.3
Granulomatous disease,chronic,autosomal recessive,cytochrome b-negative	*CYBA*	NM_000101.3
Chronic granulomatous disease,X-linked	*CYBB*[x]	NM_000397.3

Disease	Gene	Refseq
Congenital adrenal hyperplasia,Hyperaldosteronism,familial,type I	*CYP11B1*	NM_000497.3
Corticosterone methyloxidase type 2 deficiency	*CYP11B2*	NM_000498.3
Adrenal hyperplasia, congenital, due to 17-alpha-hydroxylase deficiency	*CYP17A1*	NM_000102.3
Aromatase deficiency	*CYP19A1*	NM_031226.2
Congenital glaucoma	*CYP1B1*	NM_000104.3
Adrenal hyperplasia, congenital, due to 21-hydroxylase deficiency	*CYP21A2*	NM_000500.7
Cerebrotendinous xanthomatosis	*CYP27A1*	NM_000784.3
Maple syrup urine disease, type II	*DBT*	NM_001918.3
Histiocytic medullary reticulosis	*DCLRE1C*	NM_001033855.2
Lissencephaly, X-linked	*DCX*[x]	NM_178153.2
Smith-Lemli-Opitz syndrome	*DHCR7*	NM_001360.2
Retinitis pigmentosa 59	*DHDDS*	NM_024887.3
Dihydrolipoamide dehydrogenase deficiency	*DLD*	NM_000108.4
Mental retardation, X-linked 90	*DLG3*[x]	NM_021120.3
Distrofia mucular de Duchenne, Distrofia muscular de Becker	*DMD*[x]	NM_004006.2
Primary ciliary dyskinesia	*DNAH5*	NM_001369.2
Ciliary dyskinesia	*DNAI1*	NM_012144.3
Ciliary dyskinesia	*DNAI2*	NM_023036.4
Myasthenia,limb-girdle,familial,Pena-Shokeir syndrome type I	*DOK7*	NM_173660.4
Thryoid dyshormonogenesis 6	*DUOX2*	NM_014080.4
Thyroid dyshormonogenesis 5	*DUOXA2*	NM_207581.3
limb-girdle muscular dystrophy type 2B	*DYSF*	NM_003494.3
Hypohidrotic X-linked ectodermal dysplasia	*EDA*[x]	NM_001399.4
Wolcott-Rallison dysplasia	*EIF2AK3*	NM_004836.6
Leukoencephalopathy with vanishing white matter	*EIF2B5*	NM_003907.2
Emery-Dreifuss muscular dystrophy 1,X-linked	*EMD*[x]	NM_000117.2
Cerebrooculofacioskeletal Syndrome,Cockayne syndrome,Macular degeneration	*ERCC6*	NM_000124.3
Cockayne syndrome	*ERCC8*	NM_000082.3
Glutaric acidemia IIA	*ETFA*	NM_000126.3
Glutaric acidemia IIB	*ETFB*	NM_001985.2
Glutaric acidemia IIC	*ETFDH*	NM_004453.3
Ethylmalonic encephalopathy	*ETHE1*	NM_014297.4
Chondroectodermal dysplasia	*EVC*	NM_153717.2
Ellis-van Creveld Syndrome;Meckel-Gruber syndrome	*EVC2*	NM_147127.4
Pontoneocerebellar hypoplasia	*EXOSC3*	NM_016042.3
Retinitis pigmentosa 25	*EYS*	NM_001142800.1
Hemophilia A	*F8*[x]	NM_000132.3
Hemophilia B	*F9*[x]	NM_000133.3
Aarskog-Scott syndrome; Mental retardation, X-linked 16	*FGD1*[x]	NM_004463.2
Fumarase deficiency	*FH*	NM_000143.3
Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies)	*FKRP*	NM_024301.4
Walker-Warburg syndrome	*FKTN*	NM_001079802.1
Fragile X syndrome	*FMR1*[x]	NM_002024.5
Glutamate formiminotransferase deficiency	*FTCD*	NM_006657.2
Mental retardation, X-linked 9	*FTSJ1*[x]	NM_012280.3
Glycogen storage disease Ia	*G6PC*	NM_000151.3
Favism	*G6PD*[x]	NM_001042351.2
Glycogen storage disease II / Pompe Disease	*GAA*	NM_000152.4
Krabbe disease	*GALC*	NM_000153.3
Galactose epimerase deficiency	*GALE*	NM_000403.3
Deficiencia de galactosinasa con cataracts	*GALK1*	NM_000154.1
Mucopolysaccharidosis IVA	*GALNS*	NM_000512.4

