The CRISPR Apple on the Tree of Knowledge

with Arvin M. Gouw, "The CRISPR Apple on the Tree of Knowledge Conference Highlights: CRISPR in Science, Ethics, and Religion"; Arvin M. Gouw, "Introducing the Brave New CRISPR World"; Roger R. Adams, "Moral Decisions about Human Germ-line Modification"; Constance M. Bertka, "Navigating the Future in a Sea of CRISPR Uncertainty"; and Linda Groff, "CRISPR, CRISPR on My Mind."

THE CRISPR APPLE ON THE TREE OF KNOWLEDGE CONFERENCE HIGHLIGHTS: CRISPR IN SCIENCE, ETHICS, AND RELIGION

by Arvin M. Gouw

Abstract. The Institute on Religion in the Age of Science (IRAS) asked Ted Peters, an eminent theologian and bioethicist who was at the forefront of the cloning and stem cell debates in the past few decades, and myself, a molecular biologist, to invite scholars from various fields to brainstorm the religious and ethical implications of the CRISPR revolution. We invited keynote speakers, whose talks will be covered here, as well as other speakers and poster presentations. The conference also hosted question and answer sessions, chaplain sessions, and discussions throughout the week at the beautiful Star Island in the summer of 2019. The purpose of this paper is to highlight and sample the discussions and presentations from that conference. I will organize them into three broad topics: CRISPR in science, ethics, and religion. For readers unfamiliar with CRISPR technology, this overview can also serve as an introduction to the field, and a stepping stone for future ideas for CRISPR discussions.

Keywords: biotechnology; bioethics; CRISPR; genetics

Gene editing technology has existed for over a decade; however, it has not been easily utilizable until the advent of clustered regularly interspaced short palindromic repeats (CRISPR) gene editing. Since the discovery of CRISPR gene editing, species ranging from simple bacteria to monkeys have been genetically edited. In fact, last year we heard of the infamous case of the first twins to be CRISPR-ed by He Jiankui (Gouw 2019). The Institute on Religion in the Age of Science (IRAS) Star Island Conference

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of 2019 (titled "The CRISPR Apple on the Tree of Knowledge"), to which this thematic section of *Zygon: Journal of Religion and Science* is devoted, was a multidisciplinary conference on the implications of CRISPR. Like with most revolutionary scientific discoveries, ethicists and regulators are left behind, trying to catch up with understanding both the nature and the implications of the new technology. Given that CRISPR technology can be used to edit the human genome and anything that carries DNA, there are multiple stakeholders who should be involved in discussing what this CRISPR revolution means to the public.

The IRAS asked Ted Peters, an eminent theologian and bioethicist who was at the forefront of the in vitro fertilization (IVF), cloning, and stem cell debates in the past few decades, and myself, a scientist who conducts genetics research, to invite prominent speakers from various fields to brainstorm the religious and ethical implications of the CRISPR revolution. We invited keynote speakers, whose talks will be covered here, as well as other speakers and poster presentations. The conference also hosted question and answer sessions, chaplain sessions, and multiple formal and informal discussions throughout the week at the beautiful Star Island, off the coast of New Hampshire, in the summer of 2019.

The purpose of this article is to highlight and sample the discussions and presentations from that conference; it also serves as the introduction to this thematic section of *Zygon: Journal of Religion and Science*. I will organize them into three broad topics: CRISPR in science, ethics, and religion. For readers unfamiliar with CRISPR technology, this overview can also serve as an introduction to the field, and a stepping stone for future ideas for CRISPR discussions.

Science of CRISPR

The conference began with a broad overview by me to introduce the science of CRISPR. CRISPR was discovered as a defense mechanism by bacteria against phages, or viruses (Jinek et al. 2012). Since bacteria are single-celled organisms, they do not have the luxury that multicellular organisms have to dedicate a subset of their cells to be immune cells. Scientists then discovered that bacteria are able to incorporate some segments from invading foreign viral DNA into their genomes. Upon entry of foreign DNA, an enzyme called Cas9 will cleave the foreign DNA. This simple, elegant mechanism has allowed bacteria to survive throughout their evolutionary history, and this CRISPR/Cas9 system is also found in eukaryotes and higher level organisms, such as mammals and humans. (Weatherall 2000; Bosley et al. 2015; White and Khalili 2016; Abdelrahman et al. 2018).

