Invitae Boosted Exome Informed Consent

FM146-3

DESCRIPTION OF INFORMED CONSENT PROCESS

Whole-exome sequencing can be used to help diagnose one or more hereditary conditions. The risks and the benefits of this test are explained in this consent form so that you and your healthcare professional can make an informed decision about whether or not to order the test. If you are thinking about having this test, we recommend that you have genetic counseling with a geneticist, genetic counselor, or other licensed healthcare provider, who can answer your questions and provide information about alternatives.

TEST DESCRIPTION

The Invitae Boosted Exome is a complex test that looks at a large number of genes simultaneously and is designed to identify genetic changes in your DNA that may cause disease or are important to your health in other ways. Genetic disorders are caused by changes in the DNA sequence that affect the ability of a gene to function. Most changes that cause disease affect the portions of our genes called "exons." The exons of a gene contain the genetic information your body uses to make proteins, which are molecules that carry out all the essential functions in the body. The DNA within the exons of all the genes is collectively called "the exome" and "whole-exome sequencing" is a test that looks for disease-causing changes in any gene we think could be related to your underlying clinical problem that is the reason you are having this test.

LIMITATIONS OF TESTING

I understand that:

1. Invitae will perform the Invitae Boosted Exome on my (or my child's) sample. Samples from other family members may be studied to help interpret the results.
2. This test may not be able to detect all types of DNA changes. Exome sequencing has technical limitations that may prevent Invitae from detecting certain sequence changes in the DNA.
3. Due to limitations inherent in the technology used in exome sequencing, we may not see every part of every gene we want to analyze. If any such gaps occur in your results, Invitae will provide this information in the coverage table included with your report.
4. The process of exome sequencing is not 100% error free. Possible sources of error can include: trace contamination, rare technical errors in the laboratory, DNA changes that compromise data analysis, inconsistent scientific classification systems, inaccurate reporting of family relationships, or inaccurate or incomplete description of clinical findings.
5. The analysis of variants in your exome is limited to a subset of all the variants in your exome; additional variants may exist and may contribute to or cause disease but not be identified by this analysis.
6. The field is accumulating new information at a rapid rate, therefore over time, variants that today have no association with disease may ultimately prove important for your health. Please discuss with your healthcare provider whether re-evaluation of your variants is appropriate, especially if anything about your clinical condition has changed.
7. When the test identifies a genetic change that leads to a diagnosis, there may not always be treatment options available for the identified genetic disease.
8. When the test leads to a diagnosis, there is no guarantee that the severity and clinical course of the genetic condition can be accurately predicted.
9. Although this test will analyze and detect changes in the nuclear genes associated with mitochondrial function, it does not sequence the DNA within mitochrondria. As a result, sequence changes, deletions and duplications in mitochondrial DNA are not evaluated with this test.

POSSIBLE TESTING OUTCOMES

I understand that:

1. The results of the Invitae Boosted Exome could be:
   A. Positive, and may:
      i. identify a likely diagnosis of a genetic condition.
      ii. identify a predisposition or an increased risk for developing a genetic disease in the future.
      iii. have implications for other family members.
   B. Negative, and may:
      i. reduce but not eliminate the possibility that my condition has a genetic basis.
      ii. reduce but not eliminate my predisposition or risk for developing a genetic disease in the future.
      iii. be uninformative.
      iv. not remove the need for additional testing.
   C. Of uncertain significance and may:
      i. result in the recommendation of testing additional family members.
      ii. remain uncertain for the foreseeable future.
      iii. be resolved over time if additional information becomes available regarding the identified sequence variant. My healthcare professional will be notified of clinically significant changes to the classification of variants that relate to my (or my child's) result. I understand that it is my responsibility to inform my healthcare professional if my contact information changes.
      iv. lead to the recommendation of additional tests to clarify the findings, such as a muscle or skin biopsy or imaging (MRI/CT scan) to obtain more information about the significance of the genetic change.