Disease	Gene	Refseq
Galactosemia	*GALT*	NM_000155.3
Cerebral creatine deficiency syndrome	*GAMT*	NM_000156.5
Gaucher disease, perinatal lethal	*GBA*	NM_001005741.2
Glycogen storage disease IV	*GBE1*	NM_000158.3
Glutaricaciduria, type I	*GCDH*	NM_000159.3
Charcot-Marie-Tooth Neuropathy Type 4A	*GDAP1*	NM_018972.2
Fibular hypoplasia and complex brachydactyly	*GDF5*	NM_000557.4
Mental retardation, X-linked 41	*GDI1*^{x}	NM_001493.2
Charcot-Marie-Tooth,X-linked	*GJB1*^{x}	NM_000166.5
Deafness, autosoma recessive 1A; DFNB1A	*GJB2*	NM_004004.5
Deafness, digenic, GJB2/GJB3	*GJB3*	NM_024009.2
Fabry disease	*GLA*^{x}	NM_000169.2
GM1-gangliosidosis, types I, II and III	*GLB1*	NM_000404.3
Glycine encephalopathy	*GLDC*	NM_000170.2
Inclusion body myopathy 2	*GNE*	NM_005476.7
Glycine N-methyltransferase deficiency	*GNMT*	NM_018960.5
Mucolipidosis II and III, alpha/beta	*GNPTAB*	NM_024312.4
Mucolipidosis,Type III Gamma	*GNPTG*	NM_032520.4
Hypogonadotropic hypogonadism 7 without anosmia	*GNRHR*	NM_000406.2
Mucopolysaccharidosis type IIID	*GNS*	NM_002076.3
Nystagmus 6, congenital, X-linked	*GPR143*^{x}	NM_000273.2
Hyperoxaluria, primary, type II	*GRHPR*	NM_012203.1
Mental retardation, X-linked 94	*GRIA3*^{x}	NM_000828.4
Leber congenital amaurosis	*GUCY2D*	NM_000180.3
Mucopolysaccharidosis type VII	*GUSB*	NM_000181.3
LCHAD deficiency	*HADHA*	NM_000182.4
Trifunctional protein deficiency	*HADHB*	NM_000183.2
Histidinemia	*HAL*	NM_002108.3
Neutropenia, severe congenital 3, autosomal recessive	*HAX1*	NM_006118.3
Thalassemias, alpha-	*HBA1*	NM_000558.4
Thalassemias, alpha-	*HBA2*	NM_000517.4
Thalassemia, beta	*HBB*	NM_000518.4
Tay-Sachs; GM2-gangliosidosis, several forms	*HEXA*	NM_000520.5
Sandhoff disease, infantile, juvenile, and adult forms	*HEXB*	NM_000521.3
Hemochromatosis: Type 2A; HFE2 Related	*HFE2*	NM_213653.3
Alkaptonuria	*HGD*	NM_000187.3
Mucopolysaccharidosis type IIIC (Sanfilippo C)	*HGSNAT*	NM_152419.2
Holocarboxylase synthetase deficiency	*HLCS*	NM_000411.6
HMG-CoA lyase deficiency	*HMGCL*	NM_000191.2
Hyperoxaluria, primary, type III	*HOGA1*	NM_138413.3
Síndrome 1 de Hermansky Pudlak	*HPS1*	NM_000195.4
Hermansky-Pudlak syndrome 3	*HPS3*	NM_032383.4
Hermansky-Pudlak syndrome 4	*HPS4*	NM_022081.5
17-Beta-Hydroxysteroid Dehydrogenase III Deficiency	*HSD17B3*	NM_000197.1
Bifunctional peroxisomal enzyme deficiency,Perrault syndrome 1	*HSD17B4*	NM_000414.3
3 beta-Hydroxysteroid dehydrogenase deficiency	*HSD3B2*	NM_000198.3
Mental retardation, X-linked syndromic, Turner type	*HUWE1*^{x}	NM_031407.6
Hydrolethalus syndrome 1	*HYLS1*	NM_145014.2
Retinitis pigmentosa 46	*IDH3B*	NM_006899.4
Mucopolysaccharidosis II	*IDS*^{x}	NM_000202.7
Mucopolysaccharidosis Ih	*IDUA*	NM_000203.4
Dysautonomia, familial	*IKBKAP*	NM_003640.4
Mental retardation, X-linked 21/34	*IL1RAPL1*^{x}	NM_014271.3

