



## PREIMPLANTATION GENETIC DIAGNOSIS (PGD)

### HLA MATCHING

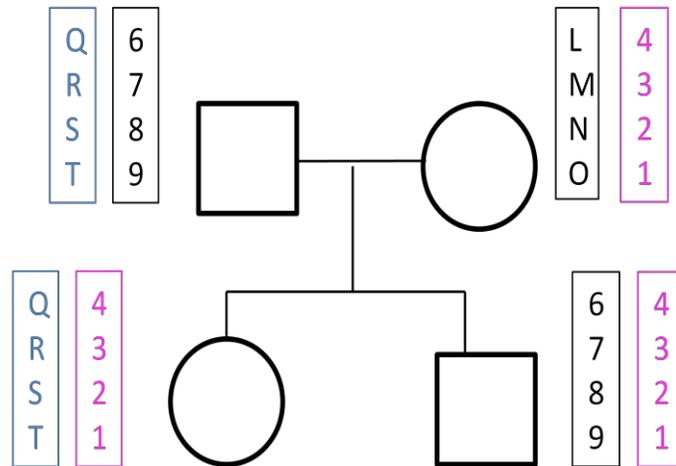
Allogeneic haematopoietic stem cell (HSC) transplantation represents the only curative option for leukemia and certain blood disorders, including  $\beta$ -thalassemia, sickle cell disease, Fanconi anemia, chronic granulomatous disease, Diamond-Blackfan anemia, Schwachman-Diamond syndrome, and Hyper IgM. The best possibilities of cure are provided by transplantation with Human Leukocyte Antigen (HLA)-identical sibling donors. Unfortunately, this ideal strategy cannot be used in the majority of cases because of the difficulty to find HLA-matched donors, even among family members.

If a pregnancy with a matched sibling is conceived, then the newborn umbilical cord blood can be collected during delivery and used to treat the affected sibling. Without intervention, there is a 25% chance of each sibling being a complete HLA match to their affected brother or sister. An increasing number of couples with a child affected by a hematological disease are requesting PGD for HLA matching to increase the chances of conceiving a healthy child who could become a future donor of umbilical cord blood stem cells to treat an affected recipient sibling.

PGD for HLA matching is used to select embryos of a HLA tissue type compatible with that of a child who is in need of a bone marrow transplant. PGD for HLA can be performed in conjunction with a single gene disorder if needed, in order to recommend embryos that are both HLA-matched to an affected sibling and free of the inherited condition.

#### **How does RGI test for HLA?**

RGI has developed a PGD strategy that is optimized for HLA matching. This procedure, called **linkage analysis**, involves generating a mini DNA fingerprint of the affected child's HLA region, and then determining if the HLA region in an embryo is the same or different. PGD for HLA includes the analysis of at least eight polymorphic (unique) genetic markers scattered through the HLA complex, and has been helpful in detecting potential recombination (the normal crossing-over process by which genes are "shuffled" when being transmitted from one generation to the next) that may compromise the likelihood of a match.



In the above figure, circles represent females; squares represent males.

The two narrow rectangles next to a particular circle or square represent the two gene copies that individual possesses. The numbers and letters represent the unique genetic sequences (linked markers) present at that location in the HLA region of the chromosome.

In the figure above, the couple (top row) has two children, a daughter (bottom left) and a son (bottom right). This couple needs an HLA match for their daughter. The daughter's two HLA copies are represented by the blue box and the pink box. The son has the pink copy in common with the daughter; however, his other copy is different; therefore, these siblings are only half-matches.

During the PGD set-up process, the linked markers are determined for each individual in the family using blood or cheek swab samples. These markers are then compared between parents and children to determine which linked markers were inherited in the child needing an HLA match (and therefore, which linked markers would be seen in an HLA-matched embryo). In this case, an embryo would need to show all of the pink markers and all of the blue markers in order to be a complete match. Any black markers seen in an embryo would mean this embryo is not a complete match.

### How many embryos will be a complete match to my child?

If PGD is being performed only to test for HLA, then 25% (1 out of 4) of the embryos are expected to be a match.

If PGD is being performed to test for HLA and a single gene disorder, then the percentage of embryos that are expected to be an HLA match AND free of the disorder will depend on the inheritance pattern of the particular condition. This percentage is often as low as 18.75% (3 in 16).

**However, it is extremely important to remember that statistics do not always hold up in small sample sizes.** Therefore, it is very possible to see a higher or lower number of healthy embryos than predicted. Healthy and HLA-matched embryos must also be developing to be considered for transfer. **Many cycles may result in having no healthy, HLA-matched, and developing embryos to transfer.**

It is also important to know that approximately 6-7% of children may be **“HLA recombinant”**. This term is used to describe a scenario in which a child has not inherited a complete HLA copy from one or both parents, which is a result of the natural process of recombination (crossing over of genes). Unfortunately, if a child is an **HLA recombinant, there is essentially no chance of finding an embryo that is a complete HLA match**. The stage at which we would determine whether or not a child is an HLA recombinant will depend on your particular situation, including prior HLA typing, number of children, and availability of your child’s grandparents to submit a DNA sample. Your genetic counselor will discuss this with you further during a consultation.

### Sample PGD results

EMBRYO #	PREDICTED DISEASE GENOTYPE	PREDICTED HLA GENOTYPE	EMBRYO TRANSFER
1	NORMAL	NON-MATCH	NO
5	AFFECTED	NON-MATCH	NO
6	NORMAL	NO RESULT	NO
9	CARRIER	MATCH	YES
13	AFFECTED	NON-MATCH	NO
14	AFFECTED	MATCH	NO

### Further information

Regardless of whether you are also interested in testing for a single gene disorder or only HLA, please review our Single Gene Information Packet since most of the information also applies to HLA testing and should answer many of your questions prior to a consultation with one of our genetic counselors.

Reproductive Genetic Innovations, LLC  
 2910 MacArthur Boulevard  
 Northbrook, IL 60062  
 Phone: 847-400-1515  
 Fax: 847-400-1516  
 Email: info@rgipgd.com  
 www.rgipgd.com