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Review

THE EMERGING ERA OF GENETICALLY ENGINEERED OFFSPRING

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Abstract

Genetically engineered offspring are produced by genetic modification to affect the characteristics of the offspring, or from an embryo chosen by pre-implantation genetic diagnosis (PGD). The main goal of designing offspring is to prevent genetically-based disorders that are caused by mutations in DNA. It is now possible to produce precisely modified designer babies—as evidenced by the advancements in mitochondrial DNA transfer and genome editing techniques. But there isn't enough information available about the risks associated with these editing tools, particularly when the changes are inherited. In addition, there are moral questions about whether or not we should use these technologies to produce designer offspring. that further study is needed to refine the technique and determine its long-term safety, and that these germ line genetic editing techniques should still be regarded as experimental operations. created and put into use a teaching module for both an advanced genetics course and a genetics course that introduces students to CRISPR-cas9 technology. The design, strategy, conceptual modelling, and implementation of CRISPR-cas9 technology are based on the current study findings about CCR5 gene editing in twin girls.

Keywords: CCR5, CRISPR-cas9, Gene-editing, Germ-line.

INTRODUCTION:

A designer baby is a child whose genetic composition has been chosen or changed, frequently to eliminate genes linked to certain illnesses or to exclude a certain gene. Pre-implantation genetic diagnosis is the process of identifying genes linked to specific diseases and traits by evaluating a large number of human embryos. Then, embryos with the desired genetic makeup are chosen. A few companies offer polygenic screening; single gene screening is a common procedure; and altering a baby's genome directly before birth is another way to change their genetic makeup. As of 2019, however, this is not a common practice and there has only been one known instance of it, involving the Chinese twins Lulu and Nana.

The desired genetic material can be added to the embryo itself, the parents' sperm and/or egg cells, or both by applying gene-editing technologies or direct cellular delivery of the desired genes. These babies are designed while still in the womb to achieve more designed, looks, skills, intelligence, and talents**.**

The goal of designer babies is to avoid inheritance defects by selecting "disease-free" embryos by pre-implantation genetic diagnosis (PGD). Certain illnesses, such as cystic fibrosis and β-thalassemia, are curable. However, genetic alteration would be required when all embryos carried the "disease genes" from a carrier couple. Scientists can now produce designer babies through newly developed DNA editing techniques [6].

HISTORY OF DESIGNER BABY

In November 2018, the 38-year-old scientist Dr. Jiankui, a skilled Chinese-American physician, revealed the birth of twin twins going by the aliases Lulu and Nana. They were the first human beings with genomes edited using CRISPR (Clustered Regularly Interspaced Short Palindrome Repeats). He stated that his goal was to modify theirCCR5 gene so the girls would be resistant to the AIDS virus, since both their parents were infected. The announcement was initially grated with jubilation by Chinese authorities, but it was later revealed that the experiments had violated the most fundamental ethical and medical standards.

He and his team extracted DNA from the placenta, umbilical cord, and cord blood of the two newborn girls and used Whole Genome Sequencing (WGS) to verify that CCR5 editing was successful. Based on the WGS data, it was determined that these samples included just two distinct CCR5 alleles, each of which accounted for around half of the sequencing reads. For Lulu, one allele remained, and the other allele had an in-frame deletion. For Nana, the two CCR5 mutant alleles represented 100% of all sequencing reads at the CCR5 target region, which suggests, quite surprisingly, that none of the mother's tissue (containing WT CCR5 allele) contaminated any of Nana's samples [7].

PRE-IMPLANTAION OF GENETIC ENGINEERING

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Pre-implantation genetic diagnosis:

Pre-implantation genetic diagnosis, often known as PIGD, is a process that involves screening embryos before implantation. The method is used in conjunction with in vitro fertilization (IVF) to produce embryos for genome analysis; ovocytes can also be checked before fertilization. The method's debut was in 1989.

