NIMGenetics
New Integrated Medical Genetics

ExoNIM®

INFORMED CONSENT

CODE.

To be filled in by the lab

Name and surname:	Date of birth:
Reason for consultation:	
Full address:	Identification/passport number:
Patient E-mail address:	Phone number:
Name of consultant:	E-mail:
Clinic/Hospital/Laboratory	Phone number:

Data obtained from this study are confidential and will be managed with the strictest confidentiality requirements.

1. I have been informed by the consultant regarding the indication, purpose, characteristics and potential risks of the exome sequencing study **(ExoNIM®)** to be performed on a sample from me or my child. I have also read the information provided about the test and my questions have been satisfactorily answered.

2. I understand the purpose and the limitations of the study, in particular that the test cannot detect mutations in intronic regions, mutations caused by insertion/deletion of 10 or more nucleotides, or the presence of unfrequent variants in the hybridization region of the oligonucleotides used.

3. I understand that a new blood sample may be required to repeat the test or to carry out additional tests.

4. I understand that the clinical interpretations of the results will be based on the scientific literature currently available, clinical data provided, and type of test requested. New medical advances and discoveries could change the interpretation of the results.

5. I understand that the test can reveal genetic information from the patient or family relatives that is unrelated to the medical concern for which the study was initially requested. I agree that the identification of pathogenic or putative pathogenic variants affecting any one of the 56 genes selected by the American College of Medical Genetics (ACMG, see Table 1 in the documentation attached) will be reported as incidental findings.

If you **DO NOT WISH** to receive this information, please indicate by placing your initials here: _____
By signing this document, I give my consent for the application of the whole exome sequencing test.

Date:

Patient/legal guardian signature:

Consultant signature:

If you are the parent or legal guardian (full name and identification/passport number):

AUTHORIZATION TO USE THE RESULTS

The results obtained can contribute to increase the analytical capacity of the test and the current knowledge state, which would benefit new studies. I therefore give my consent for my clinical information and results to be used by NIMGenetics in scientific publications, quality studies or databases in the field of healthcare. NIMGenetics will guarantee the confidentiality of the information. This authorization can be revoked by a written notification to info@nimgenetics.com.

If you **DO NOT WISH** the data obtained to be used in this way, please indicate by placing your initials here: _____

NIMGenetics S.L. Parque Científico de Madrid. C/Faraday nº 7, Campus Cantoblanco. 28049 Madrid. CIF B-85332138

Anexo 03. PG05-12. V01 21/01/2016

ExoNIM® INFORMATION

The Exome Sequencing test is carried out on extracted and purified deoxyribonucleic acid (DNA) from the sample received. This test is used to identify the genetic causes of a disease or disability in an individual. Genes contain hereditary information, and it is estimated that the cells in our body contain around 19 thousand genes. The combination of all genes of an individual is known as the genome. Exons are the regions of genes containing the information essential to produce proteins, which are fundamental elements for the normal development of a living organism. The word "exome" refers to the entire number of exons in a genome. The study simultaneously analyzes the exons of 93-97% of the genes, and compares them with healthy control samples in order to identify DNA changes associated with the medical condition of the patient. In other words, the test is aimed at identifying the DNA change/s (known as mutations) implicated in the development of the patient´s or child´s medical condition.

In addition, those changes in the DNA sequence with no clear clinical significance (known as variants of uncertain significance), which are not considered polymorphic changes (i.e., those present in the healthy population), will also be identified. In these cases, predictive bioinformatics studies will be performed in order to estimate the possible consequences, at the protein level, of the variants of uncertain significance.

A new sample may be required if the sample extracted is not optimum from a quantitative or qualitative point of view, or if additional genetic tests are required due to diagnosis complexity.

Unused samples will be stored for a maximum of 5 years, to be available in those cases where a study needs to be repeated to confirm the diagnosis. The material obtained from the DNA sample, known as the genomic library, will be destroyed after one year (Act 14/2007).

Test limitations

Certain characteristics of some exome regions make it impossible to accurately determine changes in the sequence. Thus, in exceptional cases the presence of non-frequent variants in the DNA sequence could hinder or impede the amplification of a sufficient number of sequences, making it difficult to obtain reliable results for this specific genome region. Furthermore, homopolymeric regions of 9 nucleotides or more, or regions with high complexity, cannot be accurately detected using this methodology.

