California Center for Reproductive Health

CONSENT FOR EMBRYO BIOPSY, PREIMPLNATATION GENETIC TESTING (PGT)

Preimplantation genetic testing (PGT) for Aneuploidy (PGT-A) and/or for Monogenic disorders (PGT-M) are specialized techniques designed to screen embryos for chromosomal or genetic disorders. The PGT techniques are procedures requiring removal of several cells [trophectoderm (TE) cells] from the embryo. The TE cell(s) are genetically evaluated to determine the presence or absence of specific chromosomal abnormalities and/or genetic diseases. After the genetic evaluation of embryos, they are selected for embryo transfer into the uterus, or frozen (cryopreserved) to be used later, to achieve pregnancy. The advantages of using PGT are to greatly reduce the risk of miscarriage or having a child with the chromosomal/genetic problems.

Embryo biopsy can only be done once eggs are fertilized and embryos are created, which is part of the routine IVF process. Embryo biopsy is usually performed at the blastocyst stage (usually day 5 after egg retrieval) of embryo development. Using specially designed micromanipulation tools and microscope, an opening is created in the outer shell of the embryo (*zona pellucida*), and several cells are extracted. The cell(s) removed from each embryo are then subjected to PGT using various genetic analysis techniques such as Polymerase Chain Reaction (PCR), array-Comparative Genetic Hybridization (aCGH), single nucleotide polymorphisms (SNPs), or Next Generation Sequencing (NGS).

In PCR the genetic material within the TE cell is multiplied (amplified) and then subjected to analysis to determine whether a specific chromosomal abnormality or genetic disease is present. The aCGH technique utilizes amplification of the DNA of each chromosome and the expression is compared to a standard. In NGS, millions of small fragments of DNA are sequenced in parallel and bioinformatics analyses are used to piece together these fragments by mapping the individual reads to the human reference genome; each of the three billion bases in the human genome is sequenced multiple times, providing high depth to deliver accurate data and an insight into unexpected DNA variation

In some instances, embryos determined to be free of chromosomal abnormality or genetic disease (normal embryos) are selected for fresh embryo transfer into the uterus, typically on day 6 (blastocyst stage) after the egg retrieval (one day after the embryo biopsy procedure). In most instances, all biopsied embryos are frozen (cryopreserved) at the day 5-6 stage while results of PGT analysis are pending; subsequently only those embryos labeled normal are maintained frozen for future use, while abnormal frozen embryos are discarded. Abnormal embryos, which are not transferred to the uterus or cryopreserved, may have their remaining cells tested for chromosomal abnormalities or a specific genetic condition to confirm the accuracy of the PGT procedure.

Embryo biopsy and PGT are embryology laboratory techniques involving technically extremely sensitive procedures that could possibly lead to a **WRONG DIAGNOSIS.** Specifically a wrong diagnosis may mean that a perfectly normal embryo is erroneously labeled as abnormal following PGT and is therefore not used to achieve pregnancy and often discarded; or that an abnormal embryo (containing a chromosomal abnormality or genetic mutation) is labeled as normal following PGT testing and is transferred into the uterus to achieve pregnancy. Moreover, a wrong diagnosis may mean that a female embryo is misdiagnosed as male or that a male embryo is misdiagnosed as female. Although medical studies have been conducted using these techniques, research studies are still limited.

Laboratory experience can be limited in the field of genetic testing and the likelihood of success cannot be predicted. I/We understand that embryo biopsy may result in damage to the embryos, which may result in lowered implantation rates (lower pregnancy rates), and may also lead to currently unknown risks, including congenital defects or other anomalies. However, despite some uncertainty regarding potential risks, numerous successful and healthy live births have been reported in many centers both in the United States and abroad following embryo biopsy and PGT.

Reasons for the possible failure of preimplantation genetic screening/diagnosis include, but are not limited to the following:

- Failure to obtain adequate numbers of eggs or sperm
- Failure of fertilization or embryonic development
- Failure of the embryo biopsy to obtain one or more cells for analysis
- Damage to the embryo during biopsy resulting in a non-viable embryo
- Failure of the genetic analysis to provide adequate diagnostic information
- Failure to transfer selected embryos back to the uterus and implantation
- Limitations of genetic tests used and technical challenges
- Embryo mosaicism (different cell lines within the same embryo) or embryo auto-correction
- Presence of genetic issues not detectable with currently available screening tests

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Initials

I/We have been advised that in order to undergo PGT we first have to undergo in vitro fertilization (IVF), for which I/We have given full informed consent. I/We also understand that PGT require biopsy (removal of cells) from embryos created by IVF for the purpose of chromosomal/genetic testing. I/We also understand that freezing of embryos (cryopreservation) may be necessary following embryo biopsy for PGT, for which I/We have given full informed consent.

I/We agree that since PGT techniques could possibly result in the transfer of an affected egg/embryo, should pregnancy occur, I/We agree to undergo chorionic villus sampling or genetic amniocentesis to confirm the genetic analysis. Should one or more of the fetuses be affected by the genetic disease, I/We am/are not under any obligation to terminate the pregnancy, but may choose to do so. I/We have been adequately counseled concerning chromosomal and/or genetic abnormalities and understand that chromosomal and genetic diseases may drastically reduce the quality of life or life expectancy of an affected individual. I/We understand that the laboratory director and physician may choose to use some or all of the normal embryos for transfer, but in general no more than 1-2 embryos will be transferred because of the increased risk of multiple pregnancies. I/We understand that if a multiple pregnancy occurs, further genetic testing during pregnancy becomes more difficult and at times not possible to carry out.

I/We do jointly and severally release and forever discharge Dr. Mor, Dr. Woo, the California Center of Reproductive Health and each of its employees, officers, physicians, agents, successors, and assigns from any and all claims, demands, costs, expenses and loss of services incurred as a result of the physical or mental nature of any child or children produced using these procedures.

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Initials

Certification of Informed Consent for Embryo Biopsy and Preimplantation Genetic Testing
Your signature below indicates that you have read the preceding consent, that you understand the potential risks and benefits of embryo biopsy and PGT that you have had the opportunity to ask questions, that your questions have been answered to your satisfaction, and that you consent to have the procedures enumerated herein.

PATIENT NAME (print)	**PATIENT SIGNATURE**	**DATE**
PARTNER NAME (print)	**PARTNER SIGNATURE**	**DATE**
WITNESS (print)	**WITNESS SIGNATURE**	**DATE**