CENTOGENE
THE RARE DISEASE COMPANY

NGS Panels 2020

BENEFIT FROM OUR MEDICAL EXPERTISE AND STREAMLINED GENETIC TESTING

NGS Panels 2020

Benefit from our Medical Expertise and Streamlined Genetic Testing

CENTOGENE is fully committed to bringing the best possible diagnostic solutions to our patients and their families. We always strive to incorporate the latest in-house findings and medical research in our products to improve and ease the diagnostic odyssey of rare disease patients. To reflect the fast-growing knowledge of complex associations of genes with diseases as well as to maximize clinical sensitivity, we have updated and significantly redesigned our Next Generation Sequencing (NGS) gene panels.

The gene composition of each panel has been revised to meet the latest gene discoveries as well as to provide the highest clinical validity. Additionally, we have minimized complexity and removed redundancy in the panel portfolio by creating phenotype-directed diagnostic panels, which are the most comprehensive and include all relevant genes necessary for differential diagnosis of syndromes with overlapping phenotype, therefore allowing the diagnosis of diseases that otherwise would be missed. This principle increases the clinical utility, de-risks panel choice, increases cost-effectiveness, and ultimately simplifies the diagnostic process.

When choosing one of our NGS panels, feel confident that you will receive high-quality sequencing combined with best data analysis and interpretation, which are documented in comprehensive medical reports. As always, CENTOGENE and our Customer Support Team is readily available to help in each step of your diagnostics.

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Panel Specifications

COVERAGE	≥99.5 % targeted regions covered at ≥20x. For each gene, all single nucleotide variants described in HGMD and CentoMD® are covered, including relevant deep intronic and regulatory variants.
SPECIFICITY	≥99.9 %
GENES	For a complete overview of included genes, please visit: www.centogene.com/ngspanels-medical-reporting
DELETION/ DUPLICATION	NGS-based copy number variant (CNV) analysis has a sensitivity of above 80 % for all homozygous deletions. Heterozygous CNVs spanning less than three exons cannot reliably be detected, and are therefore excluded from routine analysis, and will only be inspected and reported upon medical or technical indication.
REPORTING	Pathogenic and likely pathogenic variants are reported following ACMG classification guidelines. Variants of uncertain significance (VUS) are not reported in any of the following cases: the described phenotype(s) is explained by detected pathogenic or likely pathogenic variant(s); the detected VUS are not related to the described phenotype(s) of the patient or family members; in the lack of sufficient clinical information; and in our oncogenetic panels.
REQUESTED MATERIAL	1 CentoCard® *
TAT	25 days

*Except for: *BRCA1/BRCA2* panel and solid tumor panel, where the requested material is FFPE tissue (block or sections) or fresh tumor tissue.
For more details of accepted materials please check: https://www.centogene.com/diagnostics/how-to-order.html

CENTOGENE PANEL	SUBPANELS INCLUDED
CentoCardio™ **Genes: 219** **CentoCardio™** includes the most relevant genes for arrythmias, congenital heart disease, and cardiomyopathies. Syndromes included: Long and short QT, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia, cardiomyopathies dilated and hypertrophic, and congenital heart defects. In addition, this panel includes vascular abnormalities, such as dolichoectasia and hereditary hemorragic telangiectasia. Panel does not include analysis of *PKD1*. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Arrhythmia, hereditary panel Arrhythmogenic right ventricular cardiomyopathy panel Brugada syndrome panel Cardiomyopathy dilated panel Cardiomyopathy hypertrophic panel Catecholaminergic polymorphic ventricular tachycardia panel Congenital heart defects panel Dolichoectasia panel Hereditary hemorrhagic telangiectasia panel Heterotaxy panel Hypomagnesemia panel Long QT syndrome panel Short QT syndrome panel

CENTOGENE PANEL	SUBPANELS INCLUDED
CentoSkin **Genes: 72** **CentoSkin** is our solution for patients displaying skin disorders. Our panel includes genes for hypotricosis, epidermolysis bullosa, and congenital ichthyosis, between others. For melanoma, please check our Oncology section. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Congenital ichthyosis panel Cutis laxa panel Epidermolysis bullosa panel Ichthyosis extended panel Non-syndromic hypotrichosis panel

CENTOGENE PANEL	SUBPANELS INCLUDED
CentoDysmorph **Genes: 556** **CentoDysmorph** is designed to help physicians diagnose patients that suffer from a dysmorphic syndrome. The panel includes craniosynostosis, craniofacial disorders, cleft/lip palate, holoprosencephaly, Waardenburg syndrome, Hirschsprung disease, lissencephaly, and brain malformation disorders, among others. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Bardet-Biedl panel Cerebral cavernous malformations panel Cleft lip/palate panel Coffin-Siris syndrome panel Cornelia de Lange syndrome panel Craniosynostosis and craniofacial disorders panel Hirschsprung disease panel Holoprosencephaly panel Klippel-feil syndrome panel Lissencephaly and brain malformation panel Meckel syndrome panel Metaphyseal dysplasia panel Micro syndrome panel Microphthalmia/anophthalmia/coloboma spectrum panel Multiple epiphyseal dysplasia panel Neurofibromatosis panel Seckel syndrome panel Skeletal dysplasia ciliopathy panel Skeletal dysplasia extended panel Stickler syndrome panel Tuberous sclerosis panel Waardenburg syndrome panel

CENTOGENE PANEL	SUBPANELS INCLUDED
Ciliopathies panel **Genes: 194** Our **ciliopathies panel** includes a group of disorders causing cilia dysfunction, including Joubert Syndrome, Bardet-Biedl, COACH syndrome, primary ciliary dyskinesia, Meckel syndrome, skeletal dysplasia, situs inversus, and heterotaxy, among others. If polycystic kidney disease is suspected, CentoNephro Plus is recommended, which includes *PKD1* analysis. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Bardet-Biedl panel Ciliary (primary) dyskinesia panel Heterotaxy panel Joubert syndrome panel Skeletal dysplasia ciliopathy panel
Connective tissue and related disorders panel **Genes: 72** Our **connective tissue and related disorders panel** provides a profound one-step evaluation of several genes to detect different disorders with similar phenotypes, such as Marfan Syndrome, Loeys-Dietz, cutis laxa, Ehlers-Danlos, Stickler syndrome, and familial thoracic aortic aneurysm and dissection. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Cutis laxa panel Marfan, Ehlers-Danlos, Thoracic aortic aneurysm and related syndromes panel Familial thoracic aortic aneurysm panel Marfan, Loeys-Dietz syndrome and related disorders panel Stickler syndrome panel