Not long after this discovery, scientists built on this bacterial defense mechanism by inserting single guide RNAs (sgRNAs) specific to a gene of interest. sgRNAs have the ability to activate a host's CRISPR/Cas9 system to destroy their respective gene of interest. In other words, scientists are now able to edit any genome by exploiting this CRISPR/Cas9 system (White and Khalili 2016; Otoupal and Chatterjee 2018).

Before even getting into the ethical implications of this technology, there are some concerns about unintended scientific consequences that should be noted. First, because the human genome has about 2–3 billion base pairs, we have to make sure that the sgRNA that we design will target only one gene of interest amongst the 20–30,000 genes that we have in our DNA. Similar to small molecule drugs, our genetic targeting could end up hitting unintended targets (Grunewald et al. 2019; Herai 2019). Scientists refer to this as the "off-target effect." Second, even once we have successfully designed sgRNAs that are specific to our gene of interest, we have to be mindful of unintended on-target effects (Tuladhar et al. 2019). For example, it is widely known that sickle-cell anemia confers resistance to malaria. Therefore, suppression of sickle-cell anemia through gene editing can increase susceptibility to malaria (Jajosky, Jajosky, and Jajosky 2018; Contreras and Alviz 2019). Given the complexity of genetic networks, it is difficult and often impossible to predict all the consequences of altering even a single gene in that network. Third, we now know that environment, as well as genetics, plays a crucial role in the development of disease. In scientific terms, genes do not always dictate the ultimate phenotype. Other factors beyond genes, known as epigenetic factors, can alter or modulate specific genetic program (Janssen et al. 2019). For example, suppose I carry a gene that causes cancer. However, if that gene is bound by histones in my nucleus such that the gene cannot be activated, I will never actually develop cancer. Similarly, a CRISPR modification may be epigenetically repressed by the host cell, rendering it useless (Gouw 2019). This has led scientists to modify the epigenetic factors themselves using CRISPR (Xie et al. 2018; Xiao et al. 2019).

Beyond these scientific concerns, I briefly touched upon issues related to the ease of access to CRISPR technology. A "DIY Bacterial Genome Engineering CRISPR Kit" allows you to do CRISPR as long as you have water and microwave at home, and it is now available from Amazon for less than $180 as of January 2020. Moreover, inserting the CRISPR gene into cells, which used to require a $10,000 tool, now can be done with a new tool that only costs 23 cents to make (Byagathvalli et al. 2020). High school students have been able to perform CRISPR gene editing successfully after a short training by UC Berkeley scientists, which is also being considered in other places as part of a molecular biology workshop (Ziegler and Nellen 2019). On the positive side, the proliferation of this powerful technology due to low cost and ease of use may lead to a democratization of science, and help CRISPR therapies become widely available (Gouw 2018a). On the negative side, these same factors may lead to ineffective or harmful interventions by untrained practitioners who do not understand (or do not care about) the potential for unintended side effects, and makes it easier for unscrupulous individuals to conduct morally questionable experiments with little oversight (Ledford 2015; Wolinsky 2016).

Dr. Kareem Washington, physician scientist and faculty from Howard University, further elaborated upon the scientific context of CRISPR technology. Washington argued that genetic engineering has been done for millennia, starting with the advent of agriculture at the dawn of civilization. Selection of seeds and crops led to genetic drift and positive selection for most productive crops in agriculture. Similarly, animals have been selectively bred for specific traits. In the more contemporary context, Washington presented the birth of biotechnology using recombinant proteins in treatment, which was followed by utilizing RNA as therapy. Thus, Washington correctly noted that CRISPR is one amongst many preceding technologies in the realm of modifying genetics. Whatever ethical issues arise out of CRISPR are not novel, as they are also shared by other bioengineering technologies, be it at the protein, RNA, or DNA level. Washington interestingly proposed that retributive and distributive justice have been utilized accordingly for past technologies, and it would not hurt to keep this classic model of justice in mind when evaluating CRISPR gene editing in our current context.

