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Thinking Through the Choices Forced Upon Us by Gene Editing Technologies

by

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Whether we like it or not, we in the present generation must increasingly take our destiny into our own hands. The juggernaut of advancing technology forces upon us choices that our ancestors did not need to make. When Jesus' disciples planned their trip from Capernaum to Jerusalem, they did not have to choose between taking a train, taxi, or shuttle bus. They walked. With the advent of effective birth control technologies and artificial insemination (Assisted Reproductive Technology), we now must choose between sex-without-babies and babies-without-sex.

Just about a year ago, my brother-in-law Bill was diagnosed with an incurable infection. He was being kept alive in the hospital by a machine. What should we do? Keep him alive artificially for as long as possible? Or, should we decide the moment of death? Bill and his doctor decided he would die on a Monday. When I arrived at the hospital on that Monday, a nurse asked, "are you the relative who is a pastor? Bill's been waiting for you." She ushered me into his room.

Family members crowded the room. I offered to lead everyone in prayer. Bill said, "thanks Ted. But, keep it short, will ya?" For the next four hours after I said, "amen," we watched Bill die. The doctor entered at the last moment and wrote on his clip board, "death at 3:43pm."

The time of Bill's death was a forced choice. Had we decided to let nature and the machine take its course, it would have been our choice. Had we decided to pick a day for his death, it would have been our choice. To leave Bill's death up to nature was not an option.

CRISPR, like so many other biotechnologies, is forcing upon our generation new choices. How will we influence the genomes of plants, animals, and humans? Do we edit these genomes, or not? If we edit these genomes, what principles will guide us? To decide to refrain from such editing would in itself be a moral decision. We can no longer ask nature to take care of our morality for us.

It is time for churches and university communities along with scientists to think ethically about CRISPR and

other biotechnologies.[1] This thinking-through should not simply distinguish between good and evil, as Adam and Eve wanted to do. Rather, this thinking-through should be aimed at equipping our people to make responsible choices, choices guided by human well-being and the common good.[2]

Editing our Genome with CRISPR

Here is something you don't need to know. CRISPR stands for *Clustered Regularly Interspaced Short Palindromic Repeats*. What does this mean? In the past, our human genomes incorporated palindromic DNA repeats from bacteria and archaea which were their adaptive method for strengthening their immune systems. The summary point to get is this: palindromic repeats of DNA base pairs provide targets for the geneticist to shoot at.

Like an archer, the CRISPR researcher aims at these targets with Cas9 arrows. What's Cas9? It's an endonuclease capable of cleaving DNA. When combined with specific RNA in a system it can either insert or delete specific genetic sequences. If Cas9 is the arrow, the CRISPR archer can fire it to a specific target on a DNA

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[1] I have been pressing this point regarding the need to prepare for moral choice since publishing a treatment on genethics two decades ago, *For the Love of Children: Genetic Technology and the Future of the Family* (Louisville KY: Westminster John Knox, 1996).

[2] Pope Paul VI defined the common good as "the sum of those conditions of social life which allow social groups and their individual members relatively thorough and ready access to their own fulfillment." "Pastoral Constitution on the Church in the Modern World: *Gaudium Et Spes*, promulgated by His Holiness, Pope Paul VI on December 7, 1965," No. 26, The Holy See, accessed May 7, 2016, http://www.vatican.va/archive/hist_councils/ii_vatican_council/documents/vat-ii_const_19651207_gaudium-et-spes_en.html.

strand, cut it, insert a prescribed sequence of nucleotides, and then re-connect the DNA strand. We call this "gene editing" for short.

What is the upshot? CRISPR/Cas9 technology can be used for highly specific and convenient gene editing, either inserting sequences in target genes, deleting genes, or turning genes off. The overwhelming scientific consensus is that this technology will usher in an age of cheap and easy genetic manipulation. If we don't like the DNA nature has bequeathed us, we can employ CRISPR/Cas9 to edit it to our standards.