Disease	Gene	Refseq
Severe combined immunodeficiency, X-linked	*IL2RG*[x]	NM_000206.2
Mental retardation, X-linked 1/78	*IQSEC2*[x]	NM_001111125.2
Isovaleric acidemia	*IVD*	NM_002225.3
Thyroid dyshormonogenesis 4	*IYD*	NM_203395.2
SCID, autosomal recessive, T-negative/B-positive type	*JAK3*	NM_000215.3
Hyperinsulinemic hypoglycemia, familial, Type 2	*KCNJ11*	NM_000525.3
Mental retardation, X-linked, syndromic, Claes-Jensen type	*KDM5C*[x]	NM_004187.3
MASA syndrome / CRASH syndrome	*L1CAM*[x]	NM_000425.4
Congenital Muscular Dystrophy,LAMA2-related	*LAMA2*	NM_000426.3
Epidermolysis bullosa,junctional,Laryngoonychocutaneous syndrome	*LAMA3*	NM_000227.4
Epidermolysis bullosa, junctional, Herlitz type; non-Herlitz type	*LAMB3*	NM_000228.2
Epidermolysis bullosa, junctional, Herlitz type; non-Herlitz type	*LAMC2*	NM_005562.2
Leber congenital amaurosis	*LCA5*	NM_181714.3
Hypercholesterolemia, familial	*LDLR*	NM_000527.4
Hypercholesterolemia, familial, autosomal recessive	*LDLRAP1*	NM_015627.2
Leydig cell agenesis	*LHCGR*	NM_000233.3
Stuve-Wiedemann syndrome	*LIFR*	NM_002310.5
Wolman disease (lysosomal acid lipase deficiency)	*LIPA*	NM_000235.3
Methylmalonic aciduria and homocystinuria, cblF type	*LMBRD1*	NM_018368.3
Nonsyndromic Hearing Loss,Recessive	*LOXHD1*	NM_144612.6
Hyperlipoproteinemia,type I	*LPL*	NM_000237.2
Leigh syndrome, French-Canadian type	*LRPPRC*	NM_133259.3
Chediak-Higashi syndrome	*LYST*	NM_000081.3
Mannosidosis, alpha-, types I and II	*MAN2B1*	NM_000528.3
Methionine adenosyltransferase deficiency, autosomal recessive	*MAT1A*	NM_000429.2
3-Methylcrotonyl-CoA carboxylase 1 deficiency	*MCCC1*	NM_020166.4
3-Methylcrotonyl-CoA carboxylase 2 deficiency	*MCCC2*	NM_022132.4
Deficiencia de metilmalonil CoA epimerasa	*MCEE*	NM_032601.3
Mucolipidosis IV	*MCOLN1*	NM_020533.2
Mental retardation, X-linked, syndromic 13	*MECP2*[x]	NM_004992.3
Microcephaly,postnatal progressive,with seizures and brain atrophy	*MED17*	NM_004268.4
Familial Mediterranean fever, AR	*MEFV*	NM_000243.2
Jarcho-Levin syndrome	*MESP2*	NM_001039958.1
Ceroid lipofuscinosis, neuronal, 7	*MFSD8*	NM_152778.2
Meckel syndrome 1	*MKS1*	NM_017777.3
Megalencephalic leukoencephalopathy with subcortical cysts	*MLC1*	NM_015166.3
Malonyl-CoA decarboxylase deficiency	*MLYCD*	NM_012213.2
Methylmalonic aciduria, vitamin B12-responsive	*MMAA*	NM_172250.2
Methylmalonic aciduria	*MMAB*	NM_052845.3
Methylmalonic aciduria and homocystinuria, cblC type	*MMACHC*	NM_015506.2
Homocystinuria	*MMADHC*	NM_015702.2
Congenital disorder of glycosylation type 1B	*MPI*	NM_002435.2
Thrombocytopenia, congenital amegakaryocytic	*MPL*	NM_005373.2
Mitochondrial DNA depletion syndrome	*MPV17*	NM_002437.4
Severe X-linked myotubular myopathy	*MTM1*[x]	NM_000252.2
Charcot-Marie-Tooth disease, type 4B1	*MTMR2*	NM_016156.5
Homocystinuria-megaloblastic anemia, cbl E type	*MTRR*	NM_002454.2
Abetalipoproteinaemia	*MTTP*	NM_000253.3
Methylmalonic aciduria, mut(0) type	*MUT*	NM_000255.3
Hyper-IgD syndrome; Mevalonic aciduria	*MVK*	NM_000431.3
Deafness,autosomal recessive 3	*MYO15A*	NM_016239.3
Usher syndrome, type 1B	*MYO7A*	NM_000260.3
Mucopolysaccharidosis type IIIB (Sanfilippo B)	*NAGLU*	NM_000263.3