CENTOGENE PANEL	SUBPANELS INCLUDED
Noonan - RASopathies panel **Genes: 22** The RASopathies are a group of genetic syndromes caused by germline mutations in genes that encode components or regulators of the RAS/mitogen-activated protein kinase (*MAPK*) pathway. Our **Noonan - RASopathies panel** is intended for patients with clinical symptoms of RASopathies and includes genes related to neurofibromatosis type 1, Noonan syndrome, Noonan syndrome with multiple lentigines, capillary malformation–arteriovenous malformation syndrome, Costello syndrome, Cardio-Facio-Cutaneous syndrome, and Legius syndrome, among others. Tuberous sclerosis and McCune Albright syndrome are included for differential diagnosis. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Neurofibromatosis panel Noonan - CFC syndrome panel Tuberous sclerosis panel

CENTOGENE PANEL	SUBPANELS INCLUDED
CentoHear **Genes: 196** **CentoHear** includes genes associated with syndromic and non-syndromic hearing loss. Hearing loss is a common condition in children, affecting 1 in 100 live births. In more than 50 % of the cases, there is a genetic cause for this disorder. CentoHear includes syndromes, such as Alport, Pendred, Waardenburg, Usher, and branchio-oto-renal. In addition, CentoHear detects non-syndromic hearing loss, which accounts for 70 % of genetic causes. Both autosomal recessive and dominant cases are included in the panel. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Deafness/Hearing loss panel, comprehensive

CENTOGENE PANEL	SUBPANELS INCLUDED
Diabetes and obesity panel **Genes: 196** Our **diabetes and obesity panel** is recommended for patients with abnormalities in glucose metabolism, such as hyperinsulinemic hypoglicemia, diabetes neonatal, MODY, diabetes in adults, and familial hypercholesterolemia as well as for patients displaying insulin resistance, from mild to the severe spectrum (Donohue syndrome), and for patients with familial hyperinsulinism. Disorders caused by imprinting errors or uniparental disomy such as 6q24-related transient neonatal diabetes mellitus and Beckwith Wiedemann syndrome are not detected wtih this panel. 25 days TAT; ≥99.5 % ≥20x coverage MLPA: 15q11 CNV analysis included	Bardet Biedl panel Congenital glycosylation disease panel Diabetes neonatal panel Familial hypercholesterolemia panel Hyperinsulinemic hypoglycemia panel MODY panel Obesity panel
Pancreatitis panel **Genes: 22** Our **pancreatitis panel** includes genes associated with chronic pancreatitis and for differential diagnosis, it includes genes associated with pancreatic cancer. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Pancreatitis panel

CENTOGENE PANEL	SUBPANELS INCLUDED
Congenital adrenal hyperplasia panel **Genes: 8** Our **congenital adrenal hyperplasia (CAH) panel** is designed for patients suspected of having CAH. CAH is a group of inherited disorders characterized by improper functioning of the adrenal glands, leading to abnormal production of steroid hormones, such as a cortisol or aldosterone. Our panel includes the analysis of the *CYP21A2* gene, which codes for the enzyme 21-hydroxylase. More than 90 % of CAH cases are caused by a deficiency of this enzyme. 25 days TAT; ≥99.5 % ≥20x coverage CNV and *CYP21A2* analysis	Congenital adrenal hyperplasia panel

CENTOGENE PANEL	SUBPANELS INCLUDED
Blood coagulation panel **Genes: 71** Our **blood coagulation panel** contains genes for the molecular diagnosis of thrombophilia, thrombocytopenia, hereditary hemorrhagic telangiectasia, ARC syndrome, Hermasky-Pudlak syndrome, coagulation factor disorders, hemophilia, and platelet related disorders. This panel does not detect intronic inversions for F8. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Afibrinogenemia panel Coagulation factor disorders panel Hemophilia panel Platelet related disorders panel Thrombocytoperia panel Thrombophilia panel
Bone marrow failure / anemia panel **Genes: 162** Our **bone marrow failure / anemia panel** is intended for patients with abnormalities in more than 2 blood cell types (red blood cell, white blood cell, and platelets) who present symptoms of lethargy, recurrent infections, excessive bleeding, abnormal pigmentation, enlarged spleen, and malignancies. Some specific disorders detected with this panel are hemophagocytic lymphohistiocytosis, Seckel syndrome, thrombocytopenia, Fanconi anemia, dyskeratosis congenita, Shwachman Diamond syndrome as well as other types of anemias, such as thalassemia alpha and beta, sickle cell disease, spherocytosis, megaloblastic anemia, congenital sideroblastic, and dyserythropoietic anemia. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Bone marrow failure panel Congenital dyserythropoietic anemia panel Congenital sideroblastic anemia panel Diamond-Blackfan anemia panel Fanconi anemia panel Hemophagocytic Lymphohistiocytosis panel Megaloblastic anemia panel Seckel syndrome panel Spherocytosis panel Thrombocytopenia panel

CENTOGENE PANEL	SUBPANELS INCLUDED
CentoLiver	COMING SOON!

