Main Line Fertility
825 Old Lancaster Road, Suite 170
Bryn Mawr, PA 19087
www.mainlinefertility.com

Main Line Fertility Center (MLFC)

DNA sampling for Preimplantation Genetic Testing (PGT) of Embryos

Informed Consent Form

Your embryos can be tested for certain chromosomal or genetic abnormalities before they are transferred to the uterus. This is called preimplantation genetic testing or PGT of embryos. There are several ways to sample DNA from embryos for PGT. Your physician will recommend one.

A. YIKON non-invasive DNA sampling for PGT
B. EMBRACE non-invasive DNA sampling for PGT or
C. Traditional biopsy of cells for PGT

After the DNA samples are collected, they will be sent to a genetics lab for testing. The genetics lab has a separate informed consent form that you will need to sign.

Notes about PGT:

A percentage of your embryos should develop to the blastocyst stage. However, not all of your embryos will develop into a blastocyst, and it is possible you will not have any blastocysts. Embryos not developing to the blastocyst stage will not be tested and will be discarded.

In most cases, blastocyst embryos will be cryopreserved (frozen) after DNA sampling. The embryos reported as “euploid” or having the “normal” number of chromosomes will be considered for transfer to the uterus (womb). This embryo transfer will occur in a future frozen embryo transfer (FET) cycle. Results may take 2 weeks (or more) to be reported.

Risks and Limitations of PGT:

- MLFC is not responsible for sample damage or loss during transportation.
- It is possible that DNA from one or more of your samples may not be of sufficient quantity or quality, and a reading may not be obtained in the genetics lab. In this instance re-sampling of DNA is recommended before transfer to the uterus. This involves thawing the blastocyst, re-sampling DNA, then refreezing the blastocyst, which may potentially affect the viability of the embryo.
- It is possible that all samples tested will be reported as “abnormal”, meaning the sample has an abnormal number of chromosomes. Therefore, it is possible that no euploid embryo (embryo sample reported to have the correct number of chromosomes) will be eligible for transfer to the uterus to attempt pregnancy.
- PGT does not test for all genetic abnormalities. PGT-**A** only screens for **aneuploidy**, which is defined as too few or too many chromosomes.
- Results may be delayed because of weather, air travel problems, or other

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unforeseeable causes beyond the control of MLFC.
- The transfer of a genetically tested embryo does not guarantee pregnancy.
- Misdiagnosis may occur due to reasons such as, but not limited to, “mosaicism” of embryos. Mosaicism is defined as more than one chromosomally distinct cell type present in an embryo. Mosaicism is further described in the ART Consent.
- Prenatal testing such as chorionic villus sampling, amniocentesis, ultrasound examination of the fetus, and bloodwork post-IVF are strongly recommended.
- PGT does not guarantee the birth of a normal healthy baby.
- Although rare, the sex of the baby may be different than the sex result on the PGT report.

The purpose of this consent form is to inform you about the various methods that are available to sample DNA from your embryos.

A. YIKON Non-Invasive DNA sampling for PGT-A (ni-PGT-A)

Embryos are individually cultured in drops of media (nutrient solution). Embryos naturally release DNA into the culture media drops as they grow. Non-invasive DNA sampling for PGT for aneuploidy (incorrect or abnormal number of chromosomes) is when the culture media drop (that contains the embryo’s DNA) is collected then sent to a reference lab for genetic testing. This process is called *non-invasive PGT-A* (ni-PGT-A) because it avoids biopsy and removal of the embryo’s cells. This process is also called *non-invasive chromosomal screening* (NICS).

DNA sampling

- **ICSI (intracytoplasmic sperm injection) is required** as the in vitro fertilization method (separate consent form). One sperm is injected into each egg.
- On day 3 of culture, a small hole will be made in the zona pellucida (shell) of each embryo using approximately two laser pulses. This helps some of the DNA, which is naturally released by the embryo, to exit into the culture drop.
- Each embryo will be rinsed several times then moved into a fresh drop of culture medium on day 3.
- When an embryo has reached the expanded blastocyst stage on day 5, 6, or 7 of culture, the embryo will be removed from the culture drop, frozen, and then stored at MLFC.
- The drop of media contains the DNA that was secreted from the embryo since day 3 of culture. After the embryo has been removed, the drop will be placed into a small vial, frozen, then sent to the designated reference laboratory for genetic analysis.