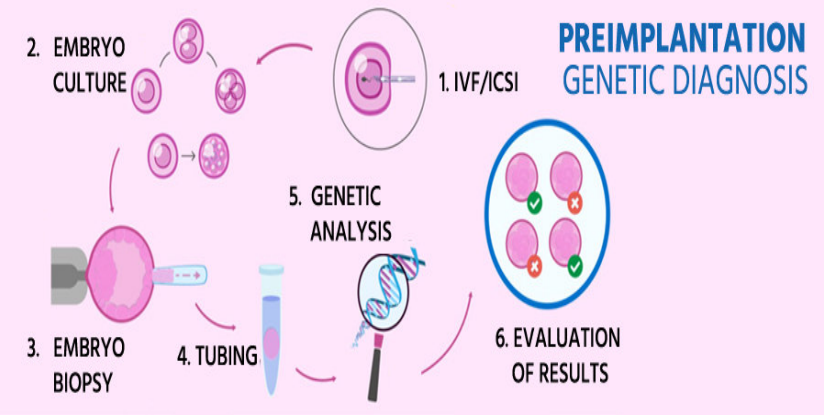

Figure-1Pre-implantation Genetic Diagnosis

Pre-implantation Genetic Testing:

• PGT-M, or pre-implantation genetic testing for monogenic diseases, is a diagnostic tool for genetic disorders resulting from mutations or changes to a single gene's DNA sequence.

• PGT-A, or pre-implantation genetic testing for aneuploidy, is a diagnostic tool for aneuploidies, or numerical abnormalities.

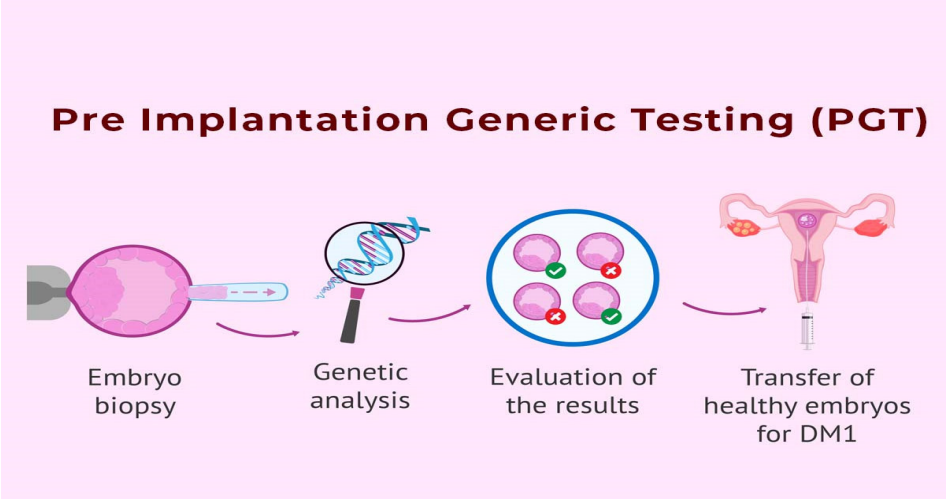

Figure- 2 Pre-implantation Generic Testing

Pre-Implantation Genetic Testing of Monogenic Disease:

PGD involves transferring only unaffected embryos, removing one or more cells from each embryo for genetic analysis, and IVF therapy for couples who may not be able to conceive a child with a single gene abnormality.

The two polar bodies, which are the result of the two meiotic divisions in the ovocyte and contain the extra maternal chromosomes, can be biopsied to check for faults in the single gene that are inherited by the mother or errors in the segregation of meiotic chromosomes. Afterwards, one or two embryonic cleavage stage cells or several blast cyst stage trophectoderm cells may be biopsied [5].

Multiple PCR for PGT-M:

Finding DNA markers that could independently determine the existence of the chromosome containing the defective gene was made necessary by the coexisting issues of ADO and contamination. This would have resulted in a diagnosis with redundancy built in (1998). In the early 1990s, A highly polymorphic class of markers known as short tandem repeats (STRs), which are widely distributed throughout the genome and consist of a short sequence of two or more bases repeated a variable number of times, was discovered and mapped as a result of the intense effort to sequence the human genome.

