JOHNS HOPKINS MEDICINE

Johns Hopkins Genomics
DNA Diagnostic Laboratory

Clinical Exome Requisition Form - Page 1

v121922

Referrer Information

Physician:

UPIN/NPI:

Genetic Counselor:

Email:

Institution:

Address:

Phone:

Fax:

Additional reports to:

Address:

Phone:

Fax:

Mandatory Signature

I have confirmed that the patient has consented for the testing ordered and that two matching identifiers are present on each page of this requisition.

Signature:

Date:

Patient Information (*two of these identifiers MUST also appear on the sample tube)

Legal Name* (Last):

(First):

Preferred Name (Last):

(First):

Date of birth* (mm/dd/yy):

Sex assigned at birth:

Gender:

Patient ID/MRN*:

Patient Address:

Billing Information (contact Billing Coordinator at 443-287-2486 prior to submitting)

Billing contact:

Phone:

Fax:

Email:

☐ Inpatient ☐ Referring Center ☐ MD Medicaid ☐ Self-pay ☐ Patient Insurance ☐ Medicare

Shipping Address: 1812 Ashland Ave, Sample Intake Rm 245, Baltimore, MD 21205

Patient Information

Patient Name:

DOB:

Proband Sample Information

Test Selection

☐ Proband-only ☐ Duo ☐ Trio ☐ Quad

☐ Include full sequence analysis and deletion testing of the mitochondrial genome

Sample Type

☐ Whole Blood
☐ Extracted DNA
☐ Saliva
☐ Cultured skin fibroblasts*
☐ Other:_____

☐ Cord blood
☐ Cleaned chorionic villi
☐ Cultured chorionic villi
☐ Cultured amniocytes

Collection Date:

Blood and saliva are **not** acceptable if the patient has:

- Received blood products <2 weeks before specimen collection. Exceptions are made for pRBC-only transfusions.
- Received an allogenic bone marrow or stem cell transplant. Cultured skin fibroblasts are the only accepted specimen type in this case.
- Active hematologic malignancy; cultured skin fibroblasts are the recommended sample type.

Contact the lab with specific questions or concerns.

Isolation or extraction of nucleic acids must be performed in a CLIA-certified laboratory or a laboratory meeting equivalent (or more stringent) requirements as determined by the College of American Pathologists (CAP) and/or the Centers for Medicare and Medicaid Services (CMS).

Family Information (if applicable)

Name (Last, First)	DOB	Relationship	Sample Type
			☐ Blood ☐ Saliva
			☐ Blood ☐ Saliva
			☐ Blood ☐ Saliva

Collection Site(s)

Ethnicity

☐ Black, African American, or of African descent
☐ East Asian
☐ Middle Eastern, Southwest Asian, North African
☐ Hispanic, Latino/Latina/Latinx
☐ Native American, Alaska Native, First Nations
☐ Native Hawaiian, Pacific Islander
☐ South Asian
☐ Southeast Asian
☐ White
☐ Other: _____

Patient Information

Patient Name:

DOB:

Phenotypic Information

Cancer

- ___ Type: _____
- ___ Location: _____
- ___ Age of onset: _____

Developmental/Behavioral

- ___ Absent speech
- ___ Aggressive behavior
- ___ Anxiety
- ___ Autistic Behavior
- ___ Cognitive impairment
- ___ Delayed speech & language development
- ___ Developmental regression
- ___ Gait disturbance
- ___ Global developmental delay
- ___ Hyperactivity
- ___ Intellectual disability
- ___ Learning disability
- ___ Memory impairment
- ___ Other: _____

Cardiac

- ___ Amyloidosis
- ___ Aortic root dilation
- ___ Arrhythmia
- ___ Atrial septal defect
- ___ Bicuspid aortic valve
- ___ Cardiomyopathy
- ___ Coarctation of aorta
- ___ Mitral valve prolapse
- ___ Patent ductus arteriosis
- ___ Prolonged QTc interval
- ___ Sudden death
- ___ Tetralogy of Fallot
- ___ Ventricular septal defect
- ___ Other: _____

Ear Defects/Hearing Impairment

- ___ Ears (shape, placement)
- ___ Conductive hearing impairment
- ___ Sensorineural hearing impairment
- ___ Other: _____

Craniofacial/Dysmorphism

- ___ Dysmorphic features
- ___ Asymmetry
- ___ Brachycephaly
- ___ Cleft lip and/or palate
- ___ Coarse facial features
- ___ Craniosynostosis
- ___ Short neck
- ___ Synophrys
- ___ Other: _____

