Reflecting on CRISPR Gene Editing

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Blessing or curse? When we reflect on new biotechnologies in health care, do we consider them a blessing or a curse? Will they be a blessing, by helping us to dismantle barriers to health care and to facilitate access to quality health care services for all citizens around the world? Or will they be a curse, adding further barriers that will inhibit or limit the availability and accessibility of health care services to people around the world today and in the future?

Some would probably prefer an inclusive approach: "both and." They would argue that rapidly developing biotechnologies are both, at the same time, a blessing and a curse. They might be a blessing for those who can benefit from them and a curse for those who are excluded from the expected potential advantages.

For others, developing biotechnologies are neither a blessing nor a curse. They are somehow in between. Some biotechnological improvements might be beneficial to selected people or even the whole world, while, at the same time, some aspects might be quite ethically problematic.

Hence, it is essential to discern. To rely solely on the distinction between "blessing" and "curse" to assess new biotechnologies in health care might be potentially limiting, generic, oversimplifying and, ultimately, unhelpful.

AN EXAMPLE: GENE EDITING

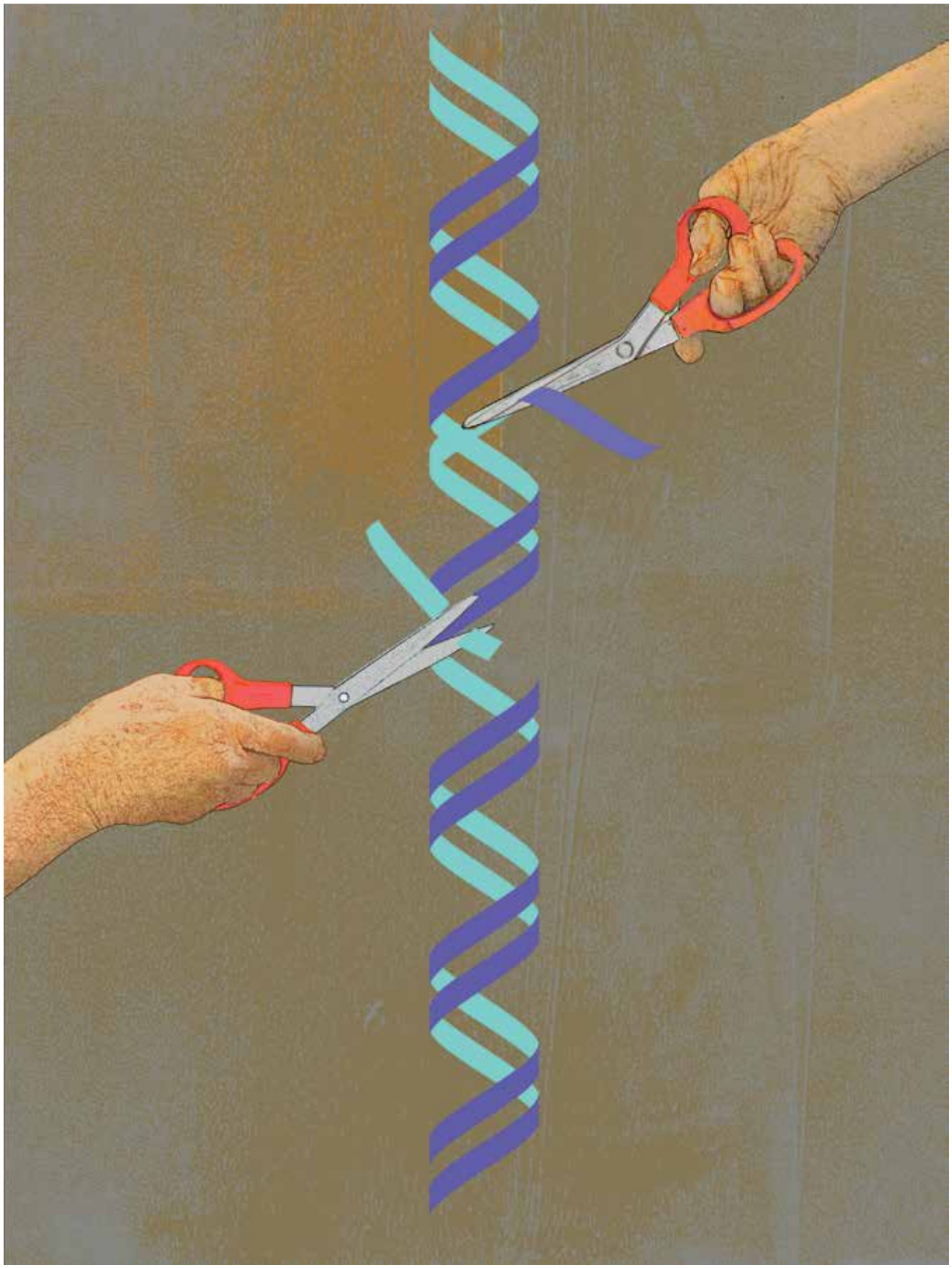
Every writer knows that, to communicate correctly, an accurate editing process is needed. Editing exists in genetics too. Nature too wants to be sure that the genetic information is correct and that any misspelling is eliminated.