CRISPR editing could be effective in genetic therapy. Already in 2017, Shoukhrat Mitalipov, who directs the Center for Embryonic Cell and Gene Therapy at Oregon Health and Science University in Portland, changed the DNA of a large number of one-cell embryos with the CRISPR gene-editing technique. His target was a gene responsible for an inherited disease, hypertrophic cardiomyopathy. Mitalopov proved the technique in principle, even though as yet clinical trials have not begun. An embryo with such a genetic alteration could be born without a predisposition to hypertrophic cadiomyopathy. If this gene editing technique would take place in somatic cells (already mature cells in an individual patient), we would have an effective therapy for a thousands of monogenic inherited disorders. And if this gene editing would take place in gametes (sperm or egg), future

generations would also be born free of this inherited threat.[3]

In addition to employing CRISPR for genetic therapy, it could also become a technique for genetic enhancement. "The term *enhancement* is usually used in bioethics to characterize interventions designed to improve human form or functioning beyond what is necessary to sustain or restore good health," according to former director of the Ethical, Legal, and Social Implications Research Program at the National Institutes of Health, Eric Juengst.[4] Might CRISPR gene editing go on sale like performance enhancing drugs to create children superior in intelligence, size, strength, and talent? Are gene therapy and gene enhancement moral equivalents? Or, do we evaluate them differently?

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[3] Steve Conner, "First Human Embryos Edited in U.S., *MIT Technology Review* (July 26, 2017) https://www.technologyreview.com/s/608350/first-human-embryos-edited-in-us/ (accessed 9/29/2017). Whether Milatopov's results can be confirmed or not is disputed by scientific skeptics. Kelly Servick, " Skepticism surfaces over CRISPR human embryo editing claims," *Science* (August 31, 2017) http://www.sciencemag.org/news/2017/08/skepticism-surfaces-over-crispr-human-embryo-editing-claims (accessed 9/29/2017). Attempts to prove in principle that CRISPR is effective in altering the genomes of pre-implantation embryos has also been going on in Asia. See: Hong Ma, Nuria Marti-Gutierrez, Sang-Wook Park, Jun Wu, Yeonmi Lee, Keiichiro Suzuki, Amy Koski, Dongmei Ji, Tomonari Hayama, Riffat Ahmed, Hayley Darby, Crystal Van Dyken, Ying Li, Eunju Kang, A.-Reum Park, Daesik Kim, Sang-Tae Kim, Jianhui Gong, Ying Gu, Xun Xu, David Battaglia, Sacha A. Krieg, David M. Lee, Diana H. Wu, Don P. Wolf, " Correction of a pathogenic gene mutation in human embryos," *Nature* 548 (24 August 2017) 413-419.

[4] Eric T. Juengst, "What Does Enhancement Mean?" in Erik Parens, ed., *Enhancing Human Traits: Ethical and Social Implications* (Washington DC: Georgetown Universitry Press, 1998) 29. Most ethicists quickly give a thumbs up to therapy but a thumbs down to enhancement, because enhancement exacerbates inequality and injustice in the social fabric. Further, enhancement de-humanizes. "I do not think the main problem with enhancement and genetic engineering is that they undermine effort and erode human agency. The deeper danger is that they represent a kind of hyperagency—a Promethean aspiration to remake nature, including human nature, to serve our purposes and satisfy our desires….And what the drive to mastery misses and may even destroy is an appreciation of the gifted character of human powers and achievements." Michael J. Sandel, "What's wrong with designer children, bionic athletes, and genetic engineering?" *The Atlantic Monthly* (April 2004) 5.

The U.S. National Academy of Sciences guides us through the thicket of enhancement deliberation.

> To begin, it is necessary to define what is meant by "enhancement." Formulating this definition requires a careful examination of how various stakeholders conceptualize "normal." For example, using genome editing to lower the cholesterol level of someone with abnormally high cholesterol might be considered prevention of heart disease, but using it to lower cholesterol that is in the desirable range is less easily characterized, and would either intervention differ from the current use of statins? Likewise, using genome editing to improve musculature for patients with muscular dystrophy would be considered a restorative treatment, whereas doing so for individuals with no known pathology and average capabilities just to make them stronger but still within the "normal" range might be considered enhancement. And using the technology to increase someone's muscle strength to the extreme end of human capacity (or beyond) would almost certainly be considered enhancement.[5]

What is needed for moral decision-making regarding genetic enhancement is the partnership of knowledge with wisdom combined with personal integrity oriented toward the common good.