Disease	Gene	Refseq
Nijmegen Breakage Syndrome (Ataxia telangectasia, type 1)	*NBN*	NM_002485.4
Norrie disease	*NDP*[x]	NM_000266.3
Charcot-Marie-Tooth disease, type 4D	*NDRG1*	NM_006096.3
Mitochondrial complex I deficiency	*NDUFS6*	NM_004553.4
Nemaline myopathy 2, autosomal recessive	*NEB*	NM_001271208.1
Mental retardation, X-linked, Asperger syndrome susceptibility, X-linked	*NLGN4X*[x]	NM_020742.3
Niemann-Pick disease, type C1	*NPC1*	NM_000271.4
Niemann-pick disease, type C2	*NPC2*	NM_006432.3
Joubert syndrome 4	*NPHP1*	NM_000272.3
Nephrotic syndrome, type 1	*NPHS1*	NM_004646.3
Nephrotic syndrome	*NPHS2*	NM_014625.3
Congenital adrenal hypoplasia,X-linked	*NR0B1*[x]	NM_000475.4
Goldmann-Favre syndrome	*NR2E3*	NM_014249.3
Hereditary insensitivity to pain with anhidrosis	*NTRK1*	NM_001012331.1
Dent disease 2	*OCRL*[x]	NM_000276.3
3-Methylglutaconic aciduria type 3	*OPA3*	NM_025136.3
Retraso mental ligado al X	*OPHN1*[x]	NM_025163.3
Ornithine transcarbamylase deficiency	*OTC*[x]	NM_000531.5
Auditory neuropathy, autosomal recessive, 1	*OTOF*	NM_194248.2
Osteogenesis imperfecta, type VIII	*P3H1*	NM_022356.3
Phenylketonuria	*PAH*	NM_000277.1
Mental retardation, X-linked 30/47	*PAK3*[x]	NM_002578.4
HARP syndrome	*PANK2*	NM_153638.3
Hypothyroidism	*PAX8*	NM_003466.3
Pyruvate carboxylase deficiency	*PC*	NM_000920.3
Hyperphenylalaninemia, BH4-deficient, D	*PCBD1*	NM_000281.3
Propionic acidemia	*PCCA*	NM_000282.3
Propionic acidemia	*PCCB*	NM_000532.4
Deafness, autosomal recessive 23	*PCDH15*	NM_033056.3
Retinitis pigmentosa 43	*PDE6A*	NM_000440.2
Pyruvate dehydrogenase E1-alpha deficiency	*PDHA1*[x]	NM_000284.3
Pyruvate dehydrogenase E1-beta deficiency	*PDHB*	NM_000925.3
Peroxisome biogenesis disorder 1A (Zellweger)	*PEX1*	NM_000466.2
Peroxisome biogenesis disorder 6A (Zellweger)	*PEX10*	NM_153818.1
Peroxisome biogenesis disorder 3A	*PEX12*	NM_000286.2
Peroxisome biogenesis disorder 5B	*PEX2*	NM_000318.2
Heimler syndrome, type 2	*PEX6*	NM_000287.3
Peroxisome biogenesis disorder 9B; Rhizomelic chondroplasia punctata, type I	*PEX7*	NM_000288.3
Glycogen storage disease,type VII	*PFKM*	NM_000289.5
Phosphoglycerate kinase 1 deficiency	*PGK1*[x]	NM_000291.3
Mental retardation syndrome, X-linked, Siderius type	*PHF8*[x]	NM_015107.2
Phosphoglycerate dehydrogenase deficiency	*PHGDH*	NM_006623.3
Polycystic kidney and hepatic disease	*PKHD1*	NM_138694.3
Ehlers-Danlos syndrome, type VI	*PLOD1*	NM_000302.3
Pelizaeus-Merzbacher disease	*PLP1*[x]	NM_000533.4
Congenital disorder of glycosylation, type Ia	*PMM2*	NM_000303.2
POLG-Related Spectrum Disorders	*POLG*	NM_002693.2
Treacher Collins syndrome 3	*POLR1C*	NM_203290.3
Muscular dystrophy-dystroglycanopathy type A, 3	*POMGNT1*	NM_017739.3
Muscular dystrophy-dystroglycanopathy type A, 1	*POMT1*	NM_007171.3
Muscular dystrophy-dystroglycanopathy type A, 2	*POMT2*	NM_013382.5