CENTOGENE PANEL	SUBPANELS INCLUDED
Bone marrow failure / anemia panel **Genes: 162** Our **bone marrow failure / anemia panel** is intended for patients with abnormalities in more than 2 blood cell types (red blood cell, white blood cell, and platelets) who present symptoms of lethargy, recurrent infections, excessive bleeding, abnormal pigmentation, enlarged spleen, and malignancies. Some specific disorders detected with this panel are hemophagocytic lymphohistiocytosis, Seckel syndrome, thrombocytopenia, Fanconi anemia, dyskeratosis congenita, Shwachman Diamond syndrome as well as other types of anemias, such as thalassemia alpha and beta, sickle cell disease, spherocytosis, megaloblastic anemia, congenital sideroblastic, and dyserythropoietic anemia. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Bone marrow failure panel Congenital dyserythropoietic anemia panel Congenital sideroblastic anemia panel Diamond-Blackfan anemia panel Fanconi anemia panel Hemophagocytic Lymphohistiocytosis panel Megaloblastic anemia panel Seckel syndrome panel Spherocytosis panel Thrombocytopenia panel

CENTOGENE PANEL	SUBPANELS INCLUDED
CentoImmuno **Genes: 208** **CentoImmuno** is our solution for immunodeficiency and severe combined immunodeficiency (SCID) disorders. Our panel includes genes targeting severe combined immunodeficiency, congenital neutropenia, primary antibody deficiency, common variable immune deficiency, chronic granulomatous disease, autoimmune lymphoproliferative, afibrinogenemia, and agammaglobulinemia. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Agammaglobulinemia panel Autoimmune lymphoproliferative syndrome panel B-negative SCID panel B-positive SCID panel Chronic granulomatous disease panel Ciliary (primary) dyskinesia panel Comprehensive SCID panel Congenital neutropenia panel Hermasky-Pudlak syndrome panel Periodic fever syndrome panel Primary antibody deficiency panel Primary Immunodeficiency (PID) panel Susceptibility to atypical mycobacterium disease panel

CENTOGENE PANEL	SUBPANELS INCLUDED
CentoICU® **Genes: 843** **CentoICU®** a comprehensive NGS panel that includes genes explicitly selected for the genetic testing of critically ill newborns and children under 24 months in intensive care units (ICU). It is designed to address multiple genetic conditions that may be present in the newborn or early childhood period, with many having overlapping phenotypes and immediate implications for treatment initiation. It allows clinicians to utilize just one single test to provide an accurate diagnosis of newborn-related diseases using dried blood spots. 15 days TAT; ≥99.5 % ≥20x coverage FAST option: 10 days TAT	CentoICU®

METABOLIC DISORDERS

CENTOGENE PANEL	SUBPANELS INCLUDED
CentoIEM **Genes: 590** Inborn Errors of Metabolism largely impact human diseases. **CentoIEM** includes a large array of different disorders and contains genes responsible for diverse phenotypes, including intermediary metabolism, such as aminoacidopathies, organic acidurias, urea cycle disorders, sugar intolerance, metal disorders, and porphyrias, among others. Cytoplasmic and mitochondrial energetic processes and metabolism affecting cellular organelles, such as lysosomal, peroxisomal, glycosylation, and cholesterol synthesis are included. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Aicardi-Goutieres syndrome panel Autoimmune lymphoproliferative syndrome panel Brain iron accumulation syndromes panel Ceroid lipofuscinosis panel Congenital glycosylation disease panel Familial hypercholesterolemia panel Fatty acid oxidation disorder panel Glycogen storage disease panel (advance) Glycogen storage disease panel (basic) Hemochromatosis panel Hemophagocytic Lymphohistiocytosis panel Leigh syndrome and mitochondrial encephalopathy panel Leukodystrophy and peroxisome biogenesis disorders panel Lipodystrophy panel Lysosomal storage disease panel Maple syrup urine disease panel Methylmalonic acidemia panel (advanced) Methylmalonic acidemia panel (basic) Mucopolysaccharidosis panel Non ketotic hyperglycinemia panel Refsum disease panel Porphyria panel Spherocytosis panel Urea cycle disorder panel

CENTOGENE PANEL	SUBPANELS INCLUDED
CentoMetabolic® **Genes: 206** **CentoMetabolic®** was developed specifically for patients suspected of having a metabolic disorder or presenting complex, overlapping symptoms, a metabolic crisis, or neurological conditions of unknown etiology. It provides short turnaround times, targeting critically ill patients in NICU/PICU, and includes enzyme-activity testing where applicable as well as a proprietary selection of biomarkers that is continually updated. 15 days TAT; ≥99.5 % ≥20x coverage CNV analysis included Complementary biochemical testing by proprietary biomarkers and enzyme-activity assays if applicable	CentoMetabolic®
CentoMito® comprehensive **Genes: 404** **CentoMito® comprehensive** covers the entire mitochondrial genome (≥97 % ≥ 200x coverage) with detection of heteroplasmy down to 5 % along with nuclear genes related to mitochondrial diseases (≥99.5 % ≥20x coverage). Mitochondrial diseases are genetic conditions that occur when mitochondria fails to produce enough energy for the cell. Genetic mutations related to mitochondria cause symptoms mainly in the organs, where energetic consumption is high. These organs include the eye, kidney, pancreas, blood, inner ear, colon, skeletal muscle, heart, and brain. 25 days TAT; ≥99.5 % ≥20x coverage (nuclear mitochondrial genes); ≥97 % ≥ 200x (CentoMito® Genome) CNV analysis included	CentoMito® comprehensive Leigh syndrome and mitochondrial encephalopathy panel Neonatal mitochondrial hepatopathies panel

CENTOGENE PANEL	SUBPANELS INCLUDED
CentoMito® Genome **Genes: 37** **CentoMito® Genome** includes mitochondrial genes. Nuclear mitochondrial genes are not included. 25 days TAT; ≥97 % ≥200x coverage ≥5 % mitochondrial heteroplasmy can be confidently detected CNV analysis included	CentoMito® Genome Leber optic atrophy panel
Diabetes and obesity panel **Genes: 196** Our **diabetes and obesity panel** is recommended for patients with abnormalities in glucose metabolism, such as hyperinsulinemic hypoglicemia, diabetes neonatal, MODY, diabetes in adults, and familial hypercholesterolemia as well as for patients displaying insulin resistance, from mild to the severe spectrum (Donohue syndrome), and for patients with familial hyperinsulinism. Disorders caused by imprinting errors or uniparental disomy such as 6q24-related transient neonatal diabetes mellitus and Beckwith Wiedemann syndrome are not detected wtih this panel. 25 days TAT; ≥99.5 % ≥20x coverage MLPA: 15q11 CNV analysis included	Bardet-Biedl panel Congenital glycosylation disease panel Diabetes neonatal panel Familial hypercholesterolemia panel Hyperinsulinemic hypoglycemia panel MODY panel Obesity panel

