Two trials show promising results with gene therapies that target sickle-cell anemia

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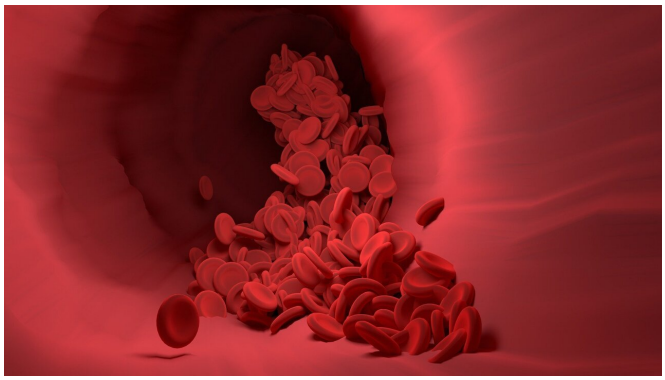

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Two teams of researchers working independently have found success in trialing gene therapies targeting sickle-cell anemia. Both teams have published papers in the *New England Journal of Medicine* describing their work and results. The first team comprised members from the U.S., Germany, Canada and France; they used the CRISPR-Cas9 gene editing system to boost the production of fetal hemoglobin in sickle-cell anemia patients. The second team comprised members from Harvard Medical School and the Dana–Farber Cancer Institute. They also sought to boost the production of fetal hemoglobin in sickle-cell anemia patients but used a different technique that involved introducing RNA via a viral carrier that altered expression of the fetal hemoglobin gene.

Sickle-cell anemia is an inherited blood disorder that predominantly occurs in people of African descent. It's caused by a mutation in a gene for the protein hemoglobin. The alterations result in stiffened red blood cells and force them into a sickle-like shape. These cells can clog blood vessels, resulting in pain for the patient, and can sometimes lead to organ damage or stroke.

Both of the new treatment options were part of clinical trials, and both aimed to alter the genes responsible for the development of sickle-cell anemia. In both cases, doctors removed some of the patients' blood stem cells and attempted to disable the genetic switch that becomes inactivated in people with the disorder. The patient was then given chemotherapy to destroy their faulty cells; the newly changed stem cells were then infused back into the patient. As time passed, the stem cells grew into normal blood cells and the patient was free of the disorder.

Both teams found success with their trials—the team using CRISPR-Cas9 carried out their first test approximately 17 months ago, and thus far, the patient has shown no signs of pain associated with sickle-cell anemia. Other patients since then have had similar results. The same team also tried a similar technique to treat patients with beta-thalassemia—another inheritable disorder in which patients make little or no hemoglobin due to genetic mutations in roughly the same areas as those with sickle-cell anemia. The second team has carried out their procedure on six patients thus far over the past several years, and to date, have not yet seen any failures.

More information: Haydar Frangoul et al. CRISPR-Cas9 Gene Editing for Sickle Cell Disease and ?-Thalassemia, *New England Journal of Medicine* (2020). DOI: 10.1056/NEJMoa2031054

Erica B. Esrick et al. Post-Transcriptional Genetic Silencing of BCL11A to Treat Sickle Cell Disease, *New England Journal of Medicine* (2020). DOI: 10.1056/NEJMoa2029392