ARUP LABORATORIES

A nonprofit enterprise of the University of Utah
and its Department of Pathology

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THIS IS NOT A TEST REQUEST FORM. Please complete and submit with the test request form or electronic packing list.

EXOME SEQUENCING INTAKE FORM

Failure to provide required information for exome testing will result in a suboptimal clinical report and delays in testing.

REQUIRED for Exome Sequencing (ARUP test code 3016583):

1. **Proband Patient Name:** ______________________ **Date of Birth:** ______________________
2. **Suspected Clinical Diagnosis:** ______________________

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Provide medical records detailing the patient's phenotype/relevant previous testing/family history or complete the Additional Clinical Information section found in this document.

3. **Parental/familial control samples (RECOMMENDED; ARUP test code 3016589). Submit comparator samples within 7 days of the proband's sample.**
   a. **Maternal Last Name, First Name:** ______________________
   Date of birth: __________ Clinically affected? ☐ No ☐ Yes: ______________________
   b. **Paternal Last Name, First Name:** ______________________
   Date of birth: __________ Clinically affected? ☐ No ☐ Yes: ______________________
   c. **Additional Familial Control (if applicable) Name:** ______________________
   Relationship to proband: ______________________
   Date of birth: __________ Clinically affected? ☐ No ☐ Yes: ______________________
4. **Ordering Provider Attestation of Informed Consent (signature required below)**

Test Purpose and Description
The purpose of exome sequencing is to identify the gene variant(s) causing a suspected Mendelian genetic condition. Testing requires drawing 2 mL of blood from which the DNA is extracted. DNA codes for genes. Most of the patient's genes will be sequenced.

Thousands of DNA variants will be detected by sequencing. DNA variants may be disease causing or harmless; however, the effect of many DNA variants is currently unknown.

Ordering Considerations
Participation in exome sequencing is voluntary. Genetic counseling is recommended before and following this complex test.

The chance a cause for the patient's medical issue(s) can be determined using this test varies and is influenced by the specific clinical features present. Diagnostic rates are highest when biological parents' samples are included as comparators for exome sequencing. Parental sequence data is used to identify de novo (new) changes in the patient's DNA, not found in either parent, that could explain the patient's disorder.

It is important that the familial biological relationships are correctly stated because undisclosed adoption or uncertain paternity will cause confusion and decrease the chance of identifying the causative disease variant.

Exome sequencing may identify genetic findings unrelated to the original reason for testing such as:

- Predict another family member has, is at risk for, or is a carrier of an unsuspected genetic condition
- Reveal nonpaternity (the person stated to be the biological father is not, in fact, the biological father)
- Indicate the biological parents of the patient are close blood relatives (consanguineous)

Reporting of Results
Results are generally available in 3–4 weeks. Variants that are known or suspected to be causative for the patient's medical issues are reported.

All variants identified in the patient that are related to the patient's primary disorder will be tested in familial controls. The status of all primary variants tested in controls will be indicated on the proband's report.

Candidate variants that are not known to be causative for the patient's medical issues, such as de novo variants (not inherited from either parent) or variants inherited from both parents in the same gene, may be reported even if the function of the gene is unknown.

Variants in genes unrelated to the patient's medical condition are not usually reported except for disease-causing secondary findings (see the Secondary Findings section below).

Because genetic knowledge is advancing at a rapid pace, reanalysis of exome sequencing data should be considered 12–18 months after testing is complete if a cause for the patient's condition was not determined. ARUP will perform reanalysis (ARUP test code 3001457) of exome data. If the report is amended, the ordering client will receive an updated report.

Limitations
Although genetic test results are usually accurate, several sources of error are possible, including clinical misdiagnosis of a condition, sample mislabeling or contamination, transfusion, bone marrow transplantation, maternal cell contamination of cord blood samples, or inaccurate information regarding biological relationships. If biological relationships are inaccurately reported, it could lead to an incorrect diagnosis or inconclusive result. ARUP will contact the referring provider if nonpaternity and/or consanguinity is detected but that information will not be included in the patient's report.

