UPMC LIFE CHANGING MEDICINE

Patient Name: _____

Identification Number: _____

**GENOME SEQUENCE ANALYSIS**
**PROBAND REQUISITION FORM**

## PATIENT INFORMATION

| First name | MI | Last name | Preferred Name |
|---|---|---|---|
| | | | |

| Date of birth | Genetic Sex (required): ☐M ☐F ☐UNK<br>Gender Identity (optional): | MRN # |
|---|---|---|
| | | |

| Address | City | State | Zip code |
|---|---|---|---|
| | | | |

| Phone |
|---|
| |

Ancestry (check all that apply)

| | | |
|---|---|---|
| ☐ White/Caucasian | ☐Native American | ☐Ashkenazi Jewish |
| ☐ Black/AfricanAmerican | ☐Central/South American | ☐Middle Eastern |
| ☐ Hispanic | ☐West/North European | ☐Other |
| ☐ Asian | ☐East/Central European | |

## ORDERING PROVIDER INFORMATION

| Physician | | |
|---|---|---|
| Address | | |
| City | State | Zip Code |
| Phone | | Fax |
| NPI# | | |

Additional Report To:

## SAMPLE INFORMATION

**(Please check one)**

☐ Blood sample

☐ Use stored extracted DNA

☐ Saliva kit requested for relatives (see Family Member Requisition)

**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.

## STATEMENT OF MEDICAL NECESSITY *(ONLY REQUIRED IF NO ELECTRONIC ORDER)*

ICD-10 Diagnoses Codes (REQUIRED)

_____ _____

_____ _____

_____ _____

I authorize and direct UPMC Clinical Genomics Laboratory (UCGL) to perform the testing indicated. I confirm that the testing requested is reasonable and medically necessary and that the test results may impact medical management and treatment decisions for this patient. and participating family members. I certify that the patient or legal guardian and participating famlily members have been informed of the risks, benefits and limitations of genetic testing. The person listed as the ordering provider is authorized by law to order the test(s) requested herein.

_____ _____

Signature of Provider (*Required*) Date

## PATIENT CONSENT (*REQUIRED*)

By signing this form I acknowledge as the patient/legal guardian that I have read the attached informed consent document and that I authorize the UCGL to perform 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.

☐ OPT-IN Please check this box if you wish to receive reportable secondary findings as identified by the ACMG. Participating family members cannot opt out if the patient has elected to receive these findings.

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

_____ _____ _____

Print name of Patient/Legal guardian Signature of Patient/Legal Guardian Date

## PAYMENT OPTIONS: SELECT ONE

**☐INSTITUTIONAL BILLING**

| Facility | Address | Contact | Phone | Email |
|---|---|---|---|---|
| | | | | |

**☐INSURANCE BILLING (copy front and back of insurance cards)**

| Primary Insurance | Insurance ID# | Name and DOB of Insured | Patient Relation to Policy Holder<br>Self Spouse Child |
|---|---|---|---|
| Secondary Insurance | Insurance ID# | Name and DOB of Insured | Prior Authorization # - Please Attach |

**☐PATIENT BILLING**

☐The patient is electing to self-pay and agrees that neither they nor UPMC Clinical Genomics Laboratory (UCGL) will submit a claim to their health insurance for testing.

REQUISITION CONTINUES ON NEXT PAGE



2CNTT **UPMC Clinical Genomics Laboratory** 300 Halket Street (Rm 4680), Pittsburgh, PA 15213 T (412)-641-2949 F (412)641-2893

**GENOME SEQUENCE ANALYSIS**
**PROBAND REQUISITION FORM**

## CLINICAL FEATURES TO BE CONSIDERED IN ANALYSIS

Please provide the following information regarding the patient 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.

