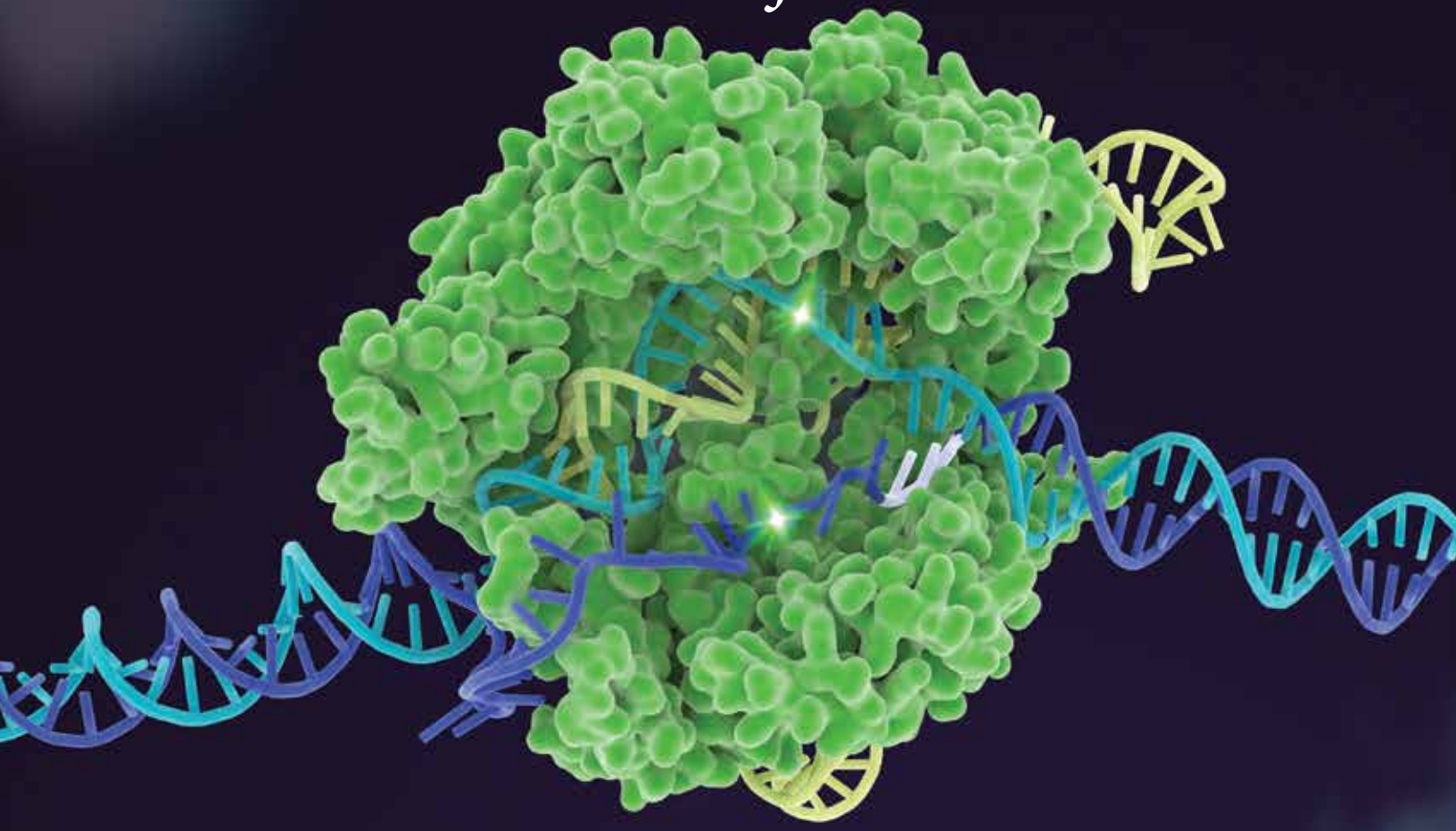
Article: Preventing Cystic Fibrosis

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: Preventing Cystic Fibrosis

Worldwide, more than 70,000 people are living with cystic fibrosis—a genetic disease that especially affects the lungs and pancreas, but also the liver, kidneys, and intestines. People with cystic fibrosis have a thick, sticky mucus that builds up in their lungs and pancreas. In the lungs, this buildup makes it difficult to breathe and leads to lung infections. The buildup of mucus in the pancreas prevents the release of digestive enzymes, leading to malnutrition and poor growth.

