The UNIVERSITY of CHICAGO
Genetic Services
www.dnatesting.uchicago.edu

EPILEPSY 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. (purple top) tube **Please contact the laboratory before obtaining an**

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:** _____
Phone: _____ Fax: _____
Email: _____

☐ **Genetic Counselor:** _____
Phone: _____ Fax: _____
Email: _____

☐ **Referring Lab:** _____
Phone: _____ Fax: _____
Email: _____

Indication for Testing (REQUIRED)

☐ **Symptomatic:** _____ ICD-10: _____

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

Testing Ordered

☐ Epilepsy Exome (proband only)

☐ Epilepsy Exome (Trio) - if ordering the Epilepsy Exome (Trio) please provide 3-10cc of blood on each parent and provide details on the parents below:

MOTHER Date Sample Drawn: _____ ☐ Sample Not Available ☐ Sample to be sent later
Name: *Last* _____ *First* _____ **Date of Birth:** _____ **MRN:** _____
☐ **Asymptomatic** ☐ **Symptomatic (attach summary of findings)**

FATHER Date Sample Drawn: _____ ☐ Sample Not Available ☐ Sample to be sent later
Name: *Last* _____ *First* _____ **Date of Birth:** _____
MRN: _____
☐ **Asymptomatic** ☐ **Symptomatic (attach summary of findings)**

Ordering Checklist

- ☐ Test Requisition Form *(required)*
- ☐ Completed Indication for Testing/ICD-10 study code *(required)*
- ☐ Completed Clinical Checklist *(required)*
- ☐ Completed Billing Information *(required)*
- ☐ Completed Epilepsy Exome Consent Form *(required)*
- ☐ Completed Research Consent Form *(recommended)*

For Office Use Only

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Epilepsy
☐ YES (see below) ☐ NO ☐ UNKNOWN
Age of onset: _____

Previous Testing for Epilepsy
☐ YES ☐ NO ☐ UNKNOWN
Please specify: _____
_____

Metabolic testing
☐ YES ☐ NO ☐ UNKNOWN
Please specify: _____
_____

Seizure type (check all that apply):
- ☐ Absence
- ☐ Atypical absence
- ☐ Atonic
- ☐ Clonic
- ☐ Complex Partial
- ☐ Early Infantile Epileptic Encephalopathy
- ☐ Febrile
- ☐ Infantile spasms
- ☐ Myoclonic
- ☐ Refractory /intractable
- ☐ Simple Partial
- ☐ Tonic
- ☐ Tonic-Clonic
- ☐ Other:_____

Other Neurological
☐ YES (see below) ☐ NO ☐ UNKNOWN
- ☐ EEG abnormalities – please specify
  _____
- ☐ Movement abnormality – please specify:
  - ☐ Dystonia
  - ☐ Ataxia
  - ☐ Chorea
  - ☐ Other_____ ___
- ☐ Encephalopathy
- ☐ Hypotonia
- ☐ Hypertonia
- ☐ Dysarthria
- ☐ Neuropathy
- ☐ Other: _____

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

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

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

Brain (Structural Anomalies) - please also provide MRI / imaging reports
☐ YES (see below) ☐ NO ☐ UNKNOWN
- ☐ Agenesis of corpus callosum
- ☐ Cortical abnormality

Please specify:_____
- ☐ Cerebellar hypoplasia
- ☐ Dandy-Walker malformation
- ☐ Hydrocephalus
- ☐ Other: _____

Craniofacial
☐ YES (see below) ☐ NO ☐ UNKNOWN
- ☐ Dysmorphic facies

Please specify: _____
- ☐ Macrocephaly, HC: _____
- ☐ Microcephaly, HC: _____
- ☐ Other: _____

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

Cutaneous
☐ YES (see below) ☐ NO ☐ UNKNOWN
Please specify:_____

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

Musculoskeletal
☐ YES (see below) ☐ NO ☐ UNKNOWN
- ☐ Digital abnormality – please specify:
  (Poly / Oligo / Other: _____)
- ☐ Limb abnormality – please specify:
  _____
- ☐ Scoliosis
- ☐ Other: _____

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

Gastrointestinal / Genitourinary
☐ YES (see below) ☐ NO ☐ UNKNOWN
Please specify:_____

Family History (please include detailed pedigree)
☐ YES (see below) ☐ NO ☐ UNKNOWN
- ☐ Family history epilepsy-please specify:
  _____
- ☐ Other: _____

Please include any additional relevant clinical information here:

The UNIVERSITY of CHICAGO
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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 Epilepsy 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 Epilepsy 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

The UNIVERSITY of CHICAGO
Genetic Services
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EPILEPSY 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 Epilepsy Exome test limits analysis of the exome sequencing data to a predefined set of 537 genes that have been associated with epilepsy. The purpose of this test is to identify the underlying molecular basis of the epilepsy in this patient/family.

Accuracy

The analysis performed is specific to genes associated with epilepsy. 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 Epilepsy 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 epilepsy 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 epilepsy 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 on genetic variants that have been reported to be pathogenic or predicted to be pathogenic or possibly pathogenic as well as unclassified variants in established genes associated with epilepsy.

What is Not Reported?

- Variants that occur in genes outside of the pre-defined set of epilepsy-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 epilepsy phenotype.
- Carrier status for recessive disorders which are not associated with an epilepsy 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. Variations 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.
- Heterozygous unclassified variants associated with a recessive disorder are not reported unless a deleterious mutation or a second unclassified variant in the same gene is also detected.
- Pathogenic mutations and 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 Epilepsy Exome

Signature of Parent /Legally Authorized Representative:

_____

Date: _____

If Legally Authorized Representative please describe relationship to individual:

_____

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: _____

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

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 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 to 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: _____