Applauding the Science of CRISPR while Doubting the Ethics of CRISPR

There is good reason for our scientists to applaud CRISPR with vigor. According to Jennifer Doudna, one of the CRISPR pioneers, "the simplicity of CRISPR-Cas9 programming, together with a unique DNA cleaving

[5] NASEM (National Academy of Science, Engineering, and Medicine). "Gene Drives on the Horizon: Report in Brief" (2016) 7; http://nas-sites.org/gene-drives/files/2015/08/Gene-Drives-Brief06.pdf (accessed 11/28/2016).

mechanism, the capacity for multiplexed target recognition, and the existence of many natural type II CRISPR-Cas system variants, has enabled remarkable developments using this cost-effective and easy-to-use technology to precisely and efficiently target, edit, modify, regulate, and mark genomic loci of a wide array of cells and organisms."[6]

Scientists are applauding. Some bioethicists are not. George Annas at Boston University's School of Public Health flashes the red light to stop all traffic. "The core challenge is what the new technology means to the human species. Is it a technology that affects our understanding of humanity and opens the door to a neo-eugenics agenda that could threaten the survival of the species?"[7] Arthur Caplan at New York University's School of Medicine flashes the yellow caution light. "In addition to the discussion about human germ line editing, CRISPR raises or revives many other ethical issues, not all of which concern only humans, but also other species and the environment."[8] If CRISPR/Cas9 threatens species survival, then this warrants a red stop light. Otherwise, a yellow caution light will suffice.

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[6] Jennifer A. Doudna and Emmanuelle Carpentier, "Genome Editing: The new frontier of genome editing with CRISPR-Cas9." *Science* 346:6213 (28 November, 2014) ; DOI: 10.1126/science.1258096.

[7] George J. Annas, "The mythology of CRISPR," *Science* 354:6309 (14 October 2016) 189. Annas proposes an international treaty to ban such biotechnologies as gene editing that would lead to species-alteration along with cloning and such. George J. Annas, Lori B. Andrews, and Rosario M. Isasi, "Protecting the Endangered Human: Toward an International Treaty Prohibiting Cloning and Inheritable Alterations," *American Journal of Law and Medicine* 28:2,3 (2002) 151-178.

[8] Arthur Caplan, Brendan Parent, Michael Shen, Carolyn Plunkett, "No time to waste—the ethical challenges created by CRISPR." *Science and Society* (August 10, 2015).
DOI 10.15252/embr.201541337| Published online 08.10.2015.

The Transhumanist Proposal for a Post-Human Species

Might someone actually wish to employ gene editing to alter the human species? Yes. A Promethean transhumanist will snap up such a technology. CRISPR/Cas9 could provide a tool in the tool box the transhumanist needs to build a super-intelligent species, a post-human species which will leave today's *Homo sapiens* in the archives of evolutionary history.

Transhumanism, also known as Humanity Plus or H+, "holds that current human nature is improvable through the use of applied science and other rational methods, which may make it possible to increase human health span, extend our intellectual and physical capacities, and give us increased control over our own mental states and moods."[9] This, according to Oxford's Nick Bostrom, a recognized H+ savant.

Bostrom tries to mollify critics who fear the extinction of the current human species by affirming genetic continuity between humanity today and post-humanity tomorrow. "There would be a continuity of differently modified or enhanced individuals, which would overlap with the continuum of as-yet enhanced humans."[10]

In sum, gene modification along with other biotechnologies could be employed today to surpass humanity and bring a superior post-humanity into

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[9] Nick Bostrom, "In Defense of Posthuman Dignity," *Transhumanism and its Critics,* eds., Gregory R. Hansell and William Grassie (Philadelphia: Metanexus, 2011) 55-66, at 55.
[10] Ibid., 60.

existence, but some continuity between the old and new species would endure.

