LG-MG-FR-006	PRE IMPLANTATION GENETIC DIAGNOSIS (PGD) INFORMATION AND CONSENT FORM FOR BALANCED REARRANGEMENT (TRANSLOCATION, INVERSION)

Purpose of the study; is examining the eggs before becoming pregnant and/or embryos fertilized via “In Vitro Fertilizasyon (IVF)” before implementation using genetic methods. 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”.

Any disease can be diagnosed before birth, chorionic villus collection (CVS) or amniocentesis methods can be used as standard methods. These two methods involve the collection of part of the baby's cells from the mother's uterus during the first trimester or the second trimester of pregnancy. The collected cells are examined to identify whether the developing baby has any defect. If a genetic abnormality is identified, parents must decide whether to pursue or terminate the pregnancy.

In Vitro Fertilization (IVF-ET)

We know that fertilization needs to be done outside in order to allow the ovum and/or embryos to be examined in vitro (in the laboratory) using the PGD method. After genetic analysis, appropriate embryos are placed in the mother's uterus. This is done using embryo transfer (ET) technique.

Examination of Chromosomes of Eggs and/or Embryos

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. This test can only detect abnormalities that may arise from a balanced translocation or inversion carried by the mother.

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 fetus.

3) **Trophectoderm Tissue Analysis**

Trophectoderm tissue analysis 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 passed both from mother and father.

4) **Translocation (Part exchange)**

Translocations are usually of two types.

a) Robertsonian translocations are the result of a chromosome binding with another chromosome. Such translocations occur between acrocentric chromosomes such as chromosomes 13, 14, 15, 21 and 22. Since the chromosomes combine to form a single new chromosome, robertsonian translocation carriers normally have 1 chromosome less (45).

b) In reciprocal translocations, two different chromosomes mutually interchange a part. Chromosomes participating in reciprocal translocation enter an unusual structure to form gamete cells (egg or sperm) during meiosis and may produce chromosomally unbalanced gametes. This can lead to infertility in balanced translocation carriers. Translocations are hereditary. They may have familial transition.

5) **Inversion (inversion)**

It is a phenomenon that a chromosome breaks at two different points and then sticks back to the former place by turning around the remaining part. Balanced inversion carriers are normal because there is no increase or decrease in genetic material, but they can produce unbalanced gametes.
There are two types of inversion:

a) Paracentric inversion: Inversions that do not include the centromere and are in one of the short or long arms.

b) Pericentric inversion: Inversions that include the centromere, resulting from two fractures in the short and long arms.

6) Study of the Chromosomes

When gametocytes form in the meiosis division, the chromosomes group together, facing each other, and then migrate (distribute) to two different poles. During this migration, chromosomes and fragments involved in translocation may be distributed in an unbalanced way instead of into two equal parts. The insemination of these unbalanced gametes results in chromosomally unstable and defective embryos. With the "segregation analysis" method all unstable distributions are identified, and the regions of the relevant chromosomes are examined to determine their potentials.
Comparative Genomic Hybridization (CGH) using Array CGH of eggs and/or embriyos is a molecular cytogenetic method that detects changes in the amount of DNA. This technique can detect 2Mb or longer imbalances (increase or decrease) that may occur in chromosomal regions involved in translocation or inversion, as well as numerical anomalies that may occur in all other chromosomes. However, even though numerical data on all chromosomes are reached, this test does not exclude microdeletions, Uniparental Disomaly (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.

7) Freezing of Untransferred Embryos

As a result of genetic tests, embryos which are normal in chromosomal sense 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 to the candidate.
We also know that PGD techniques may not produce results in balanced remodeling (about 5%). In this kind of situation, we will be informed that the test has not been performed and we will have to choose one of the following options:

a) In case of transfer of embryos and pregnancy, genetic recognition with CVS or amniocentesis methods.

b) In case of transfer of embryos and pregnancy, not selecting CVS or amniocentesis methods.

c) Freezing embryos. If the embryos are stored at the respective In Vitro Fertilization Center, accept the payment of the annual storage fee.

d) Let the embryos to deteriorate.

Proposal for Consent of the Participants of the Study to the Amniocentesis or CVS

We know that PGD is still considered as a study with a 95% diagnosis output. In addition, researchers use either "CVS" in the first trimester or "amniocentesis" in the second trimester when a pregnancy occurs; we know that they suggest the confirmation that transferred embryos do not have an abnormality for the studied chromosomes. In this case we may be asked to sign another form of consent for CVS or amniocentesis. Alternative actions, including termination of pregnancy, can be discussed with us if an abnormality that causes a disease is detected.
If we are not diagnosed using CVS or amniocentesis, this will suppress our chance to confirm our prenatal aneuploidy scan.

To Give Information to the Researchers about the Born Baby

As participants of this study, we accept that the result of your pregnancy and the health and genetic status of our born baby are transmitted to the researchers. We will get in touch with the relevant In Vitro Fertilization Center 4 weeks and 6 months after the birth.

PROFITS

This study will benefit us because it will prevent the transfer of fetuses with chromosomal abnormality and will not confront us with a decision to terminate the pregnancy, thereby increasing the likelihood of pregnancy and reducing the likelihood of abortions.

However, participating in this study does not guarantee that we will get pregnancy or that the fetus will not have any other chromosomal abnormality. These processes do not exclude anomalies that may lead to phenotypic disturbances such as micro deletions, uniparental disomia (UPD), single gene diseases and mosaicism.

ALTERNATIVES

The alternative choices we have when participating in this study are as follows:

1) There are other research centers in Turkey doing this study. We can join another PGD study in another center.

2) We can not participate in the PGD research neither here nor elsewhere. Instead, we can choose prenatal diagnosis using CVS or amniocentesis methods.

3) We may not participate to any of pre-implantation or prenatal genetic diagnosis.

CONFIDENTIALITY

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

COST

We have been informed about Chromosome Screening, Pre-Implantation Genetic Diagnosis (PGD) and IVF/ET costs. We are committed to paying.
We read, understood and accept of our own accord the objective of the PGD applications and the potential risks.
* 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. We authorize ..... which we know is a private hospital to freely practice this application, which is deemed appropriate, without any pressure and direction, completely free of our own will, along with the physician, nurse and other health professionals, and we request this procedure to be carried out. 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.

	Name-Surname	Date	Signature
Doctor			