Often, exome sequencing is not able to identify the cause of a patient's medical issues. This does not exclude the possibility that the patient has a genetic condition. Some disease-causing variants are in genes with unknown function while others may not be identifiable using this test. Examples of variants not detectable with this test include large gene deletion/duplications, variants occurring outside of the coding region and intron-exon boundaries, chromosome rearrangements, inversions, methylation abnormalities, and those causing repeat disorders. This test does not include sequencing of the mitochondrial genome.

Secondary Findings
The American College of Medical Genetics and Genomics (ACMG) recommends reporting disease-causing variants in specific genes that increase the risk for developing cancer, cardiovascular issues, metabolic disorders, problems with anesthesia, retinopathy, and other conditions where monitoring or early treatment may be available. Please refer to the latest version of the ACMG recommendations for reporting secondary findings in clinical exome sequencing for a list of genes and associated disorders tested. Additional medically actionable variants in non-ACMG genes may be reported at ARUP's discretion.

If a patient has symptoms of a condition related to an ACMG recommended gene, separate testing should be ordered, as coverage of ACMG genes may be incomplete. Only variants in ACMG genes identified by routine exome sequencing are reported. Single disease-causing variants in recessive ACMG genes are not reported.

To receive secondary findings about the patient, the patient (or their legal guardian) would need to choose to receive this information by selecting the "opt in" option on this intake form. Familial controls who undergo exome sequencing and desire a full analysis and report of their secondary findings must select the "opt in" option on this intake form and will incur a separate fee. Secondary findings will be reported for familial controls who elect to receive this information regardless of whether the finding was also identified in the patient. Parental inheritance of secondary findings identified in the patient will only be included in the patient's report if the positive parent also opts to receive secondary findings.

If a disease-causing genetic variant is identified, insurance rates, the ability to obtain disability and life insurance, and employability could be affected. The Genetic Information Nondiscrimination Act of 2008 extends some protections against genetic discrimination (genome.gov/10002328). All test results are released to the ordering healthcare provider and those parties entitled to them by federal, state, and local laws.

Access to Sequence Data/Data Sharing/Sample Storage
ARUP Laboratories will have access to the patient's sequence data from exome sequencing. Your healthcare provider and the hospital that submitted the test to ARUP can also request a copy of the sequence data.

Because ARUP is not a storage facility, most samples are discarded after testing is completed. Some samples may be stored indefinitely for test validation or education purposes after personal identifiers are removed. You may request disposal of your sample by calling ARUP Laboratories at 800-242-2787 ext. 3301.

In cooperation with the National Institutes of Health's effort to improve understanding of specific genetic variants, ARUP submits HIPAA-compliant, deidentified (cannot be traced back to the patient) genetic test results and health information to public databases. The confidentiality of each sample is maintained. If you prefer that your test result not be shared, call ARUP at 800-242- 2787 ext. 3301. Your deidentified information will not be disclosed to public databases after your request is received, but a separate request is required for each genetic test. Additionally, patients have the opportunity to participate in patient registries and research. To learn more, visit aruplab.com/genetics.

Ordering Healthcare Provider, Genetic Counselor: 1) I attest that I am the ordering healthcare provider or certified genetic counselor; 2) I have explained the purpose/benefits and limitations of the test to the patient or their legal guardian and all parental controls; 3) the patient/legal guardian and parental controls were offered copies of this consent document; 4) I have answered all of their questions regarding the purpose of the test, the reporting of primary and secondary findings, the use and retention of samples, and data sharing.

Ordering Provider/Genetic Counselor Printed Name	**Signature**	**Date**

Secondary findings identified WILL NOT be examined and reported for the patient or controls UNLESS the corresponding box is checked. A fee applies for generating a clinical report with secondary findings for control individuals.

☐ Opt in to report secondary findings for the PATIENT.
☐ Opt in to report secondary findings for the MATERNAL CONTROL.
☐ Opt in to report secondary findings for the PATERNAL CONTROL.
☐ Opt in to report secondary findings for ADDITIONAL FAMILIAL CONTROL. (name(s):________________________________)

For questions, contact an ARUP genetic counselor at 800-242-2787 ext. 2141.

EXOME SEQUENCING INTAKE FORM

Exome Sequencing Additional Clinical Information:

Please provide medical records detailing the patient’s phenotype/relevant previous testing/family history or complete the Additional Clinical Information section below. The ability to identify causative variant(s) for the patient’s presentation is influenced by the quality of the clinical information provided.