CENTOGENE PANEL	SUBPANELS INCLUDED
Atypical hemolytic uremic syndrome panel **Genes: 20** Our **atypical hemolytic uremic syndrome panel** contains genes for the molecular diagnosis of atypical hemolytic uremic syndrome. 25 days TAT; ≥99.5 % ≥20x coverage *MLPA: CFH, CFHR1, CFHR2, CFHR3, CFHR5* CNV analysis included	Atypical Hemolytic Uremic syndrome
CentoNephro **Genes: 375** Approximately 10 % of the population worldwide is affected by chronic kidney diseases. Advances in genetic techniques are providing insights into kidney disease diagnosis, pathogenesis, and therapy. **CentoNephro** offers a comprehensive tool to screen for the most prominent hereditary kidney disorders, including polycystic kidney disease, Alport syndrome, renal tubular acidosis panel, focal glomerulonephrosis panel, and primary hyperoxaluria, among others. *PKD1* analysis is not included in this panel. 25 days TAT; ≥ 99.5 % ≥20x coverage CNV analysis included **CentoNephro Plus** **Genes: 376** If polycystic kidney disease is suspected CentoNephro Plus is recommended, which includes all genes from CentoNephro Plus and *PKD1* analysis. 25 days TAT; ≥ 99.5 % ≥20x coverage CNV and *PKD1* analysis	Alport syndrome panel Bardet Biedl panel Bartter syndrome panel Ciliary (primary) dyskinesia panel Combined Pituitary hormone deficiency panel Focal glomerulonephrosis panel Heterotaxy panel Intrahepatic cholestasis panel Joubert syndrome panel Kallmann syndrome and Hypogonadotropic hypogonadism panel Leber congenital amaurosis panel Meckel syndrome panel Nephronophthisis panel Nephrotic syndrome panel Neonatal mitochondiral hepatopathies panel Polycystic kidney disease Pseudohypoaldosteronism panel Renal tubular acidosis panel Skeletal dysplasia ciliopathy panel

CENTOGENE PANEL	SUBPANELS INCLUDED
Ciliopathies panel **Genes: 194** Our **ciliopathies panel** includes a group of disorders causing cilia dysfunction, including Joubert Syndrome, Bardet-Biedl, COACH syndrome, primary ciliary dyskinesia, Meckel syndrome, skeletal dysplasia, situs inversus, and heterotaxy, among others. If polycystic kidney disease is suspected, CentoNephro Plus is recommended, which includes *PKD1* analysis. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Bardet-Biedl panel Ciliary (primary) dyskinesia panel Heterotaxy panel Joubert syndrome panel Skeletal dysplasia ciliopathy panel

CENTOGENE PANEL	SUBPANELS INCLUDED
Ataxia panel Our **ataxia panel** includes genes relevant to hereditary neurological disorders characterized by ataxia, including SCA sequencing, cerebellar ataxia, episodic ataxia, and pontocerebellar ataxia. These disorders normally share overlapping symptoms and can only be clearly differentiated by molecular genetic testing. Our ataxia panel is the best option for a patient displaying gait imbalance and uncoordinated walking (ataxia). The most common forms of inherited ataxia are caused by repeat expansion. Therefore, we recommend to pair this NGS analysis with our repeat expansion module. **Ataxia panel** **Genes: 186** Includes NGS with CNV analysis 25 days TAT; ≥99.5 % ≥20x coverage **Ataxia comprehensive panel** **Genes: 196** Includes NGS with CNV and repeat expansion analysis 25 days TAT; ≥99.5 % ≥20x coverage **Ataxia repeat expansion panel** **Genes: 13** Includes repeat expansion analysis 25 days TAT; 100 % coverage Repeat expansion analysis: *ATN1, ATXN1, ATXN10, ATXN2, ATXN3, ATXN7, ATXN8OS, BEAN1, CACNATA, FXN, NOP56, PP2R2B, TBP*	Ataxia comprehensive panel Cerebellar ataxia panel Episodic ataxia panel Pontocerebellar hypoplasia panel SCA comprehensive panel SCA repeat expansion panel SCA sequencing panel

CENTOGENE PANEL	SUBPANELS INCLUDED
Amyotrophic lateral sclerosis (ALS) panel **Genes: 36** Our **amyotrophic lateral sclerosis (ALS) panel** is designed to detect ALS, which is a progressive neurodegenerative disorder characterized by the degeneration of the upper and lower motor neurons. Most cases appear to be sporadic, but 5-10 % of cases have a family history of the disease (FALS). 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included Repeat Expansion: *C9ORF72, PRNP*	Amyotrophic lateral sclerosis (ALS) panel Amyotrophic lateral sclerosis (ALS) and Frontotemporal dementia panel
CentoICU® **Genes: 843** **CentoICU®** a comprehensive NGS panel that includes genes explicitly selected for the genetic testing of critically ill newborns and children under 24 months in intensive care units (ICU). It is designed to address multiple genetic conditions that may be present in the newborn or early childhood period, with many having overlapping phenotypes and immediate implications for treatment initiation. It allows clinicians to utilize just one single test to provide an accurate diagnosis of newborn-related diseases using dried blood spots. 15 days TAT; ≥99.5 % ≥20x coverage FAST option: 10 days TAT	CentoICU®

