

Illumina Laboratory Services

TruGenome™ Undiagnosed Disease Test Requisition Form

The TruGenome Undiagnosed Disease Test is intended to provide information to physicians to aid in the diagnosis of highly penetrant genetic diseases. The analysis and interpretation are designed to detect and report on single nucleotide variants (SNVs), small insertion/deletion events, copy number variants (CNVs), homozygous loss of *SMN1*, mitochondrial SNVs, and short tandem repeat (STR) expansions occurring at sites with associations to genetic disease. Analysis may be family-based or performed on only the proband. Family-based analyses may be composed of a trio (the proband and their biological parents), a duo (parent and child), or other family structures. Variant characteristics, clinical presentation information, plausible inheritance patterns (based on the reported family history), peer-reviewed literature, and information from publicly available data sets are used to contextualize variants identified during analysis.

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 Illumina Laboratory Services. 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 at Illumina Laboratory Services. The laboratory is CLIA-certified and College of American Pathologists (CAP)-accredited.
- Illumina Laboratory Services 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 testing, please provide:

Test Requisition Form (TRF)

- Completed and signed test requisition form. Each person who submits a sample for testing at Illumina Laboratory Services is considered a patient. For family-based analysis, complete a new TRF for each family member.
- Clinical phenotype (TRF, section 4). Only *required* for affected proband and affected family members. Section 4 may be supplemented with copies of clinical notes.
- Project Name (*if applicable*), or billing information (*if applicable*).

Patient Sample

- For information about ordering clinical whole genome sequencing or obtaining whole blood collection kits: https://www.illumina.com/clinical/illumina_clinical_laboratory/how-to-order.html

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

Illumina, Inc.
ATTN: ILS - Illumina Laboratory Services
5200 Illumina Way, Building 2, Dock 2, San Diego, CA 92122

For questions, please contact Illumina Laboratory Services at (858) 736-8080, or (855) 266-6563 (toll free), or submit a secure ticket at clinicallabservicesupport.illumina.com



1. Requested Test All fields below are required to be completed.

TruGenome Undiagnosed Disease Test (Patient only)
 TruGenome Undiagnosed Disease Test (Family-based analysis)

- *For family-based analysis, submit a test requisition form for each patient submitted for testing.*

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 to access clinical deliverables will be sent to this email address)	

Names and email addresses of other health care providers who may receive delivery notification/copy of results

First	Last	Email Address
First	Last	Email Address

3. Patient Information Each person from whom a sample is taken and submitted for testing at Illumina Laboratory Services is considered a patient. For family-based analysis, complete a separate TRF for each family member.

First	Middle Initial	Last		
Date of Birth (DD/MON/YYYY eg, 28/Feb/2017)	Biological Sex Male Female Unknown			
Ethnicity (Optional)	African Ashkenazi Jewish	Latino East Asian	European/Caucasian Middle Eastern	Asian Pacific Islander Other _____

For the person being tested with respect to this test requisition form, select the appropriate relationship to the proband below.

Name of proband: _____

Number of family members being submitted for testing:

Relationship to Proband. Select one row only for the patient named on this requisition form.	Affected Status		
	Affected	Unaffected	Unknown
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, maternal half-sister of the proband)]			

Enter Project Name: _____

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:	

5. Secondary and Incidental 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, TGFB1, TGFB2, 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** for secondary findings analysis

Patient **OPTS OUT** of 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.

Incidental findings (It is not possible to opt out of incidental findings.)

Incidental findings are defined as clinically significant variants found in genes associated with phenotypes that are unrelated to the patient's primary indication for testing. Unlike Secondary Findings, these variants are not actively sought, but may be noted during analysis. Variants with the potential to influence medical management, that meet the following criteria, and are deemed reportable by the clinical laboratory director will be returned.

- The evidence supporting the gene-disease relationship must be classified "Strong" or "Definitive" per current laboratory protocol.
- The variant(s) must reach a classification of likely pathogenic or pathogenic and occur in the correct allelic state (or zygosity) for the disease.
- Must influence medical management per the discretion of the laboratory director.
- Short tandem repeat (STR) expansions are not returned as incidental findings.

6. Patient Sample Collection Information

Date of Collection (DD/MON/YYYY eg, 28/Feb/2017)	Sample Type Blood (PAXgene or EDTA tube) DNA <i>Extracted DNA has a higher known failure rate than whole blood. Please contact the laboratory for more information. DNA must be collected from an authorized CLIA laboratory.</i>
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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 (DD/MON/YYYY eg, 28/Feb/2017)

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 (DD/MON/YYYY eg, 28/Feb/2017)

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 eg, 28/Feb/2017)	CVV