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 RAPID SEQUENCING 4500+ GENES TEST

Patient Name _____ Date of Birth _____ Sex ☐ F ☐ M

Symptoms ☐ Y ☐ N _____

Test Description and Purpose

- The Rapid Sequencing 4500+ Genes test involves decoding the DNA sequence of approximately 4,500 genes known to cause disease in humans. The purpose is to determine the cause of the patient's medical condition.

Ordering Considerations

- Participation in genetic testing is completely voluntary. Genetic counseling is required prior to and following this complex test.
- Because this test examines greater than 4,500 genes, thousands of DNA changes (variants) are detected. These variants may be harmless, disease-causing or have an unknown effect. It may be unclear whether a specific variant identified is contributing to or causing the patient's symptoms.
- This test may identify the cause of an infant's medical condition in approximately 50% of cases.
- Parental samples are required to identify new (de novo) variants present in their child that are not present in either parent. If a healthy parent carries the same variant identified in their affected child, this often decreases the chance the variant is disease-causing. If the variant is de novo, the likelihood that the variant is disease-causing is increased.
- Genetic testing results may provide information that was not anticipated, 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.
- 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, as monitoring or early treatment may be available. Parental ACMG variants will not be reported.
- Medically actionable incidental variants in genes not included in the list below may also be reported at ARUP's discretion. Note that single disease-causing variants in recessive ACMG genes are not reported.
  - **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 disease-causing ACMG variants (or other incidental findings) should NOT be reported.**

- 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, and sample mislabeling or contamination.
- 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.

Limitations of the Rapid Sequencing 4500+ Genes Test

- If the test is unable to identify the cause of a patient's medical issues, this does not exclude the possibility that the patient has a genetic condition.
- The test does not detect all variants causative for genetic disease as there are about 19,000 genes, but only the approximately 4,500 currently known to be associated with human disease are analyzed.
- Some disease-causing variants in the 4,500 genes analyzed may not be detected as they may lie in the noncoding DNA, occur within repetitive sequences or reside in other complex regions that are difficult to analyze.

Reporting of Results

- Results are typically reported within 7–28 days. All detected disease-causing variants that may be related to the patient's medical issues will be reported.
- Disease-causing variants, unrelated to the patient's symptoms, will NOT be reported unless they are in a gene included on the ACMG's list of recommended genes or are considered medically actionable incidental variants and are desired as indicated above.
- Because genetic knowledge continues to advance at a rapid pace, the interpretation of results may differ in the future. If your report is amended, your healthcare provider will be contacted and provided a copy of the updated report.

Test Improvement

- In cooperation with the National Institutes of Health's effort to improve 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. 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 www.aruplab.com/genetics/resources.
- 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.

Parent/Legal Guardian

I authorize ARUP Laboratories to perform the Rapid Sequencing 4500+ Gene test. The benefits, risks, and limitations of this testing have been explained to my satisfaction by a qualified health professional.

_____

Patient/Guardian Printed Name | Signature | Date

Ordering Healthcare Provider

I have explained this DNA test, including its risks, benefits and alternatives to the patient or legal guardian and addressed all their questions.

_____

Healthcare Provider Printed Name | Signature | Date

_____ (_____) _____(_____)_____

Specialty | Phone Number | Fax

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