CENTOGENE PANEL	SUBPANELS INCLUDED
CentoMito® comprehensive **Genes: 404** **CentoMito® comprehensive** covers the entire mitochondrial genome (≥97% ≥ 200x coverage) with detection of heteroplasmy down to 5% along with nuclear genes related to mitochondrial diseases (≥99.5% ≥20x coverage). Mitochondrial diseases are genetic conditions that occur when mitochondria fails to produce enough energy for the cell. Genetic mutations related to mitochondria cause symptoms mainly in the organs, where energetic consumption is high. These organs include the eye, kidney, pancreas, blood, inner ear, colon, skeletal muscle, heart, and brain. 25 days TAT; ≥99.5% ≥20x coverage (nuclear mitochondrial genes); ≥97% ≥ 200x (CentoMito® Genome) CNV analysis included	CentoMito® comprehensive Leigh syndrome and mitochondrial encephalopathy panel Neonatal mitochondrial hepatopathies panel
CentoMito® Genome **Genes: 37** **CentoMito® Genome** includes mitochondrial genes. Nuclear mitochondrial genes are not included. 25 days TAT; ≥97% ≥200x coverage ≥5% mitochondrial heteroplasmy can be confidently detected CNV analysis included	CentoMito® Genome Leber optic atrophy panel

CENTOGENE PANEL	SUBPANELS INCLUDED
CentoNeuro™ **Genes: 1493** **CentoNeuro™** is our largest panel, designed to detect a great array of neurological disorders from neonatal ICU cases to dementia or movement disorders in adults. This panel includes genes related to neurological diseases, such as amyotrophic lateral sclerosis, dementia, Parkinson´s, neuromuscular diseases, Charcot-Marie-Tooth, dystonia, epilepsy, autism, intellectual disability, migraine, spastic paraplegia, ataxia, Leigh syndrome, peroxisomal diseases, epileptic encephalopathies, and movement disorders, among others. If there is high diagnostic suspicion for Duchenne muscular dystrophy, we recommend that the clinician orders deletion/duplication analysis for *DMD* gene as an additional service. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	AllNeuro panel Amyotrophic lateral sclerosis (ALS) and Frontotemporal dementia panel Ataxia panel Arthrogryposis panel Dementia panel Dolichoectasia panel Dystonia panel Epilepsy panel Familial hemiplegic migraine panel Intellectual disability panel Joubert syndrome panel Kallman syndrome and Hypogonadotropic hypogonadism panel Leigh syndrome and mitochondrial encephalopathy panel Leukodystrophy and peroxisome biogenesis disorders panel Meckel syndrome panel Neonatal mitochondrial hepatopathies panel Neuromuscular panel Parkinson´s disease panel Refsum disease panel Spastic paraplegia panel Tuberous sclerosis panel Zellweger syndrome panel

CENTOGENE PANEL	SUBPANELS INCLUDED
Ciliopathies panel **Genes: 194** Our **ciliopathies panel** includes a group of disorders causing cilia dysfunction, including Joubert Syndrome, Bardet-Biedl, COACH syndrome, primary ciliary dyskinesia, Meckel syndrome, skeletal dysplasia, situs inversus, and heterotaxy, among others. If polycystic kidney disease is suspected, CentoNephro Plus is recommended, which includes *PKD1* analysis. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Bardet-Biedl panel Ciliary (primary) dyskinesia panel Heterotaxy panel Joubert syndrome panel Skeletal dysplasia ciliopathy panel
Dementia panel **Genes: 57** Our **dementia panel** includes genes causing Alzheimer's, dementia, and frontotemporal demetia, as well as genes used for differential diagnosis with overlap at any point of the natural history of the disease. Genes inside this panel have been carefully selected to increase the diagnostic yield. Actionable diseases overlapping with the phenotype are included such as Wilson disease, Niemann-Pick, and hexosaminidase A deficiency. This panel does not detect Huntington disease. 25 days TAT; ≥99.5 % ≥20x coverage Repeat expansion analysis: *ATXN2, C9ORF72, PRNP* CNV analysis included	Alzheimer dementia and dementia panel Dementia panel Frontotemporal dementia panel

CENTOGENE PANEL	SUBPANELS INCLUDED
Dystonia panel **Genes: 88** Our **dystonia panel** includes a selection of genes that help to differentiate between different types of dystonia, including isolated, dystonia plus parkinsonism, dystonia plus myoclonus, dystonia plus another dyskinesia, and complex dystonias. Additionally, our panel includes genes associated with primary familial brain calcification, disorders of heavy metal metabolism, neurodegeneration with brain iron accumulation, some lipid storage disorders, arylsulfatase A deficiency, leukodystrophies, and specific metabolic diseases necessary for differential diagnosis. Our dystonia panel provides the knowledge to help solve the genetic cause of dyskinesia. This panel does not detect Huntington disease or diseases with repeat expansion as the mechanism of disease. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Comprehensive dystonia panel Dopa-responsive dystonia panel Myoclonic dystonia panel

CENTOGENE PANEL	SUBPANELS INCLUDED
Epilepsy panel **Genes: 547** While some types of seizures are easily categorized (i.e., partial or generalized), others are not or might later develop into different types (i.e., partial seizures with secondary generalization), making targeted panel testing less likely to succeed at reaching a diagnosis. Our **epilepsy panel** is a phenotype-directed panel that covers different types of seizure syndromes, covering Dravet syndrome, early infantile epileptic encephalopathy, epilepsy partial, epilepsy generalized, epilepsy absence, myoclonic epilepsy panel, and hypomagnesemia. This panel does not include mitochondrial genes (i.e., genes causing myoclonic epilepsy with ragged red fibers -MERRF-). If the clinical suspicion is oriented towards metabolic or mitochondrial disorders, please order CentoMito® comprehensive. 25 days TAT; ≥99.5 % ≥20x coverage Repeat expansion analysis: *CSTB* CNV analysis included	Aicardi-Goutieres syndrome panel Brain iron accumulation syndromes panel Comprehensive epilepsy panel Congenital glycosylation disease panel Dravet syndrome panel Early infantile epileptic encephalopathy panel Epilepsy (absence) in childhood panel Epilepsy (generalized) with febrile seizures panel Epilepsy (partial) hereditary panel Epileptic encephalopathy panel Hypomagnesemia panel Leigh syndrome and mitochondrial encephalopathy panel Leukodystrophy and peroxisome biogenesis disorders panel Lysosomal storage disease panel Mitochondrial DNA depletion panel Myoclonic epilepsy panel Urea cycle disorder panel