### PRE/PERINATAL HISTORY
☐ Cystic hygroma [0000476]
☐ Congenital diaphragmatic hernia [0000776]
☐ Encephalocele [0002084]
☐ Increased nuchal translucency [0010880]
☐ Intrauterine growth retardation [0001511]
☐ Nonimmune hydrops fetalis [0001790]
☐ Oligohydramnios [0001562]
☐ Omphalocele [0001539]
☐ Polyhydramnios [0001561]
☐ Premature birth [0001622] Gest. Age: _____
☐ Prolonged neonatal jaundice [0006579]

### GROWTH
☐ Failure to thrive [0001508]
☐ Hemihypertrophy [0001528]
☐ Large for gestational age [0001520]
☐ Obesity [0001513]
☐ Short stature [0004322]
☐ Tall stature [0000098]

### MOTOR/COGNITIVE DEVELOPMENT
☐ Absent speech [0001344]
☐ Aggressive behavior [0006919]
☐ Anxiety [0100852]
☐ Autistic Behavior [0000729]
☐ Behavior abnormality [0000708]
☐ Delayed speech and language development [0000750]
☐ Developmental Regression [0002376]
☐ Global developmental delay [0001263]
☐ Hyperactivity [0000752]
☐ Intellectual Disability [0001249]
☐ Memory impairment [0002354]
☐ Sleep disturbance [0002360]
☐ Specific learning disability [0001328]

### METABOLIC/RESPIRATORY
☐ Abnormal activity of mitochondrial respiratory chain [0011922]
☐ Abnormal circulating metabolite concentration [0032180]
☐ Aminoaciduria [0003355]
☐ Asthma [0002099]
☐ Bronchiectasis [0002110]
☐ Elevated circulating creatine kinase concentration [0003236]
☐ Elevated hepatic transaminase [0002910]
☐ Hyperammonemia [0001987]
☐ Hyperglycemia [0003074]
☐ Hyperventilation [0002883]
☐ Hypoammonemia [0100493]
☐ Hypoglycemia [0001943]
☐ Hypoventilation [0002791]
☐ Lactic acidosis [0003128]
☐ Organic Aciduria [0001992]
☐ Pneumothorax [0002107]
☐ Pulmonary fibrosis [0002206]
☐ Respiratory insufficiency [0002093]

### STRUCTURAL BRAIN ABNORMALITIES
☐ Abnormal basal ganglia morphology [0002134]
☐ Abnormal brainstem morphology [0002363]
☐ Abnormal myelination [0012447]
☐ Abnormality of neuronal migration [0002269]
☐ Abnormal periventricular white matter morphology [0002518]
☐ Agenesis of corpus Collosum [0001274]
☐ Chiari malformation [0002308]
☐ Cerebellar atrophy [0007360]
☐ Holoprosencephaly [0001360]
☐ Hydrocephalus [0000238]
☐ Leukodystrophy [0002415]
☐ Lissencephaly [0001339]
☐ Pachygyria [0001302]
☐ Polymicrogyria [0002126]
☐ Ventriculomegaly [0002119]

### NEUROLOGICAL
☐ Abnormal nervous system morphology [0012639]
☐ Ataxia [0001251]
☐ Cerebral palsy [0100021]
☐ Cerebral visual impairment [0100704]
☐ Chorea [0002072]
☐ Dementia [0000726]
☐ Dysarthria [0001260]
☐ Dyskinesia [0100660]
☐ Dystonia [0001332]
☐ Encephalopathy [0001298]
☐ Hemiplegia [0002301]
☐ Incoordination [0002311]
☐ Infantile Spasms [0012469]
☐ Language impairment [0002463]
☐ Migraine [0002076]
☐ Myoclonus [0001336]
☐ Parkinsonism [0001300]
☐ Peripheral neuropathy [0009830]
☐ Seizure [0001250]
☐ Sensory Neuropathy [0000763]
☐ Spasticity [0001257]
☐ Syncope [0001279]
☐ Tremor [0001337]
☐ Vertigo [0002321]

### ENDOCRINE
☐ Delayed puberty [0000823]
☐ Diabetes Insipidus [0000873]
☐ Diabetes Mellitus [0000819]
☐ Hyperthyroidism [0000836]
☐ Hypophosphatemia [0002148]
☐ Hypothyroidism [0000821]
☐ Hypoparathyroidism [0000829]
☐ Maturity-onset diabetes of the young [0004904]
☐ Pheochromocytoma [0002666]
☐ Paraganglioma [0002668]

