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Illumina Clinical Services Laboratory CLIA
Certificate No.: 05D1092911

Illumina Clinical Services Laboratory

TruGenome™ Undiagnosed Disease Test Requisition Form

The TruGenome Undiagnosed Disease Test is intended to provide information to physicians to aid in the diagnosis of inherited diseases with high penetrance. Analysis and interpretation are designed to detect and report on single nucleotide variants (SNVs), small insertion/deletion events, copy number variants (CNVs), and mitochondrial SNVs that impact genes with an established association to genetic disease. Analysis is typically done as a family-based analysis (eg, a "trio" of the proband and his/her biological parents), but may be performed on a proband only. Family-based analyses may be comprised of a duo (parent and child), trio, or other higher order family structure. The analysis considers inheritance patterns consistent with the reported family history. In addition, analysis considers clinical presentation, family history, and peer-reviewed literature to contextualize resulting variants from the analyses.

This test is appropriate for situations where there are many candidate genes to evaluate, the evaluation of the genome may clarify or refine the diagnosis because the presenting set of signs, symptoms, imaging, and laboratory tests are inconclusive, or the phenotype might indicate multiple genetic conditions.

Examples of conditions for which this test is not appropriate include those caused by multiple genes, each with small effect, or gene–environment interactions. This may include diseases that are common in the population such as diabetes, immune disorders, and disorders thought to be caused by gene–environment interactions. To assess if a patient's disorder is likely to have a Mendelian etiology, the referring physician should consider other lines of evidence such as increased severity, earlier than expected age of onset, multiple affected close family members, and unexpected phenotypic complexity.

Physicians ordering this testing should understand the intended use of, and the performance characteristics of, this test. Physicians should provide pretest counseling to their patients and family members being tested to review the potential benefits, risks, limitations, and alternatives to this testing. Physicians ordering this test are responsible for obtaining informed consent from the persons being tested.

Statement Regarding the TruGenome Undiagnosed Disease Test

- The TruGenome Undiagnosed Disease Test was developed, and its performance characteristics determined, by the Illumina Clinical Services Laboratory. This test has not been cleared or approved by the US Food and Drug Administration (FDA). The laboratory is regulated under Clinical Laboratory Improvement Amendment (CLIA) as qualified to perform high-complexity testing. This test is intended for clinical purposes and should not be regarded as investigational or for research.
- The TruGenome Undiagnosed Disease Test will be performed in the Illumina Clinical Services Laboratory. The laboratory is CLIA-certified and College of American Pathologists (CAP)-accredited.
- The Illumina Clinical Services Laboratory offers several tests in addition to the TruGenome Undiagnosed Disease Test. Review the test descriptions at www.illumina.com/clinical/illumina_clinical_laboratory/trugenome-clinical-sequencing-services.html to make sure that the most appropriate test is ordered.
- Illumina cannot accept samples from New York State.

To submit a sample for sequencing, you will need:

- A fully completed test requisition form (completion of Sections 1-7 is required).
  - Note that providing phenotype information is required for analysis and interpretation. Physicians may submit copies of pertinent clinical notes as a substitute for completion of Section 4.
  - Complete Section 8, Billing Information and Signature, if applicable.
- Properly labeled sample in the collection tube.
  - Instructions are available at www.illumina.com/clinical/illumina_clinical_laboratory/how-to-order.html.
- **FOR FAMILY-BASED ANALYSES, SUBMIT A TEST REQUISITION FORM FOR EACH SAMPLE SUBMITTED FOR TESTING.**

Send the **completed** items listed above to:

Illumina, Inc.
ATTN: Illumina Clinical Services Laboratory
5200 Illumina Way
San Diego, CA 92122

Contact the Illumina Clinical Services Laboratory at 858.736.8080 if you have any questions.

Place Barcode Here

1. Requested Test

For test definition and pricing, visit www.illumina.com/clinical/illumina_clinical_laboratory/trugenome-clinical-sequencing-services.html

- ☐ TruGenome Undiagnosed Disease Test (Patient only) — FT-800-1005
- ☐ TruGenome Undiagnosed Disease Trio Test (Family-based analysis) — FT-800-1006

- ***For family-based analyses, submit a test requisition form for each sample submitted for testing.***
- *Contact the laboratory at GenomicServices@illumina.com for information about pricing for family-based analyses, including familial structures other than the standard trio (eg, duo, quad, quint, etc.)*

2. Physician and Institution Information

Authorized Physician (Print Full Name)	NPI (or License if no NPI) Number
Institution Name	Institution Address (Required for Return of Results)
Physician Office Phone Number	

Physician Email (Required: Notification of return of results and authorization codes to access clinical deliverables will be sent to this email address)

Names and email addresses of other clinicians who may receive delivery notification/copy of results

3. Patient Information

Each person submitting a sample for testing in the Illumina Clinical Services Laboratory is considered a patient. For family-based analyses, complete this section for each family member submitting a sample for testing.

First Name | Middle Initial | Last Name

Date of Birth (MM/DD/YYYY)

Sex: ☐ Male ☐ Female ☐ Unknown

☐ African-American ☐ Ashkenazi Jewish ☐ Asian/Pacific Islander ☐ Caucasian ☐ Hispanic ☐ Middle Eastern ☐ Native American ☐ Other _____

Patient Email (Required: Notification of return of results and authorization codes to access clinical deliverables will be sent to this email address)

Check one of the following boxes to indicate the person being tested with respect to this test requisition form:

- ☐ Proband (affected individual in the family who is the primary individual being tested)
- ☐ Biological mother of the proband
- ☐ Biological father of the proband
- ☐ Full brother of the proband
- ☐ Full sister of the proband
- ☐ Other [describe relationship to the proband specifically (eg, half-sister of the proband)] _____

Name of the Proband: _____

Indicate the affected status of the person being tested with respect to this test requisition form:

☐ Affected ☐ Unaffected ☐ Unknown

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4. Patient Clinical Information The clinical information on this form will be used in the clinical interpretation of the data. Failure to provide clinical information about the patient will result in delay of testing. In addition to completing the phenotype information, submit copies of relevant clinical notes and family history, if necessary.