Ordering Provider: ______________________ Provider’s Phone: ______________________
Practice Specialty: ______________________ Provider’s Fax: ______________________
Genetic Counselor: ______________________ Counselor’s Phone: ______________________

Ethnicity/Ancestry: ☐ African American/Black ☐ Asian ☐ Hispanic ☐ White ☐ Other

Genes of Interest: ______________________

Family History: ______________________

PRE/PERINATAL
- ☐ 0000776 Congenital diaphragmatic hernia
- ☐ 0001627 Congenital heart defect
- ☐ 0000476 Cystic hygroma
- ☐ 0002084 Encephalocele
- ☐ 0010945 Fetal pyelectasis
- ☐ 0007430 Generalized edema
- ☐ 0001789 Hydrops fetalis
- ☐ 0010880 Increased nuchal translucency
- ☐ 0001511 Intrauterine growth restriction
- ☐ 0002475 Myelomeningocele/ spina bifida
- ☐ 0001562 Oligohydramnios
- ☐ 0001539 Omphalocele
- ☐ 0001561 Polyhydramnios
- ☐ 0001622 Prematurity-GA at birth

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- ☐ 0003026 Short long bones
- ☐ 0001518 Small for gestational age
- ☐ ______________________

STRUCTURAL BRAIN ABNORMALITIES
- ☐ 0002134 Abnormality of basal ganglia
- ☐ 0002363 Abnormality of the brain stem
- ☐ 0001273 Abnormality of corpus callosum
- ☐ 0002269 Abnormality of neuronal migration
- ☐ 0007360 Aplasia/hypoplasia of the cerebellum
- ☐ 0012444 Brain atrophy
- ☐ 0007266 Cerebral dysmyelination
- ☐ 0006808 Cerebral hypomyelination
- ☐ 0002500 Cerebral white matter abnormality
- ☐ 0002539 Cortical dysplasia
- ☐ 0002282 Heterotopia
- ☐ 0001360 Holoprosencephaly
- ☐ 0000238 Hydrocephalus
- ☐ 0002352 Leukoencephalopathy
- ☐ 0001339 Lissencephaly
- ☐ 0002126 Polymicrogyria
- ☐ 0002119 Ventriculomegaly
- ☐ ______________________

NEUROLOGICAL
- ☐ 0100022 Abnormality of movement
- ☐ 0001284 Areflexia
- ☐ 0001251 Ataxia
- ☐ 0002015 Dysphagia
- ☐ 0001332 Dystonia
- ☐ 0100660 Dyskinesia
- ☐ 0200134 Epileptic encephalopathy
- ☐ 0001298 Encephalopathy
- ☐ 0001347 Hyperreflexia
- ☐ 0004305 Involuntary movements
- ☐ 0001250 Seizures
  - ☐ 0002121 Absence
  - ☐ 0002373 Febrile
  - ☐ 0007359 Focal
  - ☐ 0002123 Generalized myoclonic
  - ☐ 0010818 Generalized tonic
  - ☐ 0011169 Generalized clonic
  - ☐ 0012469 Infantile
  - ☐ 0002069 Tonic-clonic
- ☐ ______________________

METABOLIC
- ☐ 0040081 Abnormal CK
- ☐ 0001941 Acidosis
- ☐ 0003234 Decreased plasma carnitine
- ☐ 0003348 Hyperalaninemia
- ☐ 0001943 Hypoglycemia
- ☐ 0001987 Hyperammonemia
- ☐ 0002490 Increased CSF lactate
- ☐ 0003542 Increased serum pyruvate
- ☐ 0001946 Ketosis
- ☐ 0003128 Lactic acidosis
- ☐ 0001942 Metabolic acidosis
- ☐ 0001992 Organic aciduria
- ☐ Abnormal newborn screen

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- ☐ ______________________

DEVELOPMENTAL/BEHAVIORAL
- ☐ 0007018 Attention deficit hyperactivity disorder
- ☐ 0000729 Autistic spectrum disorder
- ☐ 0000750 Delayed speech and language development
- ☐ 0002376 Developmental regression
- ☐ 0001263 Global developmental delay
- ☐ 0001249 Intellectual disability
  - ☐ 0002187 Profound
  - ☐ 0010864 Severe
  - ☐ 0002342 Moderate
  - ☐ 0001256 Mild
- ☐ 0001270 Motor delay
- ☐ ______________________

