

## **Preimplantation Genetic Diagnosis for Single Gene Disorders**

### **What are Single Gene Disorders?**

Single gene disorders are genetic conditions caused by the alteration or mutation of one specific gene in the affected person's DNA. Examples of single gene disorders are cystic fibrosis, sickle cell anemia, Tay Sachs disease, myotonic dystrophy, and Duchenne/Becker muscular dystrophy, to name a few. Individuals with a family history of a single gene disorders are at increased risk for passing the condition onto their children. Preimplantation genetic testing is able to distinguish between genetically normal or affected embryos. Currently, this is the only way to determine whether the embryo is unaffected with the genetic condition, prior to pregnancy. [Please click here for a list of single gene disorders that have been tested by our center.](#)

### **What is preimplantation genetic diagnosis?**

By definition, preimplantation genetic diagnosis (PGD) is diagnosis of a genetic condition prior to achievement of a pregnancy. PGD was first performed in the early 1990's as a way for couples to prevent the pregnancy of a child with genetic disease. Currently, we are able to perform PGD for many genetic conditions including single gene disorders and for chromosomal abnormalities. At the Reproductive Genetics Institute, we have been performing PGD since it became available in 1990. We pioneered the polar body removal technology and are one of the most active centers offering PGD in the world. Our laboratory technicians are well trained in the techniques involved.

### **How can PGD help my family and me?**

PGD is an opportunity to reduce your chances of having a child affected by genetic disease. PGD allows the laboratory to determine prior to implantation which embryos are likely to be affected or unaffected by a particular genetic condition. Only the embryos that are predicted to be free of the genetic condition are transferred to the woman's womb. This process reduces the likelihood that a family has to make difficult decisions in a pregnancy following prenatal testing results and may alleviate much anxiety when awaiting results.

### **What is IVF?**

IVF is an abbreviation for in vitro fertilization. This refers to a process by which the eggs are retrieved from the ovaries of a woman before they are released, and fertilization of the eggs occurs in the laboratory. The resultant embryos are placed back into the woman's uterus several days later. An IVF cycle includes the woman taking injectible medications to stimulate the ovaries to produce more than one egg at a time. As one can imagine, this is a fairly complicated process which requires a number of physician visits and monitoring. IVF is required when an individual chooses to have PGD testing performed.

### **How is the testing performed?**

There are two basic types of preimplantation diagnosis—polar body analysis and embryo analysis. Both types of analysis have advantages and limitations. Polar body testing focuses on the maternal contribution, and is an earlier method of testing. Generally, polar body testing is performed in any case where the female partner of the couple carries the gene of interest (she may have the condition or she may be a carrier of that condition).

When both partners are at risk for a recessive genetic condition (e.g. cystic fibrosis) but they carry different gene changes, it is often recommended only to test for the female contribution via polar body analysis to minimize the risks of misdiagnosis. Embryo testing may account for both maternal and paternal genetic contributions but occurs later and in many circumstances has a higher chance of misdiagnosis. Therefore, this testing is performed in cases in which the male partner has the genetic condition that is being tested for or in cases where it is necessary to have paternal contribution assessed.

### **What are polar bodies?**

Polar bodies are the by-products of the egg's division. As an egg matures, it goes through a two-step division process, dividing once at the time when ovulation would occur and again at the time of fertilization. The two polar bodies are the products of this division, which are essentially being discarded by the egg (oocyte). By analyzing the polar bodies, it is possible to infer the genetic status of the oocyte. When testing for a genetic disorder, it is critical to have information from both polar bodies to get a clear picture of the genetic make-up of the oocyte.

### **What is an embryo biopsy?**

When an embryo becomes a 6-10 celled mass (approximately 3 days after egg retrieval), it becomes possible to directly test the embryo through removal of a single cell. Removal of this cell is usually not detrimental to the embryo, as all the cells are equivalent and no cell differentiation has occurred. The cell that is removed may then be analyzed to determine directly the genetic status of the embryo, both maternal and paternal.

### **How is the PGD done?**

Generally, due to the limited amount of DNA that is available for study (one single cell), and due to the limited timeframe to obtain results, a special system for testing will be set up for each family. This testing will rely on a technology known as PCR, which enables the laboratory to use a small amount of DNA and get a rapid result. A system is set up for each family, which will be dependent upon the condition being tested for. Usually, in addition to testing for the gene change, the lab will also determine linked markers, which are used in a fashion similar to DNA fingerprinting. Linkage allows the lab to have several ways to determine which gene(s) has/have been inherited. Therefore, RGI will request different types of DNA samples to prepare the case and develop a system for the family. Once this system has been created for the family, the laboratory tests it on the various samples to assure that the testing works consistently in a single cell setting.

### **When do I get results?**

Results are generally given at the time of embryo transfer. If testing is only being performed on polar bodies, results will be available for a day three transfer. If blastomere testing is necessary, the results are available on day five. Since the PGD lab will not have information regarding the status of the embryos, it is most useful to review the results at the time of transfer, when the status of the embryos has been assessed.

### **What is the accuracy of the testing?**

The accuracy of the testing will vary depending upon the genetic condition being studied, the method by which it is being studied, and the number of linked markers for the family. In addition, there will usually be a range of different accuracies for each case, as there are

several different possible outcomes. On average, for a case performed on polar bodies, accuracy will range from 95-98%, and for a case performed only on blastomeres 90-98%. It is important to keep in mind that the testing focuses in only on the condition being studied, and it is not possible to check for all genetic and/or chromosome problems at this early stage of embryo development.

### **What is the cost?**

Please contact one of our genetic counselors for updated pricing information.

### **Does PGD replace prenatal testing?**

No, PGD does not replace prenatal testing, such as chorionic villus sampling or amniocentesis. PGD is a research-based test allowing for a similar diagnosis to those available by prenatal testing. However, prenatal testing is still recommended, as this is currently the standard-of-care. Our genetic counselors can discuss what prenatal testing options are available to you.

### **Frequently asked questions**

#### *Will my insurance cover the costs of PGD?*

Because PGD testing is performed on an investigational basis, most insurance carriers will not cover the cost of PGD. As insurance policies vary, it is always to your benefit to check with your insurance carrier. It is your responsibility to contact your insurance carrier regarding your coverage.

#### *How do I get more information about PGD?*

To receive additional information, please contact our office at (773) 472-4900. You can also send an email request to [rgi@flash.net](mailto:rgi@flash.net).

#### *How do I get started?*

Please contact one of our genetic counselors for an initial consultation at (773) 472-4900. They will provide the necessary information to begin the process for your family.

#### *What are the limitations of PGD?*

As with prenatal testing, PGD is aimed at reducing your chances of having a child with genetic disease; however, it does not test for all birth defects. Every couple, regardless of their ethnic background and family history, has a 3-5% risk for birth defects, with each pregnancy.

#### *Can you also test for chromosome problems such as Down syndrome?*

In many cases, we are also able to screen for age-related chromosomal abnormalities, such as Down syndrome, in addition to testing for the specific genetic condition running in your family. There is an additional fee for this testing. Please talk with our genetic counselor to see if this testing is an option for you.

#### *Is there a waiting list?*

No. As soon as our center receives the necessary information, samples and laboratory set-up fee, we begin working on your case immediately.