CENTOGENE PANEL	SUBPANELS INCLUDED
Intellectual disability panel **Genes: 599** Our panel includes genes associated with intellectual disabilities covering all mechanisms of inheritance as well as syndromic and non-syndromic autism, microcephaly, neuronal migration disorders, developmental regression, and Aicardi Goutierres. Detection of Fragile X syndrome is possible as our panel includes repeat expansion of *FMR1*. 25 days TAT; ≥99.5 % ≥20x coverage Repeat expansion analysis: *FMR1* CNV analysis included	Aicardi-Goutieres syndrome panel Bardet-Biedl panel Mental retardation AD, AR, XL panel Mental retardation, X-linked panel Micro syndrome panel Microcephaly panel Neuronal migration disorders panel Syndromic autism panel

CENTOGENE PANEL	SUBPANELS INCLUDED
Neuromuscular panel **Genes: 276** Our **neuromuscular panel** is ideal for patients with hypotonia, weakness, and muscular diseases. It includes genes causing neurological diseases and covers disorders, such as metabolic myopathies, muscular dystrophies, Ullrich, Bethlem, Charcot-Marie-Tooth, hypotonia, congenital myasthenic syndromes, congenital myopathies, myofibrillar myopathies, and nemaline myopathies. Arthrogryposis is included for differential diagnosis of early-onset neuromuscular disorders. If there is high diagnostic suspicion for Duchenne muscular dystrophy, we recommend that the clinician orders deletion/duplication analysis for the *DMD* gene as an additional service. 25 days TAT; ≥99.5 % ≥20x coverage Repeat Expansion: *DMPK* CNV analysis included	Arthrogryposis Bethlem myopathy panel CMT neuropathy panel Congenital myasthenic syndrome panel Congenital myopathy panel Dejerine-Sottas syndrome panel Hyperekplexia panel Malignant hyperthermia panel Metabolic myopathies panel Muscular dystrophy panel Muscular dystrophy-dystroglycanopathy type A panel Myofibrillar myopathy panel Myopathy-rhabdomyolysis syndrome panel Nemaline myopathy panel Non-dystrophic myotonia congenita panel SMN negative spinal muscular atrophy panel Ullrich muscular dystrophy panel

CENTOGENE PANEL	SUBPANELS INCLUDED
Parkinson disease panel **Genes: 37** Our **Parkinson disease (PD) panel** identifies all relevant pathophysiologically genetic variants for the development and treatment of PD. Characteristic features of PD include neuronal loss in specific areas of the substantia nigra and widespread intracellular protein α-synuclein accumulation. The disease is characterized by three core motor symptoms: tremor, muscle rigidity, and bradykinesia. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Parkinson's disease panel
Spastic paraplegia panel **Genes: 65** Our **spastic paraplegia panel** is recommended for patients displaying spastic gait impairment, spastic weakness, and hyperreflexia. Our panel screens for recessive, dominant, and x-linked forms of hereditary spastic paraplegia (HSP) which can not be distinguished by clinical and neuroimaging parameters alone. For patients that also show complex HSP and display other neurological signs including ataxia, mental retardation, dementia, extrapyramidal signs, visual dysfunction, or epilepsy, we recommend CentoNeuro™. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Spastic paraplegia panel complete Spastic paraplegia panel, autosomal dominant Spastic paraplegia panel, autosomal recessive

CENTOGENE PANEL	SUBPANELS INCLUDED
BRCA1, BRCA2 panel **Genes: 2** Breast cancer is the most common type of cancer in woman constituting around 25% of all females cases. Mutations in *BRCA1* and *BRCA2* can increase the risk of developing cancer. **_BRCA1, BRCA2_ panel** Panel includes only NGS 15 days TAT; ≥99,5 % ≥20x coverage Type: Germline **_BRCA1, BRCA2_ panel Plus** Panel includes only NGS and CNV analysis 15 days TAT; ≥99,5 % ≥20x coverage Type: Germline **_BRCA1, BRCA2_ panel Combi** Panel includes NGS and MLPA 15 days TAT; ≥99,5 % ≥20x coverage Type: Germline **_BRCA1, BRCA2_ panel** Panel for somatic mutation analysis 10 days TAT; variable coverage Type: Somatic	*BRCA1, BRCA2* panel
CentoBreast® **Genes: 30** **CentoBreast®** detects mutations in the *BRCA1* and *BRCA2* genes, which are the most common hereditary causes for breast cancer. In addition, our panel includes other genes such as *ATM, BRIP1, CHEK2, PALB2, RAD51,* etc. which have also been associated with increased cancer risk. Breast cancer is one of the most common cancers in the world affecting ~12.5% of women during their lifetime, with 5–10% of these patients having a hereditary form. 15 days TAT; ≥99.5 % ≥20x coverage Type: Germline CNV analysis	Breast ovarian cancer panel CentoBreast® panel Ovarian cancer panel, targeted

CENTOGENE PANEL	SUBPANELS INCLUDED
CentoCancer® **Genes: 70** Each gene in **CentoCancer®** has been carefully selected based on its risk potential in the development of one or more of the following cancers: breast, ovarian, colorectal, gastric, thyroid, endometrial, pancreatic, melanoma, renal, and prostate. This panel is appropiate for patients with positive personal history of early-onset cancer, rare cancer, bilateral cancer, or multiple primary cancers. 15 days TAT; ≥99.5 % ≥20x coverage Type: Germline CNV analysis inluded	CentoBreast® panel CentoColon extended panel Melanoma panel Prostate cancer panel Renal cancer panel, targeted Skin cancer panel, targeted Thyroid cancer panel, targeted Uterine cancer panel, targeted
CentoCancer® comprehensive **Genes: 110** **CentoCancer® comprehensive** is our most extensive cancer panel, covering a large number of cancer-associated genes. Each gene in this panel has been carefully selected based on its risk potential in the development of one or more of the following cancers: breast, ovarian, colorectal, gastric, thyroid, endometrial, pancreatic, melanoma, renal, prostate, among others. 15 days TAT; ≥99 % ≥20x coverage Type: Germline CNV analysis included	CentoCancer® comprehensive panel Multiple endocrine neoplasius / paragenglioma / pheochromocytoma panel
CentoColon **Genes: 33** **CentoColon** detects genes that are associated with colon, pancreatic, and gastric cancer. 15 days TAT; ≥99.5 % ≥20x coverage Type: Germline CNV analysis included	CentoColon extended panel Colon cancer non-polyposis panel Colon cancer with polyps panel Gastric cancer panel, targeted Pancreatic cancer panel, targeted

