Neuberg DIAGNOSTICS | CENTER FOR GENOMIC MEDICINE

CONSENT FORM

PRE-IMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A)& STRUCTURAL REARRANGEMENTS (PGT-SR)

Neuberg Center for Genomic Medicine is a genetic testing laboratory specialized in preimplantation genetic testing for aneuploidies (PGT-A) and structural rearrangements (PGT-SR). The lab conducts genetic testing on a small sample i.e. 6-8 cells of your embryos to determine which embryo is chromosomally normal. Embryos with abnormal chromosome copy may cause failure of implantation, miscarriage, or lead to newborn with chromosomal disorder. In order for Neuberg Center for Genomic Medicine to provide your IVF center with genetic testing, we require you to read and sign this consent form.

Embryo Biopsy and PGT-A: The embryologist at your IVF lab will perform embryo biopsy to extract a few cells (Day 5/Day 6 embryo) from each of your embryos. Embryo biopsy is performed using a medical laser to extract a few cells from your embryos. The extracted cells will be prepared and shipped to Neuberg Center for Genomic Medicine for genetic testing. The embryos themselves will remain at your IVF clinic until testing is complete and embryo transfer can take place. Each biopsy sample will be analyzed using Next Generation Sequencing.

Introduction :

Pre-Implantation Genetic Testing-Aneuploidy (PGT-A):

In normal individuals, there are a total 46 chromosomes. They are present in pairs (23 pairs), with one copy being inherited from each parent (one from the mother and one from the father). Any numerical abnormality leading to extra or missing chromosome/chromosomes (47--,45--,etc) is known as chromosomal aneuploidy.
PGT-A screens for aneuploidy in all chromosomes, including the 22 pairs of autosomes and the sex chromosomes X and Y.

PGT-A is usually offered to individuals with:

- Advanced maternal age (> 35 yrs)
- Bad obstetric history
- Implantation failure
- Severe male factor infertility

PGT-A is a genetic study of the embryos produced during IVF treatment which identifies the numerical chromosome aneuploidies (imbalances). This test helps select chromosomally normal embryos and can help improve your chances of pregnancy and thereby improve pregnancy outcomes.

PGT-A is known to have the following benefits:

- Improved chance of pregnancy: PGT-A may help couples at higher risk for aneuploidy achieve pregnancies. Embryos with chromosomal abnormalities have a higher risk of getting aborted. As only embryos found to be chromosomally normal are transferred to the womb, your chances for pregnancy are increased.
- Improved pregnancy outcomes: PGT-A is able to identify most chromosomal abnormalities and allows only embryos found to be chromosomally normal to be transferred. PGT-A therefore, has the potential to substantially reduce the chance of conceiving a baby with certain chromosomal abnormalities.

Preimplantation Genetic Testing-Structural Rearrangement (PGT-SR):

It tests for specific imbalances arising from parental chromosomal rearrangements as well as other numerical or structural abnormalities across all 24 chromosomes. PGT-SR is an accepted and routine procedure in most IVF/ PGT centres. It has been developed for patients who are unable to achieve a pregnancy or at high risk of pregnancy loss and of abnormal live born births, resulting from inheritance of unbalanced products of the rearrangement. One of the parents usually has a balanced translocation, which increases the risk of having a baby with chromosomal abnormality.

PGT-SR is offered to individuals with:

One of the parents usually has a balanced chromosomal rearrangement, which increases the risk of having a baby with chromosomal abnormality.
Chromosomal rearrangements can be-

- Inversion
- Reciprocal translocation
- Robertsonian translocation

Method:

Next Generation Sequencing (NGS) is the latest technology available for preimplantation genetic testing for preimplantation genetic testing for aneuploidies as well as structural rearrangements (PGT-A and PGT-SR). NGS has various advantages over other techniques including-