This technology does not allow the identification of some types of mutations, called large deletions or rearrangements. Likewise, it cannot detect variants in non-coding DNA, mitochondrial DNA, pseudogenes, trinucleotide repeat expansions or epigenetic alterations.

During the analysis of the results, it will not be possible to assign a significant value to variants sequenced to a depth of less than 10×, which means that those variants that do not reach this value will be excluded or validated by Sanger sequencing. Also, in the trio analysis (mother / father/ child) or in the targeted exomes, the filtering process applied prevents the detection of some mutations associated with a carrier state of the patient or the parents. Germline or tissue-specific mosaicism can lead to inconclusive results.

Finally, you must be aware that some disease-causing mutations do not occur in the exons, and accordingly this test will not detect those mutations. In such cases, your doctor or genetic counselor may request additional diagnostic studies.

Results

Clinical interpretation of the results will be based on the scientific information currently available, the clinical date provided and the type of study requested. Interpretation of your results may change as medical knowledge advances and new discoveries take place. It is possible that, in the future, a new interpretation of your results may lead to new information on your medical condition. This new interpretation will have to be requested by your doctor and may imply extra costs. However, this may not be possible, and another test may be necessary which will require the new collection of samples.

This test can reveal genetic information from the patient or family relatives that is unrelated to the medical concern for which the study was initially requested. Knowing this information may cause anxiety or psychological stress. It may reveal a genetic risk to develop a disease later in life. The findings could be associated with:

- Diseases that are different from those for which the medical reason for the Exome Sequencing test was requested.
- Disorders that have no current treatment.
- Non-paternity or maternity (the father or the mother is not the biological parent) or with another unexpected familial relationship.

Following the guidelines from the American College of Medical Genetics, the report will only inform, if detected during the analysis, about those variants involving selected genes associated with medical conditions that can be validated by other diagnostic methods or require clinical intervention (Table 1). Similarly, we will NOT REPORT mutations related with genetic diseases that might or might not develop in the future, and of which the patient currently does not show any symptomatology related to them (ie. risk of cancer or Alzheimer´s disease).

Table 1: Genes selected by the ACMG (Adapted from Robert C. Green, et al (2013), Genetics in Medicine 15(7): pp 565-574).

ACTA2	*FBN1*	***MUTYH*	*PRKAG2*	*SDHD*	*TSC1*
ACTC1	**GLA*	*MYBPC3*	*PTEN*	*SMAD3*	*TSC2*
APC	*KCNH2*	*MYH11*	*RB1*	*STK11*	*VHL*
BRCA1	*KCNQ1*	*MYH7*	*RET*	*TGFBR1*	*WT1*
BRCA2	*LDLR*	*MYL2*	*RYR1*	*TGFBR2*	*APOB*
CACNA1S	*LMNA*	*MYL3*	*RYR2*	*TMEM43*	*PCSK9*
COL3A1	*MEN1*	*MYLK*	*SCN5A*	*TNNI3*	
DSC2	*MLH1*	*NF2*	*SDHAF2*	*TNNT2*	
DSG2	*MSH2*	*PKP2*	*SDHB*	*TP53*	
DSP	*MSH6*	*PMS2*	*SDHC*	*TPM1*	

All the genes selected, except GLA and MUTYH, show an autosomal dominant or semi-dominant inheritance pattern
**X-linked inheritance pattern*
***Autosomal recessive inheritance pattern*

The final report will be available within 90 working days from the date the laboratory confirms the quality of the DNA. In exceptional circumstances, this period can be extended due to methodological reasons. The report of the study will be sent to the requesting Doctor. In some cases, your Doctor will recommend genetic counseling.

Data Protection and Confidentiality Policy

In compliance with Law 41/2002 on the autonomy of patients' rights and obligations regarding clinical information and documentation and in compliance with the Organic Law 15/1999 of December 13, on Personal Data Protection, the petitioner must have the informed consent signed by the patient to carry out the requested diagnostic tests and for the purpose of its data processing. To do so, we must inform you of the obligation to inform the patients that all the data collected in the present document will be included in an automated and confidential file, duly registered with the Spanish Data Protection Agency, under NIMGenetics, S.L. ownership, for the purpose of managing the diagnostic study indicated therein and of which the patient may, at any time, exercise her rights of access, rectification, cancellation and opposition at the following address: NIMGENETICS, S.L.

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