With the complete sequencing of the human genome in the early 2000s, researchers, health care professionals and citizens expected scientists to develop genetic therapies that could treat and possibly cure many genetic diseases. Gene therapy, however, disappointed. In its initial clinical trials, the death of a few patients — both in the USA and in France — stopped the clinical trials. Scientists realized that they needed to know more about safe ways to change genes whose mutations cause genetic diseases. A safe technology to edit genes could allow for the treatment of both genetic diseases and medical conditions with a genetic component, like some cancers. Gene editing could greatly benefit human health and health care practice.

CRISPR

Under the heading "gene editing" scientists place a series of methods that can change our genetic information, our DNA. One of them, the CRISPR-Cas9 system, seems very promising.[1]

Scientists discovered that some bacteria have a built-in gene editing system that is very similar to the CRISPR-Cas9 system. Bacteria use this system to respond to invading pathogens like viruses. Hence, this system, in bacteria, works much like an immune system. Using CRISPR as a bacterial defense system, the bacteria snip out parts of the



virus DNA and keep a bit of it to help them recognize and defend against the virus next time it attacks.

CRISPR-Cas9 enables geneticists and medical researchers to edit parts of the genome by removing, adding or altering sections of the DNA sequence to one or more genes in a cell's genome.[2] It is simpler, faster, cheaper and more accurate than previous techniques of editing DNA, and it has a wide range of potential applications.

CRISPR-Cas9 editing technology could be used in three different ways: first, for basic research to study the mechanisms of gene editing in cells. To know better how this type of gene editing works could allow us to use it for beneficial purposes. Second, it could be used to edit the genetic information of human non-reproductive cells (our somatic cells). The researchers call this approach "somatic interventions." In this case, gene editing could help to edit genetic mistakes in genetic diseases. Third, gene editing could edit genes in reproductive cells (sperm and oocytes), the so-called "germ cells." These are "germline interventions." In this case, the offspring and the following generations will carry the edited genes.

SCIENTIFIC CHALLENGES AND ETHICAL ISSUES

Hence, CRISPR-Cas9 could be very promising and beneficial for human health. It might be a blessing. But the scientific excitement is cooled down because this is not an exact biotechnological tool. Improvements are needed before it can be used safely in clinical trials.

In formulating the scientific challenges that they face, scientists first stress the need of an accurate balance of risks and benefits. While gene editing could edit our genes to correct the mutations that cause diseases, these changes, instead of repairing, could introduce further modifications because of the current inaccuracy of gene editing technology.

Gene editing may cause "off-target" mutations, which can lead to further health problems, because large genomes, like the human genome, contain multiple DNA sequences identical or very similar to the intended target DNA sequence. The gene editing system is misguided by these identical or very similar sequences. Hence, in trying to assess risks and benefits, scientists ask whether gene editing is safe and irreversible.

A further concern related to safety depends on the relative simplicity and availability of this technology. To give an example, "The equipment and reagents that are needed to use CRISPR-Cas9 are already readily available to Do It Yourself (DIY) biologists."[3] Gene editing could be performed without the necessary scientific and ethical supervision. This is what happened in November 2018, when a Chinese scientist announced he performed gene editing in human embryos.[4]

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Second, gene editing could lead to ecological disequilibrium by introducing human-made genetic modifications in the environment with uncertainty about the effects. Historically, humankind does not have a good record at protecting the environment. If used without caution, gene editing could introduce genetic mutations in living organisms that could affect delicate ecosystems.

Third, gene editing technology could be used not only in the case of therapy, but to modify genetic characteristics in healthy individuals through enhancement of somatic cells and/or of germline cells.

Fourth, in the case of reproductive cells, scientists wonder what the impact of changes in our genetic information could be in the affected offspring and in the future generations that will inherit those modified genes.

TO DISCERN

The Moral Agent and Moral Agency

What can help us to discern if gene editing is a blessing or a curse? We can answer by focusing first on who is answering — the moral agent — and second on how the moral agent answers, that is, moral agency.

