LG-MG-FR-007	PREIMPLANTATION GENETIC DIAGNOSIS INFORMATION AND CONSENT FORM FOR CHROMOSOME SCREENING

INFORMATION

Preimplantation Genetic Diagnosis for Chromosome Screening

Purpose of the study; is examining the eggs before becoming pregnantand/or embryos fertilized via “InVitro Fertilizasyon (IVF) or Intra Cytoplasmic Sperm Injection (ICSI)” before implementation. If successful, these techniques will allow selection of embryos that do not carry chromosomal anomalies for implantation. All of these research techniques are called “Pre-implantation Genetic Diagnosis” or “PGD”. PGD treatment can be performed in 3 different developmental stages of embryos:

1) Polar body analysis before and after fertilization,

2) Blastomer analysis in the cleavage phase,

3) Analysis of trophoblast tissue (trophoblast cells) in blastocyst stage.

These methods can be used alone or in combination with the intention of confirming the diagnosis in case of uncertainty.

1. Polar Body Analysis

The maturing egg produces a small cell called the “First Polar Body”. The egg then produces the “Second Polar Body” following the fertilization. Since polar bodies carry the genetic information found in the egg, tests on these cells can be used to obtain information about the genetic structure of the egg.

Polar bodies are pulled out of a hole formed in the outer layer of the egg (Polar Body Biopsy). These polar bodies are used to screen for aneuploidy (chromosome aberration) in mother candidates aged 38 years and older, in mother candidates with low ovarian reserve, or in determining the maternal diseases. Genetic results are obtained before the embryo transfer. With this test, only chromosomal anomalies that can be found in the mother can be detected. Polar bodies 1 and 2 must be examined together in order to obtain a reliable result.

2. Blastomer Cell Analysis

After approximately 68-72 hours following fertilization and at least 6-8 embryo cells stage, this method is performed by taking one of the cells called blastomer on the 3rd day of embryonic development. Blastomer biopsy is used for the detection of chromosomal abnormalities that can result from both the mother and the father.

3. Trophododerm Tissue Analysis

Trophectoderm tissue biopsy is performed in the embryo on the blastocyst stage. It is usually done by taking 4-5 cells on the 5th day after fertilization. With this method, chromosomal anomalies can be detected in the embryo, which can inherit both from mother and father. When cultured to the embryonic blastocyst stage, some of the embryos with chromosomal anomalies are eliminated and only a limited part of the embryos from the beginning can reach the blastocyst stage.

Problems that can be encountered on Preimplantation Genetic Diagnosis

All patients can encounter problems during cycle. In some cases, the patient does not respond to the drug treatment and the treatment cycle can be canceled before the eggs are collected. Rarely, eggs may not be formed. In addition, there may be cases where no egg is fertilized and embryos to be subjected to genetic testing can not be obtained.

In case of male-induced infertility, if Y chromosome microdeletion encountered in the father on the genetic tests, the male embryo will be the carrier in terms of microdeletions found in the father. When transfer of these embryos is decided; should be known by the patient before the treatment begins that the child is born with a risk of infertility when he/she is married in the future.

Research shows that preimplantation embryos obtained from routine ICSI patients may contain abnormal chromosomes. We also know that as the woman's age progresses, her risk of having a baby with a chromosomal abnormality, such as Down Syndrome, increases by 40-60%. In some patients, the risk of miscarriage due to chromosomal abnormalities is also increased. PGD method can detect abnormalities in chromosomes 13, 15, 16, 17, 18, 21, 22, X and Y which are determined to be risky to give rise to disabled birth, as well as all other chromosomal anomalies which can lead to implantation failures.

We suggest that our patients should be diagnosed prenatally as there is a risk of misdiagnosis of 2 % (trophectoderm biopsy) and 5

% (polar body and blastomer biopsy) in the technique of array-comparative genomic hybridization (a-CGH) and Next Generation Sequencing techniques applied during preimplantation genetic diagnosis.

Array CGH Method

Comparative Genomic Hybridization (CGH) is a molecular cytogenetic method that detects changes in the amount of DNA. With this technique, it is possible to determine the increase or decrease in the number of chromosomes or in partial regions of the chromosome in the whole genome, and all the numerical chromosomal anomalies in the embryo can be detected.

