



## PGT FOR ANEUPLOIDY SCREENING (PGT-A)

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# MOSAIC RESULTS

*Of note, reporting preferences may differ between clinics when it comes to reporting mosaicism. This pamphlet provides information on mosaic reporting, specifically, and does not pertain to non-mosaic reporting.*

# INTRODUCTION

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*Why is it important to have an entire pamphlet about mosaic results?*

While most PGT-A results are straightforward, the interpretation of mosaic results is a bit more complicated and can depend on several different subcategories of mosaic results. Doctors and researchers in reproductive health are continuing to study the outcomes of mosaic embryo transfers. While we continue to learn, this pamphlet is intended to provide you an overview of our current knowledge on mosaic results. Importantly, some mosaic embryos have the potential to grow and develop into a healthy baby.

If you've already had a discussion with your doctor or you have done your own research on this topic, you've probably encountered a lot of new terminology that may be unfamiliar and confusing. You can read more about **related terminology** on **page 3** of this pamphlet. This pamphlet will also address questions such as **how mosaicism is detected and reported on pages 6-7**.

This pamphlet focuses on mosaic results. Igenomix also offers a more general **Results Guide** for PGT-A. Please ask us for a copy!

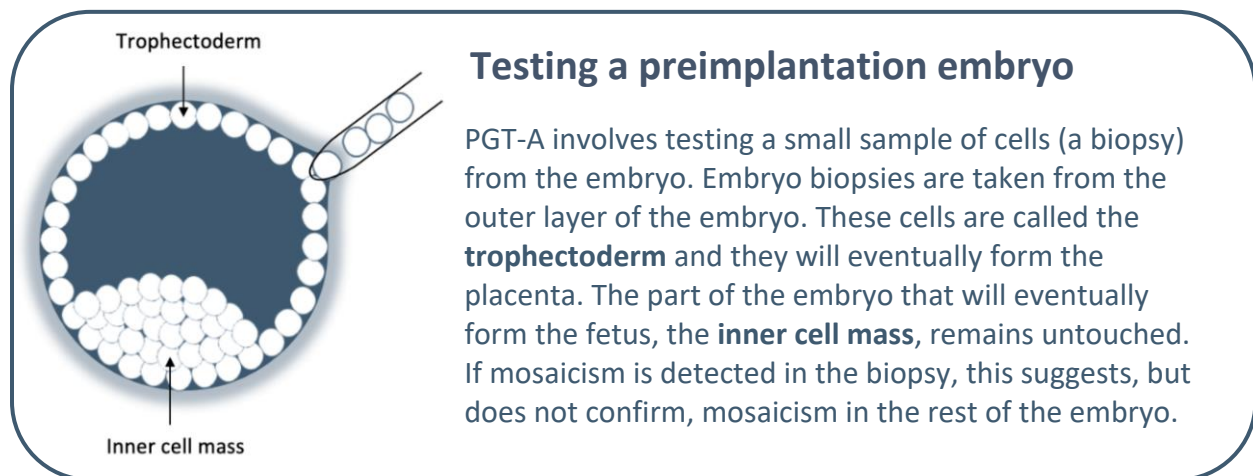
You are likely wondering what a mosaic result means for the reproductive potential of an embryo. Whether an embryo transfer will result in a successful pregnancy is influenced by several factors, including some that are specific to your clinic and to your reproductive history. For this reason, a conversation about expected reproductive potential is best addressed with your fertility provider. Here we share information about the reproductive potential of embryos reported as mosaic from studies focusing on the outcomes of transferring these embryos. You can learn more about **potential outcomes on pages 4-5** of this pamphlet.

Also check out the section of **frequently asked questions (FAQs)** found on **pages 10-11**. We hope you find this pamphlet answers many of your questions. Please do not hesitate to contact us if you would like to schedule a phone consultation with a certified genetic counselor for a discussion of your PGT-A results.

## TERMINOLOGY

Typically, human cells contain 23 pairs of chromosomes, for a total of 46.

**PGT-A (Pre-implantation Genetic Testing for Aneuploidy):** PGT-A refers to screening a biopsy of an embryo for chromosomal copy number changes.

