Gene Silencing Technologies and Mitochondrial Replacement Therapy

Gene Silencing

- Gene silencing is widely understood to be the inactivation of previously active individual genes or larger chromosome regions as a result of an epigenetic alteration of gene expression.
- There are two methods of gene silencing by manipulating mRNA:
  - RNA Interference Technology (RNAi)
  - Antisense technology

RNA Interference Technology (RNAi)

- This is a gene-silencing technology in which the gene is silenced by manipulating messenger RNA so that a harmful protein is not synthesized in the body.
- In RNA interference technology, a double helix RNA molecule is inserted in the cell which destroys a messenger RNA produced by a specific gene.

Applications

- RNA interference technology can be useful in the treatment of AIDS and it can lower the cholesterol levels in the body.
- With the help of RNAi technology, scientists are developing anti-viral defense mechanisms in COVID-19 patients.

Antisense Technology

- This type of gene silencing technology follows the Knockdown method.

Process

- If a DNA gene is having a sequence A T G C C T, then the transcripted mRNA contains a gene sequence called U A C G G A which eventually can make protein.
- So here, to silence mRNA gene, a carbon copy of RNA or an antisense strand A U G C C U is created which is carried to mRNA to block it completely.
- Now mRNA is blocked, so no further protein synthesis takes place.

Application

- Antisense technology was used to develop flavr-savr tomatoes.

RNAi Technology	Antisense Technology
Gene silencing through Knockdown method.	Gene silencing through Knockdown method.
Double helix RNA is used to destroy the mRNA.	Single helix RNA is used to block the mRNA.
New technology and more accurate.	Old technology and less accurate.

IP-IVF (Three Parent- In Vitro Fertilization)/Three Parent Baby/ Mitochondrial Replacement Therapy

Mitochondria

- Mitochondria has mDNA (maternal DNA) that has 37 genes and these 37 genes come to us from mother's mitochondria.
- A zygote contains 30000 genes from the father, 30000 genes from the mother and mitochondrial DNA or mDNA (37 genes) from the mother.
- Any defect in this m-DNA can cause diseases related to the eyes, brain, muscles, heart and liver. It may also cause a serious medical problem known as Charge Syndrome or Leigh Syndrome.
- Since mDNA is transferred from mother to child, so if the mother is having a mitochondrial defect, then it will pass on to the next generations. Both son and daughter will be diseased. The daughter will pass it onto the next generation but the son will not pass it because Mitochondria is contributed through the ovum by females only.

Three-Parent Baby Procedure

- If a mother is having a disease, then only the nucleus is taken from her ovum and mitochondrial DNA is taken from the donor mother and both this mDNA and nucleus are fused with the sperm of the father to form a zygote.
- Then after fertilization, a baby is formed which contains 37 genes from the donor mother, 30000 genes from the mother and 30000 genes from the father.
- So, the baby is called a three-parent baby.

Mitochondrial Replacement Therapy
There are 2 methods

- **Mitochondrial Spindle Transfer:** In the mitochondrial spindle, transfer mitochondria is replaced in the ovum before fertilization. This method has less risk involved, hence the more popular method.
- **Pronuclear Transfer:** In pronuclear transfer, mitochondria is replaced in the zygote after fertilization. This method has high risk involved, hence less popular.

Additional Information

- In Britain, one out of 6000 newborns suffer from mitochondrial defects and in 2015, Britain became the first country in the world to allow genetic changes in Embryos, to eliminate the mitochondrial defect.
- In 2016, the world's first three-parent baby was born, where the healthy mitochondria were obtained from another female.