



PREIMPLANTATION GENETIC DIAGNOSIS (PGD)

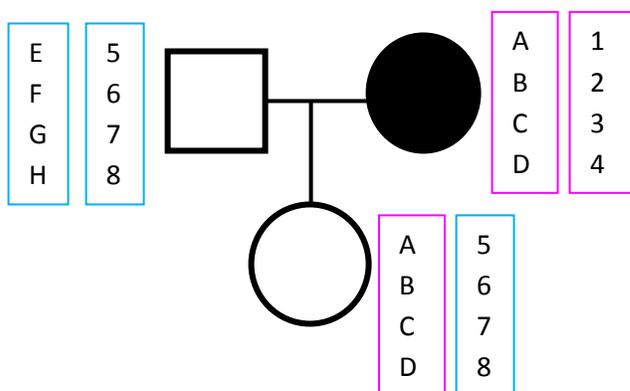
NON-DISCLOSURE TESTING

Non-disclosure testing is an option for people who are at risk of being affected by a late-onset disorder, such as Huntington’s Disease (HD), Spinocerebellar Ataxia (SCA), or Early-Onset Alzheimer’s disease, and do not wish to learn their own genetic status but would like to ensure that their children do not inherit this disease. RGI offers two different methods by which non-disclosure testing can occur.

Indirect Non-Disclosure Testing

Indirect non-disclosure testing utilizes a process called **linkage analysis**. This process involves the use of genetic markers to generate DNA “fingerprints” of the individual’s affected parent’s two gene copies, while not identifying which copy has the genetic mutation. The at-risk individual’s two gene copies are subsequently fingerprinted and matched to his/her parent’s DNA, in order to determine which gene copy was inherited by the affected vs. the non-affected parent. Our lab will only identify which of the at-risk individual’s genes are maternal vs. paternal in order to select for embryos with the gene copy that comes from the unaffected parent.

For example, the individual in the diagram below (open circle) is at-risk because her mother is affected with Huntington’s disease (shaded circle). Each pink and blue rectangle represents a copy of the HD gene, and the numbers and letters inside the rectangles represent the unique genetic sequences (linked markers) in the region of the HD gene. The individual below has a 50% chance of inheriting her mother’s affected gene copy and a 50% chance of inheriting her mother’s healthy gene copy. Her other gene copy was inherited from her father. **We do not know if the gene copy inherited from her mother is the healthy one or the affected one.** We will select for embryos that inherit the individual’s paternal gene copy (lower blue rectangle), since we do not know if the individual’s maternal gene copy (lower pink rectangle) is healthy or affected.



The following is an example of indirect non-disclosure results, based on the diagram on the previous page:

EMBRYO #	PREDICTED EMBRYO GENOTYPE	EMBRYO TRANSFER
1	Presence of patient's MATERNAL gene copy	NO
2	Presence of patient's PATERNAL gene copy	YES
3	Presence of patient's PATERNAL gene copy	YES
4	Presence of patient's MATERNAL gene copy	NO
5	Presence of patient's PATERNAL gene copy	YES

It should be noted that if the at-risk individual is unaffected with the familial genetic condition, then healthy embryos may be selected against.

Direct Non-Disclosure Testing

In direct non-disclosure testing, we send an anonymous sample of the at-risk individual's DNA for testing at a clinical laboratory that specializes in testing for the at-risk gene. **Our PGD laboratory will receive the results and will therefore know the at-risk individual's genetic status; however, this information is not disclosed to the IVF physician and is not placed in the medical chart.**

With this option, testing for aneuploidy (chromosome abnormalities) is mandatory. Chromosome abnormalities occur spontaneously during egg or sperm cell division (please see Page 12 of the Single Gene information packet for more information on this testing). If the at-risk individual is affected, we will test for both the familial genetic disease *and* chromosome abnormalities. If the at-risk individual is unaffected, we will test *only* for chromosomes. Whether the embryos are tested for the genetic disease and chromosomes or only for chromosomes is not disclosed. The results will be presented as a list of those embryos recommended for transfer, whereas it will not be disclosed why certain embryos are not recommended for transfer (i.e. affected with single gene disorder or affected with a chromosome abnormality).

The following is an example of direct non-disclosure results:

EMBRYO #	EMBRYO TRANSFER
1	YES
2	YES
5	YES
10	YES

Therefore, with the direct testing method, embryos are only selected against if they are affected with a genetic problem (either the familial genetic condition or a chromosome abnormality).

RGI strongly recommends that complete non-disclosure is maintained by all parties, including the IVF clinic involved. Our recommendation is that the patient is not provided with any information regarding the number of eggs retrieved, embryos tested, or embryos recommended for transfer, and that the results report above is not seen by the patient. The only information that should be disclosed is whether or not there is at least one embryo for transfer, and whether or not there is at least one embryo frozen. This helps to avoid any potential deduction of genetic status based on the number or percentage of embryos with normal test results.

Which option makes sense for me?

Please make sure to check with one of our genetic counselors to ensure that both options are available to you based on your family history and availability of DNA samples from other family members. If both options are a possibility, you may wish to consider the following advantages and disadvantages to each testing strategy:

Indirect Testing: This option allows for complete anonymity as no one (including our laboratory) will know your genetic status, since we will only be testing for maternal/paternal linked markers and NOT the genetic mutation. There is no risk of learning your status by seeing your results report or other medical records. However, there is the risk that we are performing unnecessary testing (and potentially selecting against healthy embryos) if you did not inherit the familial genetic condition. Additional chromosome testing is optional.

Direct Testing: With this option, our laboratory would be aware of your genetic status. Therefore, even though RGI takes every precaution against disclosure of genetic status, there is a risk for disclosure to happen. However, with this method, embryos are only discarded if they are affected with a genetic problem (either the familial genetic condition or a chromosome abnormality). Additional chromosome testing is mandatory.

Further Information:

Please review the Single Gene Information Packet since this information also applies to non-disclosure testing and should answer many of your questions prior to a consultation with one of our genetic counselors.

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