Patient Information

Patient Name:

DOB:

Phenotypic Information (continued)

Eye Defects/Vision

- ___ Cataracts
- ___ Coloboma
- ___ Corneal opacity
- ___ Ectopia lentis
- ___ External ophthalmoplegia
- ___ Microphthalmia/Anophthalmia
- ___ Myopia
- ___ Nystagmus
- ___ Optic atrophy
- ___ Ptosis
- ___ Retinal detachment
- ___ Retinitis pigmentosa
- ___ Strabismus
- ___ Other: _____

Endocrine

- ___ Hypogonadism
- ___ Delayed puberty
- ___ Precious puberty
- ___ Diabetes
- ___ Hyperinsulinism
- ___ Hyperthyroidism
- ___ Hypothyroidism
- ___ Other: _____

Gastrointestinal/Abdominal

- ___ Constipation
- ___ Diaphragmatic hernia
- ___ Diarrhea
- ___ Duodenal stenosis/atresia
- ___ Exocrine pancreatic insufficiency
- ___ Failure to thrive
- ___ Feeding difficulties
- ___ Gastroesophageal reflux
- ___ Hepatomegaly
- ___ Heterotaxy
- ___ Inflammatory bowel disease
- ___ Intrahepatic biliary atresia
- ___ Jaundice
- ___ Nausea/Vomiting
- ___ Pancreatitis
- ___ Pyloric stenosis
- ___ Splenomegaly
- ___ Tracheoesohageal fistula
- ___ Umbilical hernia
- ___ Other: _____

Patient Information

Patient Name:

DOB:

Phenotypic Information (continued)

Genitourinary

- ___ Ambiguous genitalia
- ___ Cystic kidney disease
- ___ Cryptorchidism
- ___ Horseshoe kidney
- ___ Hydronephrosis
- ___ Hypospadias
- ___ Inguinal hernia
- ___ Micropenis
- ___ Nephrolithiasis
- ___ Renal agenesis
- ___ Other: _____

Growth

- ___ Abnormal fat distribution
- ___ Failure to thrive
- ___ Obesity
- ___ Overgrowth
- ___ Short stature
- ___ Tall stature
- ___ Macrocephaly
- ___ Microcephaly
- ___ Other: _____

Hematologic/Immunologic

- ___ Allergic rhinitis
- ___ Anemia
- ___ Immunodeficiency
- ___ Neutropenia
- ___ Pancytopenia
- ___ Recurrent infections
- ___ Thrombocytopenia
- ___ Other: _____

Imaging Findings

___ Specify or provide relevant imaging reports:

Metabolic/Lab Findings

___ Specify or provide relevant lab reports/values:

Patient Information

Patient Name:

DOB:

Phenotypic Information (continued)

Musculoskeletal

- ___ Abnormal connective tissue
- ___ Abnormal form of the vertebral bodies
- ___ Abnormality of the ribs
- ___ Arachnodactyly
- ___ Arthrogryposis
- ___ Bruising susceptibility
- ___ Camptodactyly
- ___ Clinodactyly
- ___ Decreased muscle mass
- ___ Ectrodactyly
- ___ Fatigue
- ___ Hemihypertrophy
- ___ Hypotonia
- ___ Joint hypermobility
- ___ Muscle weakness
- ___ Myopathic facies
- ___ Myopathy
- ___ Osteoarthritis
- ___ Osteopenia
- ___ Pectus deformity
- ___ Polydactyly
- ___ Recurrent fractures
- ___ Rhabdomyolysis
- ___ Scoliosis
- ___ Skeletal dysplasia
- ___ Other: _____

Neurological

- ___ Ataxia
- ___ Cerebral palsy
- ___ Chorea
- ___ Cortical Visual Impairment
- ___ Dementia
- ___ Dysarthria
- ___ Dyskinesia
- ___ Dysphasia
- ___ Dystonia
- ___ Encephalopathy
- ___ Headaches
- ___ Hemiplegia
- ___ Infantile Spasms
- ___ Migraines
- ___ Myoclonus
- ___ Parkinsonism
- ___ Peripheral neuropathy
- ___ Seizures
- ___ Sensory neuropathy
- ___ Spasticity
- ___ Stroke
- ___ Tremors
- ___ Other: _____

Patient Information

Patient Name:

DOB:

Phenotypic Information (continued)

