



Intellectual Disability Exome Requisition Form

The University of Chicago Genetic Services Laboratories

5841 South Maryland Avenue, Room G701/MC0077, Chicago, IL 60637

Toll Free: 888.824.3637 | Local: 773.834.0555 | Fax: 773.702.9130

ucgslabs@genetics.uchicago.edu | dnatesting.uchicago.edu | CLIA#: 14D0917593 | CAP#: 18827-49

Patient Information

Name: Last _____ First _____ Date of Birth: _____

Gender: Male Female MRN: _____

Ethnicity: Caucasian African-American Hispanic Asian Ashkenazi Jewish Other _____

Date Sample Drawn: _____ Specimen Requirements: 3-10cc blood in an EDTA (purple top) tube DNA samples are only accepted if the DNA extraction or isolation was performed at a CLIA-certified laboratory. Please see our website for other specimen requirements.

Ordering Physician Information

REPORTING RESULTS: Reports will only be faxed out. Please check the boxes below for those who should receive by fax.

Referring Physician: _____ Genetic Counselor: _____

Phone: _____ Fax: _____ Phone: _____ Fax: _____

Email: _____ Email: _____

Referring Lab: _____

Phone: _____ Fax: _____

Email: _____

Indication for Testing Symptomatic: _____ ICD-10: _____

In addition, the following are strongly recommended to be sent with samples for the Intellectual Disability Exome: detailed clinic notes, pedigree, results of prior genetic testing, and brain imaging reports.

Parental Samples Parental samples are REQUIRED for interpretation of proband results, and there is no additional charge for parental testing as part of the Intellectual Disability Exome. Please send 3-10ccc in EDTA. Please label parental sample with full name and DOB.

MOTHER Date Sample Drawn: _____

Name: Last _____ First _____ Date of Birth: _____

MRN: _____

Asymptomatic Symptomatic (attach summary of findings)

FATHER Date Sample Drawn: _____

Name: Last _____ First _____ Date of Birth: _____

MRN: _____

Asymptomatic Symptomatic (attach summary of findings)

To be sent later – note, testing will not be initiated until both parental samples are received

Ordering Checklist

- Test Requisition Form (required)
- Completed Indication for Testing/ICD9 study code (required)
- Completed Clinical Checklist (required)
- Completed Billing Information (required)
- Completed Intellectual Disability Exome Consent Form (required)
- Completed Research Consent Form (recommended)

For Office Use Only

INTELLECTUAL DISABILITY EXOME CLINICAL CHECKLIST REQUIRED

Please check all clinical features that apply, and use the additional space provided at the bottom of the form if needed

Perinatal History

- YES (see below) NO UNKNOWN
 Abnormal prenatal development - please specify: _____

Cognitive / Developmental findings

- YES (see below) NO UNKNOWN
 Cognitive impairment (please provide details): _____
 Developmental regression
 Global developmental delay
 Mild Moderate Severe
 Motor delay
 Speech delay

Behavioral findings

- YES (see below) NO UNKNOWN
 Autism spectrum disorder
 Behavioral / Psychiatric abnormality - please specify: _____

Neurological findings

- YES (see below) NO UNKNOWN
 Seizures
 Movement abnormality – please specify:
 Ataxia
 Dystonia
 Chorea
 Other: _____
 Encephalopathy
 Hypertonia
 Hypotonia (muscular)
 Spina bifida
 Additional findings: _____

Brain (Structural Anomalies) - please also provide MRI / imaging reports

- YES (see below) NO UNKNOWN
 Agenesis of corpus callosum
 Cortical dysplasia
 Cerebellar hypoplasia
 Dandy-Walker malformation
 Heterotopia
 Hydrocephalus
 Lissencephaly
 Polymicrogyria
 Pachygyria
 Other: _____

Craniofacial features

- YES (see below) NO UNKNOWN
 Cleft lip and/or palate
 Craniosynostosis
 Dysmorphic facies
Specify: _____
 Macrocephaly, HC: _____
 Microcephaly, HC: _____

Hearing/Vision findings

- YES (see below) NO UNKNOWN
 Vision abnormality – please specify: _____
 Hearing impairment – please specify: _____
 Other: _____

Growth findings

- YES (see below) NO UNKNOWN
 Failure to thrive
 Overgrowth
 Short stature
 Hemihypertrophy
 Other: _____

Gastrointestinal (GI) findings

- YES (see below) NO UNKNOWN
please specify: _____

Cutaneous findings

- YES (see below) NO UNKNOWN
please specify: _____

Cardiac findings

- YES (see below) NO UNKNOWN
 Arrhythmia
 Heart malformation – please specify: _____
 Other: _____