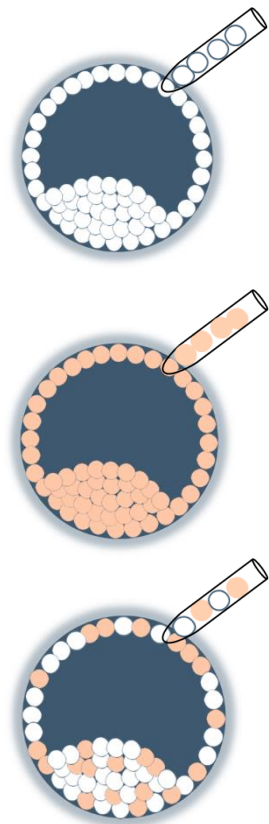


There are three main categories of informative PGT-A results:

**Euploid** refers to embryos with the typical chromosome copy number. Each of the first 22 chromosomes have a copy number of 2. The sex chromosomes typically come as a pair, too, either XX or XY. Euploid embryos are the most likely to result in a successful pregnancy and birth of a healthy baby.

**Aneuploid** refers to embryos with extra or missing chromosomes. One or more chromosomes were observed to have a copy number change (e.g., 1 or 3 copies instead of the typical 2 copies). Aneuploid embryos are less likely to implant. Those that implant are most likely to result in pregnancy loss or an ongoing pregnancy with a chromosome condition.

**Mosaic** refers to embryos that have both euploid and aneuploid cells. When cells in the biopsy are a mix of euploid and aneuploid, mosaicism can be detected based on intermediate chromosomal copy number changes. Mosaicism can be reported as high level or low level.



## OUTCOMES OF MOSAIC EMBRYO TRANSFER

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Several studies have examined pregnancy outcomes following transfer of embryos reported as mosaic.

There are two primary outcomes when an embryo reported as mosaic is transferred:

1. A seemingly healthy ongoing pregnancy/live birth.
2. Failed implantation or early miscarriage.

If an embryo is mosaic for a chromosome abnormality, it is possible that euploid cells within the embryo will progress and aneuploid cells will not, resulting in a healthy child. It is also possible that the aneuploidy will disrupt the development of the embryo, preventing implantation or causing early miscarriage.

Current studies show that the likelihood of an ongoing pregnancy affected by a mosaic chromosome abnormality is low (<1%). However, progression of aneuploid cells in a pregnancy or live birth cannot be ruled out, and **there have been rare case reports of both high and low mosaicism persisting throughout the pregnancy.**

There remains limited clinical data regarding the long-term outcomes of children resulting from mosaic embryo transfers.

Several studies have explored the outcomes of mosaic embryo transfer. Success rates vary by study. **Overall, mosaic embryos have between a 15-45% chance of resulting in ongoing pregnancy or live birth.** Factors that may influence the reproductive success of a mosaic embryo include:

## THE LEVEL OF MOSAICISM

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Studies show that most embryos in the low mosaic range have high reproductive potential, equal to or only slightly lower than that of euploid embryos. Whereas some studies suggest slightly lower rates of pregnancy and higher rates of miscarriage compared to euploid embryos, studies done by Igenomix show that the reproductive potential of low mosaic embryos is equivalent to that of euploid embryos. Although we cannot test the entire embryo, studies show that a low mosaic result is most likely to correspond to an otherwise euploid embryo.

Embryos in the high mosaic range have lower reproductive potential than euploid or low mosaic embryos but higher than aneuploid embryos. Concordance studies show that a high mosaic result is more likely to correspond to an embryo where the majority of the cells, including those of the inner cell mass, are aneuploid.

## THE TYPE OF MOSAIC ANEUPLOIDY

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Studies suggest that the type of mosaic aneuploidy may be more relevant for determining the outcome of a mosaic embryo transfer, rather than the specific chromosome involved in the aneuploidy. For example, embryos reported as mosaic for a segmental aneuploidy (partial monosomy or partial trisomy) have been shown to have higher reproductive potential as compared to embryos reported as mosaic for a whole chromosome aneuploidy.