Pre/Perinatal History

- ___ Increased NT/Cystic hygroma
- ___ Intrauterine growth retardation
- ___ Nonimmune hydrops fetalis
- ___ Oligohydramnios
- ___ Omphalocele
- ___ Polyhydramnios
- ___ Two vessel cord
- ___ Prematurity
- ___ Other: _____

Respiratory

- ___ Asthma
- ___ Hypoventilation
- ___ Laryngomalacia
- ___ Pneumothorax
- ___ Pulmonary fibrosis
- ___ Respiratory insufficiency
- ___ Other: _____

Skin/Hair

- ___ Abnormal blistering of the skin
- ___ Abnormality of hair
- ___ Abnormality of nail
- ___ Abnormal skin pigmentation
- ___ Abnormality of teeth
- ___ Other: _____

Structural Brain Abnormalities

- ___ Abnormal myelination
- ___ Abnormality of basal ganglia
- ___ Abnormality of brainstem
- ___ Abnormality of periventricular white matter
- ___ Abnormality of the corpus callosum
- ___ Aplasia/hypoplasia of cerebellum/vermis
- ___ Arnold Chiari malformation
- ___ Encephalocele
- ___ Heterotopia
- ___ Holoprosencephaly
- ___ Hydrocephalus/Ventriculomegaly
- ___ Leukodystrophy
- ___ Lissencephaly
- ___ Pachygyria/Polymicrogyria
- ___ Other: _____

Vascular

- ___ Arterial aneurysm/dissection
- ___ Arterial calcification
- ___ Arterial tortuosity
- ___ Arteriovenous malformation
- ___ Epistaxis
- ___ Lymphedema
- ___ Pulmonary hypertension
- ___ Other: _____

Additional Clinical Information/ Genes of Interest/ Previously Reported Variants

My Choices - Patient

Secondary Findings Reported to Me

Secondary findings are genetic changes that are likely to cause specific conditions other than the primary reason for testing in me/my child. Only conditions with clear management guidelines are included, and not every possible disease is covered. The DNA Diagnostic Laboratory largely follows the ACMG version 3 guidelines for reporting secondary findings. With respect to TTN-associated DCM, our current policy is to report truncating variants in the A-band alone.

- ☐ Yes, I would like secondary findings to be analyzed for me/my child.
- ☐ No, I would not like secondary findings to be analyzed for me/my child.

Research

De-identified clinical and genetic information may be used in academic case research and/or publications. The ordering provider may reach out to me to obtain additional information and/or photos. Additionally, if the results of clinical exome sequencing are negative, the ordering provider may re-contact me about follow-up research sequencing opportunities.

- ☐ Yes, I agree to my/my child's de-identified sample being used for research.
- ☐ No, I do not agree to my/my child's de-identified sample being used for research.

Sequence Data Given to My Provider

My provider can have a copy of the raw sequence data from my exome test (called a variant call file or VCF). My provider may request the raw data to further analyze genetic changes that may be associated with my/my child's primary medical concerns. This information will not be used for research purposes or shared with other providers or insurers unless otherwise discussed with me.

- ☐ Yes, I allow the lab to release my raw data to my referring provider.
- ☐ No, I do not allow the lab to release my raw data to my referring provider.

Statement of Consent - Patient

My ordering provider has reviewed OR I have read the Clinical Exome Sequencing Informed Consent document in its entirety. I have had the opportunity to ask questions of the provider about Exome Sequencing. I grant permission for the DNA Diagnostic Laboratory at Johns Hopkins University to perform clinical exome sequencing for me and/or my child. I have chosen to either opt-in or opt-out of receiving secondary findings, being re-contacted for research, and allowing my referring provider to request access to the VCF as detailed above. I understand the benefits, risks, and limitations of exome sequencing.

Patient Name (Print):

Signature: Date:

Relationship to patient (if not self):

My Choices - Family Member

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Family Member Name (Print):

Signature: Date:

Relationship to patient:

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Signature: Date:

Relationship to patient:

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Family Member Name (Print):

Signature: Date:

Relationship to patient:

Informed Consent

Exome Sequencing

Exome sequencing is a genetic test that analyzes a patient's genetic material, or DNA. Genes are the instructions that tell cells and bodies how to grow and develop. They are made up of DNA. Changes in genes, or variants, may contribute to a patient's health concerns. All people have many changes in their genetic information. Only some of these variants are known to result in genetic conditions. Exome sequencing is able to analyze many genes at once to look for variants that may provide a genetic diagnosis. Understanding the cause of a patient's health concerns may provide insight into what can be expected for the patient in the future, whether other family members may be at risk for carrying the variant, and what the risk is for recurrence. Although exome sequencing is able to read through many genes, it is not able to read through the entirety of the patient's genetic information. The goal of exome sequencing is to identify a genetic cause for a patient's health concerns.