Despite Bostrom's attempt to calm critics, this transhumanist vision causes bioethicists to tremble in their Nikes. They fear that such playing God will lead to a recklessness that might put an end to our species before a superior one can emerge. Hava Tirosch-Samuelson unleashes a barrage of criticism. "The transhumanist project is misguided because of its mechanistic engineering-driven approach to being human, its obsession with perfection understood in terms of performance and accomplishments rather than moral integrity, and its disrespect for the unknown future. Transhumanism is a utopian vision that, like all utopias, has gone awry because it mistakenly believes that the ideal is realizable in the present instead of remaining just a beacon for the future."[11]

Perhaps we should acknowledge that the transhumanist vision is grand, big, comprehensive, and dramatic. Long before we open the gate to a post-human species, however, our society will likely follow a long rocky path requiring careful baby steps. We are already on that

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[11] Hava Tirosch-Samuelson, "Engaging Transhumanism," Ibid., 19-52, at 47. Theologian and bioethicist Ronald Cole-Turner is much more open to a marriage between secular transhumanism and Christian spirituality. "Human transformation is central to Christian thought." Ronald Cole-Turner, "Introduction: The Transhumanist Challenge," *Transhumanism and Transcendence,* ed., Ronald Cole-Turner (Washington DC: Georgetown University Press, 2011) 1-18, at 5. On the one hand, self-identified atheist and transhumanist Russell Blackford complains about me for being too critical of H+: "Peters has adopted...a disdainful attitude toward transhumanist thought." Russell Blackford, "Trite Truths about Technology: A Reply to Ted Peters," Ibid., 176-188, at 187. On the other hand, transhumanism critic, theologian Celia Deane-Drummond warns that I am too cozy with the movement. "I am more wary of the slide from enhancement to transhumanism than are authors such as Ted Peters." Celia E. Deane-Drummond, *Christ in Evolution* (Minneapolis: Fortress Press, 2009) 259.

path, actually. What should be our next baby step? Should we look ahead at a red light or a yellow light?

Formulating CRISPR Ethics

CRISPR ethics, like all ethical deliberation, is future oriented. I define ethics as reflection on how to make a better future. I think of ethics proleptically. That is, we begin with a vision of a transformed future and then pave a road with transformative actions that will help get us there. When it comes to scientific and technological advance, proleptic or anticipatory ethics takes into account the many unknown factors or even pot holes that might require a detour or circumnavigation. Yet, the vision of a transformed future, like the star followed by the Magi, provides our moral beacon.

When it comes to gene editing combined with other biotechnologies and medical research, we must project a vision of a future characterized by optimum human health, planetary flourishing, and universal participation in the common good.[12] If we begin with such a vision, then we can measure the potential contributions of CRISPR gene editing accordingly.

The caveat is that we must admit that we are not in complete control of what happens. Despite our attempt to engineer our bodies and engineer our future, contingent events and side effects and unforeseen negative repercussions will ineluctably require repeated changes in

[12] For proleptic ethics, see: Ted Peters, *God--The World's Future* (Minneapolis: Fortress Press, 3rd ed., 2015) Chapter 14.

course. Bioethical seer Hans Jonas (whom Mark Richardson will examine closely) alerts us to this caveat. "The gap between the ability to foretell and the power to act creates a novel moral problem."[13] This leads Jonas to a disposition of caution, the need to recover respect; he advises humility in the face of the subtle and complex whole of evolution we still do not, and cannot, know in its entirety.

I recommend that we proceed through a yellow traffic light, developing and applying CRISPR/Cas9 while invoking the Precautionary Principle (PP). There is no warrant either theologically or ethically for putting up a red light or stop sign to halt this particular technology. Theologically, I want to say this: human creativity belongs inherently to the *imago Dei,* because we are created by the God who does new things (Isaiah 65:17).[14] Human creativity even in self-transformation should be morally guided, not squashed.

Human creativity must be ethically thought of in terms of our relationship to self, God, and the world. The implication is this: if genome modification has the potential for improving human health, then the divine image of God at work in us will lead us to toward stewarding CRISPR's benefits. If we think of human society as the divine image

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[13] Hans Jonas, *The Imperative of Responsibility: The Search for an Ethic in a Technological Age,* (Chicago: u. of Chicago Press, 1984) 8.