- High accuracy
- High number of probes
- Not susceptible to signal saturation, and signal noise.
- Detection of mosaicism
- Each sample is assigned an additional molecular code in NGS, eliminating the possibility of error since the moment of collecting material from the embryo. In addition, the test credibility is enhanced by a direct connection of DNA reading with the obtained information.
- Embryo safety-reducing the number of biopsies for the diagnosis: Usually just one embryo biopsy is sufficient to obtain a reliable result.
- The same embryo biopsy can be used to carry out PGT-M to select healthy embryos not having the monogenic disorder followed by PGT-A/SR to look at chromosomal abnormalities and select healthy embryos further.
- The NGS method is considered to be referential for all the other techniques: DNA sequencing is described as the reference method (model for others), mainly due to the direct nature of the genetic material reading. Other methods (FISH and microarrays) use markers and light as change markers and indirectly test the genetic material. For this reason, these methods are currently being abandoned for the use of NGS.
- Lower costs of test: The special design of the Next Generation Sequencing apparatus allows for a significant reduction in the cost of tests in comparison with existing methods. .

Limitations:

- PGT-A/ PGT-SR will not detect conditions caused by single gene mutations, such as cystic fibrosis or Tay-Sachs disease. The general risk of having a baby with a birth defect or genetic condition, with or without IVF, is around 3 to 4 percent. PGT-A/ PGT-SR is not performed, nor is it able to appreciably alter this background number. The purpose of PGT-A is, instead, to identify what are believed to be the best embryos for transfer to the womb to increase your chances of pregnancy and substantially reduce the chance of conceiving a baby with certain chromosomal abnormalities.
- Preimplantation genetic testing is limited by the technology and the number of cells examined. Therefore, it is recommended that any patient who conceives after this technique should consider routine prenatal diagnosis through amniocentesis to confirm PGT-A/ PGT-SR results. Congenital abnormalities, birth defects, genetic abnormalities, mental retardation and other possible deviations from normal can occur following In Vitro Fertilization (IVF), and may also occur following the transfer of embryos that have undergone PGT-A/ PGT-SR. Damage or destruction of the embryo is also a potential risk of PGT-A/ PGT-SR, although this risk is small.
- The vast number of animal and human studies shows that microsurgery of the embryo does not seem to affect the normal development of the baby. The thousands of children born following an embryo biopsy since 1989 provide evidence of no deleterious effects as a result of the biopsy process. Despite this data, however, it is important to be aware that some rare, unrecognized potential risk does exist and can never be entirely ruled out.

Misdiagnosis:

There is a chance of misdiagnosis with every sample analyzed.

- With embryo testing, it is possible for a chromosome anomaly to be present in a cell, yet not in other cells of the same embryo and vice-versa. This condition is called mosaicism. PGT-A/SR tests only a limited number of cells which might not be representative of the complete embryo. It is also important to understand that PGT-A/ PGT-SR represents the theoretical and practical limits of any medical diagnostic test.
- Diagnostic errors may be encountered, even in the absence of mosaicism and , are unable to eliminate risks completely. However, utmost importance is placed on reducing the risk of misdiagnosis.

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No normal embryos:

There is a chance that your results may reveal that all embryos tested have chromosomal abnormalities and, therefore, are not suitable for transfer.
Transfer of normal embryos:
In a few instances, embryos found to be genetically normal may not result in a pregnancy, or continue to delivery due to other biological reasons. They may may cease to develop, altogether, prior to transfer into the womb.
We have reviewed the costs of treatment and will be personally responsible for all expenses. The expenses include, but are not limited to, hospital charges, laboratory charges, and physician professional fees.

Patient Initial_____ Partner Initial_____

Please read and acknowledge the following items by initialing each:

- Patient Initial_____ Partner Initial_____
  I request the following test:
  ☐ NGS-PGT-A (24 chromosome preimplantation genetic testing for aneuploidies using Next Generation Sequencing)
  ☐ NGS-PGT-SR (24 chromosome preimplantation genetic testing for chromosomal abnormalities/ rearrangements using Next Generation Sequencing)

- Patient Initial_____ Partner Initial_____
  I confirm my wish to have a small sample from each of my/our embryos biopsied for the purpose of identifying embryos without chromosomal abnormality.