Disease	Gene	Refseq
Antley-Bixler syndrome with genital anomalies and disordered steroidogenesis	*POR*	NM_000941.2
Deafness, X-linked 2	*POU3F4*[x]	NM_000307.4
Ceroid lipofuscinosis, neuronal, 1	*PPT1*	NM_000310.3
Renpenning syndrome	*PQBP1*[x]	NM_005710.2
Pituitary hormone deficiency, combined, 2	*PROP1*	NM_006261.4
Arts syndrome	*PRPS1*[x]	NM_002764.3
Hiperfenilalalinemia, deficneincia BH4, A	*PTS*	NM_000317.2
Mitochondrial myopathy and sideroblastic anemia	*PUS1*	NM_025215.5
McArdle disease	*PYGM*	NM_005609.3
Hyperphenylalaninemia, BH4-deficient, C	*QDPR*	NM_000320.2
Carpenter syndrome	*RAB23*	NM_183227.2
Histiocytic medullary reticulosis,Severe Combined Immune Deficiency	*RAG2*	NM_000536.3
Congenital Myasthenic Syndrome,Pena-Shokeir syndrome type I	*RAPSN*	NM_005055.4
Pontoneocerebellar hypoplasia	*RARS2*	NM_020320.4
Microphthalmia, isolated 3	*RAX*	NM_013435.2
Leber congenital amaurosis 13	*RDH12*	NM_152443.2
Retinitis Pigmentosa,Recessive	*RLBP1*	NM_000326.4
Anauxetic dysplasia	*RMRP*	NR_003051.3
Retinitis pigmentosa 2	*RP2*[x]	NM_006915.2
Leber congenital amaurosis 2	*RPE65*	NM_000329.2
Cone-rod dystrophy, X-linked, 1	*RPGR*[x]	NM_000328.2
Coffin-Lowry syndrome	*RPS6KA3*[x]	NM_004586.2
Retinoschisis	*RS1*[x]	NM_000330.3
Dyskeratosis congenita,autosomal recessive,5	*RTEL1*	NM_032957.4
Disqueratosis congénita, autosómica recesiva, 5	*SACS*	NM_014363.5
Pontocerebellar hypoplasia type 2D	*SEPSECS*	NM_016955.3
Emphysema due to AAT deficiency	*SERPINA1*	NM_000295.4
Muscular dystrophy, limb-girdle, type 2D	*SGCA*	NM_000023.3
Muscular dystrophy, limb-girdle, type 2E	*SGCB*	NM_000232.4
Limb-girdle muscular dystrophy,type 2F	*SGCD*	NM_000337.5
Severe autosomal recessive muscular dystrophy of childhood - North African type	*SGCG*	NM_000231.2
Mucopolysaccharidisis type IIIA (Sanfilippo A)	*SGSH*	NM_000199.5
Charcot-Marie-Tooth disease, type 4C	*SH3TC2*	NM_024577.3
Familial hypokalemia-hypomagnesemia	*SLC12A3*	NM_000339.2
Andermann syndrome	*SLC12A6*[x]	NM_133647.1
Allan-Herndon-Dudley syndrome	*SLC16A2*	NM_006517.4
Salla disease	*SLC17A5*	NM_012434.4
Carnitine deficiency, systemic primary	*SLC22A5*	NM_003060.3
Citrullinemia, adult-onset type II; type II, neonatal-onset	*SLC25A13*	NM_014251.2
Hyperornithinemia-hyperammonemia-homocitrullinuria syndrome	*SLC25A15*	NM_014252.3
Carnitine-acylcarnitine translocase deficiency	*SLC25A20*	NM_000387.5
Achondrogenesis Ib	*SLC26A2*	NM_000112.3
Congenital secretory diarrhea,chloride type	*SLC26A3*	NM_000111.2
Deafness, autosomal recessive 4, with enlarged vestibular aqueduct	*SLC26A4*	NM_000441.1
Arthrogryposis,mental retardation,and seizures	*SLC35A3*	NM_012243.2
Glycogen storage disease Ib	*SLC37A4*	NM_001164277.1
Hereditary acrodermatitis enteropathica	*SLC39A4*	NM_130849.3
Cystinuria	*SLC3A1*	NM_000341.3
Albinismo oculocutaneo tipo 4	*SLC45A2*	NM_016180.4
Folate malabsorption, hereditary	*SLC46A1*	NM_080669.5
Corneal dystrophy, Fuchs endothelial, 4	*SLC4A11*	NM_032034.3
Thyroid dyshormonogenesis 1	*SLC5A5*	NM_000453.2

