PsiGenex™

Informed Consent Form

For Preimplantation Genetic Testing for Aneuploidies (PGT-A) using Next Generation Sequencing (NGS)

Patient's Name

Patient's Date of Birth

Principle of The Test

The Principle of Preimplantation Genetic Testing for Aneuploidy using Next Generation Sequencing is to increase the IVF implantation success rate by only transferring embryos that do not have detectable chromosomal abnormalities into the uterus.

Description of The Disease

Normally, there are 23 pairs of chromosomes in a human cell, for a total of 46 chromosomes. Each of these chromosomes has a characteristic appearance and is assigned a number or letter. Twenty-three chromosomes usually come from the genetic mother and are contained in the egg, and 23 chromosomes come from the genetic father and are derived from the sperm. Although you or your spouse and /or the egg donor or sperm donor are believed to be genetically normal individuals, an abnormal number of chromosomes can result spontaneously from the maturation of an egg, maturation of the sperm or during the process of embryo division before the embryo is transferred back into the uterus. Such numerical abnormalities in chromosome counts are called aneuploidy. A common example of aneuploidy is an extra chromosome number 21 (Down Syndrome or Trisomy 21). It has been determined that many human embryos fertilized in vitro may contain chromosomal abnormalities. It is possible that a single batch of embryos may have more abnormal embryos than normal ones.

Description of The Test

PGT-A using NGS is a six step procedure, usually performed by different individual experts and laboratories. The following are the **six steps** involved:

1. Producing embryos by in-vitro fertilization (IVF) at the IVF clinic of your choosing.
2. Embryo biopsy, in order to remove and analyze cells from the embryo, at the IVF clinic of your choosing.
3. Cell preparation performed by an embryologist or technician at the IVF clinic of your choosing.
4. Transportation of the samples in Step 3 by courier from the IVF lab to PsiGenex Lab.
5. Cell analysis performed by PsiGenex Lab.
6. Preparation of a PGT-A report by which is sent to your IVF clinic and your doctor.

Biopsy of The Embryo and Preparation of The Cell

To test the cells, an embryologist from your IVF clinic makes an opening in the covering of the embryo and removes multiple cells from the embryo via aspiration with a pipette. The embryo biopsy is performed at Day 5/6 of embryo development (trophectoderm biopsy). The embryo is kept in culture and the cells that were removed from the embryo are washed, transferred to a small test tube and sent to PsiGenex Lab for analysis. Please read and sign the consent form for embryo biopsy given to you by your IVF clinic, which will explain the risks of this embryo biopsy procedure.

Transport of The Cell

After the cells have been biopsied and placed in test tubes, your IVF clinic sends the tubes to PsiGenex Lab for analysis using express courier service.

Meaning of a Positive or Negative Test Result

Negative result
A normal or euploid embryo has 46 complete chromosomes, including 22 pairs of autosomes and a pair of sex chromosomes. A euploid result will be reported if two chromosomes for each autosome and two sex chromosomes are detected.

Positive result
Loss and /or gain of a copy or combination of any chromosomes. These embryos are at high risk of being chromosomally abnormal and might not be compatible with life.

Limitations

Preliminary studies have demonstrated NGS to be similar in accuracy to other validated methods being used clinically to perform PGT-A in human preimplantation embryos. Nevertheless, NGS is a relatively new experimental technique and as such, the exact accuracy and potential limitations of the technique have not yet been conclusively determined. NGS is being introduced into clinical practice since it can potentially offer some advantage in the near future such as screening for additional genetic abnormalities, testing more embryos at one time, carrying out more than one type of genetic test on a single biopsy sample and a higher rate of accuracy than other available methods. However, there are unknown risks which cannot be quantified of using PGT-A with NGS at this time.

Risks

It is critical that patients refrain from sexual intercourse for a period of time beginning fifteen (15) days prior to the date that the patient's eggs are retrieved, and ending not before the date the patient receives conclusive result of a pregnancy test performed by the patient's physician. Abstention from intercourse is required because sperm may survive up to fifteen (15) days in vivo. As such, it is possible that sperm from intercourse may result in fertilization and implantation of an embryo, in addition to, or instead of, fertilization and implantation resulting from IVF. This would negate the results of PGT-A testing.