Types of Results

There are several types of results that may be reported by exome sequencing:

- POSITIVE: A positive result indicates that a genetic change has been identified in a gene known to be responsible for a genetic condition. This may or may not provide a cause or diagnosis for the patient's health concerns. It is possible that this test may identify more than one genetic change. It is possible that other family members may carry the same genetic change.
- NEGATIVE: A negative result indicates that no known genetic cause for the patient's medical concerns was found. A negative result does not mean that there is not a genetic cause for the patient's health concerns. Future genetic testing may be able to identify additional genetic changes.
- UNCERTAIN: A variant of uncertain significance (VUS) indicates that a genetic change was identified in a gene, but that there is not yet enough information known about the consequences of a particular change or gene to determine whether it has health care significance. Testing of additional family members may be recommended to better understand the effect of an uncertain variant.

Family Member Testing

Obtaining samples from the patient's biological family members may aid in the interpretation of exome sequencing results. If a genetic change is identified in a patient, the family member samples may be tested for the same change. This may indicate whether or not the change was inherited or de novo (new to the patient). Family member samples will only be analyzed in the event that a genetic change is identified in the patient.

Secondary Findings

Exome sequencing analyzes many genes all at once. Accordingly, it is possible to find genetic changes in genes that are not related to the patient's primary health concerns. These results are called secondary findings. The American College of Medical Genetics and Genomics (ACMG) recommends that laboratories report such findings in genes that are known to cause specific actionable inherited conditions. Examples include hereditary cancer and heart syndromes, among others (please see attached table). Some of these conditions may not present until adulthood and may have a significant impact on the patient's and family member's healthcare and/or reproductive risk. If the patient is found to have a genetic change associated with one of these conditions, the family member's samples will be analyzed for the same change. A complete list of these genes will be provided to the patient/parent/guardian. Secondary findings will only be analyzed and reported if the patient/parent/guardian consents to receive them.

Informed Consent (continued)

Results Reporting

Results of exome sequencing will be reported to your ordering provider. Additionally, the provider may wish to get a copy of the raw sequence data, also known as the variant call file (VCF), after results are returned. Results that will be reported include positive results in the genes analyzed, variants of uncertain significance in the genes analyzed, and secondary findings if the patient/parent/guardian consents to receive them. A negative result does not rule out a disease-causing genetic change in the genes analyzed. Changes that are not believed to affect the patient's health will not be reported. Changes that are known to be risk-factors but not causative of disease may not be reported.

Risks

It is possible that this test may result in an uncertain result or identify unexpected secondary findings. It is possible that this test may reveal unexpected familial relationships (i.e. consanguinity, non-paternity, etc.). Results of this test may affect the healthcare and/or reproductive decisions of both the patient and their family members. Results may also affect the patient's and/or family member's ability to buy life, disability, and long-term care insurance in the future. Additionally, it is possible that exome sequencing may not be covered in full by the patient's health insurance plan. Although unlikely, there is a possibility for laboratory error to occur. Genetic counseling is recommended prior to consent for exome sequencing and after results are returned.

Limitations

Although exome sequencing analyzes many genes at once, it does not analyze all genes and all types of genetic changes. It is possible that this test may not identify the genetic change responsible for the patient's medical concerns. This test may identify a change in a gene, but does not have the ability to predict long-term prognosis. Interpretation of results is based on our current understanding of genetics. It is possible that results may change in the future upon reanalysis.

Research

If the patient/parent/guardian provides permission, de-identified clinical and genetic information may be used in academic case reports and publications. The ordering provider may reach out to the patient/parent/guardian for additional information and/or photos. Additionally, if the results of the clinical exome sequencing are negative, the ordering provider may re-contact the patient/parent/guardian regarding follow-up research sequencing opportunities.

Privacy Protections

The results of clinical exome sequencing will be released only to providers authorized by the patient/parent/guardian. In addition, The Genetic Information Nondiscrimination Act (GINA) protects most individuals from discrimination by employers and/or health insurers on the basis of genetic test results. In an attempt to better understand the field of genetics and variant interpretation, the DNA Diagnostic Laboratory may share de-identified genetic information in healthcare databases.