The Torch
Vol. 3 (25)

Stem cells and CRISPR-Cas9 for sickle cell treatment

Prama Ghosh

Sickle cell disease (SCD) is an inheritable disease caused due to mutations in a single gene. In this disorder, there is a single substitution on chromosome 11, where glutamic acid is replaced by valine in the sixth codon of the β-globin gene. The modified β-globin gene produces an abnormal haemoglobin S (HbS) which alters red blood cell (RBC) rheology and lifespan. This monogenic disorder affects around 300,000 people every year and results in serious mortalities all around the world. To date there is no definitive treatment for the disease; only two FDA-approved medications are available to lessen the disease's severity. Rapid and substantial progress in genome editing approaches is significant as a curative option in this case. Haematopoietic stem cell transplantation (HSCT) and gene therapy are promising therapeutic approaches. Among other approaches, patient-derived haematopoietic stem/progenitor cells (HSPCs) can be used to correct the underlying mutation causing the disorder. The induction of foetal haemoglobin expression can also be used to prevent the sickling of the RBCs. Further, creating corrected induced pluripotent stem cells (iPSCs) would allow the derivation of a population with 100% corrected cells. Genome engineering has been revolutionised by the discovery of the gene-editing technology, CRISPR/Cas9 (clustered regularly interspaced short palindromic repeats/CRISPR associated protein 9.) In this genome editing technology, a specific RNA sequence called guide RNA recognises the DNA region of interest and directs the effector Cas protein for editing. This cost-effective, easily applicable and highly efficient technique can be used to correct the SCD mutation or induce foetal haemoglobin (HbF) expression in ex vivo cell culture conditions and mouse models. Proof-of-principle studies have proven this technique to be effective. However, the safety of this technique still needs to be addressed and clarified. The efficiency of cutting and editing both non-homologous end joining (NHEJ) and homology directed repair (HDR)), specificity and delivery methods have to be improved before translating it into a routine procedure that can be used to treat SCD.

Keywords: Sickle cell disease, Genome editing, Transplantation, Mutation, Gene therapy

Citation:
Prama Ghosh. Stem cells and CRISPR-Cas9 for sickle cell treatment. The Torch. 2022. 3(25). Available from: https://www.styvalley.com/pub/magazines/torch/read/stem-cells-and-crispr-cas9-for-sickle-cell-treatment.