MUSCULOSKELETAL
- ☐ 0002804 Arthrogryposis multiplex congenita
- ☐ 0003199 Decreased muscle mass
- ☐ 0001371 Flexion contracture
- ☐ 0001528 Hemihypertrophy
- ☐ 0001252 Hypotonia
- ☐ 0001276 Hypertonia
- ☐ 0001382 Joint hypermobility
- ☐ 0002808 Kyphosis
- ☐ 0040064 Limb abnormality
- ☐ 0001324 Muscle weakness
- ☐ 0003198 Myopathy
- ☐ 0010442 Polydactyly
- ☐ 0002757 Recurrent fractures
- ☐ 0002650 Scoliosis
- ☐ 0004322 Short stature
- ☐ 0002652 Skeletal dysplasia
- ☐ 0001257 Spasticity
- ☐ 0001159 Syndactyly
- ☐ 0001762 Talipes equinovarus
- ☐ 0000098 Tall stature
- ☐ 0000925 Vertebral column abnormality
- ☐ ______________________

CRANIOFACIAL
- ☐ 0000271 Abnormal facies
- ☐ 0000306 Abnormality of the nose
- ☐ 0000290 Abnormality of the forehead
- ☐ 0000175 Cleft palate
- ☐ 0410030 Cleft lip
- ☐ 0001363 Craniosynostosis
- ☐ 0000286 Epicanthus
- ☐ 0000316 Hypertelorism

- ☐ 0000601 Hypotelorism
- ☐ 0000256 Macrocephaly
- ☐ 0000252 Microcephaly
- ☐ ______________________________

EYE AND VISION

- ☐ 0000526 Aniridia
- ☐ 0000528 Anophthalmia
- ☐ 0000618 Blindness
- ☐ 0000589 Coloboma
- ☐ 0000519 Congenital cataract
- ☐ 0000568 Microphthalmia
- ☐ 0000639 Nystagmus
- ☐ 0000648 Optic atrophy
- ☐ 0000508 Ptosis
- ☐ 0009919 Retinoblastoma
- ☐ 0000486 Strabismus
- ☐ 0000505 Visual impairment
- ☐ ______________________________

EAR AND HEARING

- ☐ 0000377 Abnormal external ear
- ☐ 0000405 Conductive hearing impairment
- ☐ 0000410 Mixed hearing impairment
- ☐ 0000407 Sensorineural hearing impairment
- ☐ ______________________________

CARDIAC

- ☐ 0001713 Abnormal cardiac ventricle
- ☐ 0002616 Aortic root dilatation
- ☐ 0011675 Arrhythmia
- ☐ 0001631 Atrial septal defect
- ☐ 0001647 Bicuspid aortic valve
- ☐ 0001638 Cardiomyopathy
- ☐ 0001680 Coarctation of aorta
- ☐ 0001642 Pulmonary stenosis
- ☐ 0001636 Tetralogy of Fallot
- ☐ 0001629 Ventricular septal defect
- ☐ ______________________________

RESPIRATORY

- ☐ 0002104 Apnea
- ☐ 0002883 Hyperventilation
- ☐ 0002791 Hypoventilation
- ☐ 0008751 Laryngeal cleft
- ☐ 0001601 Laryngomalacia
- ☐ 0002205 Recurrent respiratory infections
- ☐ 0002878 Respiratory failure
- ☐ 0002093 Respiratory insufficiency
- ☐ 0002107 Pneumothorax
- ☐ 0002206 Pulmonary fibrosis
- ☐ 0002575 Tracheoesophageal fistula
- ☐ 0002779 Tracheomalacia
- ☐ ______________________________

GASTROINTESTINAL

- ☐ 0002251 Aganglionic megacolon
- ☐ 0002910 Elevated hepatic transaminase
- ☐ 0001508 Failure to thrive
- ☐ 0001543 Gastroschisis
- ☐ 0001399 Hepatic failure
- ☐ 0002240 Hepatomegaly
- ☐ 0002021 Pyloric stenosis
- ☐ 0001744 Splenomegaly
- ☐ 0002013 Vomiting
- ☐ ______________________________