## THE SPECIFIC MOSAIC CHROMOSOME

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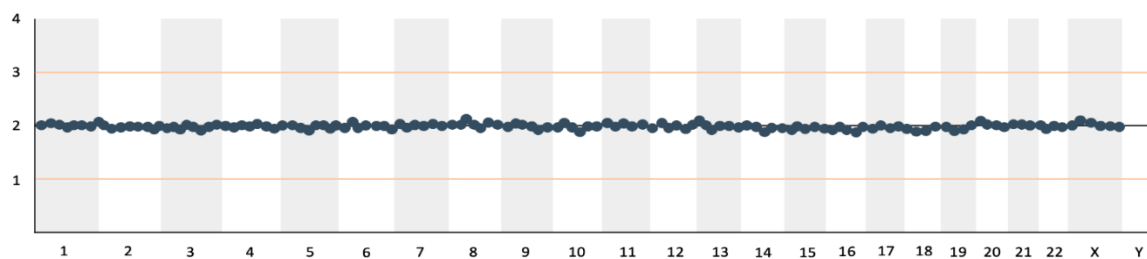
The specific mosaic chromosome involved has little impact on the chance for a pregnancy to occur, and the chance for mosaicism to persist throughout the pregnancy is generally low for all chromosomes. However, there may be some additional counseling considerations for chromosomes associated with viable aneuploidy syndromes, including chromosomes 13, 18, 21, and X.

While studies have not thus far demonstrated increased risks for pregnancies or babies born with an aneuploidy syndrome, the data are very limited. Many providers remain cautious about transferring embryos mosaic for the chromosomes associated with viable aneuploidies.

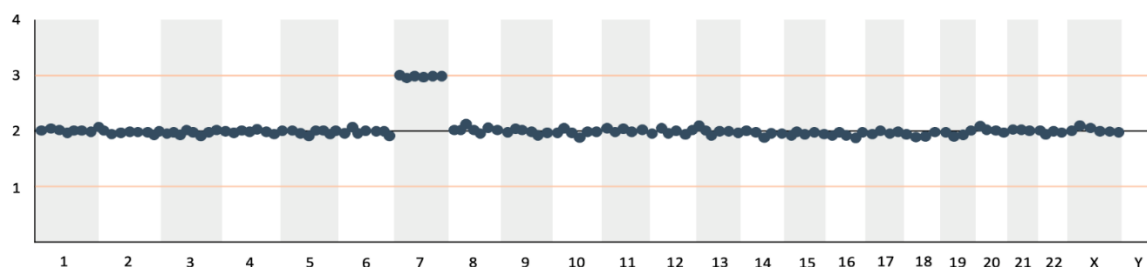
## DETECTION OF MOSAICISM

Cells from the sample are analyzed together as a whole instead of individually. Therefore, a mosaic result is not actually the direct observation of both euploid and aneuploid cells in the embryo sample. Rather, PGT-A compares the relative number of copies of each chromosome in the sample.

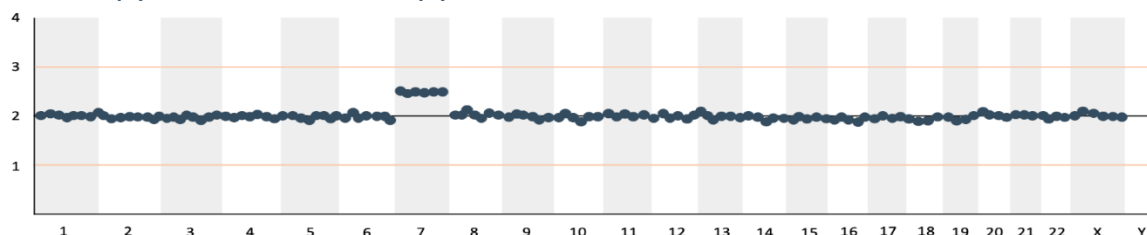
A **euploid** result is reported when the number of sequencing reads, representing the amount of DNA, from each chromosome falls on the baseline, determined to be copy number 2.



Chromosome reads that deviate from copy number 2 are an indication of aneuploidy. An increase to copy number 3 (extra chromosome) or a decrease to copy number 1 (missing chromosome) suggests that the chromosomal abnormality is present in every cell of the biopsy. These results are reported as **aneuploid**.

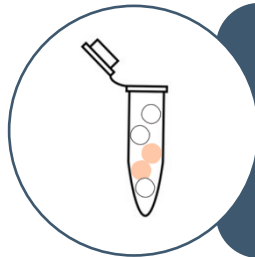


**Mosaicism** is reported when an intermediate copy number change (between 1 and 2 or between 2 and 3) is detected. If a chromosome has 2 copies in some cells but 3 copies in other cells, then the content of DNA for that chromosome will fall between copy number 2 and copy number 3.

