UPMC LIFE CHANGING MEDICINE

Patient Name: _____
Identification Number: _____
Facility: _____

WHOLE EXOME & MITOCHONDRIAL GENOME SEQUENCING FAMILY MEMBER REQUISITION

FAMILY MEMBER INFORMATION (Please Print)				PROBAND INFORMATION (Please Print)
First Name / MI / Last Name / Preferred Name				Name of Proband:
DOB (mm/dd/yy)	MRN#	Genetic Sex (required): ☐M ☐F Gender Identity (optional):		DOB: Sex ☐M ☐F ☐UNK
Address		Phone		Relationship to Proband
City	State	Zip Code		Provider

SAMPLE INFORMATION

Sample Instruction based:

☐ Send saliva kit to address above

☐ Use stored extracted DNA

☐ Blood draw planned

Does this individual have a history of:

☐Blood Transfusion ☐ Hematologic Malignancy ☐ Bone Marrow Transplant ☐ NONE

If the answer is yes to any of these questions, please contact the laboratory to discuss before sending a sample.

PARTICIPANT CONSENT (*REQUIRED*)

By signing this form I acknowledge as the related family member/their legal guardian that I have read the attached informed consent document and that I authorize the UCGL to perform whole exome and mitochondrial genome sequencing as described. Genetic variants that are present in a family member but not in the proband will NOT be detected and therefore not reported. Inheritance of variants present in both a proband and their relative WILL be detected and reported. This includes secondary findings, if the proband has opted to receive them.

☐ OPT-IN: Please check this box if you wish to be recontacted for future research opportunities should they become available.

_____	_____	_____
Print name of Relative/their Legal guardian	Signature of Relative/their Legal guardian	Date

REQUISITION CONTINUES ON NEXT PAGE

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WHOLE EXOME & MITOCHONDRIAL GENOME SEQUENCING FAMILY MEMBER REQUISITION

FAMILY MEMBER CLINICAL HISTORY

Please provide the following information regarding the family member to be tested. Phenotypes listed are in HPO terms with the corresponding HPO number (https://hpo.jax.org/app/) This information is needed to facilitate interpretation of whole exome sequencing results.

☐ Negative/None

PRE/PERINATAL HISTORY
☐ Premature birth [0001622]

GROWTH
☐ Failure to thrive [0001508]
☐ Obesity [0001513]
☐ Short stature [0004322]
☐ Tall stature [0000098]

MOTOR/COGNITIVE DEVELOPMENT
☐ Aggressive behavior [0006919]
☐ Anxiety [0100852]
☐ Autistic Behavior [0000729]
☐ Delayed speech and language development [0000750]
☐ Hyperactivity [0000752]
☐ Intellectual Disability [0001249]
☐ Learning Disability [0001328]
☐ Sleep disturbance [0002360]

CRANIOFACIAL/DYSMORPHISM
☐ Abnormal facial shape [0001999]
☐ Oral cleft [0000202]
☐ Macrocephaly [0000256]
☐ Microcephaly [0000252]
☐ Short neck [0000470]

HEARING IMPAIRMENT
☐ Conductive hearing impairment [0000405]
☐ Mixed hearing impairment [0000410]
☐ Sensorineural hearing impairment [0000407]

GASTROINTESTINAL FINDINGS
☐ Constipation [0002019]
☐ Diarrhea [0002014]
☐ Gastroesophageal reflux [0002020]
☐ Inflammatory bowel disease [0002037]
☐ Pancreatitis [0001733]
☐ Pyloric Stenosis [0002021]
☐ Vomiting [0002013]

GENITOURINARY
☐ Abnormality of the genitourinary system [0000119]
Specify: _____ [_____]
Specify: _____ [_____]

HAIR & SKIN FINDINGS
☐ Abnormal Blistering of the Skin [0008066]
☐ Abnormal nail growth [0030807]
☐ Alopecia [0001596]
☐ Anhidrosis [0000970]
☐ Eczema [0000964]
☐ Hemangiomas [0001028]
☐ Hypermelanotic macule [0001034]
☐ Hyperextensible skin [0008067]
☐ Hyperpigmentation of the skin [0001000]
☐ Soft skin [0000977]
☐ Telangiectasia [0001009]

STRUCTURAL BRAIN ABNORMALITIES
☐ Agenesis of corpus Collosum [0001274]
☐ Chiari malformation [0002308]
☐ Ventriculomegaly [0002119]

NEUROLOGICAL FINDINGS
☐ Abnormality of nervous system [0000707]
☐ Ataxia [0001251]
☐ Dementia [0000726]
☐ Migraine [0002076]
☐ Parkinsonism [0001300]
☐ Peripheral neuropathy [0009830]
☐ Seizure [0001250]
☐ Sensory Neuropathy [0000763]
☐ Syncope [0001279]
☐ Tremor [0001337]
☐ Vertigo [0002321]