INVITAE BOOSTED EXOME RESULT REPORTING

I understand that:

1. The Invitae Boosted Exome is performed to identify a potential genetic basis for the condition affecting me (or my child). We will report results that may help answer that question.
2. Our ability to interpret the large amount of genetic information generated by whole-exome sequencing greatly benefits from our ability to review the submitted clinical history, family history, and genetic information of the submitted family members, and currently available genetic information in medical literature and databases. Submission of a detailed clinical description of the affected family members, their relevant medical records, and a complete pedigree is therefore essential.
3. During this focused evaluation of my (or my child's) exome, variants may be identified that are not directly obvious or relevant to my (or my child's) presenting symptoms, but still considered to be of clinical importance. When a disease-causing or likely disease-causing variant is identified outside of the indication for testing, this is considered an "incidental finding". Incidental findings that have significant medical implications and management options for the patient will be reported with an appropriate explanation, but incidental findings associated with adult-onset disorders for which there are no currently available interventions will not be reported. This policy concerning returning incidental findings is distinct from the optional secondary findings discussed below.
4. Invitae's clinical reports are released only to the certified healthcare professional(s) listed on the test order form. Clinical reports are confidential and will only be released to other medical professionals with my explicit written consent. It has been explained to me that my (or my child's) clinical report will be available for me to view or download from the Invitae website (www.invitae.com/patients) after it has been released by my healthcare professional(s). Alternatively, my (or my child's) clinical report can be made immediately available upon completion of the test with the prior approval of my healthcare professional, as indicated through the test ordering process.

FAMILY RELATIONSHIPS

I understand that:

1. Results from the Invitae test are analyzed with the assumption that correct information on family relationships has been provided. For example, this test may detect misattributed paternity, revealing that the presumed father of the patient is not the true biological father. It may be necessary to report these findings to the individual who requested testing.

PRIVACY

I understand that:

1. It is my responsibility to consider the possible impact of my (or my child's) test results as they relate to insurance rates and obtaining disability or life insurance and employment. The Genetic Information Non-discrimination Act (GINA), a federal law, provides some protections against genetic discrimination. For information on GINA, visit www.genome.gov/10002328
2. My (or my child's) data and personal information will be stored and protected in strict confidence complying with regulatory requirements (e.g., HIPAA and equivalent protections), and acknowledge that I have read and understand Invitae's Privacy Policy and Notice of Privacy Practices (www.invitae.com/privacy). My (or my child's) individually identifiable health information (i.e., "Protected Health Information" under HIPAA) will NOT be used in FOR-PROFIT research without my additional, explicit consent.

DATA/RESULTS RETENTION

I understand that:

1. In accordance with CLIA, CAP, and California guidelines, the genetic data obtained from the Invitae Boosted Exome are stored for a minimum of seven years.

DNA SAMPLE STORAGE

New York State residents only: I understand that:

1. My (or my child's) DNA sample can be retained for greater than 60 days after the completion of testing. _____ INITIAL HERE

SECONDARY FINDINGS

There are genetic conditions that are considered "actionable" because they are medically treatable or avoidable. Professional organizations, including the American College of Medical Genetics, have recommended that while sequencing an exome, an additional evaluation to identify any disease-causing changes in a group of medically actionable genes be offered to all patients and relatives who are having their exomes sequenced, even if it is not related to the condition for which the exome test was ordered. These conditions include some forms of hereditary cancer, cardiac conditions, and other medically important conditions. Because changes in these genes represent an additional analysis beyond what is being performed for the primary indication for testing, it is your decision if you would like to know this information or if you would prefer to only learn about genetic changes related to the primary test indication. All individuals who choose to receive secondary findings will receive a separate report with the results. The decision to receive or not receive these secondary findings should be made with your clinician at the time the exome order is placed.

For more information regarding the ACMG recommendations, please see:
www.nature.com/gim/journal/vaop/current/pdf/gim2016190a.pdf

BY SIGNING BELOW, I ATTEST THAT

I have read and understand the information provided on this form and have had an opportunity to have any questions answered by my healthcare provider.

Patient signature	Date
Patient name (please print)	Email address
Signature of parent/guardian, if patient is a minor	Date
Parent's/guardian's name (please print)	Email address

HEALTHCARE PROVIDER STATEMENT

By signing below, I attest that I am the referring physician or authorized healthcare professional. I have explained the purpose of test described above. The patient has had the opportunity to ask questions regarding this test and/or seek genetic counseling. The patient has voluntarily decided to have this test performed by Invitae.

Healthcare provider signature	Date