Hematologic/Immunologic findings

- YES (see below) NO UNKNOWN
 Immunodeficiency
 Anemia/neutropenia/pancytopenia
 Other: _____

Musculoskeletal findings

- YES (see below) NO UNKNOWN
 Congenital diaphragmatic hernia
 Digital abnormality – please specify: (Poly / Oligo / Other: _____)
 Limb abnormality – please specify: _____
 Limb joint contracture(s)
 Scoliosis
 Other: _____

Genitourinary findings

- YES (see below) NO UNKNOWN
 Genital system abnormality - please specify: _____
 Kidney abnormality - please specify: _____
 Other: _____

Family History

- YES (see below) NO UNKNOWN
 Parents with 2 or more miscarriages
 Other relatives with similar clinical history (please include detailed pedigree)

Please include any additional relevant clinical information here:

In addition to this checklist, please send the following: detailed clinic notes, pedigree, results of prior genetic and metabolic testing.

BILLING OPTIONS

All samples received with incomplete billing information will delay processing time.
 Test cancelled while "in progress" will be billed for the amount of work completed up to that point.
 Please note, we do not currently offer direct insurance billing for our Intellectual Disability Exome.
 Please forward all billing questions to: youtlaw@bsd.uchicago.edu or call (773-834-8220).

Patient Name: Last _____ First _____ (MI): _____ Date of Birth: _____

1.) Institutional Billing *(Pre-payment is required for all samples referred from outside the US or Canada.)*

Billing Institution: _____ PO#: _____

Financial Contact: _____ Phone: _____ Fax: _____

Address: _____ City: _____ State: _____ Zip: _____

Email (required): _____

2.) Self-Pay

We accept all major credit cards. Please call our office (773-834-8220) for credit card processing.



Important notice: We will not be responsible for refunding any "cost differential" that may occur as a result of a patient seeking any type of reimbursement.

Wire Transfer *(Please include 'Genetics Services Laboratories' and invoice numbers to ensure proper receipt.)*

Electronic funding information, as follows: The Northern Trust Bank – **(Physical Address)** 50 S. LaSalle Street, Chicago, IL 60675
 ABA/Routing No.: 071000152, International SWIFT Code: CNORUS44, University of Chicago Wire Account No.: 28509

Amount \$ _____ (USD) Date of Transfer: _____ Name of Institution: _____

Check/Money Order **(Make check/money order payable to: The University of Chicago Genetic Services)** Amount Enclosed \$ _____
 (Please note: All bank fees for returned checks will be added to the original charge of patient invoice)

We currently only offer institutional billing and self-pay for our Intellectual Disability Exome. Insurance prior authorization is not absolutely mandatory before sending a sample to our laboratory. Insurance prior authorization services are offered as a courtesy and can be requested PRIOR to sending a sample to our laboratory (please see website for prior authorization request form). Samples received with appropriate billing information (institutional billing or self-pay) will be processed accordingly

INTELLECTUAL DISABILITY EXOME CONSENT FORM

The Division of Biological Sciences | University of Chicago Medical Center
REQUIRED

Patient Name: _____

Date of Birth: _____

Overview

Exome sequencing attempts to evaluate the coding regions of approximately 20,000 genes in the genome. This is called the 'exome'. The exome represents only 1.5% of the genome and comprises the majority of DNA variations that cause human disease. The UCGS Intellectual Disability Exome test limits analysis of the exome sequencing data to a predefined set of 1918 genes that have been associated with intellectual disability. The purpose of this test is to identify the underlying molecular basis of the intellectual disability in this patient/family.

Accuracy

The analysis performed is specific to genes associated with intellectual disability. Accurate interpretation of test results may require an accurate report of the patient's medical and family history. There is always a small possibility of an error or failure in sample analysis; this is always a possibility with complex testing in any laboratory. Extensive measures are taken to avoid these errors. The accuracy of genetic testing is limited by the methods employed, and sometimes by the nature of the condition for which testing is requested.

Limitations

Not all the exons in the genes being analyzed are targeted and captured due to certain inherent characteristics of the genome. Approximately 90-95% of exons are targeted in the diagnostic Intellectual Disability Exome test. In addition, there is limited or no coverage in regions outside of the exome.

Certain types of mutations are not detectable by this test. This methodology will not detect trinucleotide repeat expansions, low level mosaicism or copy number variation mutations (i.e. such as the deletion or duplication of an exon). Other types of rare genetic variation can interfere with this analysis.