Risks of Shipping and Transport

PsiGenex, its employees, contractors, consultants and authorized agents, agree to provide its best efforts to receive the material in a container provided by PsiGenex or the selected courier. Weather and travel conditions may delay the receipt of samples. PsiGenex shall not be responsible for the safety,

physical integrity or identity of the material before it was placed and transported in the container by the patient, physician, program facility, or any designated agent including commercial shipping companies and couriers and/or before it is received by PsiGenex. The transporting of the material involves certain risks to that material, and of this material may be damaged or destroyed. I agree to accept any and all risks involved in the transporting of the materials, I hereby release PsiGenex, its employees, contractors, consultants and authorized agents from any kind and all responsibility for the safety and integrity of the materials, prior to the possession and control of PsiGenex. I acknowledge that PsiGenex makes no guarantees as to the security or method of the packing or transfer method. Since PsiGenex did not process this material initially, it cannot be held responsible for errors that may have occurred in sample identification or handling prior to arrival at PsiGenex. I am aware that this form is a release of liability, and I sign it of my own free will.

Risk of Natural Disaster or Other Unforeseen Circumstances

Samples may be destroyed or lost in circumstances beyond PsiGenex's control including, but not limited to natural disasters such as hurricanes, floods and fires, human events such as terrorist attacks or other major disruptions, and / or other cause beyond reasonable control such as mechanical, electronic, or communications failure. PsiGenex cannot be held liable for such losses.

Inherent Procedural Risk

The actual biopsy of an embryo can carry a risk. There may be a risk of decreased viability of the embryo from the biopsy procedure as well as a potential for unknown consequences to a live born child. PsiGenex will not be held liable if the biopsy is not adequately performed. PGT-A using NGS is considered an experimental treatment and widespread studies on humans have not been done.

Risk of All Embryos Being Abnormal

The test may find that none of the embryos are normal, and there may be no embryos to transfer. The likelihood that this will happen is influenced by a variety of factors, the most important of which is usually the age of the woman producing the eggs.

Risk of No Results

Some embryos will have no diagnosis, due to the loss of biopsied cells, or poor DNA quality (often found in damaged or dying cells). Embryos without a result can still be transferred, but all the possible advantages of PGT-A will not apply. In addition, sometimes the analysis may not be clear for one of the chromosomes being tested. This embryo could be transferred, but the possible advantages of PGT-A may not apply.

Risk of Misdiagnosis

There is a chance of misdiagnosis due to test error or mosaicism. Mosaicism is when there is more than one chromosomally distinct cell line in the same embryo. This occurs by chance during embryo development. As a result, it is possible that a chromosomally normal embryo may be incorrectly identified as an abnormal embryo and therefore not substituted in the uterus, or that a chromosomally abnormal embryo is incorrectly identified as a normal embryo, and transferred into the uterus.
This technique can only assess the sampled tissue. The remainder and undiagnosed portion of the embryo may be different. If the sampled cells are different than the rest of the embryos, a misdiagnosis may occur.

In the event that a pregnancy is achieved, PGT-A does not guarantee the fetus will not have birth defects or genetic abnormalities. PGT-A does not guarantee the birth of a healthy baby, or the birth of any baby at all.

PGT-A does not eliminate the risk of all genetic defects. A normal result refers only to aneuploidy. It does not test for or report structural abnormalities, single gene disorders, or any other genetic defects.

PGT-A should not be considered a replacement for prenatal testing. PsiGenex recommends prenatal diagnostic testing when pregnancy is achieved.

Risk of Multiple Pregnancies

Replacing two or more embryos classified as normal by PGT-A may significantly increase the risk of multiple pregnancies (twins, triplets, etc.). PsiGenex recommends discussing the risk of multiple pregnancies with your physician and the advantages of only placing one embryo into the uterus at each attempt at pregnancy.

Risk of Miscarriage

It is not possible to guarantee that a pregnancy will occur with uterine placement of embryos that have been chromosomally screened.

Possible Benefits

Many embryos with chromosome abnormalities are indistinguishable morphologically and developmentally from chromosomally normal ones. Thus, without PGT-A, an embryologist cannot differentiate normal embryos from aneuploid embryos and you could have aneuploid embryos transferred into your uterus.

Preimplantation Genetic Screening can determine whether the embryo could potentially be affected by a chromosomal abnormality. Therefore, your chance of conceiving a baby with a chromosomal abnormality will be reduced after PGT-A. However, PsiGenex strongly advises you to undergo prenatal genetic testing during the resulting pregnancy in order to confirm that the procedure was accurate and that your baby is, in fact, chromosomally or genetically normal.

Several recent blinded and randomized studies, as well as multiple observational studies, have shown that day-5 biopsy coupled with comprehensive chromosome screening (such as the one performed with NGS), significantly improve implantation rates, pregnancy rates and reduce the risk of miscarriage.

Alternatives

The alternative to PGT-A is to attempt to conceive a pregnancy through in vitro fertilization without genetic testing. Alternatives to PGT-A during pregnancy include prenatal testing for abnormalities. You are not obligated to undergo PGT-A even if your physician recommends it. You should have prenatal testing when you become pregnant. This risks, benefits and alternative of this testing should be discussed thoroughly with your genetic counselor, obstetrician or the person performing/ ordering the tests. Although these tests may serve as alternatives to PGT-A, PGT-A is not a substitute for routine prenatal testing.

