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CGT ONE Test Requisition Form

The fields marked with * are required in order to perform the test requested

*ANALYSIS REQUESTED

*Name of condition:_____

*Name of gene(s):_____

CLINICIAN INFORMATION

*Clinic:_____

*Referring doctor:_____

Contact person: _____

*Email address for delivery of results:_____

Address: _____

City: _____ Province: _____ Postcode: _____

PATIENT AND SAMPLE DETAILS

*Name:_____*Surname(s):_____

*Date of birth:_____

MRN/Unique Patient ID (UPI):_____

*Date of sample collection:_____

*Sex: ☐ Male ☐ Female

Ethnic Group: ☐ Caucasian ; ☐ East Asian; ☐ South Asian; ☐ Arab

☐ Ashkenazi; ☐ Hispanic; ☐ Romani; ☐ Afro-_____

Donor (Mark ONLY if this is the case) ☐

CLINICAL INFORMATION AND INDICATION OF TEST

*Blood transfusion (<60 days):	☐ NO	☐ YES
*Congenital or acquired chimera:	☐ NO	☐ YES
*Bone marrow transplant:	☐ NO	☐ YES
*Diagnosed or clinical suspicion:	☐ NO	☐ YES
*Known carrier:	☐ NO	☐ YES
*Family history:	☐ NO	☐ YES; Please specify:_____
*Partner Carrier/Diagnosed:	☐ NO	☐ YES; Please specify:_____
*Medical/genetic reports:	☐ NO	☐ YES; Please attach if yes

Doctor authorization

I certify that the patient and prescribing doctor's details given in this request form are accurate to the best of my knowledge and that I have requested the test indicated above based on my professional criteria. I have explained the limitations of this test and have answered any questions based on medical judgement. I understand that Igenomix may require further information and I agree to provide this information if necessary.

Doctor's signature _____ Date: _____/_____/_____

Patient consent

By signing this application form, I voluntarily ask Igenomix to perform the test indicated above. I have read and received a copy of the informed consent included in these pages. I have also been adequately informed of the risks, benefits and limitations of this test.

Patient's signature_____ Date: _____/_____/_____

INFORMED CONSENT FOR THE CGT ONE GENETIC SEQUENCING TEST

DESCRIPTION, PURPOSE AND ADVANTAGES OF ANALYSIS

Some of the medical pathologies that may be passed on to offspring during pregnancy or at birth do not have a known genetic component and/or the risk of their recurrence in future pregnancies is low. Others, however, have a defined genetic component and can pose a high risk of recurring in the following pregnancies. When the disorder is caused by an abnormality in a known specific gene –monogenic diseases–, the gene can be studied and, based on the result obtained, preventive measures can be taken before a new pregnancy.

There are currently around 4,500 known monogenic diseases (http://www.omim.org/statistics/entry) and thanks to major developments in scientific study and techniques, tests with high detection rates are available to study the presence of genetic abnormalities or DNA sequence mutations. However, detecting the genetic cause or determining the follow-up medical advice will depend on the pathology.

The CGTOne test is designed to analyse the DNA sequence of one or more genes that cause a specific monogenic hereditary disorder in order to identify one or more mutations that help confirm a clinical diagnosis. It works by analysing the sequence of a gene or panel of genes depending on the disorder to study.

This test should be recommended preferably for clinically diagnosed individuals. Otherwise, the test may be recommended for healthy individuals, for example, parents of a child with a disorder from whom no biological matter is preserved. In this second context, CGTOne involves a screening test. Lastly, CGTOne may be recommended as a screening test for an individual who provides the gametes in an assisted reproductive procedure, when it is known that the other member of the couple is a carrier of a specific gene mutation.

PROCEDURE, RISKS AND LIMITATIONS

The process for conducting the test is as follows:

1. Extraction of a blood sample.
2. Extraction of DNA from the biological sample.
3. Laboratory protocol for massive parallel sequencing of important gene regions of the gene(s) where the majority of the known mutations of the disorder under study are located.
4. Bioinformatic analysis of the sequencing results.
5. Validation of results.

