2nd International and 10th National Biotechnology Congress of Islamic Republic of Iran
August 29-31, 2017
Seed and plant Improvement Institute, Karaj, Iran
دومین همایش بین المللی و دهمین همایش ملی بیوتکنولوژی جمهوری اسلامی ایران
۷-۹ شهریور ماه ۱۳۹۶
کرج، سالن همایش های موسسه تحقیقات اصلاح و تهیه نهال و بذر

Molecular PGD for finding HLA match embryo for stem cell therapy in Fanconi anemia

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Introduction

Pre-implantation genetic diagnosis (PGD) is a technic that has been applied for couples with known genetic disorders to prevent the birth of children affected by monogenic defects.

In molecular PGD, the blastomeres are biopsied from 8-cell stage embryos, via in vitro fertilization. Therefor abnormalities in embryos are detectable before transferring them in to the mother's uterus.

PGD make the opportunity to diagnose the disease status, chromosomal aneuploidies, HLA typing and sex selection simultaneously.

Fanconi anemia is a genetically heterogeneous disease with autosomal recessive inheritance. It is characterized by physical abnormalities, bone marrow failure and increased risk for malignancy.

This article presents experience of molecular PGD to select unaffected and HLA-matched blastomere/s for the purpose of transplanting to his affected sibling.

Keywords

PGD, HLA, Fanconi anemia, IVF

Material & Method

After genetic consolation, peripheral blood samples were collected in tubes containing EDTA and genomic DNA was extracted using salting out method.

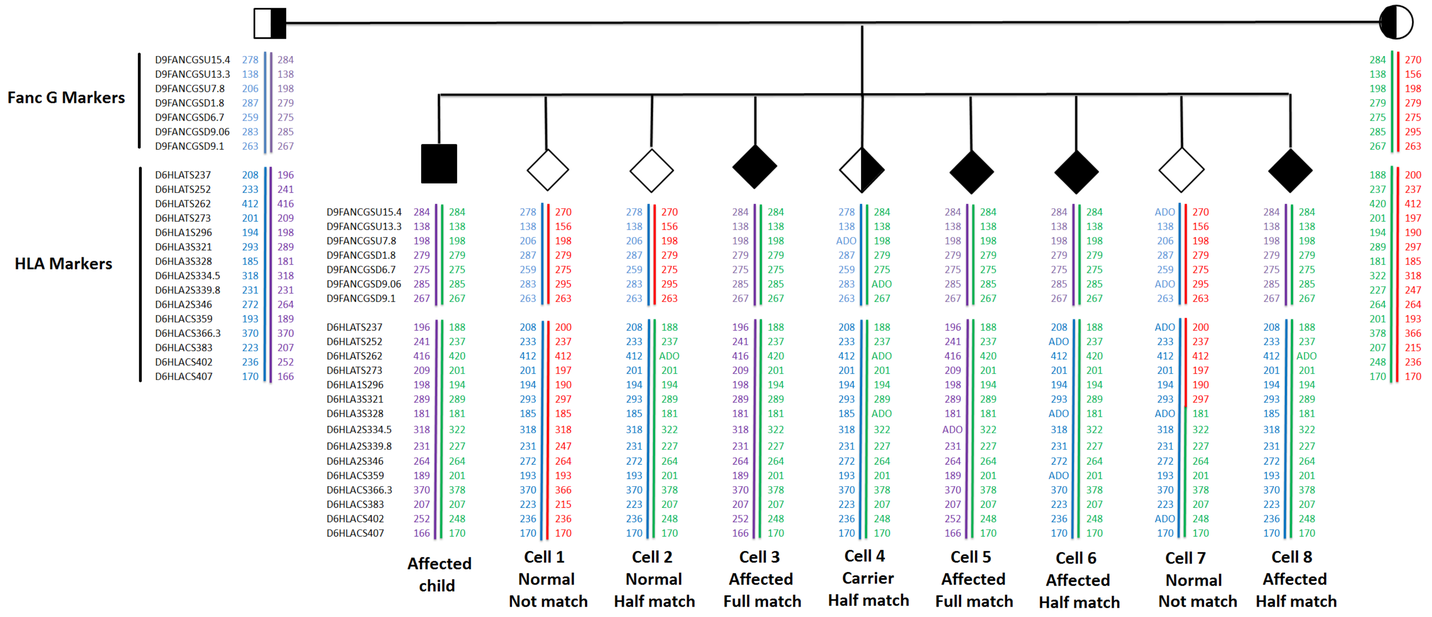
Homozygosity mapping with help of polymorphic STR markers were performed on each blastomere for FANC G gene to track the defective alleles in the family. Simultaneously, haplotype analysis was done to find the HLA matched embryo for all members of the family. Additionally, the possibility of the presence of the causative mutation in FANC G gene was tested by Sanger sequencing.

Result

From 8 investigated blastomeres, 3 were normal (1 half-matched HLA, 2 not matched HLA). 1 carrier with half-matched HLA. 4 affected (2 full matched HLA, 2 half-matched HLA).

Conclusion

PGD prepare a chance to have a healthy child who can donate stem cells for the treatment of affected child. This method is a reliable technique with 99.9% accuracy, Results obtained from haplotype mapping in parallel with direct mutation detection.



Haplotype illustrating embryos