Pathogenic variants may be present in a region of a gene not covered by this test. Absence of findings for any particular gene does not mean that there are no pathogenic variants present in that gene.

It is the responsibility of the referring physician, or a health care professional designated by the physician, to understand the limitations of the testing ordered, and to educate the patient regarding these limitations.

Testing & Analysis Pipeline

Of the thousands of variants identified by exome sequencing, a list of variants that are located within a predefined set of genes that have been associated with intellectual disability is generated. Most variants identified as part of exome sequencing will NOT undergo interpretation by a laboratory staff member. Only those variants identified that fall within a gene associated with intellectual disability and are considered to be potentially relevant to the patient's condition are reviewed by a team of Board-Certified PhD geneticists, MD geneticists, and genetic counselors who will determine the likelihood of the variant being related to the patient's disorder.

What is Reported?

UCGS will report any variants interpreted as pathogenic or likely pathogenic in the predefined set of 1918 genes. In some cases, variants of unknown significance will be reported if the variant is strongly suspected to be associated with the patient's clinical findings.

What is Not Reported?

- Variants of unknown clinical significance in the pre-defined set of intellectual disability-associated genes, that are considered unlikely to be the cause of the patient's intellectual disability based on the clinical information provided.
- Single heterozygous unclassified variants associated with a recessive disorder.
- Variants that occur in genes outside of the pre-defined set of intellectual disability-associated genes.
- Variants that occur in genes defined as medically actionable by the American College of Medical Genetics and Genomics (ACMG), unless they are associated with an intellectual disability phenotype.
- Carrier status for recessive disorders which are not associated with an intellectual disability phenotype.
- Benign sequence changes not associated with disease and are commonly identified in healthy people.
- Synonymous (silent) sequence changes not associated with a change in the amino acid.
- Variations associated with increased or decreased risk to develop common disorders (like high blood pressure) or involved in drug metabolism.
- Variants that have been associated with an increased risk for diseases that might present at an advanced age (like Alzheimer's Disease) in which there is no treatment or preventative measures.
- Variants in genes with no current known association with disease.

Implication of Results

Because the implications of genetic testing results can be complex, involving both medical and emotional and social issues, results will only be reported through the referring physician or a professional designated by the physician, such as a genetic counselor. The issues associated with some types of genetic testing are particularly sensitive. Therefore, the laboratory reserves the right to provide testing only if genetic counseling can be provided.

Confidentiality

Results and patient information are confidential and will only be released to the referring physician, unless written consent for further distribution is provided or the laboratory directors are required by law to release this information. For patients within The University of Chicago affiliated centers, policy may require that reports are provided to the medical records department.

Consent for Intellectual Disability Exome

Signature of Patient/Parent/Legal Guardian:

Relationship to patient: _____

Date: _____

Referring Clinician

By signing this consent form, the referring clinician 1) indicates that this consent form has been reviewed with the patient and/or the patient's parent or guardian, and 2) accepts responsibility for pre- and post- test genetic counseling.

Signature of Referring Clinician:

Date: _____

RESEARCH CONSENT FORM – The University of Chicago
The Division of Biological Sciences | University of Chicago Medical Center
RECOMMENDED BUT OPTIONAL

CONSENT/AUTHORIZATION BY SUBJECT FOR PARTICIPATION IN A RESEARCH PROTOCOL FOR THE BETTER UNDERSTANDING OF THEIR GENETIC CONDITION

Protocol Number: 11-0151

Name of Subject : _____

Date of Birth: _____

STUDY TITLE: Molecular Genetic Studies of Rare Orphan Genetic Disease

Research Team: Soma Das, Ph.D.
 5841 S. Maryland Ave. Room L-155 MC 0077, Chicago, IL 60637
 773-834-0555

You are being asked to allow your child to participate in a research study that may help us learn more about the genetic condition for which your child is being tested. This consent form describes the study, the risks and benefits of participation, as well as how your confidentiality will be maintained. Please take your time to contact us with questions and feel comfortable making a decision whether to participate or not. If you decide to participate in this study, please sign this form.

Why is this study being done?

You have already consented to clinical genetic testing for your child. We are asking you to also participate in further studies. The purpose of these studies is to learn more about the genetic cause of diseases tested for in our lab, gather more information about these disorders, and experiment with new methods that may be better for testing.

What is involved in the study?