### CARDIAC FINDINGS
☐ Abnormal heart morphology [0001627]
☐ Amyloidosis [0011034]
☐ Aortic root aneurysm [0002616]
☐ Arrhythmia [0011675]
☐ Atrial septal defect [0001631]
☐ Bicuspid aortic valve [0001647]
☐ Bradycardia [0001662]
☐ Coarctation of aorta [0001680]
☐ Dilated cardiomyopathy [0001644]
☐ Heterotaxy [0030853]
☐ Hypertension [0000822]
☐ Hypertrophic cardiomyopathy [0001639]
☐ Mitral valve prolapse [0001634]
☐ Noncompaction cardiomyopathy [0012817]
☐ Patent ductus arteriosus [0001643]
☐ Patent foramen ovale [0001655]
☐ Prolonged QTc interval [0005184]
☐ Sudden death [0001645]
☐ Supraventricular tachycardia [0004755]
☐ Tetralogy of Fallot [0001636]
☐ Ventricular septal defect [0001629]

### VASCULAR SYSTEM
☐ Arterial calcification [0003207]
☐ Arterial dissection [0005294]
☐ Arterial tortuosity [0005116]
☐ Arteriovenous malformation [0100026]
☐ Epistaxis [0000421]
☐ Lymphedema [0001004]
☐ Pulmonary arterial hypertension [0002092]
☐ Pulmonary venous hypertension [0030950]
☐ Stroke [0001297]
☐ Vascular dilatation [0002617]

### HAIR & SKIN
☐ Abnormal Blistering of the Skin [0008066]
☐ Abnormal nail growth [0030807]
☐ Alopecia [0001596]
☐ Anhidrosis [0000970]
☐ Coarse Hair [0002208]
☐ Eczema [0000964]
☐ Generalized Hypertrichosis [0004554]
☐ Hemangioma [0001028]
☐ Hyperextensible skin [0008067]
☐ Hypermelanotic macule [0001034]
☐ Hyperpigmentation of the skin [0001000]
☐ Hypohidrosis [0000966]
☐ Hypopigmentation of the skin [0001010]
☐ Ichthyosis [0008064]
☐ Skin Rash [0000988]
☐ Soft Skin [0000977]
☐ Sparse hair [0008070]
☐ Telangiectasia [0001009]



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## CLINICAL FEATURES continued

**MUSCULOSKELETAL**
- ☐ Abnormal form of the vertebral bodies [0003312]
- ☐ Abnormal rib morphology [0000772]
- ☐ Arachnodactyly [0001166]
- ☐ Clinodactyly [0030084]
- ☐ Decreased muscle mass [0003199]
- ☐ Ectrodactyly [0100257]
- ☐ Exercise intolerance [0003546]
- ☐ Hemihypertrophy [0001528]
- ☐ Hypertonia [0001276]
- ☐ Hypotonia [0001252]
- ☐ Joint Hypermobility [0001382]
- ☐ Muscle weakness [0001324]
- ☐ Myalgia [0003326]
- ☐ Myopathic facies [0002058]
- ☐ Osteoarthritis [0002758]
- ☐ Osteopenia [0000938]
- ☐ Pectus carinatum [0000768]
- ☐ Polydactyly [0010442]
- ☐ Recurrent Fractures [0002757]
- ☐ Rhabdomyolysis [0003201]
- ☐ Scoliosis [0002650]
- ☐ Skeletal Dysplasia [0002652]
- ☐ Syndactyly [0001159]

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

**GENITOURINARY**
- ☐ Ambiguous Genitalia [0000062]
- ☐ Cryptorchidism [0000028]
- ☐ Horseshoe Kidney [0000085]
- ☐ Hydronephrosis [0000126]
- ☐ Hypospadias [0000047]
- ☐ Inguinal hernia [0000023]
- ☐ Micropenis [0000054]
- ☐ Nephrolithiasis [0000787]
- ☐ Polycystic kidney dysplasia [0000113]
- ☐ Proximal Tubulopathy [0000114]
- ☐ Renal Agenesis [0000104]
- ☐ Renal dysplasia [0000110]
- ☐ Umbilical hernia [0001537]

**GASTROINTESTINAL**
- ☐ Aganglionic megacolon [0002251]
- ☐ Constipation [0002019]
- ☐ Diarrhea [0002014]
- ☐ Duodenal stenosis [0100867]
- ☐ Episodic Vomiting [0002572]
- ☐ Failure to thrive [0001508]
- ☐ Feeding difficulties [0011968]
- ☐ Gastroesophageal reflux [0002020]
- ☐ Gastroparesis [0002578]
- ☐ Hepatomegaly [0002240]
- ☐ Inflamation of the large intestine [0002037]
- ☐ Pancreatitis [0001733]
- ☐ Pyloric Stenosis [0002021]
- ☐ Splenomegaly [0001744]
- ☐ Tracheoesophageal Fistula [0002575]
- ☐ Vomiting [0002013]