MUSCULOSKELETAL FINDINGS
☐ Arachnodactyly [0001166]
☐ Exercise intolerance [0003546]
☐ Hemihypertrophy [0001528]
☐ Hypertonia [0001276]
☐ Hypotonia [0001252]
☐ Joint Hypermobility [0001382]
☐ Muscle weakness [0001324]
☐ Myalgia [0003326]
☐ Osteoarthritis [0002758]
☐ Osteopenia [0000938]
☐ Pectus carinatum [0000768]
☐ Scoliosis [0002650]

EYE DEFECTS & VISION
☐ Abnormality of vision [0000504]
Specify:_____[_____]
☐ Ptosis [0000508]
☐ Retinal detachment [0000541]
☐ Strabismus [0000486]

ENDOCRINE
☐ Delayed puberty [0000823]
☐ Diabetes Insipidus [0000873]
☐ Diabetes Mellitus [0000819]
☐ Hyperthyroidism [0000836]
☐ Hypothyroidism [0000821]
☐ Hypoparathyroidism [0000829]
☐ Maturity-onset diabetes of the young [0004904]

METABOLIC/RESPIRATORY FINDINGS
☐ Abnormal circulating metabolite concentration [0032180]
☐ Asthma [0002099]
☐ Increased CPK [0003236]
☐ Pneumothorax [0002107]
☐ Pulmonary fibrosis [0002206]

CARDIAC FINDINGS
☐ Abnormal heart morphology [0001627]
☐ Amyloidosis [0011034]
☐ Arrhythmia [0011675]
☐ Bradycardia [0001662]
☐ Dilated cardiomyopathy [0001644]
☐ Hypertension [0000822]
☐ Mitral valve prolapse [0001634]
☐ Prolonged QTc interval [0005184]
☐ Supraventricular tachycardia [0004755]

VASCULAR SYSTEM
☐ Arteriovenous malformation [0100026]
☐ Epistaxis [0000421]
☐ Stroke [0001297]
☐ Vascular dilatation [0002617]

HEMATOLOGIC/IMMUNOLOGIC FINDINGS
☐ Anemia [0001903]
☐ Immunodeficiency [0002721]
☐ Neutropenia [0001875]
☐ Pancytopenia [0001876]
☐ Recurrent infections [0002719]
☐ Thrombocytopenia [0001873]

CANCER
☐ Type of cancer _____
☐ Age at Diagnosis _____
☐ Family History of Cancer (attach pedigree)

OTHER FEATURES
Phenotype [HPO# https://hpo.jax.org/app/]
_____ [_____]
_____ [_____]
_____ [_____]
_____ [_____]
_____ [_____]

ADDITIONAL HISTORY (or attach records)

INFORMED CONSENT

ABOUT THE UPMC WHOLE EXOME & MITOCHONDRIAL GENOME SEQUENCING TEST

Whole exome sequencing is a complex genomic test that looks at thousands of genes at once. It is designed to identify genetic changes in your DNA (genetic material) that may cause the medical condition your provider is concerned about in your family member. Most changes that cause disease affect the parts of our DNA called "exons." Only about 1.5% of all the DNA is located in the exons. However, testing the exons finds many of the genetic changes which are known to cause disease. All of the exons of all the genes together is called the "whole exome." This test will sequence, or "read" the patient's whole exome.

Mitochondrial DNA (mtDNA) encodes 37 genes and is exclusively maternally inherited. Disorders of mitochondrial energy metabolism, or oxidative phosphorylation (OXPHOS) disorders, are characterized by reduced activity of one or more mitochondrial respiratory chain complexes. Mitochondrial testing to be completed by UCGL or under certain circumstances may also be performed by PerkinElmer laboratory.

The purpose of this test is to determine if there is a possible genetic reason for your family member's health condition. Finding a genetic cause may improve future medical care and treatment options and inform family planning.

Detailed medical and family history are needed for accurate interpretation of results. Clinical photographs can also be helpful.

Genetic counseling and/or clinical genetics consultation is recommended before and after whole exome sequencing. Clinical reports are released only to the certified healthcare professional(s) listed on the order form. You may choose to request a copy of the clinical report from the healthcare professional who ordered the test.

FAMILY MEMBER TESTING

Any samples submitted to assist in the analysis of the patient's exome (such as the parents or a sibling) will have sequencing performed but will not be analyzed separately. They will only be utilized if submitted before the patient's data is analyzed, or within 30 days of receipt of proband, whichever is first.

Family member data are ONLY used for interpretation of the patient's whole exome sequencing findings. Genetic variants that may be in a family member, but are NOT present in the proband, will not be detected and therefore are not reported.

Genetic testing may reveal that the true biological relationships in a family are not as they were reported. This includes non-paternity (the stated father of an individual is not the biological father) and consanguinity (the parents of an individual are related by blood). Incorrect information about the biological relationships in your family may result in incorrect interpretation of results, incorrect diagnoses, and/or inconclusive test results. If you have any concerns about any such issues, please discuss them confidentially with your genetic counselor or ordering provider.