When novel biotechnological developments are discussed, questions about the moral agent and moral agency are often phrased with the expression "playing God," to mean that, with their research, scientists are doing what pertains to God. By playing God, the argument goes, scientists make themselves as God and abuse the creative power that should be left to the divine. Playing God is portrayed as an ethically problematic concept that shows perversion of the moral agent and of moral agency. Hence, some biotechnological developments are a curse because they lead us to playing God.

In the ethical literature, however, there are also more nuanced interpretations of playing God. Both a Protestant theologian, the late Allen Verhey and a Catholic theologian, Cynthia Crysdale argue that playing God could be interpreted in more positive ways by stressing the role and responsibility assigned to the ethical discernment of moral agency in decision making concerning new biotechnologies.[5] Hence, we should be playing God responsibly.

The late 20th-century Catholic theologian Karl Rahner, SJ, and, more recently, the Protestant theologian Philip Hefner, stressed this positive understanding of responsibility by arguing that human beings are "co-creators."[6] By using their creative power, which is God's gift, human beings are neither presuming to be God, nor abusing of their role as creatures. They are not playing God, in the negative sense. On the contrary, they collaborate with God's continuous creative work in our creation for the health, well-being and flourishing of humankind and of everything that is created on the Earth and in the universe.

Hence, whether the stress is on "playing God" arguments or on human beings as co-creators, in both cases the emphasis is on the moral agent and on moral agency. Theological discourse proposes that, in today's society, citizens and believers reflect on the scientific, ethical, social and religious challenges raised by introducing new biotechnologies by focusing on who we are as moral agents, on the goals that we pursue, the means that we are using, the circumstances that characterize our decision-making process, and the foreseen consequences.

What is presupposed is that human beings are able to make rational, responsible and wise decisions that protect human dignity as well as the whole creation. Moreover, what is implied is human accountability.

Principles

Theological discourse also proposes a third ethical resource that allows us to act justly: principles. Many authors focus on the so-called four principles of bioethics: respect for autonomy, beneficence, non-maleficence, and justice, formulated since 1979 by Thomas Beauchamp and James Childress in their *Principles of Biomedical Ethics*.[7]

Principles are important resources in moral reasoning. Beauchamp and Childress placed principles at the forefront of biomedical ethics. The principle of respect for autonomy led to articulating the practice of informed consent and to containing paternalistic attitudes that dominated medical practice. Beneficence and non-maleficence express the goals and the methods that should inform health care by promoting one's well-being and avoiding any harm. Finally, for Beauchamp and Childress, justice is distributive justice — what assures to each one one's due.

The principle of precaution, as a variation of the non-maleficence principle, which means avoiding doing harm, is also proposed. There are two reasons for this precaution. First, unpredictable consequences could lead to negative outcomes that could harm human health and the environment. Second, scientists want to avoid negative public reactions, with possible negative consequences for their research and funding goals.[8]

Although the principle of precaution was originally applied to ecological ethics, some authors

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suggest that it might also address new biotechnological developments, including gene editing. In the U.S., two Protestant theologians—Ted Peters and Gilbert Meilaender—rely on it in their recent articles on CRISPR. They both use a traffic metaphor. For Peters, at the traffic light, the yellow invites us to proceed with caution. Hence, "The proceed-with-caution bioethicist looks both ways on yellow, but drives forward." We should "proceed with constant risk-assessment."[9]

Meilaender asks whether to drive through at the yellow light is the best way of proceeding. Should we purse research with caution? He wonders why "we do not ask ourselves whether there may be some research—even possibly beneficial research—that should not be done no matter what its benefits may be."[10]

Meilaender also invites us to consider what could be virtuous behavior in the situations we are facing. Hence, virtues are a fourth relevant ethical resource that could help us to discern by addressing questions regarding upcoming new biotechnologies and their implementation in health care settings.

Virtues

Virtues help us to act for the right good, at the right time, in the right way. Virtuous people promote virtuous dynamics in a virtuous society. Hence, virtues concern single individuals, communities, groups, institutions and the whole society. Which virtues are more appropriate in an increasingly technologically developing world? I mention prudence and justice. More might be needed, however.

First, prudence promotes careful discernment while we are investigating and exploring the possibilities offered by developing biotechnologies. Prudence invites us to examine critically our expectations and to define how we should act.

Even when genes will be edited, at least two further factors intervene in regulating and in modulating genetic information: first, the cell messengers — the various types of RNAs. Second, the cell environment. Within genetics, epigenetics studies the changes in organisms caused by the modification of their gene expression rather than the alteration of the genetic code itself. Definitely, to modify genetic information is a complex matter.

