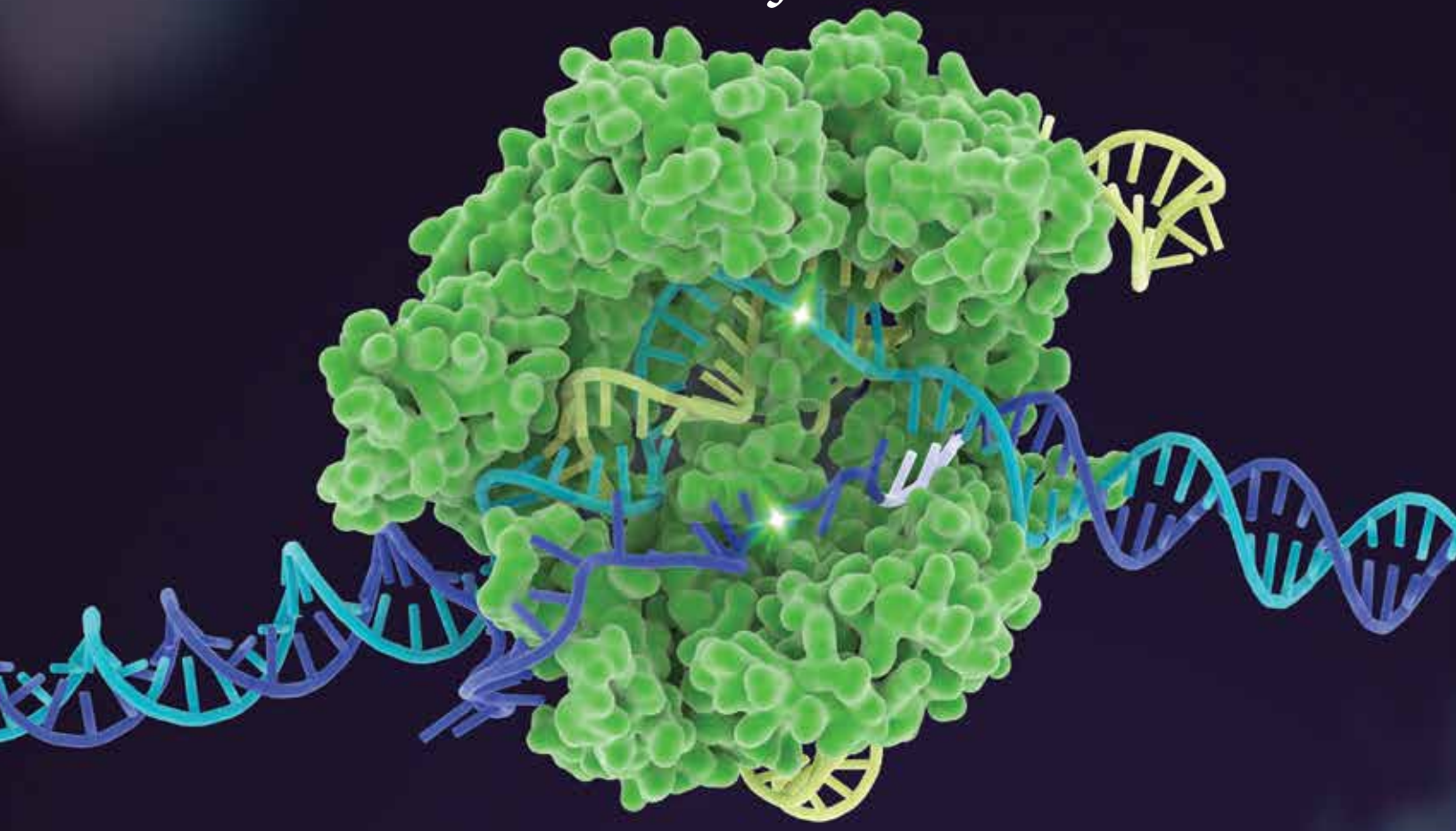
Article: Treating Sickle Cell Disease

Excerpt from

The Power of CRISPR



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Cover art: Cas9 (green) and guide RNA (gold) bound to a target DNA site (blue), making a cut in each strand (white flashes). Copyright © 2022, Janet Iwasa, for IGI.

