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Informed Consent for Pre-Implantation Genetic Testing (PGT-A)

INTRODUCTION:

This document discusses pre-implantation genetic testing (“PGT”) and also serves as your authorization to biopsy your embryo(s) and give the biopsied specimen(s) to an outside genetic laboratory to perform PGT on your embryo(s). The purpose of the PGT is to attempt to increase the likelihood of achieving a pregnancy and a child free of certain chromosomal disorders. You will have received and signed a separate informed consent for the IVF Cycle. This consent deals only with the major components involved in PGT-AL: the embryo biopsy and chromosome testing. PGT will be performed by evaluating embryos for the correct number or arrangement of chromosomes, with the intent of selecting those embryos for transfer with a greater chance of establishing a pregnancy free from the genetic problem being tested.

(The box(es) below applicable for your clinical situation will be marked.)

- Aneuploidy - The condition where there are either extra or too few chromosomes is called aneuploidy. When there is a normal number of 46 chromosomes present, it is referred to as euploid.
- Translocation - The presence of a translocated chromosome (chromosomal rearrangement) can cause the embryo to have too many copies or parts of one chromosome and too few copies or parts of the other (“unbalanced state”). This may lead to embryo death, miscarriage, or the live birth of an infant with substantial medical problems.
- Inversion – When a single chromosome breaks in two places and the material in-between is realigned upside down. The presence of this inversion chromosome in eggs or sperm can result in an embryo with too many or too few copies of genes located on this chromosome.
- Deletion – Involve the loss of a chromosome segment, resulting in a chromosome imbalance. Carriers of microdeletion syndromes can transmit this genetically imbalanced chromosome to their offspring resulting in a fetus that fails to grow, results in miscarriage, or a child with medical problems.
- Duplication – The addition of a chromosome segment that results in a chromosome with extra genetic material. Carriers of duplications may exhibit clinical abnormalities that can be transmitted to offspring.

PREIMPLANTATION GENETIC TESTING

During fertilization, the egg provides a set of chromosomes and the sperm provides another set, resulting in two of each chromosome. However, sometimes genetic abnormalities occur in the formation of sperm or eggs resulting in embryos with too many or too few chromosomes (aneuploidy), or too many or too few parts of specific chromosomes (translocation or inversion). For example, when there is an extra copy (three chromosome 21's), the embryo may result in an individual with Down syndrome (Trisomy 21). Aneuploidy or an “unbalanced state” in a developing embryo may be associated with:

1. Failure to achieve a pregnancy. Studies have demonstrated that the majority of embryos obtained following IVF that fail to implant in the uterus or result in a miscarriage are aneuploid or “unbalanced”.
2. Loss of a pregnancy. Chromosomal abnormalities are the most common reason for miscarriages
3. Offspring born with aneuploidy or an “unbalanced state”. The medical outcome and the quality of life achieved by children born with these genetic abnormalities will vary depending on which chromosome(s) is affected.

To evaluate the embryos, two technical procedures must be performed: Embryo Biopsy and Preimplantation Genetic testing. Our usual practice is to biopsy trophoctoderm cells (around the actual embryo) from a blastocyst embryo during IVF process. This is performed by making a small opening in the zona pellucida (the outer membrane surrounding the embryo) followed by the removal of the cell(s) using a very fine needle. After the cell(s) are removed from the embryo(s), the embryo(s) are returned to the incubator, where they remain until the PGT results return. In the meantime, the cells that were removed are coded and then given to the genetic laboratory where analysis of the cells will take place. Currently Next generation Sequencing (NGS) is the technology used to identify abnormalities.

PREPARATION FOR EMBRYO TRANSFER AFTER PGT

After chromosomal analysis is performed the results are forwarded from the genetic laboratory to your physician who will discuss your options following the results of testing. These issues include, but may not be limited to:

- A. What will be done with embryos that are not transferred or to abnormal embryos?
- B. What are the consequences of transferring an embryo with a chromosomal abnormality?
- C. What are the consequences of transferring a mosaic embryo ?