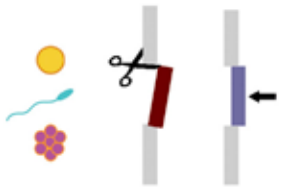
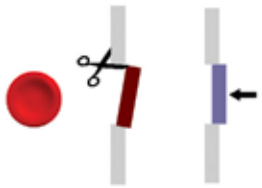
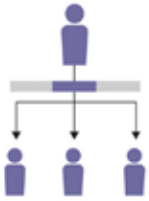
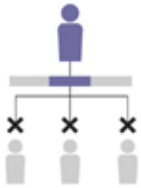
Cystic fibrosis makes it difficult to breathe.

Cystic fibrosis is caused by mutations to the cystic fibrosis transmembrane conductance regulator (CFTR) gene. This gene provides instructions for cells to make a certain type of protein, a channel protein. The channel protein helps regulate the amount of water outside cells, leading to the trait of having mucus of the right consistency. Mutations to the CFTR gene result in channel proteins that do not function properly, and very little water can cross through the channel proteins. These mutations lead to the trait of having thick mucus.

CRISPR and Germline Editing

Like sickle cell disease, CRISPR has the potential to be used as a treatment for people living with cystic fibrosis. However, there may be a way to prevent people from having these genetic diseases in the first place. If scientists can perform CRISPR on sperm, eggs, fertilized eggs, or embryos to change the mutated version of the CFTR gene to the healthy gene, any resulting organisms would be born without cystic fibrosis. Editing the genes of sperm, eggs, fertilized eggs, or embryos is called *germline editing*. By performing CRISPR at this early stage, any resulting organism would have the healthy version of the gene in all of its cells, including the organism's own sperm or egg cells. This means that all future generations would be healthy too. In contrast, when gene editing is used as a treatment for people already living with the disease (somatic gene editing), changes to the genes will not be passed down, and future generations can still get the disease.

Article: Preventing Cystic Fibrosis (continued)

	Germline gene editing	Somatic gene editing
Edit	 Edits are made to genes of sperm, eggs, fertilized eggs, or early embryos. The changes are then copied to all the new cells.	 Edits are made to genes only in specific types of cells that cause the disease. No other cells are affected.
Future generations	 The edited gene is passed down to future generations.	 The edited gene is not passed down to future generations.

As with other CRISPR gene-editing applications, this procedure carries the risk of making edits 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 cells further develop. 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. These errors can lead to health issues that are impossible to predict. Unlike using CRISPR to treat diseases in adults, these unknown changes to an organism's DNA would be passed down to future generations.

Although there is great potential for CRISPR to make a positive impact on the quality of people's lives, society must make ethical judgements and determine the limits of such a powerful technology. Germline editing using CRISPR can be used to prevent organisms from being born with genetic diseases such as sickle cell or cystic fibrosis. However, people may want to use CRISPR germline editing for a wide range of applications, for example, to make cosmetic changes, such as hair or eye color; to enhance specific parts of the body, such as having larger, leaner muscles; or to reduce the likelihood of developing certain disorders or diseases, such as Alzheimer's.

In the United States, germline editing for humans is banned. However, other countries differ in how they apply their regulations, and some researchers in China have been prosecuted for illegally using CRISPR to conduct germline editing in human embryos. It is up to society to determine if, when, and where to draw the line.