Disease	Gene	Refseq
Hartnup disorder	*SLC6A19*	NM_001003841.2
Lysinuric protein intolerance	*SLC7A7*	NM_001126106.2
Cystinuria	*SLC7A9*	NM_014270.4
Spinal muscular atrophy, type I	*SMN1*	NM_000344.3
Niemann-Pick disease, type A	*SMPD1*	NM_000543.4
Spastic paraplegia 11, autosomal recessive	*SPG11*	NM_025137.3
Spastic paraplegia 7, autosomal recessive	*SPG7*	NM_003119.3
3-Oxo-5 alpha-steroid delta 4-dehydrogenase deficiency	*SRD5A2*	NM_000348.3
Lipoid adrenal hyperplasia	*STAR*	NM_000349.2
Multiple sulfatase deficiency	*SUMF1*	NM_182760.3
Leigh syndrome, due to COX deficiency	*SURF1*	NM_003172.3
Epilepsy, X-linked, with variable learning disabilities and behavior disorders	*SYN1*[x]	NM_133499.2
Tyrosinemia, type II	*TAT*	NM_000353.2
Osteopetrosis autosomal recessive 1	*TCIRG1*	NM_006019.3
Spastic paraplegia 49,autosomal recessive	*TECPR2*	NM_014844.4
Hemochromatosis, type 3	*TFR2*	NM_003227.3
Thyroid dyshormonogenesis 3	*TG*	NM_003235.4
Ichthyosis, congenital, autosomal recessive 1	*TGM1*	NM_000359.2
Segawa syndrome, recessive	*TH*	NM_199292.2
Mental retardation, X-linked 12/35	*THOC2*[x]	NM_001081550.2
Thyroid hormone resistance	*THRB*	NM_000461.4
Joubert syndrome 2	*TMEM216*	NM_001173990.2
Thyroid dyshormonogenesis 2A	*TPO*	NM_000547.5
Ceroid lipofuscinosis	*TPP1*	NM_000391.3
Ventricular tachycardia, catecholaminergic polymorphic	*TRDN*	NM_006073.3
Bardet-Biedl syndrome,Bardet-Biedl syndrome 11	*TRIM32*	NM_012210.3
Liver failure acute infantile	*TRMU*	NM_018006.4
Olivopontocerebellar hypoplasia	*TSEN54*	NM_207346.2
Hypothryoidism, congenital, nongoitrous 4	*TSHB*	NM_000549.4
Hyperthyroidism	*TSHR*	NM_000369.2
Mental retardation, X-linked 58	*TSPAN7*[x]	NM_004615.3
Trichohepatoenteric syndrome 1	*TTC37*	NM_014639.3
Ataxia with isolated vitamin E deficiency	*TTPA*	NM_000370.3
Mitochondrial DNA depletion syndrome 1 (MNGIE type)	*TYMP*	NM_001953.4