To process the sample, the test request form will need to be correctly filled out. Otherwise, the analysis may be put on hold until the information required has been given to the laboratory.

Given the complexity of the genetic tests and the significant implications of the test results, the results obtained must be interpreted in conjunction with other clinical data, within the general context of a medical practice run by health professionals. The result reports are strictly confidential.

The biological sample –in this case, blood– to be used in the genetic test, will be obtained using standard techniques with little or no risk to the patient's health, and will be analysed by the Igenomix Group ("Igenomix"). Nevertheless, Igenomix reserves the right to carry out part or all of the analyses included in the test through Third Party Laboratories certified with recognised international quality standards, or failing this, they will be periodically assessed by Igenomix. Any results obtained in this way will be inspected by Igenomix and this circumstance will be indicated in the final report issued.

Methodologically, the sequencing or reading of the gene or panel of genes is massive sequencing, also known as New Generation Sequencing (NGS), carried out in parallel or Massive Parallel Sequencing (MPS).

Despite being carried out properly, the following technical limitations exist:

a. Using NGS, the CGTOne test analyses the DNA gene sequence to identify the mutation(s) based on current knowledge at the time the test is done, with the following limitations:

   i. The test does not identify 100% of mutations in the particular gene(s), as some of them may be found in regions with a lack of coverage, outside the gene regions under study, such as regulatory regions of the gene expression or deep intronic regions (beyond positions +3 and -3).

   ii. DNA changes caused by large reordering (deletions and duplications) cannot be efficiently detected using MPS.

   iii. Trinucleotide expansions are not detected.

   iv. The presence of low frequency polymorphisms may lead to false negatives.

b. The test can identify variants known as "variants of uncertain significance" (VUS); which are DNA variants for which there is insufficient clinical information to classify them as causes of pathologies. Although they could be identified, it is not possible to use this information to obtain a specific clinical recommendation.

c. A negative test result does not rule out the presence of somatic or germline mosaicism that creates differences in the DNA between tissues. These types of mosaicism are created after the fusion of parental gametes and can affect a part of, one or several complete tissues. This mosaicism cannot be detected if the tissue where it was created is not studied and also if it is not present in a significant portion of its cells. In any case, the incidence of this happening is relatively low.

d. A positive or negative CGTOne test result does not exclude the possibility of the onset of another genetic disorder in offspring, for example, due to the formation of a de novo mutation. These de novo mutations develop spontaneously every certain number of pregnancies (varying depending on the different genes, and in any case with a low incidence rate).

e. There may be other medical reasons that invalidate the test and which should be researched by the doctor before proposing the test, such as the presence of congenital or acquired chimera, temporarily through blood transfusion, or permanently through bone marrow transplant. The congenital

chimerism develops when two twin embryos become one; the likelihood of this happening is low or very low. Allogenic bone marrow transplants generate chimera or coexistence of the patient's own cells with others from the donor, including the possibility of an exclusive donor cell colonisation. It is important to consider that these circumstances will lead to discrepant findings if the analysed sample comes from peripheral blood. Scientific literature outlines the possibility of working with a saliva sample to avoid possible discrepancies in genetic findings when it comes to bone marrow transplants.

f. Like all laboratory tests, there is a small chance that this result is inaccurate for procedural reasons: an error during collection or with the sample label, an error in the processing, or the collection or interpretation of data.

DATA PRIVACY, STORAGE AND RESEARCH USE OF SAMPLES

Your privacy is a priority for the Igenomix Group ("Igenomix"). Your identity and all data referring to your personal information will be confidential and only Igenomix personnel will be permitted access to this information, along with the relevant authorities when required by the laws of the applicable jurisdiction. You will find further information on the Igenomix Privacy Policy, along with all your rights at www.igenomix.com, or this information may be provided to you upon request by sending an email to privacy@igenomix.com.