CENTOGENE PANEL	SUBPANELS INCLUDED
Myeloid tumor panel **Genes: 22** Our **myeloid tumor panel** targets important regions within 22 genes that are frequently mutated in myeloid malignancies. Myeloid malignancies are clonal diseases of hematopoietic progenitor cells. Myeloid tumors represent the fourth most frequently diagnosed cancer in economically developed countries. The majority of myeloid tumors contain high numbers of somatic mutations, which are genetic changes that are not inherited but created within the tumor itself. Unlike inherited "germline" mutations, these somatic mutations are not transmitted to offspring. Somatic mutations significantly contribute to the pathogenesis, progression, and prognosis of myeloid malignancies. Diseases covered in this panel include: Acute myeloid leukemia (AML), chronic myeloid leukemia (CML), myelodysplastic syndrome (MDS), myeloproliferative neoplasms (MPN), chronic myelomonocytic leukemia (CMML), and juvenile myelomonocytic leukemia (JMML). 10 days TAT; >97 % >200x coverage Type: Somatic	Myeloid tumor panel

CENTOGENE PANEL	SUBPANELS INCLUDED
Solid tumor panel **Genes: 149** Our **solid tumor panel** provides full sequencing of 106 selected cancer-associated genes as well as the hotspot analysis of relevant cancer regions in 43 genes. It detects over 5,000 validated oncogenic variants and includes the latest evidence-based variants associated with treatment decisions in solid tumors. The panel has more than 25 genes with approved targeted therapies or those that are being currently tested in clinical trials. Furthermore, somatic variants with an impact on prognosis of the individual tumor or on the efficacy of standard anti-tumor therapy are captured. It covers more than 100 different types of somatic cancers, including adrenal, colon, hepatic, prostate, renal, skin, testicular, thyroid, glioma, esophageal, endometrial, and breast cancer, among others. The panel provides a better understanding of tumor behavior as well as its likelihood to respond to a treatment, contributing to tailored medicine for the patient, thus frequently leading to a better outcome or reduced adverse effects. 10 days TAT; >97 % >200x coverage Type: Somatic	Solid tumor panel

CENTOGENE PANEL	SUBPANELS INCLUDED
CentoVision **Genes: 378** **CentoVision** is carefully designed to find the genetic basis of eye diseases, including those that are the leading causes of blindness among infants (Leber congenital amaurosis), children (early-onset retinitis pigmentosa), and adults (pattern dystrophy). Our panel includes the most common ophthalmology diseases, such as congenital glaucoma, retinitis pigmentosa, Stargardt disease, Stickler syndrome, achromatopsia, and Usher syndrome, among others. It also screens for different types of albinism (oculocutaneous and ocular) as well as Hermasky-Pudlak syndrome. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Achromatopsia panel Albinism panel Bardet-Biedl panel Cataract panel Cone-rod and cone dystrophy panel Flecked retina panel Glaucoma panel Hermansky-Pudlak syndrome panel Leber congenital amaurosis panel Meckel syndrome panel Microphthalmia/anophthalmia/coloboma spectrum panel Oculomotor apraxia panel Ophthalmoplegia progressive external panel Optic atrophy panel Retinitis pigmentosa panel, autosomal dominant Retinitis pigmentosa panel, autosomal recessive Stargardt disease panel Stickler syndrome panel Usher syndrome panel Vitreoretinopathy and Wagner syndrome panel

CENTOGENE PANEL	SUBPANELS INCLUDED
Abnormal mineralization panel **Genes: 69** Our **abnormal mineralization panel** includes osteogenesis imperfecta, osteopetrosis, high bone density disorders, and differential diagnosis genes necessary to discriminate the real genetic cause. Actionable diseases, such as hypophosphatasia, are also included in our panel. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included	Abnormal mineralization panel Osteogenesis imperfecta and low bone density disorders panel Osteopetrosis and high bone density disorders panel

CENTOGENE PANEL	SUBPANELS INCLUDED
Pulmonary panel **Genes: 92** Our **pulmonary panel** includes genes for the diagnosis of central hypoventilation, surfactant metabolism, comprehensive pulmonary diseases, and pulmonary hypertension among others. 25 days TAT; ≥99.5 % ≥20x coverage Repeat expansion analysis: *PHOX2B* CNV analysis included	Central hypoventilation syndrome panel Comprehensive pulmonary disease panel Pulmonary hypertension panel Surfactant metabolism dysfunction panel

CENTOGENE PANEL	SUBPANELS INCLUDED
CentoScreen® **Genes: 330** **CentoScreen®** is our comprehensive screening panel including autosomal and X-linked disorders. It provides the opportunity to make informed decisions and review the range of options available to guide pregnancy and family planning. **CentoScreen® Solo** Includes complete panel evaluation with CNV analysis of 34 genes. 15 days TAT;~99%>20x coverage **CentoScreen® Paired Pack** Includes complete panel evaluation with CNV analysis of 34 genes + risk gene analysis of the partner. 15 days TAT;~99%>20x coverage **CentoScreen® Duo** Includes complete panel evaluation with CNV analysis of 34 genes for each partner. 15 days TAT;~99%>20x coverage	CentoScreen®

CENTOGENE PANEL	SUBPANELS INCLUDED
Infertility panel **Genes: 94** Our **infertility panel** is recommended for patients trying to conceive for one year or longer, with known fertility problems, who have experienced more than one miscarriage, with irregular or absent menstruation, with low sperm count, form, or movement, or with secondary sexual features. Our panel includes the most important genes related to infertility in males and females. Knowing the exact cause of infertility allows for better diagnostic decisions and enables enhanced counseling for parents. 25 days TAT; ≥99.5 % ≥20x coverage CNV analysis included Repeat expansion analysis: *AR, FMR1* MLPA: Aneuploidy, AZF region	Female infertility panel Male infertility panel Global infertility panel

The CENTOGENE Advantage

A comprehensive diagnostic solution beyond DNA testing

OUR DIAGNOSTIC SERVICES ARE MORE THAN LABORATORY AND BIOINFORMATICS.