During this study, Dr. Das and her team will collect information about your child for this research. We may contact your doctor for additional Protected Health Information (PHI) about your child, which consists of any health information related to your child's diagnosis (such as date of birth, medical record number, primary diagnosis, clinical features, relevant and family history, and outcome). The data collected will be used to develop a database of patients being tested for genetic diseases and will be kept for the duration of the database. This study will look at how often different genetic mutations happen and clinical information related to the mutation.

When our lab is researching new genes or testing methods that are related to your child's diagnosis, we may include your child's sample with others from similar patients in a small study before offering this new test. This data will help in directing doctors about the likelihood of a positive or negative test result in their patient. We may also use your child's sample to set up new methods that will improve the clinical testing in our laboratory. Your child's clinical information and sample, without any identifiers, may also be shared with other researchers that are interested in this specific condition.

How long will I be in the study?

Your child will likely remain in this study as long as his/her DNA sample remains in our laboratory. If you want your child's sample to be removed from the study at any time, please contact us, and the sample will not be used for further studies. Existing results will remain in our database until the study ends.

What are the risks of the study?

There are no known added risks of the research. No additional information will be obtained from your child as all of the information has already been collected as part of clinical genetic testing or evaluation by your doctor.

Are there any benefits to taking part in the study?

If you agree to take part in this study, there may be direct medical benefit to your family. We may identify a cause for the genetic disease in your family. If a mutation is identified in your child's DNA through our testing, your child's doctor will be notified and will receive a clinical report. Our study may also be helpful in finding the genetic causes of disease and will benefit doctors and patients as a group.

What other options are there?

You may choose not to participate.

What are the costs?

There will be no additional costs to your child or your insurance company resulting from this research study. However, you or your insurance company will be responsible for costs related to your usual medical care.

Will I be paid for my participation?

You and your child will not be paid to participate.

What about privacy?

Study records that identify your child will be kept private. All of your child's personal information will be entered into a password-protected database to prevent access to non-authorized personnel. If your child's data is shared with other researchers, all patient identifiers will be removed. Data from this study may be used in medical journals or presentations. If results from this study or related studies are made public in a medical journal, individual patients will not be identified. If we wish to use a patient's identity in a medical journal, we will ask for your permission at that time.

As part of the study, Dr. Das and her team will report any positive results of further testing to your child's doctor and/or genetic counselor. Dr. Das may also share these results, without your name or date of birth, with other researchers.

People from the University of Chicago, including the Institutional Review Board (IRB), a committee that oversees research at the University of Chicago, may also view the records of the research. If health



RESEARCH CONSENT FORM – The University of Chicago
The Division of Biological Sciences | University of Chicago Medical Center
RECOMMENDED BUT OPTIONAL

information is shared outside the University of Chicago, the same laws that the University of Chicago must obey may not protect your child's health information. Dr. Das does not have to give you any results that are not important to your child's or your family's health at that time.

The research team will keep this consent form for at least six years. The study results will be kept in your child's research record and be used by the research team indefinitely. When the study ends, your child's personal information will be removed from all results. Any information shared with your child's doctor may be included in your child's medical record and kept forever.

The Genetic Information Nondiscrimination Act (GINA) is a federal law that may help protect you from health insurance or employment discrimination based on genetic information. GINA is a federal law that will protect you in the following ways:

- Health insurance companies and group plans may not request genetic information from this research;
- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums;
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

What are my rights as a participant?

Taking part in this study is optional. You may choose not to participate at any time during the study. Choosing not to participate or leaving the study will not affect your child's testing at the University of Chicago.

If you choose to leave the study and you do not want any of your child's future health information to be used, you must inform Dr. Das in writing at the address on the first page. Dr. Das may still use your child's information that was collected before your written notice. You will be given a signed copy of this form. This consent form does not have an expiration date.

Who do I call if I have questions or problems?

If you have further questions about the study, please call 773-834-0555.

If you have any questions about your rights in this research study you may contact the IRB, which protects participants in research projects. You may reach the Committee office between 8:30 am and 5:00 pm, Monday through Friday, by calling (773) 702-6505 or by writing: University of Chicago, Institutional Review Board, 5841 S. Maryland Ave., MC7132, I-625, Chicago, IL 60637.

Consent

PARENT/GUARDIAN/ OR LEGALLY AUTHORIZED REPRESENTATIVE:

I have received information about this research project and the procedures. No guarantee has been given about possible results. I will receive a signed copy of this consent form for my records.

I give my permission for my child/relative/the person I represent to participate in the above research project.

**Signature of Parent/Guardian/
Legally Authorized Representative:**

Date: _____

WITNESS

Signature of Witness:

Date: _____