Reason for referral for testing:

Main clinical features and phenotypes present in the patient under the appropriate category:
Abnormality of:

☐ Head or neck:	
☐ Eye:	
☐ Ear:	
☐ Voice:	
☐ Thoracic cavity:	
☐ Cardiovascular system:	
☐ Breast:	
☐ Respiratory system:	
☐ Limbs:	
☐ Musculature:	
☐ Skeletal system:	
☐ Connective tissue:	
☐ Digestive system:	
☐ Nervous system:	
☐ Genitourinary system:	
☐ Immune system:	
☐ Endocrine system:	
☐ Blood and blood-forming tissues:	
☐ Metabolism/homeostasis:	
☐ Integument:	
☐ Growth abnormality:	
☐ Prenatal development or birth:	
☐ Neoplasm:	
☐ Other:	

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5. Secondary Findings Interpretation

Select one of the two options below (required):

A secondary findings analysis is available for each individual being tested as part of the TruGenome Undiagnosed Disease Test. This analysis includes a targeted screen of variants that meet the current test definition in genes recommended for reporting of secondary findings by the American College of Medical Genetics and Genomics (ACMG). The list of genes included in this analysis are:

BRCA1, BRCA2, TP53, STK11, MLH1, MSH2, MSH6, PMS2, APC, MUTYH, BMPR1A, SMAD4, VHL, MEN1, RET, PTEN, RB1, SDHD, SDHAF2, SDHC, SDHB, TSC1, TSC2, WT1, NF2, COL3A1, FBN1, TGFBR1, TGFBR2, SMAD3, ACTA2, MYH11, MYBPC3, MYH7, TNNT2, TNNI3, TPM1, MYL3, ACTC1, PRKAG2, GLA, MYL2, LMNA, RYR2, PKP2, DSP, DSC2, TMEM43, DSG2, KCNQ1, KCNH2, SCN5A, LDLR, APOB, PCSK9, ATP7B, OTC, RYR1, CACNA1S

☐ **Patient OPTS IN to secondary findings analysis**

☐ **Patient OPTS OUT to secondary findings analysis**

Important points to consider:

- Opting out of secondary findings analysis means that a targeted search for variants in the list of genes recommended by the ACMG for reporting of secondary findings will not be performed.
- Incidental findings (variants classified as pathogenic or likely pathogenic in genes that are unrelated to the patient's primary indication for testing and deemed reportable by the clinical laboratory director) will still be returned, if identified.
- If an individual opts out of the analysis, incidental findings related to ACMG guidelines may still be reported if the finding lies within a large reportable CNV that contains multiple genes, including those on the ACMG list.
- In the case of a family-based analysis (eg, the TruGenome Undiagnosed Disease Trio Test), identification of secondary findings in family members who opt in for the analysis may inform carrier status of other members of the family, even those who choose to opt out of the analysis.

6. Patient Sample Collection Information

Instructions are available at www.illumina.com/clinical/illumina_clinical_laboratory/how-to-order.html

Date of Collection (MM/DD/YYYY)	Sample Type
	☐ Blood (PAXgene or EDTA tube) If other sample type, contact the laboratory at GenomicServices@illumina.com

7. Physician Signature

Please review the Illumina Patient Informed Consent Form with your patient prior to ordering this test.

I certify that (i) the patient (or authorized representative on the patient's behalf) has given his/her informed consent (which includes written informed consent or written authorization when required by law) to have this genetic test performed, (ii) the informed consent obtained from the patient meets the requirements of applicable law and Illumina Patient Informed Consent, and (iii) I am a medical doctor with the proper licensing in my country to order this testing. I agree to provide Illumina, or its designee, any and all information reasonably required for this genetic testing to be performed.

Authorized Physician Signature (required) **Date (MM/DD/YYYY)**

8. Billing Information/Payment

- **NOTE: If you are part of a participating project or existing contract, payment information is not required.**
- The Responsible Party identified below agrees to pay the full price of the test. Illumina will not begin processing the sample until payment arrangements have been made. Testing will be delayed if payment arrangements have not been made.
- Illumina does not bill health insurers or institutional billing departments. If reimbursement is necessary or desired, the Responsible Party will make his/her own arrangement to receive reimbursement.

Select the most appropriate billing option (this is the Responsible Party)

☐ Facility/Contract Billing ☐ Facility/Physician billing must be prearranged	☐ Patient/Legal Guardian/Other
Facility Name	Name (Name of Responsible Party)
Address	Billing Address
City / State / Zip	City / State / Zip
Purchase Order No. / Contact Person	Phone / Email
Phone / Email	

I agree that I am financially responsible for the full amount of the test price.

Responsible Party Acknowledgement and Signature **Date (MM/DD/YYYY)**

Select your payment option Bill my credit card for 100% prepayment Illumina can only accept credit cards from the US and Canada.	Cardholder Name Card Number	
Card Type ☐ Visa ☐ Mastercard ☐ American Express	Exp Date (MM/YYYY)	CVV

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