SNPs and Karyomapping:

Multiplex fluorescence PCR presents a challenge in that, while the chemicals are reasonably inexpensive, the initial work to find useful markers for a particular family or inherited ailment and optimize their amplification at the single cell level is labor- and time-intensive. Moreover, in many families it may be challenging to find fully informative closely connected markers. As a result, many possible options may be tested before a final combination is determined, which may only be partially informative or have a weaker desirable relationship with the mutant gene.

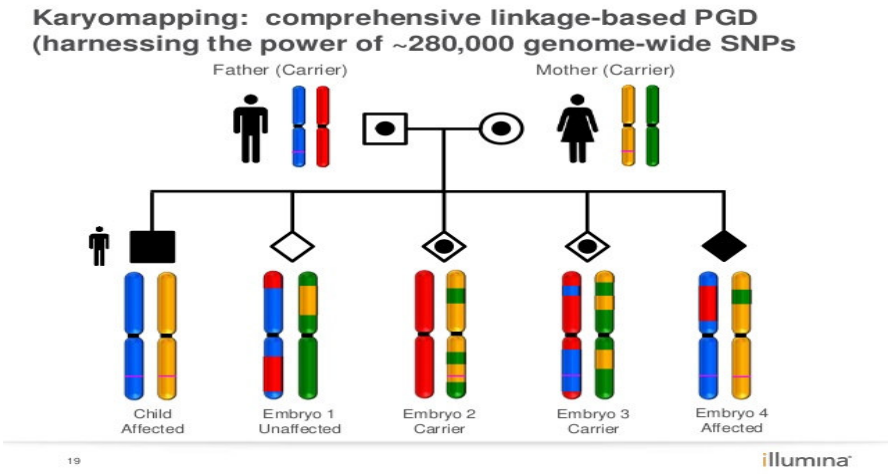

Figure-3 Karyomapping

METHODS OF GENETICALLY ENGINEERED OFFSPRING

1. CRISPR
2. Gene Editing Model
3. Embryo Editing

CRISPR:

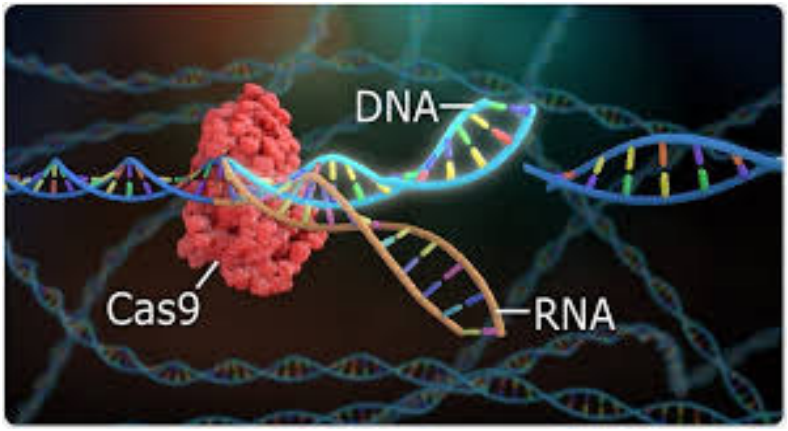

Figure-4 CRISPR Generation

Mammalian genomes are hard to work with since they have billions of base pairs. The development of homologous recombination (HR) has allowed us to accurately alter the genome and achieve the desired results. On the other hand, accurate HR-mediated modification happens in only one in 106–109 cells. Zinc finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs), and the RNA-guided DNA endonuclease Cas9 (CRISPR/Cas9) are just a few of the programmable nuclease-based genome editing tools that have been developed recently and allow for effective genetic modifications of many species [1]

Gene Editing Model

Genomic editing tools are becoming common place in both research and in higher education, necessitating critical dialogues on ways to effectively bring this technology into the undergraduate classroom. Genomic editing technologies in educational settings where wet-lab resources are unavailable are cost prohibitive, or in situations that require on-line learning [2].

Embryo Editing:

Dr. Jiankui aimed to produce embryos resistant to the majority of HIV strains. The majority of HIV strains utilise a protein that is encoded by the gene CCR5 to enter cells. His goal was to prevent this protein from being produced in any of the offspring derived from the altered embryos. In the beginning, he brought in eight couples, one of which had an HIV-positive father and the other hoping to prevent HIV from ever entering their child's life [3].

