TruGenome™ Undiagnosed Disease Test

Who should order the TruGenome Undiagnosed Disease Test?
The TruGenome Undiagnosed Disease Test is intended to be ordered by physicians for patients affected by a suspected genetic disease of single-gene etiology (Mendelian) when previous genetic testing has not resulted in a diagnosis and/or an effective treatment plan. Examples include mitochondrial disorders, inherited cardiomyopathies, and multiple-symptom conditions (e.g., seizure disorders, congenital defects, dysmorphic features, neurodegenerative conditions).

Why should I order a whole-genome vs. a whole-exome test?
Whole-genome sequencing provides the most comprehensive coverage of known disease-causing mutations and enables the most thorough analysis of the human genetic code currently available. Our whole-genome sequencing test also provides a platform for future analyses and discovery as the scientific literature expands.

What is interpreted by the TruGenome Undiagnosed Disease Test?
A case manager from the Illumina Clinical Services Laboratory team of medical geneticists and genetic counselors will define the parameters of the test based on the patient’s medical history. As the ordering physician, you will have the opportunity to contribute and review. The interpretation will focus on variants in a defined list of genes based on the phenotype. If parental samples will be sequenced as well, inheritance patterns will be used to identify genes with known autosomal recessive or de novo variants. Additionally, interpretation is performed on variants located in genes recommended by the American College of Medical Genetics (ACMG) and a set of alleles that have established associations to drug metabolism, according to the Clinical Pharmacogenomics Implementation Consortium (CPIC) and U.S. Food and Drug Administration (FDA) guidelines. These interpretations are provided in separate reports. A list of alleles associated with specific drug responses are available on the TruGenome Clinical Sequencing Services page.

What will I receive with the TruGenome Undiagnosed Disease Test?
You will receive a clinical report that includes an interpretation of genomic findings, details on clinically significant findings and the associated conditions, and references from which clinical associations were drawn. Additionally, a separate clinical report is provided that includes interpretation of variants associated with drug response, information about the drug, and the predicted implications of the drug.

Do you support testing of family members?
Yes, trio testing is available for the TruGenome Undiagnosed Disease Test. Trio testing includes testing of the patient and both parents. Testing of family members beyond a trio will be considered on a case-by-case basis. Contact the Illumina Clinical Services Laboratory by email at everygenome@illumina.com or by phone at 858.736.8080 for more information.

Why do you recommend trio testing for the TruGenome Undiagnosed Disease Test?
Trio testing can confirm whether observed variants are new in the patient or inherited from one or both parents. This information can be used to expand search parameters beyond genes associated only with particular diseases to include any that show de novo or autosomal recessive patterns of inheritance. Trio testing is expected to increase the likelihood of finding the causative variant or variants.

What if the patient’s parents are not available to participate?
Though having the parents’ genetic information enables faster and often more effective analysis, the Illumina Clinical Services Laboratory can perform the TruGenome Undiagnosed Disease Test on the patient only. We will work with you to design a list of priority genes based on the patient’s symptoms. Genetic experts in the Illumina Clinical Services Laboratory will evaluate all variants found within those genes and interpret them according to the guidelines discussed in this document.
What are the chances you will find something with the TruGenome Undiagnosed Disease Test?
The TruGenome Undiagnosed Disease Test is most likely to find something meaningful when the condition is purely genetic in nature. The likelihood of finding the causative variant or variants varies according to the details of each case, including phenotype, previous testing, inheritance pattern, and other factors. Contact the Illumina Clinical Services Laboratory at 858.736.8080 or email everygenome@illumina.com for more information.

Will I receive updates to my clinical report as new variant-to-disease associations are discovered?
The Illumina Clinical Services Laboratory will provide updates to the original clinical report in the following situations:

1. If, through our standard process of interpreting variations within a patient's DNA, we change a classification of a variant based on new information so that it becomes clinically reportable, or was thought to be clinically reportable but now can be ruled out. Example: data from a new clinical study result in a variant classification change from variant of unknown significance to likely pathogenic. In this example, all previous reports generated with that variant will be updated and a new report will be sent to the original ordering physician.

2. The ordering physician requests to have a patient's genome reinterpreted. Requests for reinterpretation can be made at any time; however, they are limited to one time per year. An additional fee is required for this request.

3. A new version of the test is available containing new features or enhancements. An additional fee is required for this update.