ARUP LABORATORIES | NATIONAL REFERENCE LABORATORY

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

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INFORMED CONSENT FOR EXOME SEQUENCING WITH SYMPTOM-GUIDED ANALYSIS

Patient Name _____ **Date of Birth** ___/___/___ **Sex** ☐ **F** ☐ **M**

Symptoms ☐ **No** ☐ **Unknown** ☐ **Yes** (please describe) _____

If this individual is a parent of a child being tested, provide child's name: _____

Test Description/Purpose
Genes hold the DNA code for making proteins that compose our bodies. Exome sequencing involves examining the DNA code of ~19,000 genes. Thousands of DNA variants are detected. Some variants are disease-causing while others are harmless or have an unknown effect. The purpose of the test is to identify the variant(s) causing the patient's suspected genetic disorder.

Ordering Considerations
Participation in exome sequencing is voluntary. Genetic counseling is required prior to, as well as following, this complex test.

Parental samples are critical to the interpretation of the patient's results. A cause for the patient's medical issue(s) is determined in ~45% of cases when both parents' samples are submitted for full exome sequencing, in ~35% of cases when only targeted sequencing of parental samples is ordered, and in only ~20% of cases when parental samples are not provided.

Exome sequencing results may provide unexpected information, such as:

- Identifying a genetic risk unrelated to the original reason for testing.
- Predicting another family member has, is at risk for, or is a carrier of a genetic condition.
- Revealing non-paternity (the person stated to be the biological father is not, in fact, the biological father).
- Suggesting the parents of the individual tested are blood relatives.

If a 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 (http://www.genome.gov/10002328). All test results are released to the ordering healthcare provider and those parties entitled to them by state and local laws.

The American College of Medical Genetics and Genomics (ACMG) recommends that disease-causing variants in the following genes be reported, whether or not they are related to the patient's condition. Monitoring or early treatment may be available for these conditions. Single disease-causing variants in recessive ACMG genes are not reported. Other medically actionable incidental variants in non-ACMG genes may be reported at ARUP's discretion.

ACMG genes associated with tumors/cancer syndromes: Hereditary breast and ovarian cancer (*BRCA1, BRCA2*), juvenile polyposis (*BMPR1A*, *SMAD4*), Li-Fraumeni (*TP53*), Peutz-Jeghers (*STK11*), Lynch (*MLH1, MSH2, MSH6, PMS2*), familial adenomatous polyposis (*APC*), *MUTYH*-associated polyposis, Von Hippel-Lindau (*VHL*), multiple endocrine neoplasia type 1 (*MEN1*), multiple endocrine neoplasia type 2/ familial medullary thyroid cancer (*RET*), PTEN hamartoma tumor (*PTEN*), retinoblastoma (*RB1*), hereditary paraganglioma-pheochromocytoma (SDHA, SDHB, SDHC, SDHD), tuberous sclerosis complex (*TSC1, TSC2*), WT1-related Wilms (*WT1*), neurofibromatosis type 2 (*NF2*).

ACMG genes associated with cardiovascular (heart) problems/syndromes: Ehlers-Danlos IV (*COL3A1*), Marfan (*FBN1*), Loeys-Dietz (*TGFBR1*, *TGFBR2*), familial thoracic aortic aneurysms and dissections (*SMAD3, ACTA2, MYH11*), hypertrophic cardiomyopathy/ dilated cardiomyopathy (*MYBPC3, MYH7, TNNT2, TNNI3, TPM1, MYL3, ACTC1, PRKAG2, GLA, MYL2, LMNA*), catecholaminergic polymorphic ventricular tachycardia (*RYR2*), arrhythmogenic right ventricular cardiomyopathy (*PKP2, DSP, DSC2, TMEM43, DSG2*), Romano-Ward long QT types 1, 2, and 3, Brugada (*KCNQ1, KCNH2, SCN5A*), familial hypercholesterolemia (*LDLR, APOB, PCSK9)*.

ACMG genes associated with other conditions: Wilson's disease (*ATP7B*), malignant hyperthermia (*RYR1, CACNA1S*), ornithine transcarbamylase deficiency (*OTC*).

Initial here ☐ **if findings or variants detected in ACMG genes should NOT be reported.**

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ARUP Laboratories will have access to the patient's sequence data from exome testing. Your health care 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. All New York samples are discarded 60 days following test completion. 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 the understanding of specific genetic variants, ARUP submits HIPAA-compliant, de-identified (cannot be traced back to the patient) genetic test results and health information to public databases. Confidentiality of each sample is maintained. You may choose not to share your test result by calling ARUP Laboratories at (800) 242-2787, ext. 3301. Your de-identified information will not be shared with public databases after the request is made, but a separate request is required for each genetic test. For more information, see www.aruplab.com/genetics.

Limitations of Exome Sequencing

- 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. Exome sequencing does not detect all disease-causing variants because some genes and variants cannot be analyzed by this test. The function of many genes is still unknown; therefore, variants identified in these genes are not currently interpretable. Because genetic knowledge continues to advance at a rapid pace, the interpretation of the result may change in the future. If the report is amended, the patient's provider will be contacted and provided a copy of the updated report.
- Exome sequencing may fail to detect variants in ACMG-recommended genes. Only disease-causing variants in ACMG genes that can be identified with routine exome analysis will be reported.
- Variants that do not appear to be related to the patient's medical condition will not be reported. The only exception to this is disease-causing ACMG variants or possibly other incidental variants if elected on this consent form.
- Although genetic test results are usually accurate, several sources of error are possible, including: clinical misdiagnosis of a condition, inaccurate information provided regarding family relationships, sample mislabeling or contamination, transfusion, bone marrow transplantation, and maternal cell contamination of prenatal or cord blood samples. Reporting of Results
- Results are typically reported in 10-12 weeks.
- Variants that are predicted to be related to the patient's medical issues will be reported. De novo DNA changes in genes of unknown function may also be reported.
- Disease-causing variants in the ACMG-recommended gene list will be reported unless declined above. Family members who have full exome sequencing and complete a separate exome consent form will receive a separate report describing whether or not any ACMG variants were identified.

Patient/Legal Guardian: I authorize ARUP Laboratories to perform exome sequencing on my (or my child's) sample. The risks, benefits, and limitations have been explained to my satisfaction by a qualified health professional.

Patient/Guardian Printed Name	Signature	Date

Ordering Healthcare Provider: I have explained exome sequencing, including its risks, benefits and alternatives to the patient or legal guardian, and answered all their questions.

Healthcare Provider Printed Name	Signature	Date

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