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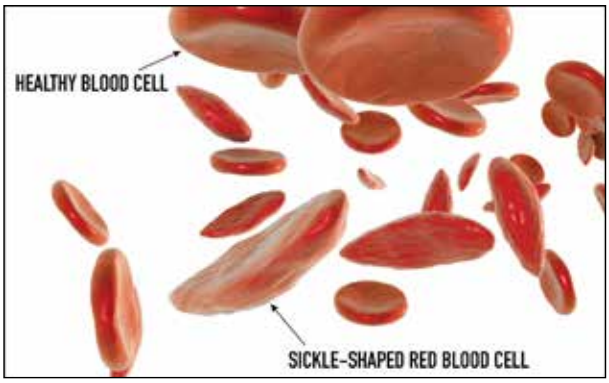
Article Introduction: The Ethics of CRISPR

In 2012, scientists developed CRISPR, a new gene-editing technology. However, the debate around whether scientists should edit organisms' genes has been around much longer. Scientists have been manipulating genes since the 1970s. Since that time, scientists and others have debated how and when this technology should be used. As technology improves, it becomes even more necessary to ask questions like these:

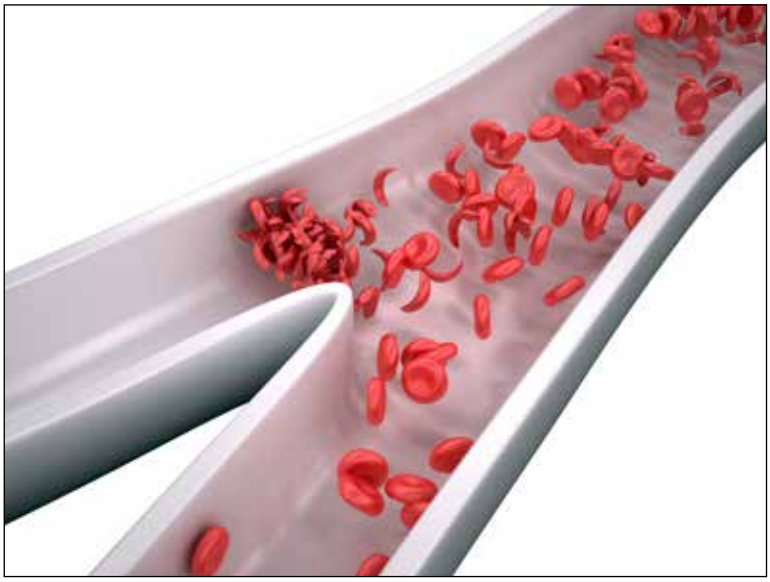
- Should people be able to edit organisms' genes?
- If people are able to edit organisms' genes, who should be able to do it, which organisms' genes should be edited, and for what purpose?
- How might changing an organism's genes affect the environment and future generations?
- Will gene editing be accessible to all people or to just a select few?

Article: Treating Sickle Cell Disease

Sickle cell disease is an inherited blood disorder affecting approximately 100,000 Americans. Typically, red blood cells are smooth and round, but a person with sickle cell disease has red blood cells that are stiff and irregularly shaped. Their shape looks like a crescent moon, or sickle, which is where the disease gets its name. The irregularly shaped red blood cells do not glide through the blood vessels like the round, smooth ones. They tend to pile up, stopping proper blood flow and preventing oxygen from getting to vital organs and tissues. This leads to fatigue, episodes of pain, swelling of the hands and feet, and frequent infections. Complications such as stroke or organ damage can even lead to death.



Sickle cell disease affects a person's red blood cells, causing them to have an irregular shape.



