ARUP LABORATORIES

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INFORMED CONSENT FOR EXOME SEQUENCING WITH SYMPTOM-GUIDED ANALYSIS

Patient Name _____**Date of Birth** __/__/__ **Gender [] Female [] Male**

Symptoms: [ ] No [ ] Yes, please describe: _____

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

Test Description/ Purpose

DNA provides instructions for making proteins that compose our bodies. Exome sequencing involves deciphering the majority of protein-coding genes. The purpose of the test is to establish a diagnosis for individuals with a suspected genetic disorder.

Ordering Considerations

- Genetic counseling is required prior to, as well as following, this complex test.
- Parental samples, and those from other affected and/or unaffected family members, are requested to aid interpretation of the patient's results. A cause for the individual's medical issue(s) is determined in approximately 35% of cases when both parents' samples are submitted and in only 20% of cases when parental samples are not available.
- The results of exome sequencing may be upsetting. This may include learning that the patient's health is at risk, another family member is affected with or a carrier of a genetic condition, or the biological relationships among family members are different than assumed (e.g. non-paternity).
- If a gene variant is identified, insurance rates, the ability to obtain disability or life insurance and employability could be affected. Federal law provides some protections regarding genetic discrimination (http://www.genome.gov/10002328).
- 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. Medically actionable incidental variants in genes not included in the list below may be reported at ARUP's discretion.
    - 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 (*PGL1, PGL2, PGL3*, *PGL4*), tuberous sclerosis complex (*TSC1, TSC2*), WT1-related Wilms (*WT1*), neurofibromatosis type 2 (*NF2*).
    - 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)*.
    - Genes associated with other conditions: Wilson's disease (*ATP7B*), malignant hyperthermia (*RYR1, CACNA1S*), ornithine transcarbamylase deficiency (*OTC*).

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

- De-identified samples are standardly used for future test development and improvement. All samples from New York State are disposed of 60 days after testing is complete.

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Patient Name_____

Limitations of the Exome Sequencing

- Often exome sequencing is not able to identify the cause of a patient's medical issues. Exome sequencing does not detect all disease-causing variants because not all genes and variants can be analyzed. The function of many genes is unknown; therefore, variants currently identified in these genes are not interpretable. If exome sequencing does not establish a genetic diagnosis, it is still possible for the patient to have a genetic condition.

- Exome sequencing may fail to detect variants in some of the ACMG recommended genes. Only disease-causing ACMG variants, that can be identified with routine exome analysis, will be reported. If the patient or a family member has symptoms of one of the conditions tested for in the ACMG list of genes, additional testing should be ordered specifically for that condition as coverage of the ACMG genes may be incomplete.

- Although DNA testing is usually very accurate, several sources of error are possible such as mislabeling of or mixing of blood samples, inaccurate or incomplete clinical information or information regarding family relationships.

- Because exome sequencing examines approximately 19,000 genes, tens of thousands of DNA variants are detected. These variants may be harmless, disease-causing or have an unknown effect. Even if a disease-causing variant is detected, it may not be possible to predict if the patient will develop the disease or the severity of symptoms.

- Because genetic knowledge continues to advance at a rapid pace, the interpretation of results may change in the future.

Reporting of Results

- Results are typically reported in 16 weeks. A healthcare provider may request reexamination of specific genes for 24 months following receipt of results.

- 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 this exome consent form will receive a separate report describing whether or not any ACMG variants were identified.

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 Name Printed: _____**Signature**_____ **Date**_____

Ordering Health Care Provider:
I have reviewed the content of this consent form with the patient or legal guardian and answered all questions.

Printed Name _____**Signature** _____ **Specialty**_____

Date _____Phone number_____Fax_____