[14] Creativity and future orientation belong to a healthy theological anthropology. "The ELCA values genetic science as an expression of the human responsibility to learn and predict, imagine and invent for the sake of stewarding creation." *Genetics, Faith, and Responsibility* (2011), The Evangelical Lutheran Church in America Social Statement; http://download.elca.org/ELCA%20Resource%20Repository/GeneticsSS.pdf (accessed 9/30/2017).

on Earth, then our creative advance in human health along with ecological health through advancing medical technology would be a fitting expression of that divine image.

This leads to three middle axioms. First, gene editing of somatic cells for purposes of therapy should be a moral no brainer. Proceed.[15] Second, gene editing of somatic cells for purposes of enhancement raises ethical questions of definition, equal access, and fairness. Yet, nothing about essential human nature would be threatened by such enhancement. Proceed only after widespread public discussion and consent.[16] Third, gene editing of the human germ line that could have consequences for generations to come, however, deserves a precautionary pause before deciding to go forward.[17]

"Where ethicists become most concerned is when germ cells are the target of CRISPR. Any changes in the germ cells can be potentially passed down to future generations, essentially introducing those changes into the human

[15] "The ethical norms and regulatory regimes developed for human clinical research, gene transfer research, and existing somatic cell therapy are appropriate for the management of new somatic genome-editing applications aimed at treating or preventing disease and disability." NASEM, 6.
[16] "Genome editing for purposes other than treatment or prevention of disease and disability should not proceed at this time, and that it is essential for these public discussions to proceed any decisions about whether or how to pursue clinical trials of such applications." NASEM.9.
[17] "Heritable genome-editing research trials might be permitted, but only following much more research aimed at meeting existing risk/benefit standards for authorizing clinical trials and even then, only for compelling reasons and under strict oversight." NASEM 7.

population."[18] We need caution here. So, I recommend we try this on for size: “Yes, but not yet.”[19]

Applying the Precautionary Principle to Gene Editing

I recommend that we pause when the yellow light is flashing, but we proceed with our drive toward gene editing. The yellow light should remind us of the Precautionary Principle or PP, originally formulated for ecological ethics but equally applicable to genetic stewardship. There are many versions, but I rely on the so-called Wingspread version of the PP as it was formulated at the 1992 United Nations Conference on Environment and Development: “When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically. In this context the proponent of the process or product, rather than the public, should bear the burden of proof.”[20]

The proof need not have slam dunk finality, but the future forecast must incorporate the best knowledge and wisdom available at the time of choice. Exploring possible

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[18] Steven Novella, "CRISPR and the Ethics of Gene Editing." *Science Based Medicine* (December 2, 2015);
https://www.sciencebasedmedicine.org/crispr-and-the-ethics-of-gene-editing/ (accessed 11/28/2016).

[19] Ted Peters, "CRISPR, the Precautionary Principle, and Bioethics," *Theology and Science* 13:3 (July 2015) 1-4; DOI: 10.1080/14746700.2015.1056583. See also: Ted Peters, "Should CRISPR Scientists Play God?" *Religions* 8:61 (2017) . DOI: 10.3390/rel8040061.

[20] Wingspread Statement on the Precautionary Principle, 1998.
http://www.gdrc.org/u-gov/precaution-3.html (accessed 12/15/2016).

futures cannot go on indefinitely. At some point, researchers need to leap forward. The choice to move forward must be informed by the best knowledge and formed by persons who appeal to the common good.

