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 health care professional or genetic counselor 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 health care provider, who can answer your questions and provide information about alternatives.

TEST DESCRIPTION

The Invitae Boosted Exome is a complex test that is designed to identify genetic changes in 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. These changes can be as small as a single base pair or may involve larger losses or gains of genetic information. The majority of changes that we currently understand to be disease-related 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 process that looks for disease-causing changes in the exons of nearly all genes. Although this test sequences the entire exome, the analysis is focused on determining which DNA sequence changes are related to the underlying clinical symptoms of the patient.

LIMITATIONS OF TESTING

I understand that:

1. Invitae will perform the Invitae Boosted Exome on my (or my child's) sample. Additional family member samples may be used to help interpret the results.
2. This test may not be able to detect all types of DNA changes. Whole exome sequencing has technical limitations that may prevent Invitae from detecting certain sequence changes in the DNA due to poor quality of the DNA specimen, inherent DNA sequence properties, or other limitations.
3. Due to innate limitations of the technology used in whole exome sequencing, gaps in sequence coverage can rarely occur in genes of interest. If there are any gaps in your results, Invitae will inform you.
4. Possible sources of error can include: trace contamination, rare technical errors in the laboratory, rare DNA changes that compromise data analysis, inconsistent scientific classification systems, inaccurate reporting of family relationships or inaccurate clinical diagnosis information.
5. 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.
6. 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.
7. Although this test will analyze and detect changes in the nuclear genes associated with mitochondrial function, it does not sequence the mitochondrial genome. 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.. reveal the diagnosis of a genetic condition.
        ii. reveal 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 health care 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 health care 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, imaging (MRI/CT scan), or a functional study of the genetic change to obtain more information.

INVITAE BOOSTED EXOME RESULT REPORTING

I understand that:

1. A single report will be issued for me (or my child), regardless of how many additional family member samples are submitted. The report may include genetic information about other family members. Family members who have submitted samples may not wish to know this information, and the possibility of finding out this information needs to be discussed in advance of carrying out the testing.
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 essential.
3. DNA changes that we believe to be associated with a disease are included in the report and may be confirmed by a second alternative test method.
4. The Invitae Boosted Exome is performed to determine if there is a genetic basis for the condition affecting me (or my child). We will report results that may help answer that question.
5. During this focused evaluation of my (or my child's) exome, variants may be identified that potentially indicate a result of clinical concern that is not directly relevant to my (or my child's) presenting symptoms. When a disease-causing or likely disease-causing variant is identified outside of the indication for testing, this is considered an incidental finding. We will not report incidental findings associated with adult-onset disorders for which there are no interventions currently available. Other variants that have significant medical implications for the patient will be reported with an appropriate explanation.
6. 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 on the test order form.

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. This test may detect misattributed paternity, for example 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

I understand that:

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

SECONDARY FINDINGS

Professional organizations, including the American College of Medical Genetics, have determined that when disease-causing changes are discovered in a gene known to be associated with a significant medical condition, this information should be disclosed by the laboratory who discovered the genetic change, even if it is not related to the condition for which the test was ordered. These conditions include some forms of hereditary cancer, cardiac conditions and late onset adult diseases. Because changes in these genes can affect medical treatment, 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 opt in to receiving secondary findings will receive a separate report with the results.

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

I opt in to receiving secondary findings:

○	**Patient name**	**Signature**
○	**Parent name**	**Signature**
○	**Parent name**	**Signature**

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