We would like to inform you that your personal data will only be processed to: (1) Fulfil the obligations arising from the provision of the services contracted by you; (2) Check and guarantee the quality of the services provided (internal audits, quality controls, laboratory validation studies); (3) For educational purposes, provided that it remains anonymous throughout and you cannot be identified during the analysis of the data, which will be removed from any publication; (4) For research purposes, scientific publications and presentations, provided that it remains anonymous throughout and you cannot be identified during the analysis of the data, which will be removed from any publication; (5) Personally address any doubts or suggestions made by the patient during the process and monitor the proper performance and resolution of the test, including the indefinite retention of your data, except where local laws of the applicable jurisdiction state otherwise; and (6) Contact you in the future to request an evaluation of the services received, send commercial communications (including 'cross-selling' and 'upselling') from associated companies, and also to invite you to participate in market research and the development of new products.

You also declare that you understand and accept that you will not obtain, either now or in the future, any economic benefit for any research carried out, and that there is no intention to compensate you for the products developed from any research.

The sample will be analysed by Igenomix or an associated group selected by Igenomix on an international level. Igenomix reserves the right to carry out part or all of the analyses included in the test through Third Party Laboratories certified with recognised international quality standards, or failing this, they will be periodically assessed by Igenomix. Any results obtained in this way will be inspected by Igenomix and this circumstance will be indicated in the final report issued.

Pursuant to the laws on the Protection of Personal Data[1], the requesting party must have the patient's consent to perform the diagnostic tests requested and to process their data. You may, at any time, exercise your rights regarding access, rectification, opposition, erasure, automated decisions, limitation, portability, by sending an email to privacy@igenomix.com, providing proof of the requesting party's identity.

IN RELATION TO THE RESULTS OF MY CGT TEST, I WISH: (INDICATE AN OPTION OF YOUR CHOICE)

☐ Not to directly receive information. I do not wish to access any information related to the results. However, if the information obtained is necessary to avoid serious damage to my health or that of my biological relatives, information may be given to me or to a legally authorized representative. In any event, the communication would be limited exclusively to the data necessary for that purpose.

☐ To receive the final conclusions: I would like the IGENOMIX Medical Team / Geneticist to inform me about the final conclusions of the study, accepting that such conclusions might mean the risk of transmitting hereditary diseases under study to my offspring, even though I may not currently show any symptoms of such pathologies.

The result of the CGTOne test will be available and it will be sent to me within a period of no more than 25 business days following receipt of the sample at the Igenomix facilities. A small percentage of samples may be delayed due to unforeseeable causes.

The result of the CGTOne test is limited to the moment when it is carried out and to the state of the art at the time, detecting only mutations that can be identified with our methodology.

I declare that I have received adequate Genetic Counselling from qualified MEDICAL / CLINIC / GENETIC COUNSELLING personnel who have offered me information about the importance of the test, including possible alternatives that I may choose in view of the results thereof, and who are available to me for any questions or additional genetic counselling that I may require once the results of the CGTOne test are known.

HAVING READ AND UNDERSTOOD THE FOREGOING, I AM AWARE OF:

The indications, procedure, success rate, risks and complications of the proposed treatment, as well as the financial cost of said test(s).

The fact that medical staff are at my disposal to expand on any aspect of the information that is not sufficiently clear to me.

I have understood the explanations given to me in clear and simple language, and the doctor who saw me allowed me to make comments, clarifying any issues I raised and informing me that I may freely withdraw my consent at any time.

I am satisfied with the information received and I freely consent to my blood sample being sent to the Igenomix facilities for the purpose of carrying out the indicated test(s).

I also accept that the results of the test(s) may be passed on to my doctor, so that he or she can advise me correspondingly.

[1] **For non-US patients:** customers residing outside the United States under certain jurisdictions may at any time request to have their personal information deleted from our active databases, subject to the applicable laws and regulations in each jurisdiction. Although we can delete your personal information from our active databases, part or all of your personal information shall remain stored in back-up files for the purpose of complying with legal, regulatory or other requirements. Information that has already been coded and/or anonymised may not be recoverable or traceable for destruction, deletion or modification. If you wish to have your personal information removed from our active databases, please contact us at privacy@igenomix.com.