RISKS:

We understand that there may be risks associated with these procedures. In addition to the risks listed below, there may be other risks not yet identified. These risks include, but are not limited to, the following:

1. Embryos may theoretically be damaged during the biopsy procedure resulting in a decrease in their ability to develop. However, it has not been determined if some undetected damage may result in a decrease in implantation, an increased risk of obstetric complications, fetal abnormalities, or may lower the chance of achieving a pregnancy. To date, there is no known risk of damage to a blastocyst embryo (day 5 or 6).
2. A diagnosis may be made on an embryo that is incorrect. Some embryos may contain cells that are genetically normal and, within the same embryo, other cells which are abnormal. This is called mosaicism. For this reason, a diagnosis may be incorrect; the chance of an incorrect diagnosis is significantly lower with a blastocyst embryo biopsy since multiple cells are removed and analyzed. This may result in the transfer of an embryo carrying a chromosome abnormality or the failure to transfer a normal embryo. Based upon world-wide data, it is estimated that there is < 1% chance that an incorrect diagnosis may occur due to biopsy of a blastocyst embryo that contains mosaicism.
3. A diagnosis on an embryo cannot be made. We also understand that the genetic testing procedure(s) may fail to yield a clear or any diagnosis. The embryo's from which these cells were taken cannot therefore be determined to have the genetic disorder being tested or be free of it.
4. With any technique necessitating mechanical support systems, equipment failure can occur and that the physicians, scientists, employees, staff, or consultants Island Reproductive Services and Reproductive Center of Central New Jersey are not to be held liable for any destruction or damage caused by or resulting from any malfunction of equipment, failure of utilities, strike, cessation of services, or other labor disturbance, any war, acts of public enemy, or weather disturbance, any fire, wind, earthquake, flood, or other acts of God.
5. With the handling of microscopic material, human error can occur. It is also possible for an embryo(s) or embryo biopsy(ies) to become lost or damaged during procedures, the handling, and shipping process.

BENEFITS:

Participation in these procedures may increase the live birth rate and decrease the risk of miscarriage from IVF. PGT may also decrease the chance of having a certain genetic abnormality or abnormalities in embryos that are transferred or in children conceived. PGT might also reduce our risk of a multiple pregnancy with single embryo transfer..

ALTERNATIVE TREATMENT:

We have been informed that the only known alternative treatments are: 1) to attempt pregnancy without embryo biopsy and therefore risk conceiving a genetically abnormal child 2) to choose not to conceive a pregnancy at all; or 3) to use donor sperm and/or donor eggs as may be applicable to minimize the risk of a genetic abnormality.

CONFIDENTIALITY:

We understand that information that is obtained from us, including answers to questionnaires, history, laboratory data findings, or physical examination will be kept strictly confidential. However, your records, just like hospital records, may be subpoenaed by court order or may be inspected by federal regulatory authorities. In order to assure that Food and Drug Administration (FDA) regulations are being followed, it may be necessary for a representative(s) of the FDA to review our medical records, or the Society for Assisted Reproductive Technology (SART) in conjunction with the Center for Disease Control (CDC), or consortium collaboration.

ACKNOWLEDGEMENT

Island Reproductive Services and Reproductive Center of Central New Jersey believe that it is important for you to understand what the processes of EMBRYO BIOPSY and PGT testing involved, and how they work, as detailed above. It is essential that you evaluate the risks and benefits they present and the alternatives available, so that you may make an informed decision as to whether Embryo Biopsy and genetic testing are appropriate for you.

Initial

Female Partner

I/We acknowledge a process that included a consultation with my/our physician during which my/our medical circumstances were discussed regarding IVF and an IVF informed consent was signed.

I/We acknowledge that through a process of informed consent which has included a consultation with my/our physician during which my/our individual medical circumstances were discussed, has informed us of the procedures involved in embryo biopsy and genetic testing, as well as their risks and benefits, including the likelihood that these procedures will not result in pregnancy and the possibility of damage (including birth defects) of children born through this process. We have also discussed the possible alternative treatments, if any, available in our particular circumstances.

