

What is CombiPGD™?

CombiPGD is a test designed for couples with an increased risk of having a child with a specific genetic disorder or chromosomal abnormality based on their own genetic status. The goal of PGD is to identify which embryos are unaffected with the disorder of concern. PGD is available for:

Single Gene Disorders

When both parents are carriers of a recessive genetic disorder or one parent has a mutation associated with a dominant genetic disorder, they are at increased risk of having an affected child. Using DNA samples from you, your partner, and a reference family member, PGD determines which chromosome(s) carry the disease-causing mutation(s). This information provides the disease status for each embryo. The reference family member is typically a first degree relative (e.g. child, sibling, parent) whose disease/carrier status is known.

Chromosome Translocations

Individuals with a balanced chromosomal translocation typically do not experience any symptoms associated with their chromosomal alteration, however, the gametes (eggs or sperm) have a significantly increased chance of carrying a chromosomal imbalance. PGD determines whether or not a chromosomal imbalance is present in each embryo.

PGS Aneuploidy Screening

As part of the CombiPGD process (for both single gene disorders and chromosome translocations), embryos are also screened for chromosomal abnormalities. Chromosomes are the structures inside of our cells that contain the genetic information needed for our bodies to grow, develop, and maintain our health. Changes to the number or structure of the chromosomes may cause failure of an embryo to implant, result in a miscarriage, or lead to the birth of a baby with developmental, intellectual and/or physical abnormalities. The goal of aneuploidy screening is to identify embryos that are chromosomally normal, and thus have the best chance of successfully implanting and maintaining a pregnancy.

Additional information is also available at

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Understanding Preimplantation Genetic Diagnosis (PGD)

Better Care.

Improved Outcomes.




CombiMatrix

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High-Tech. High-Touch.

CombiPGD Using Karyomapping

CombiMatrix utilizes a technique called Karyomapping, which investigates hundreds of thousands of points along all 23 pairs of chromosomes.

For single gene disorders, Karyomapping compares genetic markers between you, your partner and one or more reference family members to determine which chromosome(s) carry the mutation(s). This information is then used to determine whether or not an embryo has inherited the affected chromosome(s).

For chromosomal translocations, Karyomapping is able to identify how many copies of the chromosomes involved in the translocation are present, which determines whether or not the embryo has a chromosomally unbalanced form of the balanced parental translocation.

Karyomapping is also used to simultaneously determine how many copies of any given region of a chromosome are present. Although the focus is on whole chromosome aneuploidy, which is the most common cause of failed implantation and/or early miscarriage, gains and losses of chromosomal segments larger than 30 Mb in size (segmental aneuploidy) may also be detected, and are anticipated to be associated with a similar risk.

Added Benefits of Aneuploidy Screening

In addition to increasing the likelihood of a successful pregnancy for any couple, aneuploidy screening may be of particular benefit to couples who:

- Have experienced one or more failed IVF cycles
- Have a history of recurrent miscarriage
- Prefer to have a single embryo transferred
- Have had a previous pregnancy or child with a chromosomal abnormality
- Are at increased risk for aneuploidy due to advanced maternal age

How Is PGD Performed?

At 5 to 6 days following fertilization, several cells from the outer layer of the embryo (the trophoctoderm) will be biopsied and sent to CombiMatrix for analysis. Your embryos will stay at your local fertility laboratory, and your physician will send the biopsy samples to CombiMatrix. Each individual embryo biopsy is bar-coded to provide optimal security and accuracy throughout the testing process.

Is PGD Covered By My Insurance?

Most insurance plans provide very limited or no benefits for assisted reproductive treatments, such as IVF and IVF-related testing. However, you should check with your insurance provider to determine whether you may be able to submit a claim for PGD testing.

CombiMatrix is dedicated to making PGD testing affordable so that more families can benefit from this technology. Prior to your procedure, CombiMatrix will work with your reproductive health care specialist to provide you with information regarding your financial responsibility, and can also assist you in filing a claim with your insurance once testing has been completed. Please note that payment in-full is required before any testing can be initiated.

What Is The Timeline For The PGD Process?

Because each patient's situation is unique, there is a necessary preparatory period prior to initiating PGD. Karyomapping allows us to significantly reduce that time compared to other techniques of PGD. Below is an outline of the PGD referral and testing process:

1. **Initial Referral** Your doctor will complete and submit a PGD Patient Referral Form, including all relevant genetic testing results (i.e. mutation analysis for single gene disorders or karyotype reports for chromosome translocations). Please note that for single gene disorders, if a specific mutation has not yet been identified in your family, PGD cannot be performed.
2. **Initial Genetic Counseling** Within 72 hours of receiving the referral, a CombiMatrix genetic counselor will contact you to schedule an initial telephone consultation. The purpose of this initial consultation is to review the test results, obtain a detailed family and medical history, and for single gene disorders, identify any suitable family members who could serve as a test reference.
3. **Medical Team Review** The CombiMatrix Medical Team will review your case to ensure that there are sufficient genetic markers within and surrounding the gene (single gene disorders) or chromosomal region (chromosomal translocations) of concern. The vast majority of cases will be suitable for PGD by Karyomapping, however, it is possible that Karyomapping may not be the best method for PGD, due to decreased coverage of the region of concern or, for single gene disorders, a lack of a suitable reference. If this is determined to be the case, you and your doctor will be notified immediately.

4. **Second Genetic Counseling Consultation** Once your case has been approved, you will be asked to schedule a second genetic counseling telephone consultation to review the design of the testing for your specific situation, discuss the requested reference family member (for single gene disorders only), and review the risks and benefits of PGD with PGS for Aneuploidy. Following this consultation, you and your partner will sign a consent form, pay a deposit of \$500 (which is applied to the cost of the testing) and receive DNA collection kits. You and your doctor will also receive a personalized letter from the genetic counselor summarizing the consultation.
5. **PGD Test Set-Up** For single gene disorder cases, the patient, partner and reference family member's DNA will be run together to optimize the testing. If the reference sample provided is not suitable, a sample from another family member(s) may be requested. If there are any concerns regarding the unique PGD test setup for your family, our medical team will inform both you and your doctor. Since chromosome translocation cases do not require a reference family member, there is no additional test set-up step required for these cases. Patients typically begin their cycle at this point.
6. **Embryo Testing and Post-Test Genetic Counseling** Once we receive the embryo biopsies in our laboratory, testing will be initiated, with results typically available in 12-14 calendar days. After discussing the results with your doctor, a CombiMatrix genetic counselor will follow-up with you to answer any additional questions.

About CombiMatrix

CombiMatrix is a genetic testing laboratory whose mission is to provide specialized genetic tests that make a difference. Our testing services provide patients and physicians with information that can assist in making more informed care decisions.