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Proposal on use of Artificial Horizontal Gene Transfer to Cure Hereditary Hemochromatosis

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Description

HFE gene is present in various organisms and is responsible for the production of HFE protein that regulates the amount of Iron in the body. Mutation in the HFE gene of Homo sapiens sometimes lead to a condition called as Hereditary Hemochromatosis (HHC) (High Iron Load). This aggravates changes in physiology of various systems in the body that leads to multitude of secondary diseases such as cirrhosis, ascites, infertility etc [1].

The two most common types of mutations that are most common in Homo sapiens that cause HHC are:

C282Y

The C282Y mutation is the most common mutation. In C282Y mutation the nucleotide number 845 which usually is guanine is replaced with adenine which results in the transcribed protein to have tyrosine instead of cysteine at amino acid number 282 [2].

H63D

The H63D mutation replaces cytosine with guanine at nucleotide number 184 which in turn causes the transcribed protein to contain aspartic acid in place of histidine at amino acid number 63. In this mutation, an increase in the ferritin concentration and hemoglobin level of a body is observed [2].

To find a long-term cure of this disease using the innovative techniques being discovered every day, this paper was a proposal of radical solution to Type I Classic hemochromatosis that employs use of interspecies HFE gene closely resembling Homo sapiens and putting it into the genome of Homo sapiens.

Methodology

To find the species whose HFE gene resembles the most with the Homo sapiens BLAST (Basic Local Alignment Search Tool).

The results that were found when the Homo sapiens HFE gene (Ascension Number: NM_000410.4) was used as a query was that HFE gene of Pan Troglodytes (Ascension Number: XM_031011852.1).

To find the degree of similarity in the above-mentioned genes, Multiple Sequence Alignment program was used. The results showed that 348/348 (100%) amino acids of Pan Troglodyte HFE gene aligned with the HFE gene of Homo sapiens (Figure 1).

Figure 1. Pairwise alignment result of Homo sapiens HFE protien *vs.* Pan Troglodytes HF protein.

Proposed Solutions for HHC Reversal

There are various proposed solutions given on the foundation of horizontal interspecies transgenesis, that is transgenesis of Pan Troglodyte HFE gene in the human genome to correct the HHC.

Few of the ways to carry out the above mentioned are as follows:

- Since length of DNA being constraint, the lentiviral and adenoviral vectors are ruled out and the proposed vector is Epstein Bar Virus which holds large transgenic capacity up to 120 kb [3].

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Use of CRISPR-cas based gene-editing technology and stem cell therapy. Based on this model the *in vivo* experiment for transgenesis of the hepatic cells and the hematopoietic stem cells for reversing the C282Y mutation should be possible by using the CRISPR-cas technology.

Conclusion

The Genetic Analysis of Homeostasis Iron Regulator (HFE) Gene and Protein in Homo Sapiens and its Future Aspect in Treatment of Classic (Type-I) Hereditary Hemochromatosis is the first proposal and case for the artificial horizontal interspecies transgenesis coupled with CRISPR-cas or vector transgenesis to reverse various genetic diseases such as Classic Type–I HHC.

Although the artificial horizontal interspecies transgenesis coupled with CRISPR-cas or vector transgenesis lucrative option that science can use for reversal of the various genetic diseases, but this is just a basic and rudimentary theory that cannot be established in the practical form due to constraints such as cost and lack of engineering method.

Therefore, in conclusion the implementation of the proposed cures of Classic Type I HHC wouldn't be possible as of now.

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