JOHNS HOPKINS MEDICINE

Johns Hopkins Genomics
DNA Diagnostic Laboratory

Clinical Exome Requisition Form - Page 1

v031825

Referrer Information

Physician: | UPIN/NPI:

Additional provider: | 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):

Name (if different than legal name) Last: | First:

Date of birth* (mm/dd/yyyy): | Sex assigned at birth: | Gender:

Patient ID/MRN*:

Patient Address:

Billing Information (contact Billing Coordinator at 667-306-8282 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
☐ Buccal Swab (2)
☐ Cultured skin fibroblasts
☐ Cord blood
☐ Cleaned chorionic villi
☐ Cultured chorionic villi
☐ Cultured amniocytes

Collection Date:

Blood, saliva, and buccal samples 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

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, GA:
___ 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 3.2 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

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 3.2 guidelines for reporting secondary findings. With respect to TTN-associated DCM, our current policy is to report truncating variants in the A-band alone. I understand that my DNA will be analyzed for secondary findings only if a secondary finding is reported for the patient on this test.

- ☐ 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 - Family Member

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.

Family Member Name (Print):

Signature: Date:

Relationship to patient:

My Choices - Family Member

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 3.2 guidelines for reporting secondary findings. With respect to TTN-associated DCM, our current policy is to report truncating variants in the A-band alone. I understand that my DNA will be analyzed for secondary findings only if a secondary finding is reported for the patient on this test.

- ☐ 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 - Family Member

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.

Family Member Name (Print):

Signature: Date:

Relationship to patient:

My Choices - Family Member

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 3.2 guidelines for reporting secondary findings. With respect to TTN-associated DCM, our current policy is to report truncating variants in the A-band alone. I understand that my DNA will be analyzed for secondary findings only if a secondary finding is reported for the patient on this test.

- ☐ 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 - Family Member

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.

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.