However, even though numerical data on all chromosomes are reached, this test does not exclude microdeletions, Uniparental Disomy (UPD), triploidy, tetraploidy, some phenotypic features that may arise from mutations, and mosaicism.

After genetic screening, it can be determined that the entire embryos are abnormal. In this case there will be no embryo suitable for the transfer.

Preimplantation Genetic Screening using Next Generation Sequencing (NGS)

aCGH uses thousand of probes hybridized to the genomic DNA of embryo. These probes are distributed through the out whole genome and enable us to give diagnosis of for each chromosome.

However, as a result of developments in sequencing technology, the sequencing of the entire genome has become effective at affordable costs. Using Next Generation Sequencing (NGS) techniques, the whole genome of the embryo can be amplified and sequenced and this data can be analyzed to detect aneuploidies in chromosomes. The advantages of NGS method to aCGH is that it has more resolution with more sensitivity and mosaicm can be detected better by this method. Because of these reasons NGS has become highest quality of PGS techniques and is started be used widely all over the world.

Freezing Untransferred Embryos

As a result of genetic tests, embryos which are chrosomally normal but not transferred, will be frozen after confirmation from couples. The frozen embryos may then be thawed upon request of the couples for a new transfer and transferred.

If you have read and understood this form written to inform you, if you understood and accept that the Preimplantation Genetic Diagnosis (PGD) application is necessary for the health of your probable baby, please write your name and surname in the following spaces with your own handwriting.

CONFIDENTIALITY

Information obtained about us in this study will be kept confidential and our identity will not be revealed without our consent.

COST

We have been informed about the cost of this study, embryo, Pre-implantation Genetic Diagnosis (PGD) and IVF/ET costs. We are committed to paying.

* As per the Patients' Rights Regulation; 1 form copy will be given to you. Notify us when the form is not given.

CONSENT

The details of the applications, the duration, the possible outcomes and the complications, the risks, the consequences that would arise if we don't accept the treatment were explained in detail.

In brief we understood;

1) Following IVF/ICSI fertilization, first and second polar (pole) bodies may be removed by biopsy and/or

2) On the 3rd day following IVF/ICSI fertilization, one cell of the appropriate embryos will be removed by biopsy,

3) On the 5th day following IVF/ICSI fertilization, 2-5 cells of the embryo will be removed by biopsy,

4) Cells obtained by biopsy will be examined for the detection of numerical abnormalities of all chromosomes,

5) As a result of the tests made, all eggs or embryos may be found abnormally,

6) If there is no normal embryo, multiple IVF applications may be required,

7) There may be a probability of misdiagnosis about 5% for polar cell or blastomer cell analysis and 2% for trophecoderm tissue analysis,

8) With this test, abnormalities such as microdeletions, Uniparental Dizomi (UPD), triploidy, tetraploidy, mosaicism and some phenotypic features that can arise from mutations can not be detected,

9) Prenatal diagnosis (chorion villus biopsy, amniocentesis or cordocentesis) should be performed in order to confirm the diagnosis if pregnancy has occurred but 0.5% chance of pregnancy loss is possible.

We had the opportunity to ask questions and discuss the procedures to be followed, and we received satisfactory answers. We have been informed about the costs of these operations. We authorize …… Hospital, which I know to be a private hospital, with physicians, nurses and other health workers, for making this application freely without any pressure or directing, with our own will. We GIVE PERMISSION to make this application with our own consent.

We have read, understood and fully accepted all the steps mentioned above.

	Name-Surname	Date	Signature
Mr.			
Mrs./Ms.			
Translator			

CERTIFICATION

I certify that I have given consultancy service the above named spouses and that I disclose the relevant procedures, benefits, risks, alternatives and costs by answering their questions in my knowledge.

I believe that they fully understand my explanations and the answers to their questions.

Every step from the beginning to the end of the PGD process is carried out in accordance with the International PGD Guideline, which is specially prepared for the PGD. In accordance with the content and context of the “Convention on the Protection of Human Rights and Dignity in the Presence of Biology and Medical Practice”, it has been published in the 10 June 1998 dated 23368 numbered Official Gazette by Ministry of Health that gender determination can not be made in human embryos other than medical reasons.

All transactions made and information obtained will be protected in our center by adhering to the confidentiality conditions between the patient and the physician. Your personal identity will not be identified in any future medical studies or publications.

	Name-Surname	Date	Signature
Doctor			