JOHNS HOPKINS
MEDICINE

Johns Hopkins Genomics
DNA Diagnostic Laboratory

Clinical Exome Requisition Form - Page 1

v120320

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 been 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:

☐ Referring Center ☐ Maryland Medicaid ☐ Self-pay ☐ Patient Insurance ☐ Medicare

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

Patient Name*:

DOB*:

Patient Sample Information

Test Type

- ☐ Proband
- ☐ Trio
- ☐ Duo
- ☐ Quad

Sample Type

- ☐ Blood
- ☐ Saliva

Collection Date:

Collection Site:

Submission Checklist

- ☐ Contact Billing Coordinator at 443-287-2486
- ☐ Obtain informed consent from proband and/or family members
- ☐ Complete Phenotypic Information section (Pages 3-5)
- ☐ Sign page 1 indicating that the provider has ensured that all necessary information is complete
- ☐ If you are a Hopkins provider, enter test order in EPIC (place test order BEFORE proband blood is drawn)
- ☐ Send this requisition form, signed consent forms, and all samples to JH Genomics

Family Information

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

Collection Site(s)

Ancestry

- ☐ Caucasian
- ☐ Northern European
- ☐ Western European
- ☐ Eastern European
- ☐ Middle Eastern
- ☐ African American
- ☐ African
- ☐ Hispanic
- ☐ Central/South American
- ☐ Caribbean
- ☐ Asian
- ☐ Pacific Islander
- ☐ Native American
- ☐ Other

Relevant Family Information/Pedigree

Patient Name*:

DOB*:

Phenotypic Information

Pre/Perinatal History

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

Growth

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

Developmental/Behavioral Findings

- ☐ 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:

Eye Defects/Vision

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

Ear Defects/Hearing Impairment

- ☐ Ears (shape, placement), specify:
- ☐ Conductive hearing impairment
- ☐ Sensorineural hearing impairment
- ☐ Other:

Craniofacial/Dysmorphism

- ☐ Dysmorphic features, specify:
- ☐ Asymmetry
- ☐ Brachycephaly
- ☐ Cleft lip and/or palate
- ☐ Coarse facial features
- ☐ Craniosynostosis
- ☐ Short neck
- ☐ Synophrys
- ☐ Other:

Hematologic/Immunologic Findings

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

Respiratory Findings

- ☐ Asthma
- ☐ Hypoventilation
- ☐ Laryngomalacia
- ☐ Pneumothorax
- ☐ Pulmonary fibrosis
- ☐ Respiratory insufficiency
- ☐ 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:

Phenotypic Information (continued)

Gastrointestinal/Abdominal Findings

- ☐ 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:

Cardiac Findings

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

Musculoskeletal Findings

- ☐ 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:
- ☐ Syndactyly
- ☐ Other:

Cancer

Type:

Location:

Age of onset:

Neurological Findings

- ☐ 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:

Vascular Findings

- ☐ Arterial aneurysm/dissection, specify:
- ☐ Arterial calcification
- ☐ Arterial tortuosity
- ☐ Arteriovenous malformation
- ☐ Epistaxis
- ☐ Lymphedema
- ☐ Pulmonary hypertension
- ☐ Other:

Phenotypic Information (continued)

Endocrine Findings

- ☐ Hypogonadism
- ☐ Delayed puberty
- ☐ Precious puberty
- ☐ Diabetes
- ☐ Hyperinsulinism
- ☐ Hyperthyroidism
- ☐ Hypothyroidism
- ☐ Other:

Genitourinary Findings

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

Skin/Hair Findings

- ☐ Abnormal blistering of the skin
- ☐ Abnormality of hair, specify:
- ☐ Abnormality of nail, specify:
- ☐ Abnormal skin pigmentation, specify:
- ☐ Abnormality of teeth, specify:

Imaging Findings

Specify or provide relevant imaging reports:

Metabolic/Lab Findings

Specify or provide relevant lab reports/values:

Genes of Interest

Previously Reported Variants

Additional Clinical Information *(if referring to Epic note, please provide the date and author of note)*

My Choices - Patient

Secondary Findings Reported to Me

Secondary findings are genetic changes that are likely to cause specific conditions other that 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 follows the ACMG guidelines for reporting secondary findings.

- ☐ 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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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.