BIOARRAY
Diagnóstico Genético

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INFORMED CONSENT FOR EXOME SEQUENCING USING NEXT GENERATION SEQUENCING

Purpose

Exome sequencing consists of sequencing the portion of the genome with coding genes. This region comprises approximately 1% of the entire genome, and it is estimated to contain 85% of all mutations responsible for pathologies.

The purpose of this analysis is the identification of mutations causing the pathology that the patient presents at the time of the analysis.

Characteristics of the analysis

When is the analysis performed?

The analysis can be performed at any time, provided that there is a suspicion of genetic pathology.

How is it performed?

The exome sequencing requires obtaining DNA from the patient, usually from peripheral blood (5mL in EDTA tube). After this, the regions to sequence are captured or amplified, followed by their sequencing by Next Generation Sequencing. By comparison with a reference genome, a list of all the detected alterations is obtained. These variants are analysed by multiple bioinformatics tools and compared with different data bases in order to identify all the alterations that are potentially causative of genetic pathology. Finally, among all of them, the purpose is identifying the one that is related with the phenotype of the patient.

The Next Generation Sequencing is a technique with a relatively high rate of false positives, so any variant reported in the results will be tested by a second technique, such as capillary sequencing.

Which members of my family will be analysed?

Determining what people of my family will be analysed depends on the family structure and who is affected by the pathology. In the majority of the cases, the affected patient and their progenitors will be analysed, although for progenitors only the mutations which were found in the patient, considered to have pathology implications, will be analysed. In other cases, children' siblings or distant family members could be included in the study. The decision about which people to analyse will be made in consultation with your doctor, with the aim of get the higher possibility to find the genetic pathology cause. In the case of trio studios, one report will be issued.

Do I need genetic counseling?

Due to the complexity of the analysis and the results that could be obtained, it is highly recommendable to receive genetic counseling before and after the analysis.

Limitations

Will all the genes be completely analysed?

The exome sequencing aims at analysing most of the more than 20,000 genes in the human genome. However, for technical and biological reasons this cannot be possible. Nowadays, information is obtained from more than 90% of the exome, but some parts of the exome may be excluded from the analysis. It cannot be completely excluded that there are no mutations in these regions that are the cause of pathology. The report shall reflect the coverage of the exome obtained.

Do I need to do additional tests?

Next generation sequencing is not able to accurately detect trinucleotide repeat expansions, such as the causative for Fragile-X syndrome, Huntington's disease or myotonic dystrophy. If any of these pathologies is suspected, the relevant analysis should be performed.

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Also, exome sequencing capability to detect deletions and duplications is limited. For this reason, sometimes it is recommendable to perform the exome sequencing and a CGH microarray.

Finally, sometimes the complete sequencing of a gene which has obtained low coverage may also be recommended.

Results report

What will I be informed of?

With the exome analysis a great number of alterations are detected. Some of them could be classified as pathological but lying on genes that do not have relation with the pathology for which the test was indicated and for which symptoms have not yet been developed (e. g. cancer, adult-onset neuromuscular disease, etc.). For some of these conditions you have the option of not being informed.

Additionally, alterations for which there is not enough scientific evidence to determine the pathology implication could be found. These alterations will be reviewed periodically.

The report will include all pathological alterations, likely pathological or of unknown significance occurring in genes which could explain the patient's phenotype.

If you wish, you can also be informed of the following (check a box with your option):