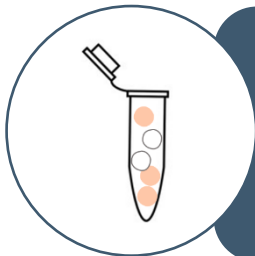


## INTERMEDIATE COPY NUMBER VARIATION

When an intermediate copy number variation is detected, the embryo is reported as mosaic. The level of mosaicism is determined by the degree of copy number variation.

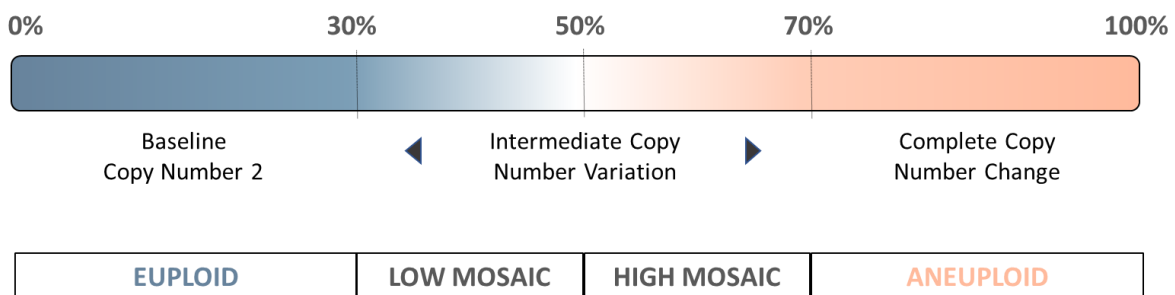


**Low level mosaicism** suggests that the majority of cells are euploid. Chromosomes are reported as low mosaic if the chromosomal copy number variation in the biopsy is between 30-50%.



**High level mosaicism** suggests that the majority of the cells in the biopsy are aneuploid. Embryos are reported as high mosaic if the chromosomal copy number variation in the biopsy is between 50-70%.

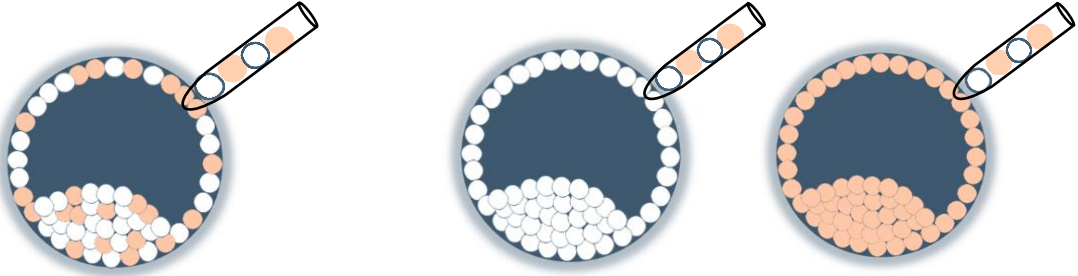
The scale below shows another representation of copy number variations. Intermediate copy number variations between 30% and 70% fall within the mosaic range and can be either a mosaic monosomy or a mosaic trisomy. Intermediate copy number variations below 50% would be reported as low mosaic and above 50% would be reported as high mosaic.



You may have noticed in the graphs on the previous page that the sequencing reads appear wavy across the chromosomes. Because of this waviness, it is difficult to provide a more refined percentage of copy number variation beyond the general categories of euploid, low mosaic, high mosaic, and aneuploid.

## LIMITATIONS

PGT-A is a screening test. Testing is done on a biopsied sample of cells, which typically represents the status of the whole embryo. False mosaic results are possible.

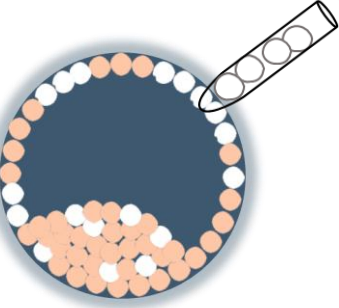


**True mosaic result**

**False mosaic results**

While a mosaic result suggests that the embryo is mosaic, the mosaic result from the biopsy may not actually represent the embryo. The embryo may be entirely euploid or entirely aneuploid. There are biological and technical limitations.