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Costs

Fees for PGT-A are in addition to the cost of the IVF cycle. Your IVF clinic or PsiGenex will advise you of the fees. Please review the packet and contact the financial coordinator with questions.

Confidentiality

Your IVF clinic will receive the final report. Confidentiality of your records will be maintained at all times except as required by state or federal law or in order to comply with a court order. The Food and Drug Administration (FDA), Center of Disease Control (CDC) and Department of Health may inspect the records. In the future other institutional, profession and governmental organizations may have jurisdiction in this area and study the records.

Genetic Consultation Before and After PGT-A

It is recommended that you have a consultation with a genetic counselor that specialized in PGT-A before and after the procedure. This can be arranged by your IVF clinic.

Specimen Retention

The cells to be tested will be destroyed during the process of the analysis. This will usually occur within 5 days of the biopsy. If the test was not performed for any unusual reason, the sample will be destroyed after 60 days of receipt, as stipulated by standard laboratory rules.

I/We hereby authorize PsiGenex to retention the PGT-A embryos biopsy specimen until further notice. Please note that any biological sample (including DNA) will be destroyed after 60 days unless a longer period of retention is expressly authorized by the patient.

Initials of both partners _____ / _____

I/We hereby authorize PsiGenex to discard PGT-A embryos that have been determined to be chromosomally and genetically abnormal for embryo transfer. I/We also understand that if the embryos were cryopreserved prior to obtaining the PGT-A results then the chromosomally and genetically abnormal embryos will be thawed and discarded.

Initials of both partners _____ / _____

Follow Up Testing and Consultation

Prenatal testing during pregnancy can be carried out invasively or non-invasively. Your obstetrician, or someone he or she refers to you to, can perform these tests. If prenatal diagnostic testing is not performed, cord blood at the time of the delivery should be analyzed for chromosomes. If a pregnancy loss occurs, we request the chromosome studies be performed on the products of conception. All result from genetic testing of the pregnancy or the child up to the age of one year should be forwarded to PsiGenex. This information will remain confidential and will be used to monitor outcomes of the PGT-A program. The Food and Drug Administration (FDA), Center of Disease Control (CDC) and Department of Health may inspect the records at PsiGenex. In the future other institutional, professional, and governmental organization may have jurisdiction in this area and study the records.

Test scope

According to the Civil Rights Law on Genetic Testing in NY, no other tests other than those authorized shall be performed on the biological sample(s).

Arbitration

Arbitration is a method of resolving dispute without going through the court system. By agreeing to the arbitration set forth below I am giving up / waiving the right to a jury trial as to all claims covered by such arbitration agreement. Any controversy or claim arising out of or relating to services provided by PsiGenex shall be finally resolved by arbitration pursuant to the Rules of the American Arbitration Association. Any such arbitration shall take place in the State of New York and shall be governed by New York law, before a single arbitrator chosen in accordance with the Rules. I further agree that the award in such proceeding shall be final and binding on the parties. Mode of communication to initiate arbitration process will be via certified/registered mail.

I have read the entire consent form, or it has been read to me. I understand that PGT-A by NGS has benefits and risks, some of which may be unknown at this time. I acknowledge that PGT-A by NGS is a new technology which will bring new information as time progresses and unforeseen issues that may affect the quality of the results. Accordingly, the test and report of the results is likely to change in the future. I wish to proceed with PGT-A for aneuploidy using NGS analysis of cells biopsied at the day-5 stage of preimplantation embryo development.

I also understand that undergoing PGT-A for aneuploidy does not eliminate the need for standard prenatal testing. The need for prenatal testing remains the same whether or not PGT-A for aneuploidy is performed. Understand that if I have questions about prenatal testing I may ask my obstetrician or I may request a referral to a genetic counselor.

I acknowledge that PGT-A is not a perfect science and I agree to hold PsiGenex harmless for the birth defects and / or chromosomal abnormalities that may result to any child I have as a result of transferring an embryo that tested normal. I understand that PsiGenex cannot guarantee me a child that is free of birth defects or chromosomal abnormalities.

I have been given the opportunity to ask questions about PGT-A by NGS procedure and the contents of this consent form. If I think of additional questions, I may contact my physician, genetic counselor, or nurse.

Partner 1 (Print Full Name)	**Partner 1 (Signature)**	**Date**
Physician/Counselor (Print Full Name)	**Witness (Signature)**	**Date**
Partner 2 (Print Full Name)	**Partner 2 (Signature)**	**Date**
Physician/Counselor (Print Full Name)	**Witness (Signature)**	**Date**