- Patient Initial_____ Partner Initial_____
  I understand that all embryos may be at risk of having chromosomal abnormality.

- Patient Initial_____ Partner Initial_____
  I understand that PGT-A/PGT-SR testing for chromosomal abnormalities does not eliminate the need for routine prenatal testing such as chorionic villus sampling (CVS) or amniocentesis. The need for these tests remains the same, whether or not I choose to have PGT-A.

- Patient Initial_____ Partner Initial_____
  I hereby confirm that this test is not intended by any means to be used for sex selection of the baby.

I hereby confirm that I have been notified that the NGS-24TM provided by Supratech will never provide any details about the sex of the embryo. In cases Sex chromosomal abnormalities are present, the report may include a remark suggesting abnormal sex chromosomes but in no way suggest the nature of the abnormalities and the particular sex chromosome/s involved.

Patient's Full Name:_____Age:_____

Partner's Full Name:_____

Address:_____

_____

All of our questions have been answered, and we know that any future questions concerning our care will be answered by our physician. We have been assured that all information about us obtained during these procedures will be handled confidentially and that neither our identity nor specific medical details will be revealed by clinic personnel without our consent.

After the embryo transfer, we wish that those embryos that have been determined to be affected with disease, and therefore not frozen for future transfer, be sent to the Neuberg Centre for Genomic Medicine to confirm affected status. These embryos will be discarded after conformational testing.

No guarantee has been given to us regarding the outcome of this test. We have been strongly advised to have prenatal diagnosis testing to confirm PGT results, and we understand the risk associated with not having prenatal testing. We also understand the risks involved with chorionic villus sampling (CVS) and amniocentesis. If we elect to have prenatal testing performed, we agree to have the sample tested at the Neuberg Centre for Genomic Medicine.

We have been informed that some studies report that congenital abnormalities, birth defects, genetic abnormalities, mental retardation, and/or other possible differences may occur in children born following IVF, cell biopsy, and PGT testing. We understand that these problems also occur in 3-5% of children resulting from natural conception without PGT.

We are aware that additional genetic alterations associated with our specific disease but not identified in us might exist in an embryo and will not be examined.

We have been informed of the possible risks and consequences associated with PGT-A/SR testing.
We have had the opportunity to ask questions and discuss the procedure and we have received satisfactory answers. We consent to these procedures.
Your identity and your all personal information shall be kept confidential. Relevant authorities will be permitted access to this information by the law of the applicable jurisdiction. The Health Authorities shall have access to them to review medical records. As part of their occupational duties, the personnel with access to your personal details shall be subject to permanent professional secrecy.

Acknowledgement

- I acknowledge that I have read and understood this written material.
- I understand the purpose, risks and benefits of this procedure.
- I am aware that there may be other risks and complications, not discussed, that may occur. During the course of the procedure, unforeseen conditions may be revealed requiring the performance of additional procedures.
- Technical problems with the instrumentation may prevent the completion of the procedure. No guarantees or promises have been made to me concerning the results of this procedure or any treatment that may be required as a result of this procedure.

PATIENT CONSENT

This procedure has been explained to me in a language that I understand. I have been given the opportunity to consider other options and alternatives. I have been counselled about the risks, benefits and limitations of this test. I willingly request NCGM to carry out this test. I opt in to donate extra DNA material, if available, for research.
I have read and have received a copy of the consent form.

Husband Name:_____ Wife Name:_____

Husband Signature:_____ Wife Signature:_____ Date, Time and Place:_____

DOCTOR AUTHORIZATION

I certify that the information on this form is correct to the best of my knowledge. I have requested this test based on my professional clinical judgement. I have counseled the patient about the possible testing outcomes and have explained the limitations of this test. I agree to share any other information if requested by the providers.

Doctor Name:_____

Signature:_____ Date, Time and Place:_____

Embryologist Name:_____ Signature:_____ Date:_____

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