**CRANIOFACIAL/DYSMORPHISM**
- ☐ Abnormal facial shape [0001999]
- ☐ Coarse facial features [0000280]
- ☐ Craniosynostosis [0001363]
- ☐ Macrocephaly [0000256]
- ☐ Microcephaly [0000252]
- ☐ Oral cleft [0000202]
- ☐ Short neck [0000470]

**EYE DEFECTS & VISION**
- ☐ Microphthalmia [0000568]
- ☐ Myopia [0000545]
- ☐ Nystagmus [0000639]
- ☐ Optic atrophy [0000648]
- ☐ Optic neuropathy [0001138]
- ☐ Ptosis [0000508]
- ☐ Retinal detachment [0000541]
- ☐ Rod-cone dystrophy [0000510]
- ☐ Strabismus [0000486]

**CANCER**
- ☐ Type of cancer_____
- ☐ Age at Diagnosis_____
- ☐ Family History of Cancer (attach pedigree)

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

**OTHER FEATURES**
Look up at: https://hpo.jax.org/app/

Phenotype [HPO]

_____ [ ]
_____ [ ]
_____ [ ]
_____ [ ]
_____ [ ]
_____ [ ]
_____ [ ]
_____ [ ]
_____ [ ]

**Additional history: You may also reference clinical notes/results or attach information**

Inheritance for the following previously reported variants is requested. A copy of the clinical lab report(s) must be attached.

Gene _____ Variant _____ Test _____
Gene _____ Variant _____ Test _____
Gene _____ Variant _____ Test _____
Gene _____ Variant _____ Test _____



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## INFORMED CONSENT

### ABOUT THE GENOME ANALYSIS TEST

Genome sequence analysis simultaneously evaluates both the protein-coding and non-coding regions of the nuclear genome. The non-coding regions include promoter, intronic and untranslated regions. An individual's nuclear genome represents approximately 20,000 genes. This test also includes screening for a select group of repeat expansion disorders. In addition, this test analyzes the mitochondrial DNA (mtDNA) genome which 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. While much of the data generated from sequencing the genome is not well understood at this time, genome sequencing may potentially detect pathogenic variants that are not assessed by exome sequencing.

The purpose of this test is to determine if there is a possible genetic reason for the patient'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 are recommended before and after the test is performed. 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 TESTING

Any sample submitted to assist in the analysis of the patient's genome (such as the parents, sibling or other relative) 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 members are ONLY used for better interpretation of the patient's genome sequencing findings. Genetic variants that may be in a family member, but are NOT present in the proband, 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.

### GENOME ANALYSIS RESULT REPORTING

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

You can also choose to receive secondary findings. The American College of Medical Genetics and Genomics (ACMG) identified a subset of 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.

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. If samples from parents, siblings or other relatives were utilized as part of the interpretation of the patient's genome test, the results will indicate if the variant(s) were de novo (new event), or inherited from the mother, the father or present in a sibling or other relative.

**INFORMED CONSENT continued**

## POSSIBLE TEST RESULTS

The genetic variants found by 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 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 (UCGL) 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 genome sequencing 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. Some parts of our DNA are naturally difficult to analyze because of features like repetitive sequences, very similar gene copies, or high GC content. These areas may produce lower-quality data and increase the chance that some variants are missed. Genome sequence analysis also has technical limits. It generally cannot detect certain types of changes, such as balanced structural rearrangements, low-level mosaicism, methylation abnormalities, or changes in highly repetitive regions. Mitochondrial DNA sequencing has its own limitations as well; variants present at very low levels (below about 5–10%) may not be detected, and the accuracy of finding deletions or duplications is not fully established. The repeat expansion disorder screening included in this test can only suggest that certain genes are unlikely to explain the patient's symptoms. It is not intended to provide a diagnosis.

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 gene(s) 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. UCGL 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.

UPMC LIFE CHANGING MEDICINE

**GENOME SEQUENCE ANALYSIS**
**PROBAND REQUISITION FORM**

## 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)



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