WHOLE EXOME & MITOCHONDRIAL GENOME SEQUENCING RESULT REPORTING

In general, the laboratory will only report results that may explain the patient's clinical features.

You will also receive secondary findings *if* the primary patient has chosen to receive secondary findings. The American College of Medical Genetics and Genomics (ACMG) identified 81 genes and disorders for which treatment is available that may reduce morbidity and/or mortality. These findings may be unrelated to the reason for referral but may impact medical decision-making if identified. Only DNA changes known to cause disease will be reported. For more information about the ACMG recommendations, refer to https://www.sciencedirect.com/science/article/pii/S1098360023008791?via%3Dihub

Due to limited knowledge on their genetic causes, variants related to complex multifactorial diseases such as asthma, lupus, and type 2 diabetes, will not be reported.

Genetic variants not known to be clinically relevant will not be reported.

One report is generated for the patient. Since samples from the patient and other family members will be utilized as part of the interpretation of the patient's exome test, the patient's report will indicate if a variant is detected in the family member tested.

CONSENT CONTINUES ON NEXT PAGE

INFORMED CONSENT continued

POSSIBLE TEST RESULTS

The genetic variants found by whole exome and mitochondrial genome sequencing will be classified according to the guidelines from the American College of Medical Genetics and Genomics (ACMG). Three possible test results include:

- Positive: pathogenic or likely pathogenic variant) a variant was found that likely caused the patient's condition or carries an increased risk for developing the disorder in the future. This result may be important for other family members.
- Negative: no disease-causing variants were found. This result does not eliminate the possibility of a genetic condition not discovered by this test.
- Variant of uncertain clinical significance (VUS): A genetic variant was found, but it is currently unknown whether that change could have caused the patient's condition. A VUS may be benign or disease-causing, but more research is needed.

Because medical and scientific knowledge are constantly changing, new information that becomes available in the future may replace or add to the information UPMC Clinical Genomics laboratory used to interpret the results.

RISKS & LIMITATIONS

As with all laboratory testing, there is a small risk of getting an erroneous result.

Because many different genes and conditions are being analyzed, there is a risk that genetic information will be revealed that is not directly related to the reason WES was ordered. This information might relate to diseases or symptoms that may develop in conditions that have no current treatment. The severity and clinical course of the genetic condition may not be known.

Additional variants may exist and may contribute to or cause disease but not be identified by this analysis. Whole exome sequencing has technical limitations and generally is not able to detect larger deletions/duplications or structural rearrangements, low level mosaicism, deep intronic variants, methylation abnormalities or repetitive sequence changes. Mitochondrial DNA sequencing also has technical limitations. Variants below 5-10% allele fraction may not be detected and the sensitivity/specificity of the detection of deletions and duplications has not been established.

Interpretation of findings is limited by what is currently known about the genes and diseases being tested.

DATA & UPDATED INFORMATION

Information about genetic disease is continually changing. Additionally, a patient's clinical presentation or family history may also change over time. It is the responsibility of the patient and ordering provider to be aware of any changes in the patient's symptoms and to communicate them to the laboratory. The laboratory will also re-contact the referring physician if the lab learns that new information about the genes tested has been identified.

The physician can initiate a request for variant interpretation review, reanalysis of sequencing data and release of raw data. There may be a charge associated with such requests.

Sharing health history and genetic information can ultimately help health care providers deliver better care for their patients and provide researchers opportunities to make discoveries. UPMC submits de-identified information to public databases to contribute to the advancement of medical knowledge.

PRIVACY/PATIENT CONFIDENTIALITY

The United States Federal Government has enacted the Genetic Information and Non-discrimination Act (GINA) that prohibit discrimination, based on genetic test results, by health insurance companies and employers. These laws also prohibit unauthorized disclosure of this information. For more information you can visit https://www.eeoc.gov/laws/statutes/gina.cfm However, this law does not consider the possible impact these results may have on obtaining disability or life insurance.

Data and personal information will be stored and protected in strict confidence complying with regulatory requirements (e.g., HIPAA and equivalent protections), and I acknowledge that I have read and understand UPMC's privacy policy.

CONSENT CONTINUES ON NEXT PAGE

INFORMED CONSENT continued

CANCELLATION OF TESTING

Request to cancel testing will be required within one business day of sample receipt. If the laboratory has already started the testing process, I will be responsible for the cost of the test. Written documentation of the request to stop testing will be required. My provider can contact the laboratory for the cancellation form.

INTERPRETER'S STATEMENT

Execute if an interpreter is provided to assist the individual in understanding this informed consent form:

I have translated the information and advice presented orally to the individual to be treated by the person obtaining this consent.

In addition, I have sight translated the consent form (read it aloud in his/her language). To the best of my knowledge and belief he/she understood this explanation.

_____
Cyracom ID (if applicable)

_____
Print Name

_____
Signature (Not required if a Cyracom interpreter was used)