We are complex beings. We always try to simplify complexity. Prudence might lead us to address the complexity as it is, without oversimplifying it. From the Catholic point of view, prudence and the willingness to protect both the most vulnerable among us now and future generations lead to critical examination of any experimentation involving germline cells and human embryos.

Second, justice should not be limited to distributive justice, to give to each one one's own. In its full sense, justice aims at promoting just social dynamics within society. Hence, justice demands social justice, a comprehensive concern and care for the less well off. Concretely, when we reflect on gene editing technologies, justice requires that we aim at the promotion of health for each person and for the whole society. Together with health care practice, public health and global health should be on the top of our justice agenda. Society should be committed to promote health care locally and globally, by strengthening health care systems and health care delivery in every country. Health is both an individual and collective challenge and responsibility. To promote health requires more than aiming at eliminating diseases by editing our genes.

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Catholic bioethics raises both the personal and social awareness of what is required from individuals and civil society if we truly want to promote personal and social health integrally and globally. Catholic bioethics demands that contemporary societies strive to promote the well-being of individuals and social contexts by addressing all the social factors that inhibit personal and social flourishing, and by eliminating any inequity, including racial inequities and any inequity affecting persons with disability and those who are sick. Hence, social justice leads to a comprehensive approach to health that aims at promoting the well-being of individuals and societies.

Moreover, justice also demands public engagement. National and international regulations can further contribute to protect citizens globally —

now and in the future. Hopefully, these multiple ethical resources will help us to discern whether CRISPR, and any new biotechnology, is a blessing or a curse, or both, or neither.

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NOTES

1. The acronym CRISPR-Cas9 means Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)–associated system (Cas). See Paul Scherz, "The Rapidly Evolving Debate over CRISPR," *Health Care Ethics USA* 27, no. 2 (2019): 24-29; Kevin T. FitzGerald, "CRISPR: What Potential? What Peril? Who Decides?," *Health Care Ethics USA* 25, no. 4 (2017): 1-5; Nicanor Pier Giorgio Austriaco, "Genome Editing with CRISPR," *Ethics and Medics* 41, no. 3 (2016): 1-3.
2. See Paul Scherz, "The Mechanism and Applications of CRISPR-Cas9," *The National Catholic Bioethics Quarterly* 17, no. 1 (2017): 29-36.
3. Todd Kuiken, "Learn from DIY Biologists," *Nature* 531, no. 7593 (2016): 167-68, at 167. See http://parts.igem.org/CRISPR.
4. See Jon Cohen, "Inside the Circle of Trust," *Science* 365, no. 6452 (2019): 430-437.
5. Allen Verhey, "'Playing God' and Invoking a Perspective," *The Journal of Medicine and Philosophy* 20, no. 4 (1995): 347-64; Allen Verhey, ""Playing God': Invoking a Perspective," *Pro Rege* 25, no. 1 (1996): 18-28; Cynthia S. W. Crysdale, "Playing God? Moral Agency in an Emergent World," *Journal of the Society of Christian Ethics* 23, no. 2 (2003): 243-59.
6. See Karl Rahner, "The Experiment with Man: Theological Observations on Man's Self-Manipulation," in *Theological Investigations* (New York: Herder and Herder, 1972), 205-24; Karl Rahner, *Foundations of Christian Faith* (New York: Seabury, 1978), 35; Philip J. Hefner, *The Human Factor: Evolution, Culture, and Religion* (Minneapolis: Fortress Press, 1993).
7. Thomas L. Beauchamp, James F. Childress; *Principles of Biomedical Ethics*, 8th ed. (Oxford: Oxford University Press, 2019).
8. The principle of precaution was formulated at the 1992 United Nations Conference on Environment and Development. See *Wingspread Statement on the Precautionary Principle* (1998), http://www.gdrc.org/u-gov/precaution-3.html. See also UNESCO, *The Precautionary Principle* (2005): 14, http://unesdoc.unesco.org/images/0013/001395/139578e.pdf 419. Quoted in Ted Peters, "Should CRISPR Scientists Play God?" *Religions* 8, no. 4 (2017): 61, https://doi.org/10.3390/rel8040061.
9. Peters, "Should CRISPR Scientists Play God?" See also Ted Peters, "Flashing the Yellow Traffic Light: Choices Forced Upon Us by Gene Editing Technologies," *Theology and Science* 17, no. 1, (2019): 79-89.
10. Gilbert Meilaender, "Gene Editing: Promise and Peril," *Commonweal* 144, no. 7 (2017): 12-15.

JOURNAL OF THE CATHOLIC HEALTH ASSOCIATION OF THE UNITED STATES www.chausa.org

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Reprinted from *Health Progress*, January – February 2020