It is not possible with PGT-A to determine the chromosomal makeup of each cell in the embryo. Therefore, even with a euploid result, mosaicism cannot be ruled out.



**Mosaicism cannot be ruled out**

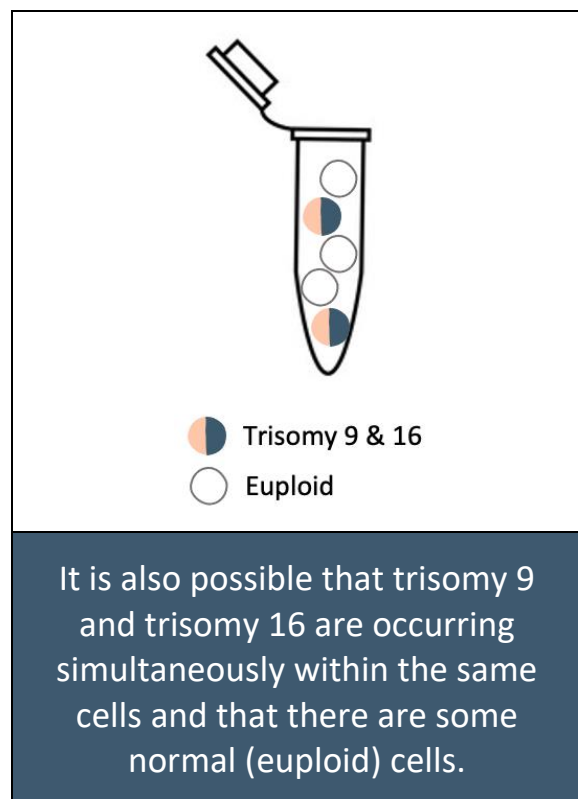
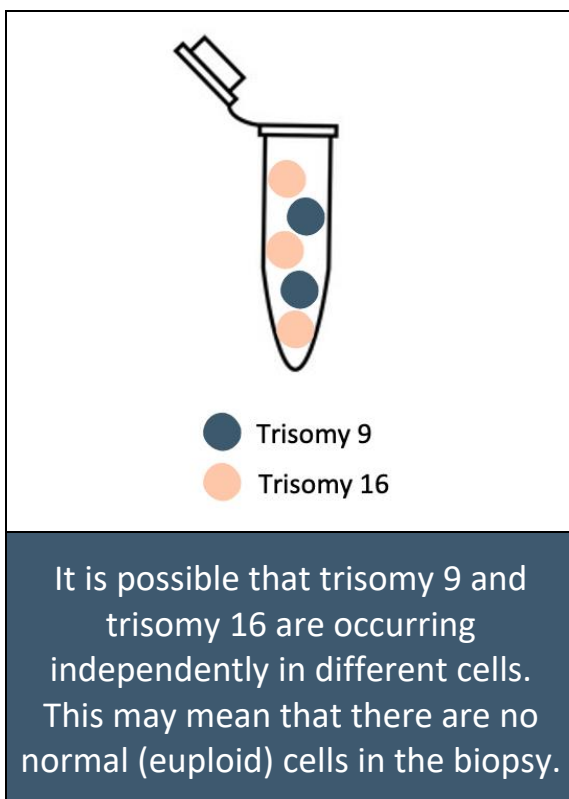
If mosaicism is *not* noted in the biopsy sample it is unlikely to be present; however, this possibility cannot be ruled out.



## LIMITATIONS OF COMPLEX MOSAIC RESULTS

When 2-5 chromosomes with intermediate copy number changes (gain or loss) are detected in an embryo sample, the embryo is reported as **complex mosaic aneuploid**.

Given that each cell in an embryo biopsy cannot be analyzed individually, it can be challenging to interpret complex mosaic results. For example, if intermediate copy number gains of chromosome 9 and chromosome 16 are reported, this could occur through different mechanisms:



If there are no euploid cells in the embryo, the embryo would have low reproductive potential. Unfortunately, PGT-A cannot confirm that euploid cells are present in the embryo even when reported as mosaic.