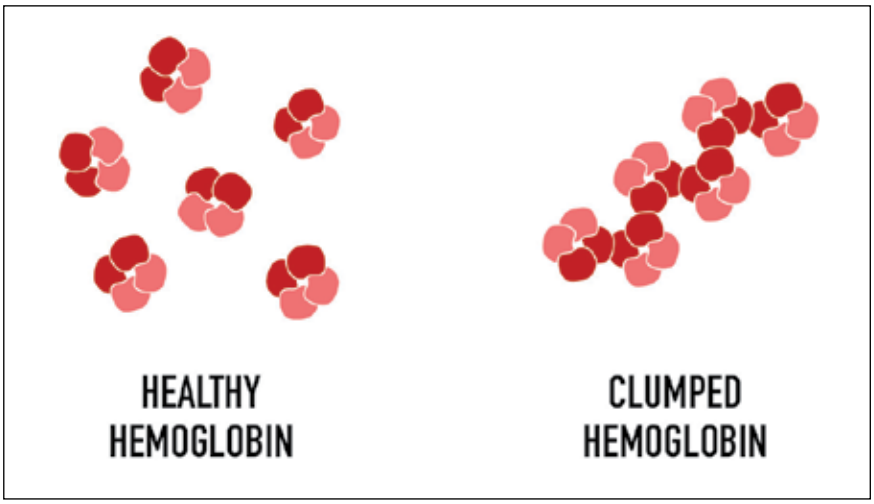
Round red blood cells glide easily through blood vessels (right vessel). Sickle-shaped red blood cells tend to cause blockages (left vessel) that prevent oxygen from reaching some organs and tissues.

Image credits: (top) Kateryna Kon/Shutterstock.com, (bottom): decade3d - anatomy online/Shutterstock.com

Article: Treating Sickle Cell Disease (continued)

Red blood cells contain a protein called hemoglobin, which is responsible for carrying oxygen to the cells of the body. People with sickle cell disease have hemoglobin proteins that can still carry oxygen, but the hemoglobin molecules stick to one another. All the hemoglobin sticking together causes the red blood cells to have a sickle shape.

The changes in the hemoglobin protein that lead to sickle cell disease are caused by a mutation in one of the genes that provides instructions for the hemoglobin protein. Genes are sections of DNA that provide a cell with instructions to make a particular protein. Hemoglobin is a protein made of four individual protein subunits. The mutation that leads to sickle cell disease is found on the gene that codes for two of those subunits. A small change to the DNA changes the instructions, which leads the cell to produce slightly different hemoglobin proteins that stick to one another in long fibers. These fibers are what lead to the trait of sickle-shaped red blood cells.



Hemoglobin usually exists as free-floating individual protein molecules. A person with the mutated version of the hemoglobin gene produces hemoglobin proteins that stick together in long fibers. These stiff fibers make the red blood cells inflexible and distort them into a sickle shape.

Article: Treating Sickle Cell Disease (continued)

CRISPR and Sickle Cell Disease

The mutation that leads to sickle cell disease is just a single error in the DNA, making it a strong candidate for treatment using CRISPR gene-editing technology. To use CRISPR to change the gene to the healthy version, scientists are working on using a protein called Cas9, which can find and cut the mutated version of the gene. Once the gene is cut, the DNA can be edited to the healthy version of the gene. Scientists hope that they will be able to treat sickle cell disease by using CRISPR in stem cells taken from the patient's bone marrow. Stem cells are special cells that have the ability to become many other types of cells in the body. Bone marrow stem cells can become red blood cells. Once the hemoglobin gene in the stem cells is edited using Cas9, the stem cells will have the healthy version of the gene. If the procedure works as intended, the stem cells will develop into healthy red blood cells that produce healthy hemoglobin in the patient's body.

Editing genes with CRISPR has risks and possible side effects. There is a chance that edits can be made to the wrong gene; this is called an off-target effect. Although many off-target effects can be eliminated in the lab, there is no guarantee that all of them would be caught. The result of an off-target effect is unknown until the patient develops symptoms. In addition, there is a risk that after Cas9 cuts the gene, the repair does not happen as planned. In that case, the result is also unknown.

Side effects from off-target effects and repair errors have not yet been observed in patients participating in CRISPR clinical trials. However, this technology is still quite new, so scientists must closely monitor all patients for any immediate or long-term side effects.