GENITOURINARY

- ☐ 0000812 Abnormal internal genitalia
- ☐ 0000062 Ambiguous genitalia
- ☐ 0000028 Cryptorchidism
- ☐ 0000085 Horseshoe kidney
- ☐ 0000126 Hydronephrosis
- ☐ 0000047 Hypospadias
- ☐ 0008738 Partially duplicated kidney
- ☐ 0000113 Polycystic kidney dysplasia
- ☐ 0000107 Renal cyst
- ☐ 0000104 Renal agenesis
- ☐ 0000089 Renal hypoplasia
- ☐ 0000069 Ureter abnormality
- ☐ 0000795 Urethra abnormality
- ☐ ______________________________

SKIN AND HAIR

- ☐ 0008066 Blistering of skin
- ☐ 0000957 Café-au-lait spot
- ☐ 0005306 Capillary hemangioma
- ☐ 0001595 Hair abnormality
- ☐ 0000974 Hyperextensible skin
- ☐ 0000953 Hyperpigmentation of skin
- ☐ 0000998 Hypertrichosis
- ☐ 0001010 Hypopigmentation of skin
- ☐ 0008066 Ichthyosis
- ☐ 0001597 Nail abnormality
- ☐ 0001581 Recurrent skin infections
- ☐ ______________________________

HEMATOLOGY AND IMMUNOLOGY

- ☐ 0001928 Abnormality of coagulation
- ☐ 0004432 Agammaglobulinemia
- ☐ 0001903 Anemia
- ☐ 0031020 Bone marrow hypercellularity
- ☐ 0001878 Hemolytic anemia
- ☐ 0002721 Immunodeficiency
- ☐ 0001888 Lymphopenia
- ☐ 0001875 Neutropenia
- ☐ 0001876 Pancytopenia
- ☐ 0002719 Recurrent infections
- ☐ 0004430 Severe combined immunodeficiency
- ☐ 0001873 Thrombocytopenia
- ☐ ______________________________

ENDOCRINE

- ☐ 0000834 Abnormality of adrenal glands
- ☐ 0008226 Androgen insufficiency
- ☐ 0008258 Congenital adrenal hyperplasia
- ☐ 0000819 Diabetes mellitus
- ☐ 0000873 Diabetes insipidus
- ☐ 0001738 Exocrine pancreatic insufficiency
- ☐ 0000821 Hypothyroidism
- ☐ 0000829 Hypoparathyroidism
- ☐ ______________________________

CANCER

- ☐ Type of cancer __________________
- ☐ Age of diagnosis _________________
- ☐ Family history of cancer and affected relatives

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OTHER

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EXOME SEQUENCING INTAKE FORM

PREVIOUS TESTING (provide copy of abnormal results)

Echocardiogram: ☐ Not performed ☐ Normal ☐ Abnormal ____________________
EEG: ☐ Not performed ☐ Normal ☐ Abnormal ____________________
EMG/NCV: ☐ Not performed ☐ Normal ☐ Abnormal ____________________

Gene testing: ____________ ☐ Normal ☐ Abnormal ____________________
Gene testing: ____________ ☐ Normal ☐ Abnormal ____________________
Karyotype: ☐ Not performed ☐ Normal ☐ Abnormal ____________________

Prenatal genomic microarray:
☐ Not performed ☐ Normal ☐ Abnormal ____________________

Postnatal genomic microarray:
☐ Not performed ☐ Normal ☐ Abnormal ____________________

MRI (brain): ☐ Not performed ☐ Normal ☐ Abnormal ____________________
MRI (other): ☐ Not performed ☐ Normal ☐ Abnormal ____________________
CT (brain): ☐ Not performed ☐ Normal ☐ Abnormal ____________________
CT (other): ☐ Not performed ☐ Normal ☐ Abnormal ____________________
Muscle biopsy: ☐ Not performed ☐ Normal ☐ Abnormal ____________________
Ultrasound: ☐ Not performed ☐ Normal ☐ Abnormal ____________________
X-ray: ☐ Not performed ☐ Normal ☐ Abnormal ____________________

Other test:____________ ☐ Normal ☐ Abnormal ____________________
Other test:____________ ☐ Normal ☐ Abnormal ____________________
Other test:____________ ☐ Normal ☐ Abnormal ____________________