Oculocutaneous albinism	*TYR*	NM_000372.4
Oculocutaneous albinism type 3	*TYRP1*	NM_000550.2
Lucey-Driscoll syndrome	*UGT1A1*	NM_000463.2
Mental retardation, X-linked, syndromic 14	*UPF3B*[x]	NM_080632.2
Deafness, autosomico recesivo 18a	*USH1C*	NM_005709.3
Usher syndrome, type 1G	*USH1G*	NM_173477.4
Retinitis pigmentosa 39	*USH2A*	NM_206933.2
Mental retardation, X-linked 99	*USP9X*[x]	NM_001039590.2
Choreoacanthocytosis	*VPS13A*	NM_033305.2
Cohen syndrome	*VPS13B*	NM_017890.4
Pontocerebellar hypoplasia,type 2e	*VPS53*	NM_001128159.2
Pontocerebellar hypoplasia type 1A	*VRK1*	NM_003384.2
VSX2-related Microphthalmia	*VSX2*	NM_182894.2
Severe congenital neutropenia X-linked	*WAS*[x]	NM_000377.2
Usher syndrome, type 2D	*WHRN*	NM_015404.3
Werner syndrome	*WRN*	NM_000553.6
Xeroderma pigmentosum,type 1	*XPA*	NM_000380.3
Xeroderma pigmentosum,group C	*XPC*	NM_004628.4

Disease	Gene	Refseq
Mental retardation, X-linked syndromic, Raymond type	*ZDHHC9*[x]	NM_016032.3
Spastic paraplegia 15	*ZFYVE26*	NM_015346.3
Mental retardation, X-linked 97	*ZNF711*[x]	NM_021998.4

[x] X chromosome-linked diseases

The average coverage of all the studied regions is approximately 60X. Virtually all coding regions of the genes included are covered at least 10X.

Complementary genetic diagnosis studies performed:

- MLPA-qPCR SMN1 gene for the detection of exon 7 deletion related to spinal muscular atrophy. In turn, polymorphism c. *3 + 80 T > G is also examined to determine the 2+0 genotype of output carriers.

- MLPA-qPCR HBA1 and HBA2 genes for the detection of alpha-thalassemia-related deletions/duplications.

- TP-PCR, study of triples of the FMR1 gene related to Fragile X syndrome.

The sensitivity of variants detection is lower in genes with highly homologous regions (pseudogenes) and homopolymeric regions (poly-T, poly-A...).