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Limitations

- Rinsing embryos and making a small hole in the shell on day 3 of embryo culture is not standard operating procedure at MLFC, and it is only performed in preparation for YIKON ni-PGTA.
- The presence of contamination with external DNA, mainly from maternal cumulus cells surrounding the eggs could interfere with the results.

Alternatives

An alternative to ni-PGT-A is no PGT or traditional biopsy for PGT-A.

B. EMBRACE Non-Invasive DNA Sampling for PGT-A (ni-PGT-A) –by Igenomix

EMBRACE is a new non-invasive test used to *prioritize* embryos for transfer. Embryos release small DNA fragments (cell-free DNA) into the culture media in which they are grown. The analysis of the cell-free DNA in the culture medium gives an estimate of the embryo's chromosomal content. The EMBRACE assessment is most effective during the embryo's later stage of development, at least 6 days after egg retrieval.

The number of chromosomes is assessed, without biopsy, in order to identify embryos with the best chance of resulting in a healthy baby. This information can be used to establish the order of priority for embryo transfer. The embryos with higher Euploidy Scores (higher probability of having the correct number of chromosomes) are prioritized as the first candidates for tranfer. The goal of the assessment is to allow all embryos to remain candidates for transfer and not to exclude any embryos with reproductive potential.

DNA sampling:

- Retrieved eggs can be inseminated using ICSI (intracytoplasmic sperm injection) or standard in vitro fertilization (IVF)
- After 4 days of development, each embryo will be rinsed and transferred to a fresh drop of culture medium
- As the embryo grows, cell-free DNA is slowly released into the medium
- At day 6 or day 7, the blastocyst-stage embryo will be removed from the culture drop and frozen
- The culture medium containing cell-free DNA will be collected, placed into an individual sterile tube, and transported to the Igenomix genetics laboratory.

Limitations:

- A multicenter study performed by IGENOMIX shows the **concordance rate of chromosome analysis with blastocyst culture medium (EMBRACE) with the trophectoderm biopsy is 78%**, meaning that the chromosome analysis results between the culture medium (EMBRACE) and embryo

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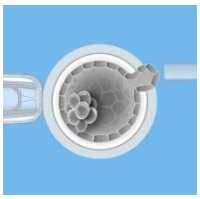
biopsy were the same 78% of the time.
- EMBRACE cannot detect mosacism at this time and will not be reported
- Rinsing embryos on day 4 of embryo culture is not standard protocol at MLFC, and it is only performed in preparation for EMBRACE ni-PGT-A.
- Culturing all embryos to day 6 is not standard protocol at MLFC, and it is only performed in preparation for EMBRACE ni-PGT-A. MLFC standard protocol is to freeze embryos on the day that they develop to the blastocyst stage, which could be day 5, day 6, or day 7 of culture. Culturing all embryos to day 6 or 7 could result in more hatching or hatched blastocysts.
- The presence of contamination with external DNA, mainly from maternal cumulus cells surrounding the eggs, could interfere with the results.
- Other limitations are described in the the EMBRACE consent form.

Alternatives:

An alternative to ni-PGT-A is no PGT or traditional biopsy for PGT-A, which is described below.

C.Traditional biopsy for PGT



Traditional biopsy for PGT has been available for over ten years, and it requires the embryologists to remove a small number of cells from the outer layer of a blastocyst-stage embryo in a process known as **embryo biopsy**. Cells are removed from the trophectoderm, which is the part of the embryo that develops into the placenta. First, a small hole is made in the zona pellucida (shell) using laser pulses. Next, approximately 5-7 cells are suctioned into a pipette, and laser pulses and suction are used to remove the biopsied cells from the remainder of the embryo. Embryo biopsy is performed when a good-quality embryo develops into a blastocyst on day 5, 6, or 7 of culture. The cell sample from biopsy will be sent to the designated reference laboratory for genetic testing, whereas the embryo/s are typically frozen and stored in a cryotank at MLFC.

