

Preimplantation Genetic Diagnosis, by Dana Pauling

Dana Pauling, a Genetic Counselor from the Reproductive Genetics Institute (RGI) reviewed the reproductive option of Preimplantation Genetic Diagnosis (PGD) for FA and HLA. PGD makes it possible to diagnose genetic disease in fertilized eggs/embryos before a pregnancy occurs. RGI has performed PGD for ~300 different genetic conditions and can be done for any FA family as long as the FA gene and DNA mutation(s) have been identified. This procedure can also be used to test for HLA status to provide a sibling who is free of FA and a potential stem cell donor for a future transplant.

In Vitro Fertilization (IVF) is necessary in order to perform PGD. Both the IVF and the PGD process can be done in Chicago at the Reproductive Genetics Institute, requiring a one time stay of 7-10 days. Alternatively the couple can opt to do the IVF at a local center and the PGD with RGI. RGI has worked with over 150 IVF centers throughout the country and outside of the United States.

PGD can only be offered if the exact gene and DNA mutations have been identified. The PGD process first requires RGI to obtain DNA samples from the couple and their offspring in order to design a reliable, accurate testing system to help determine the status of the embryos. This PGD setup process includes confirmation of the DNA mutations and the analysis of informative linked markers. The linked markers are used like a DNA fingerprint, as a back up method to help determine the status of each embryo. Linked markers are also used to determine the HLA status of the embryo. The setup process takes about 4-8 weeks to complete. Once the PGD setup is complete and the couple has completed their IVF workup, they will be allowed to start the IVF medication process. The testing system is then applied to eggs and embryo created through an IVF cycle.

With FA, there are 3 chances in 4 that a blastomere will be free from FA (a carrier or a normal, non-carrier), and a 1 in 4 chance that an embryo will be an HLA match to the FA sibling. Therefore there is a 3/16 chance per embryo that it will be free from FA *and* will be an HLA-matched donor for an FA sibling. In general the biopsy procedure itself is believed to cause harm to the developing embryo less than 1% of the time.

Fourteen FA families have worked with RGI to attempt to achieve a healthy pregnancy. These families experienced 44 IVF cycles. In total 45 embryos were transferred to the mothers (59% had an embryo transfer) resulting in 7 pregnancies. Six healthy babies have been born (including one set of twins) and one pregnancy resulted in a miscarriage. The pregnancy rate for FA parents has been ~27% per cycle (if they had an embryo for transfer). Much depends on the age and fertility characteristics of each couple as well as if they are doing additional testing like HLA matching and aneuploidy screening. An embryo can not be transferred unless it passes all of the genetic testing AND is developing.

Preimplantation Genetic Diagnosis is expensive, and insurance is unlikely to cover the cost. PGD related fees include an initial one-time set-up fee (\$3,500-\$5,000 depending

the FA mutations, \$4,000 for HLA testing), and an analysis fee of \$2500-\$5000, the total cost is approximately \$23,000 for each reproductive cycle.

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