## FREQUENTLY ASKED QUESTIONS

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### **Does mosaicism become more likely with age?**

Mosaicism typically occurs after fertilization, with aneuploidy affecting a subset of an embryo's cells. Chromosome abnormalities that occur after fertilization are random and occur with similar frequency in all age groups. However, mosaic results are actually observed a little less frequently for those in older age groups simply because non-mosaic aneuploidy (pre-fertilization) is more common.

### **How common are mosaic results?**

Based on Igenomix internal data, mosaicism is reported in approximately 8% of embryos that undergo PGT-A.

### **What do I do with my mosaic embryos?**

Options for embryos reported as mosaic may differ across clinics. These options may include: transferring the embryo(s), storing the embryo(s) for future consideration, or discarding the embryo(s). You will need to consult with your physician to know your clinic's policies.

### **Is there the option to do a re-biopsy?**

A re-biopsy is not typically recommended, as results of the second biopsy would not override the results of the first. Differing results between the first and second biopsy would only confirm that the embryo is mosaic, which is already suspected based on the initial biopsy. It is not possible to determine whether the results of the first biopsy or the results of the second biopsy are more representative of the embryo as a whole.

### **Does Igenomix recommend transferring an embryo reported as mosaic?**

Igenomix recommends euploid and most low mosaic embryos for transfer. Euploid embryos are the most likely to implant, develop to term, and result in a healthy live birth. Transfer of an embryo reported as mosaic may be considered following genetic counseling and discussion with a physician. The reproductive potential of low mosaic embryos has been shown to be similar to that of euploid embryos with low risk of persisting mosaicism. Clinics and specialists have varying opinions regarding embryos reported as mosaic. The decision whether to transfer an embryo reported as mosaic is ultimately that of the patient and their physician.

## FREQUENTLY ASKED QUESTIONS

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### **Do I need to do prenatal testing after transferring a mosaic embryo?**

As for all pregnancies, prenatal evaluation and testing should be offered to you and discussed with your obstetrician or prenatal genetic counselor. Options include fetal anatomy scans, non-invasive prenatal testing (NIPT) performed on a pregnant person's blood sample, and diagnostic testing performed through chorionic villus sampling (CVS) or amniocentesis.

Prenatal testing recommendations following transfer of a mosaic embryo are controversial. Some providers may encourage diagnostic testing while others feel the risks of prenatal diagnosis, while low, are greater than the risk for mosaicism to persist through the pregnancy. Be sure to provide a complete copy of your PGT-A report, which will include information about how to interpret mosaic results in embryos, to your prenatal provider.

### **Is there genetic testing available during a pregnancy to assess for mosaicism?**

Diagnostic testing is best suited to evaluate prenatal mosaicism. Chromosome analysis can be performed on samples obtained during pregnancy from an amniocentesis or chorionic villus sampling (CVS). Amniocentesis is the only method by which fetal DNA (rather than placental DNA) can be analyzed. NIPT is considered a screening tool and has limitations in detecting mosaicism.

Although there is no evidence for an increased risk of uniparental disomy (UPD) following mosaic embryo transfer, additional assessment if diagnostic testing is elected may be considered following transfer of an embryo with mosaicism of chromosomes associated with UPD, including chromosomes 6, 7, 11, 14, and 15, and 20.

## CONCLUSIONS

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We understand that mosaic results can be challenging to understand, and we hope that the information shared in this pamphlet makes the result interpretation a lot clearer. Igenomix genetic counselors are available to speak with you about your mosaic results and other PGT-A results. The goal of genetic counseling is not to tell you what to do or not to do, but rather to provide information to enable you to make the best decisions about your medical care and embryo transfer decisions. You may also find it valuable to consult with a genetic counselor outside of Igenomix and throughout your reproductive journey.

This result guide is intended to provide an overview of your mosaic PGT-A results. This guide is not intended to replace genetic counseling. If you still have questions as to what your results mean after reading through this guide and reviewing the results with your providers, you are welcome to schedule an appointment with a genetic counselor at Igenomix. Please note that embryos are frozen and kept at the fertility clinic, and any decisions regarding embryo transfer, discard, or storage are made with the physician.

**Contact us at:**

Genetic Counseling department: (786) 485-0014, [gc@igenomix.com](mailto:gc@igenomix.com)  
Igenomix Customer Support: (305) 501-4948, [infousa@igenomix.com](mailto:infousa@igenomix.com)