Risks and Limitations:
Although rare, it is possible that some or all embryo(s) may be damaged during biopsy. The risk of damage to the embryo can be related to embryo quality, thus only good quality blastocysts will be biopsied.

Alternatives:
An alternative to traditional biopsy for PGT is either no PGT or ni-PGT-A.

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"MOSAIC" RESULT

It is possible for a percentage of your embryos to be reported as "mosaic", which means that some of the cells in the embryo may be euploid (normal number of chromosomes) and some may be aneuploid (abnormal number of chromosomes). Healthy pregnancies have been reported after transferring mosaic embryos to the uterus (womb). Embryos have been reported to be able to "self-correct", meaning that the aneuploidy cells become apoptotic (nonviable) or ultimately in the placenta instead of the inner cell mass (ICM) that develops into the fetus. The risk associated with transferring a mosaic embryo depends upon which chromosome/s are affected. If you are interested in transferring an embryo reported to be mosaic, it is required that you have a consultation with a licensed genetics counselor, who will explain the risks. The genetic counselor's written report must be sent to your MLFC physician, and you and your partner (if applicable) must sign a separate consent form before transferring an embryo reported to be mosaic.

EMBRYOS THAT HAVE BEEN REPORTED TO HAVE ABNORMAL NUMBER OF CHROMOSOMES (ANEUPLOID) OR GENETICALLY ABNORMAL

I/We understand that by consenting to PGT that some or all of my/our embryos may be reported to be chromosomally or genetically abnormal. This means that the DNA sample was reported to have an abnormal number of chromosomes or it is affected by a specific genetic disease for which you have ordered testing. It is MLFC policy that embryos reported as abnormal cannot be transferred to the uterus to attempt pregnancy at the MLFC. You may transport or ship your embryos to another fertility center or long-term embryo storage facility.

CRYOSTORAGE AND FEES

All embryos (including those that are abnormal and have the incorrect number of chromosomes) will remain frozen in cryostorage until MLFC receives a ***Consent to Discard Embryo/s*** signed and notarized by both partners. You will be financially responsible for storage fees of all embryos.

QUESTIONS

If you have any questions about the DNA sampling and PGT process, please call **484-380-5200** or contact the following embryologists at MLFC:

Jennifer Jones at Jennifer.jones@mainlinefertility.com
Beth Raneiro at beth.wigo@mainlinefertility.com
Sharon Anderson, PhD Lab Director at 484-380-4884 or sharon.anderson@mainlinefertility.com

Please note that the embryologists at the MLFC are not geneticists. For specific questions about genetic testing of embryos or interpretation of results, please consult a genetic counselor or your physician.

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I/We have been given the opportunity to ask our physician questions about PGT and the contents of this consent form.

I acknowledge that I have read and understood the information provided above regarding DNA sampling, PGT, and the risks, and I agree and consent to DNA sampling for PGT at the Main Line Fertility Center as my signature below testifies:

X_____ _____
Patient Signature Date

_____ _____
Patient Name Date of Birth

_____
Email Address

Notary Public
Sworn and subscribed before me on this _____ day of _____, _____.

_____ _____
Notary Signature Date

X_____ _____
Partner Signature Date

_____ _____
Partner Name Date of Birth

Notary Public
Sworn and subscribed before me on this _____ day of _____, _____.

_____ _____
Notary Signature Date

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If signed in the office:
Statement by Witness (must be employee of Main Line Fertility Center)
I declare that the person(s) who signed this document is/are personally known to me and appear(s) to be of sound mind and acting on their own free will. They signed this document in my presence.
_____ Photo ID checked
_____Form of photo ID: valid Driver's License Passport Non-Driver's License

	Patient	**Partner**
Witness Name:	_____	_____
Witness Signature:	_____	_____
Date:	_____	_____