PROCEDURE:

- The technology of gene therapy is based on the effective delivery of the corrective genes and to do this, scientists have developed gene delivery vehicles called vectors.
- These vectors encapsulate therapeutic gene for delivery into the target cells. Many of the vectors currently in use are based on attended or modified version of viruses [4].
- Plasmids, which are circular pieces of DNA extracted from bacteria, are also used as vectors.
- The therapeutic gene to be transferred is extracted from the cell of a healthy individual.

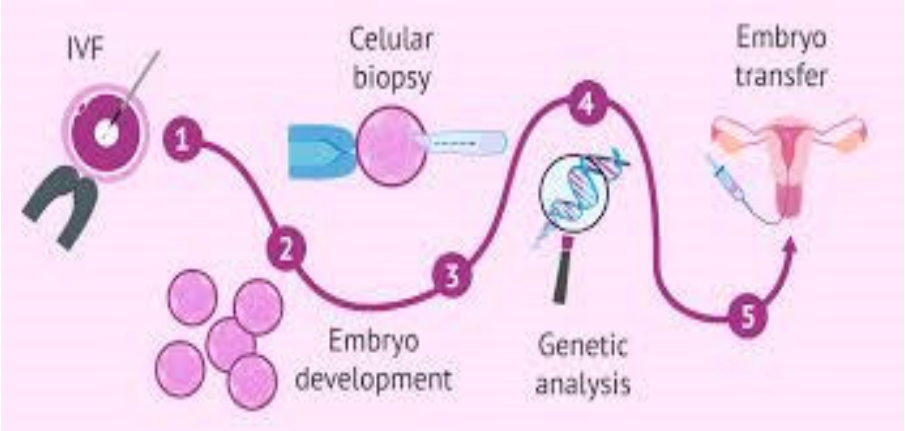

Figure-5 Procedure of Gene editing therapy

- The gene is extracted by cutting the DNA using restriction enzymes.
- There are different types of restriction enzyme, each being specific to the location of the DNA chain that it will cut.
- The section of cut DNA to be intact then a technique called electrophoresis is used to separate the selected pieces of DNA and remove the genes that contained the DNA sequence that coded for the polypeptides needed.

Viral Vectors:

Viruses infect cells by transfusing their genetic material into a host cell, using the host cellular machinery to generate viral proteins needed for replication and proliferation. By modifying viruses and loading them with the therapeutic DNA or RNA of interest, it is possible to use these as a vector to provide delivery of the desired gene into the cell.

Non-Viral Vectors:

Non-viral methods of nucleic acid transfect ion involved injecting a naked DNA plasmid into cell for incorporation into the genome. This method used to be relatively ineffective with low frequency of integration, however, efficiency has since greatly improved, using methods to enhance the delivery of the gene of interest into cells. Furthermore, non-viral vectors are simple to produce on a large scale and are not highly immune genetic.

ADVANTAGES:

- Designer Babies could also be a way to prevent those who have genetic disorders.
- Allows couples to balance gender in their families.
- Increase the likelihood of a healthy baby.
- Reduces changes of miscarriage.
- Reduces changes of termination due to disorder.
- Can be used to save lives.

DISADVANTAGES:

- High-cost leads to gap in society.
- Killing embryos that could have grown into humans.
- These genetic techniques are very expensive.

ETHICS OF GENETICALLY ENGINEERED OFFSPRING:

A designer baby is a child created by *in vitro* genetic engineering to have specific features, such as gender selection or reduced disease risk. Designer babies were mostly the stuff of science fiction before genetic engineering and in vitro fertilization (IVF) were developed. But, the idea of designer kids is becoming more and more likely due to the quick development of technology both before and after the start of the twenty-first century [8].

CONCLUSION:

Genetic editing and modification have come a long way in the last few decades, with successful cases documented in the literature. But there's still uncertainty about these operations' long-term safety. There is debate over whether these methods can be applied to treat severe hereditary illnesses. Although the treatments are not yet ready for clinical use, we think that research should go on to advance the field's technological capabilities and evaluate its long-term effects.

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