1. **Carrier status of autosomal recessive pathologies**. A recessive pathology is one that requires two mutations in the same gene to cause the disease (a heredity alteration of each progenitor). A person with a single mutation in this gene would be an asymptomatic carrier of the disease, but this information can be important for reproductive counseling. An example would be cystic fibrosis. It should be noted that in case of finding an alteration in a recessive gene but that it is related to the phenotype of the patient, this would be reported to determine with your doctor if additional tests are needed.
   - ☐ YES, I want to be informed of the alterations for which I am carrier.
   - ☐ NO, I do not want to be informed of the alterations for which I am carrier.
2. **Pharmacogenetic variants**. These alterations do not directly cause pathology, but may be related to how your body metabolizes certain medications, such as chemotherapy, antipyretics, antidepressants, etc. These changes may not be important at the time of analysis, but they can help you to know how this medication would work if you need it.
   - ☐ YES, I want to be informed of the alterations related with pharmacogenetics.
   - ☐ NO, I do not want to be informed of the alterations related with pharmacogenetics.
3. **Clinically actionable genes.** There are mutations that, without being related to the patient's phenotype, affect genes that cause pathology considered clinically actionable because they have a clear significance for your health or your family's. For them there is treatment or preventive actions that can be performed to reduce the risk of suffering a pathology. The American College of Medical Genetics has published a guide with a list of genes that fall into this category. The list of genes can be consulted on their website (www.acmg.net).
   - ☐ YES, I want to be informed of the alterations found in the genes recommended by the ACMG.
   - ☐ NO, I do not want to be informed of the alterations found in the genes recommended by the ACMG.
4. Adult-onset findings, unrelated to the phenotype of the patient, for which there is no defined clinical action (ONLY IN THE CASE OF ADULTS). These are alterations that cause an adult-onset pathology for which there is no medical action to take. An example would be Alzheimer's disease.
   - ☐ YES, I want to be informed of alterations in genes causing diseases for which no action can be taken.
   - ☐ NO, I do not want to be informed of alterations in genes causing diseases for which no action can be taken.

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What does a negative result mean?

A negative result does not completely exclude that there is a genetic cause behind the patient's phenotype. The reason is that these mutations may lie in uncovered regions, affect genes whose involvement in the phenotype is not known at the time of the study, or they may not be classified as pathological or probably pathological at that time.

Will my results be reviewed periodically?

We periodically review old cases based on the new scientific evidence that has emerged. If as a result of this, new information related to the patient's phenotype is discovered, we would like to issue an updated report reflecting it. This does not mean a complete review of all your data.

- ☐ YES, I want to be informed if new information appears that substantially affects the result of this test.
- ☐ NO, I don't want to be informed if new information appears that substantially affects the result of this test.

Turnaround time for report

Results usually take 90 days. It is advisable that applicants receive genetic counseling before and after collection of the sample. If you wish, a copy of the report can be sent to a doctor of your choice.

Revoking consent

This consent and the authorization to carry out the test can be revoked at any time by both parties.

Contact details

You can contact Bioarray laboratory at any time to receive more information by writing to the email address info@bioarray.es or by calling +34 966 261 268.

By signing this document, the applicant certifies that he/she has read and understood the information, has received the requested explanations, has understood them and is satisfied with them.

DATA PROTECTION

In accordance with data protection regulations, we provide you with the following treatment information:

Responsible party: BIOARRAY, S.L.

Rights that assist you: access, rectification, portability, deletion, limitation and opposition.

More treatment information: http://bioarray.es/en/

BIOARRAY S.L. is responsible for the processing of personal data of the Interested Party and informs that these data will be treated in accordance with the provisions of Regulation (EU) 2016/679 of April 27 (GDPR) and Organic Law 3/2018 of 5 December (LOPDGDD), so the following treatment information is provided:

Purposes and legitimation of the treatment

By the legitimate interest of the responsible party (GDPR, Article 6.1.f): maintaining a professional relationship, sending communications, analysing data and publishing scientific and informative articles.

By consent of the interested party (GDPR, article 6.1.a): sending communications, analysing data and publishing scientific and informative articles.

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Data retention criteria: will be kept for no longer than necessary to maintain the end of the treatment and when it is no longer necessary for this purpose, they will be eliminated with adequate security measures to guarantee the pseudonymization of the data or the total destruction thereof.

Communication of the data: the data will not be communicated to third parties, except legal obligation.

I give my consent for the storage and preservation of the samples for possible use in the research on genetic disease and I authorize the transfer of the results of the clinical studies in an anonymous form for the study and pharmacological development, the sending of communications, data analysis and publication of scientific and informative articles:

- ☐ Yes
- ☐ No

Please sign two copies of this consent. Return one of the signed copies to the laboratory along with the sample and the form.

Signature of patient / parent:

Name: _____

Date: _____

Signature of the Doctor:

Name: _____

Date: _____

Signature of the parents (only for Exome Trio test):

Name: _____

Date: _____

Name: _____

Date: _____