The PP ranks options according to risk due to unknown contingencies. Gene editing for therapeutic purposes or even enhancement purposes of an existing individual carries low risk. Gene editing of gametes that would affect the germ line for generations into the future, however, carries increased risk due to increased unknown contingencies. Some concerned scientists, led by Edward Lanphier, president of Sangamo and chairman of the Alliance for Regenerative Medicine in Washington DC, have sounded an alarm: "In our view, genome editing in human embryos using current technologies could have unpredictable effects on future generations. This makes it dangerous and ethically unacceptable. Such research could be exploited for non-therapeutic modifications. We are concerned that a public outcry about such an ethical breach could hinder a promising area of therapeutic development, namely making genetic changes that cannot be inherited."[21]

Note how these scientists have provided two reasons for precaution. First, unpredictable consequences risk negative impact. This in itself warrants appeal to the PP. Second, scientists want to avoid offending the public who might shut off the supply of their research money for

[21] Edward Lamphier, Fyodor Urnov, Sarah Ehlen Haecker, Michael Werner, and Joanna Smolenski, "Don't Edit the Human Germ Line," *Nature* 521:117 (2015); http://www.nature.com/news/don-t-edit-the-human-germline-1.17111.

non-germline research. The first seems to nest fittingly as a matter for ethical deliberation, while the second seems laughably self-serving.

Now let us ask: is my support for PP only a smoke screen? Does PP surreptitiously turn the traffic light red?[22] Dana Carroll and Alta Charo are suspicious here. "Critics [of CRISPR] will also point to the intrinsic uncertainty about downstream effects, and will invoke some form of the precautionary principle, which demands a strong justification before permitting any risk-creating activity, with risk defined both in terms of known hazards and unknown possibilities. The latter, of course, is incapable of measurement, which is where the precautionary principle can be stretched into a generalized prohibition."[23] It is not my intention to stretch the PP into a "generalized prohibition." I recommend a yellow traffic light, not a red one.

Dana Caroll and Alta Charo spell out what the yellow caution light might entail for CRISPR decision-makers. "Ultimately, the issues are whether the beneficial uses of genome editing are adequately safe and acceptable,

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[22] Otherwise conservative Valparaiso bioethicist Gilbert Meilaender entertains a cautionary approach to heritable germ line editing trials while recognizing that caution does not mean that they must be prohibited. "Which is to say, it sets before us a yellow light." Gilbert Meilaender, "Is Caution Enough? The Promise and Peril of Gene Editing," *Commonweal* 44:7 (April 4, 2017) 12-15, at 13. Caution just may lead to the decision to stop. "No doubt it is generally wise to let a yellow light make us cautious. But there may also be moments when we should remember that there always remains another possibility and that moral seriousness might sometimes be measured by our willingness to be as wise as kindergarteners and to know when to 'stop, stop, stop'." Ibid., 15.

[23] Dana Carroll and Alta Charo, "The societal opportunity and challenges of genome editing," *Genome Biology* (2015) 16:242; DOI 10.1186/s13059-015-0812-0; http://godandhumangenetics-slc2017.org/sites/rms.clphost.com/files/carrollcharo_genomebiol_2015.pdf (accessed 9/30/2017).

whether regulatory oversight appropriately balances realistic risk assessment with achievement of the anticipated benefits, and whether there are any other factors that point towards promoting or impeding its use."[24]

Here is the hinge on which both the ethical and public image arguments swing: the distinction between genome editing in somatic cells and in germ cells. Everyone would approve morally of therapeutic gene editing in somatic cells such as the research on inherited heart disease mentioned above. But, germ line cells seem to be treated as if they have laboratory leprosy. A voluntary moratorium in the scientific community could be an effective way to discourage human germ line modification and raise public awareness of the difference between these two techniques. Such a moratorium would obey the PP while giving the public time to join the applause for our laboratory geneticists.

Conclusion

CRISPR confronts our society with an inescapable demand to choose, with a forced option. We and our neighbors along with our world leaders cannot help but choose whether or not to alter the genomes of plants, mosquitoes, or human beings. To elect to snuff CRISPR and let nature take its course would require just as much ethical deliberation and commitment as spelling out a precautionary policy or, thirdly, allowing *laissez faire*

[24] Ibid.

capitalism to run over our genomes like a bull dozer. The near and medium range futures of gene editing will be the result of a moral choice, one choice or another. The task of the church and the university in the company of our best scientists, who are concerned about the moral integrity of our shared future, is to prepare the present and the next generations with the ability to make wholesome choices based upon a transformative vision guided by the common good.