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Genome editing for Huntington's disease

Dharani A

Huntington’s disease (HD) is an autosomal dominant genetic disorder in which nerve cells in certain parts of the brain degenerate. It is the most common inheritable neurodegenerative disease that is currently incurable and fatal too. It is caused by a genetic defect on chromosome 4 as a result of over the repetition of CAG sequences. This CAG sequence is the disease-causing copy of the huntingtin (HTT) gene that encodes the protein huntingtin. In a normal individual, CAG sequences repeat 10 to 28 times; whereas, it is 36 to 120 times for persons with HD. The presence of this expanded CAG leads to the production of a mutant protein which disrupts important cellular functions of the brain. Since huntingtin is an essential protein that prevents apoptosis of nerve cells, and helps in vesicle and organelle transport, it is essential to get expressed from the HTT gene. By using CRISPR-Cas9, mutant HTT gene can be disrupted, which could disable the production of the mutant protein. The Cas9 nuclease and a single guide RNA (sgRNA) of the CRISPR-Cas9 system bind to Cas9 and directs it to a targeted site (of HTT gene) following which Cas9 introduces a DNA double-strand break (in CAG sequences of HTT gene) thereby facilitating an error-prone DNA repair pathway to disrupt the gene expression. Hence CRISPR-Cas9-mediated gene editing could be used in combination with cell replacement therapy in the future to treat Huntington’s disease in an effective manner.

Keywords: HuntingtonÃ¢â‚¬Ëœs disease, Chromosome 4, CAG repeats, Huntingtin, Protein, Gene editing, CRISPR-Cas9

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