CentoCard®

Our quick, cost-effective, and hassle-free solution for shipment of clinical blood samples for genetic testing. Collected samples are unaffected by shipping time and temperature, and a single card enables genetic and metabolic testing.

CentoPortal®

A user-friendly and fully secure online service designed to assist in ordering tests, transferring patient data, administering patients' samples, and accessing your diagnostic reports 24/7. Please go to: www.centoportal.com

Extended Phenotyping

Structuring your patient's symptoms into Human Phenotype Ontology (HPO) terms ensures the best quality of clinical information for data interpretation.

CentoMD®

Our extensive rare disease data repository with over 400,000 analyzed case and more than 12 million unique variants supports our world-class medical interpretation.

Data Safety and Research Use

With transparent and easy-to-understand consent forms, your patients can make educated decisions without worrying about data protection. By consenting to the research and storage option, you and your patients will advance research, the understanding of rare diseases, and the quality of future diagnoses and therapies.

Variant Reclassification Program

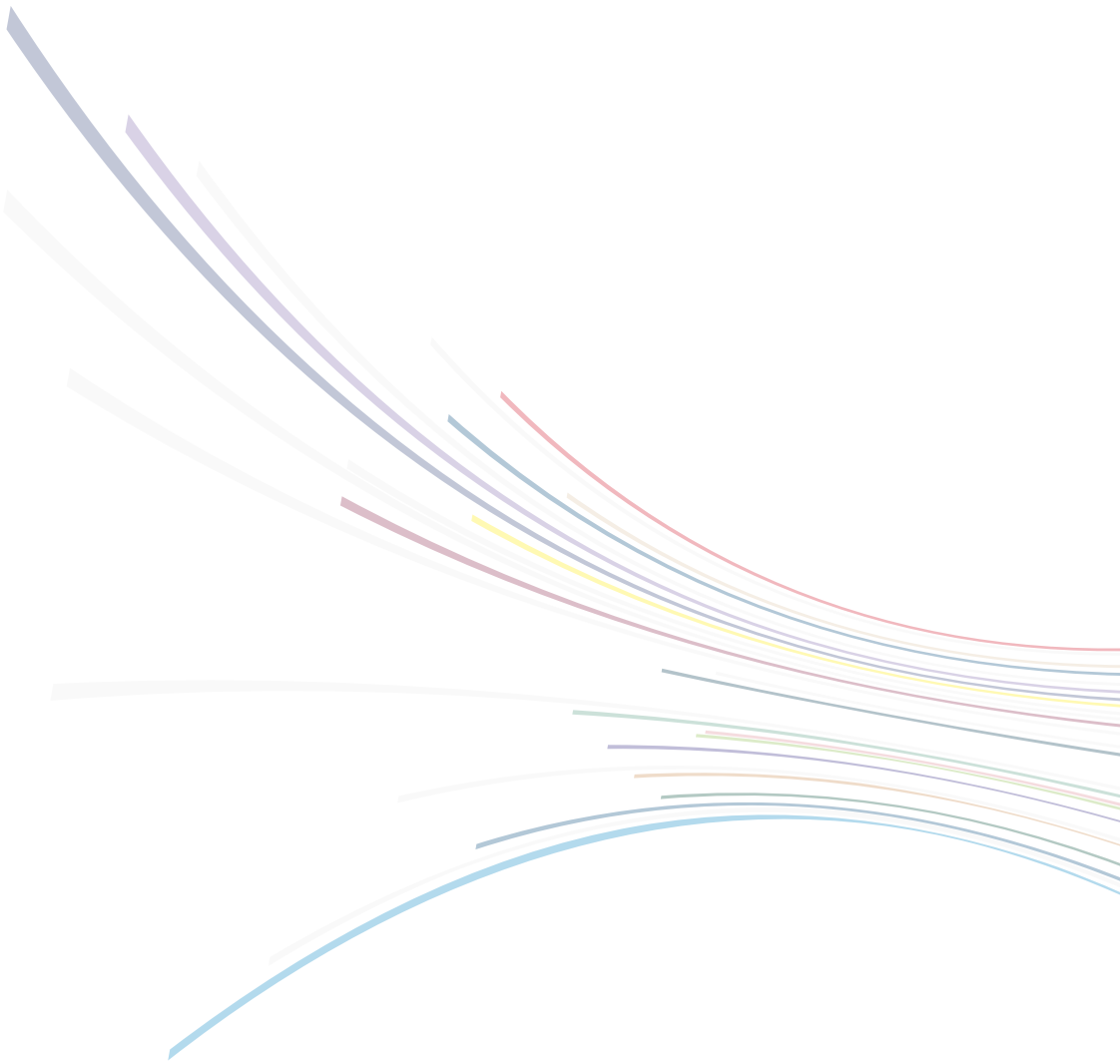
CENTOGENE has a highly robust and ongoing variant reclassification program based on new genetic evidence. If re-classification affects the nature of the genetic diagnosis of the patient, physicians will be notified free of charge.

Multiomics Testing

Continuous research identifies and validates biomarkers, increasing disease understanding and enabling therapy monitoring. This has already added diagnostic certainty to lysosomal storage disorders and other diseases.

World-Class Expertise

CENTOGENE's reputation is built on an international team of genetic and bioinformatics experts, the latest lab technology, continuously improved processes and protocols, and unique data analysis software.



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For further information and support, please contact our closest representative or our customer support team, easily accessible by phone or email.

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