I/We understand that Embryo Biopsy is usually performed the fifth or sixth day after retrieval, when the embryos are at the blastocyst stage.

I/We understand that there are fees for both the embryo biopsy and PGT. I/We assume responsibility for payment of those fees.

I/We understand that the information regarding my/our participation in treatment will be kept confidential except if it is required by a court order or by law. However, I/we give permission to collect information regarding my/our participation and to publish it so long as such information does not specifically identify us. I/We understand that data from my/our ART procedure will be provided to the Center for Disease Control and Prevention (“CDC”). The 1992 Fertility Clinic Success Rate and Certification Act requires that the CDC collect data on all ART cycles performed annually in the United States and report success rates using these data. Because sensitive information will be collected on me/us, the CDC applied for and received an “assurance of confidentiality” for this project under the provisions of the Public Health Service Act, Section 308(d). This means that any information that the CDC has that identifies me/us will not be disclosed to anyone else without my/our prior written consent.

I/We understand that I/we may withdraw from the program at any time by notifying our doctor. We will still incur all costs if embryo biopsy has already been performed.

I/We understand that the financial responsibility for any medical treatment that I/We, or my/our offspring, require as a result of my/our participation in treatment including but not limited to treatment for injury or pregnancy, will be solely my/our own financial responsibility.

I/We understand that the cell(s) evaluated by our genetic testing technology may not represent all of the cells in the embryo and in fact the fetus may carry genetic defects arising from these or other chromosomes. In addition, we understand that the results of the biopsy and genetic testing have an inherent error rate resulting in some embryos that are normal being diagnosed as abnormal, and other embryos diagnosed as normal may be, in fact, abnormal. This procedure cannot be guaranteed to produce a child without genetic defects.

I/We understand that should IVF with PGT lead to an early viable pregnancy, it has been recommended that we still perform invasive or non-invasive genetic screening.

I/We acknowledge that any technique necessitating mechanical support systems, equipment failure can occur and that the physicians, scientists, employees, staff, or consultants of our doctors are not to be held liable for any destruction or damage caused by or resulting from any malfunction of equipment, failure of utilities, strike, cessation of services, or other labor disturbance, any war, acts of public enemy, or weather disturbance, any fire, wind, earthquake, flood, or other acts of God, or failure of any other laboratory.

I/We understand that any procedure involving handling of microscopic material, human error can occur. It is also possible for cell(s) or embryo(s) to become lost/ damaged during these procedures.

I/We have had adequate opportunities to discuss embryo biopsy and PGT with the physicians, geneticist, and/or with the staff and to ask, and to have answered, any questions. I/We have had ample time to reach my/our decision freely, without pressure or coercion.

I/We understand that embryo biopsy and or genetic testing are new technologies and that, accordingly, the entire spectrum of potential dangers and risks to both mother and fetus(s) is unknown and cannot be predicted.

I/We give permission to Island Reproductive Services/Reproductive Center of Central New Jersey to discard any embryos found to be aneuploid (abnormal number of chromosomes) after 60 days of results unless we specifically and in writing request otherwise. In the event of a chromosomal abnormality in which a viable, but affected child could be born (Trisomy 13,18, 21, 45X, 47XXY) my physician will discuss this with me prior to discarding those embryos in case I/We wish to pay to keep them frozen.

I/We understand that the office policy is never to transfer a mosaic embryo with more than 1 affected chromosome. The transfer of a mosaic embryo requires medical and genetic counseling in advance.

THEREFORE, In light of careful consideration of the risks and potential benefits of embryo biopsy and PGT, I/we the undersigned, voluntarily request, authorize and direct the physician(s), embryologist, staff and nurses and other professional personnel and parties performing services to perform any and all procedures necessary for embryo biopsy and PGT, as well as any such additional procedures that may become necessary.

Patient Name

Patient Signature

Date

Partner Name

Partner Signature

Date

Witness or Notary

Witness or Notary Signature

Date