Beta-Thalassemia: A review of HBB and research proposal

Alexia Myers

Abstract

Hemoglobin subunit beta (HBB) is the gene that encodes instructions for the beta-globin protein. Beta-globin is highly important in creating hemoglobin, which allows red blood cells to carry oxygen throughout the bloodstream. Mutations in the HBB gene cause many genetic blood disor-

severity, can cause severe anemia and fatigue. Studies have been done to attempt to treat beta-thalassemia through lentiviral vectors in human patients and CRISPR/Cas9 editing on mouse models. However, CRISPR/Cas9 editing to correct the HBB gene has not been done in a clinical trial. This brief literature review and research proposal aim to address this gap in knowledge regarding CRISPR/Cas9 editing of the HBB gene and gene therapy treatment of beta-thalassemia in human patients in vivo.

The phenotype

Beta-thalassemia is an inherited blood disorder caused by genetic mutations. It triggers the body to produce less hemoglobin than an individual without the genetic disorder (Mayo Clinic, 2021). Hemoglobin is an iron-containing protein that enables red blood cells to carry oxygen (Mayo Clinic, 2021). Most living things, humans included, need oxygen to survive. With low levels of hemoglobin, red blood cells are impaired in their oxygen-carrying abilities. If red blood cells are slowly carrying oxygen or

symptoms of beta-thalassemia are weakness, pale skin, and slow growth in children (Mayo Clinic, 2021). Most notably, beta-thalassemia can cause

forms of beta-thalassemia may not require treatment, but severe forms may require regular blood transfusions to introduce more hemoglobin into the bloodstream (Mayo Clinic, 2021). Patients with severe beta-thal-

are unable to maintain a hemoglobin level of about 5 gm/dl (Przylepa and McKusick, 2021). Beta thalassemia is relatively rare in the United States but is one of the most common autosomal recessive disorders in the world (National Organization for Rare Disorders, 2018). Approximately 1
-

tomatic version of beta-thalassemia (National Organization for Rare Disorders, 2018). The disorder is particularly prevalent in the Mediterranean, Middle East, Africa, Central Asia, the Indian Subcontinent, and the Far East (National Organization for Rare Disorders, 2018). Individuals with these
-

semia or the mutations running in their family. Sickle-cell anemia, which is caused by mutations in the same gene, is more prevalent in the regions as well. Sickle-cell anemia is caused by mutant beta globin that sickles or has an abnormal crescent-like shape, while the absence of the beta chain is what causes beta-zero thalassemia (Przylepa and McKusick, 2021).

My interest in this subject started when my father was diagnosed with beta-thalassemia earlier this year. When I heard this diagnosis, the disorder was new to me. I had never heard of beta-thalassemia, let alone any other type of thalassemia. When I did research, I found that the gene that can cause beta-thalassemia also can cause sickle-cell anemia. According to my father, he gets tired very easily and is anemic, but he does

Myers, personal communication). After the discovery of my father's diagnosis, I became highly interested in the subject. I was curious as to how

thought his diagnosis was interesting for many reasons, though. First,

childhood. It is very unusual for his diagnosis to come in his mid-forties. According to Mayo Clinic, some babies show symptoms of beta-thalas-

hemoglobin gene do not have beta-thalassemia symptoms (Mayo Clinic, 2021). Since my father was unaware that he had beta-thalassemia for so

Another reason that I became interested in the subject is because it is a genetic disorder, and beta-thalassemia is passed from parents to chil-

beta-thalassemia, there is a chance that both I and my sister are. Also,

disorder down to my children. Even if it is a mild case, it can be passed

mentioned previously, individuals of African descent are more susceptible to beta-thalassemia. My father is of African descent, which means that the disorder could run in the family. However, since no one in our

Beta-thalassemia, depending on its severity, could potentially be a life-threatening genetic disorder. Genetic blood disorders such as sickle-cell anemia and beta-thalassemia are great candidates for gene therapy, as issues with red blood cells and hemoglobin are dangerous to the survival s [illegible] MedlinePlus Genetics, 2022). He

gene that is responsible for the protein-coding instructions for beta-globin. It is located on chromosome 11 at position 15.4. HBB is made up of three exons, with the third one being the largest. The HBB gene is conserved in the chimpanzee, rhesus monkey, dog, mouse, and rat genomes. In addition, 11 organisms have orthologs with the human gene HBB.

considered for gene therapy. Particularly, beta-thalassemia and sickle-cell

means of new techniques of recombinant DNA analysis (Przylepa and McKusick, 2021). In general, the molecular pathology of disorders resulting from mutations in the non-alpha-globin gene region is the best known, this

Jinek, M et al. (2012, June 28). A Programmable Dual-RNA–Guided DNA Endonuclease in Adaptive Bacterial Immunity. *Science*. https://www.sci-

cell defects in two common blood disorders. *Science*. https://www.sci-
-
fects-two-common-blood-disorders

Gene Therapy to Treat Beta-Thalassemia. *GEN - Genetic Engineering and Biotechnology News*. https://www.genengnews.com/industry-news/fda-approves-bluebird-bios-lentiviral-gene-therapy-to-treat-beta-thalassemia/
Mayo Clinic. (n.d.). Hemoglobin test. https://www.mayoclinic.org/tests-procedures/hemoglobin-test/about/pac-20385075
Mayo Clinic. (2021, November 17). Thalassemia - Symptoms and causes.https://www.mayoclinic.org/diseases-conditions/thalassemia/symptoms-causes/syc-20354995

iPSC T⊨HWU🕷Q