To zoom out from anthropocentrism, Gary Sherman, who previously worked for the Food and Drug Administration (FDA), reoriented us to CRISPR applications in plants. Sherman presented the massive problem of food shortages that we have faced throughout human history. Solomon Katz, Emeritus Professor of Anthropology at the University of Pennsylvania, also agreed that human applications of CRISPR may not be the most urgent or cost-effective use of genetic engineering. Sherman argued that many people reject the use of CRISPR (or any genetic engineering) in crops due to a fear of genetically modified organisms (GMOs). Similar to Washington, Sherman argued that genetic selection was done for millennia prior to the advent of biotechnology through ancient farming techniques. Sherman then fervently argued that organic farming techniques are less controlled and less efficient in using natural resources. With the advent of global warming and decreasing arable land, we do not have the luxury of entertaining the inefficient farming techniques employed in organic farming. Moreover, Sherman argued that organic farming leaves many variables untested, unlike in modern scientific farming or in GMO farming. Katz agreed that the whole food production chain needs to be evaluated, not just the genetics of the food itself.

Sherman's most compelling argument for the audience was when he argued that foreign genetic material cannot do anything to us. Sherman catalogued and calculated the enormous amounts of DNA and mutated DNA from our food intake during the conference. He correctly noted that GMO modification contributes only a single specific mutation as opposed to thousands of random mutations that we had already consumed by the second day that we were on Star Island. Sherman proceeded to argue that if CRISPR editing can increase farm productivity through modified crops, it would be immoral not to take advantage of it.

Switching gears from sharing what CRISPR is and what it can do in biomedicine and agriculture, Nadine Vicenten, from Harvard's Personal Genetics Education Project (pgEd.org), explained the role of public science education. Vicenten presented all the efforts that pgED has done so far in outreach programs on personal genomics education to various public sectors. Vicenten argued that science education is crucial to prevent patronizing scientists from dictating the use of CRISPR to the public. Vicenten highlighted the fact that science education requires participation of various communities, including religious communities. Vicenten presented an insight from one of her outreach programs: some Muslims felt that CRISPR-editing pigs for their organs could be "haram," or "forbidden." However, other Muslims argued that this might not be the case, because of the difference of interpretation of the regulations in Islam. Overall, Vicenten convinced all speakers and the audience at IRAS that scientists would benefit greatly from input from the public on the implementation and application of their technologies and discoveries.

In summary, the scientist speakers at IRAS agreed that we still need to learn a lot more about CRISPR. However, we all agreed that CRISPR has great potential to solve many problems in many aspects of life. Last but not least, we all agreed that we need input from all stakeholders in this new technology to guide us on how to best develop and implement it.

Ethics of CRISPR

For an introduction of the ethical dilemmas associated with CRISPR technology, our conference co-chair, Ted Peters, presented the long history of ethical debates associated with various genetic advances in the past decades. Peters began by presenting the history of the advent of genetic cloning with Dolly. Peters pointed out that genetic essentialism and determinism lie behind the fears of cloning. If our DNA makes us who we are, then cloning disrupts our notion of self-identity. Peters conceded the fact that scientists acknowledge that life is not all about the DNA, but also environmental factors, as demonstrated by the emerging field of sociobiology. However, Peters argues that sociobiology has merely expanded genetic determinism to genetic *plus* environmental determinism. Though the argument of Nature vs. Nurture is a false dichotomy, a sociobiologist's proposal of Nature *and* Nurture as the key to life presents the same deterministic fallacy.

Peters then presented the history of the stem cell debate, where the ethical arguments have not only revolved around genetic essentialism, but have also reflected on the permanence of the genetic modification. Peters highlighted the importance of distinguishing germline versus somatic modification. Despite other disagreements with William Hurlbut, an adviser to President George W. Bush who was key in government's decision on the use of embryonic stem cells for research (W.B. Hurlbut 2006; J.B. Hurlbut and Robert 2012), Peters agreed that germline modification should be put on hold (Peters 1995). Germline modifications affect not only the edited individual, but all the future progenies of that individual. This distinction of stem cell therapy for germline versus somatic cells has arisen again in the current CRISPR debates.

Overall, Peters upheld the precautionary principle when it comes to CRISPR. The precautionary principle supports neither a complete ban nor unrestricted use of CRISPR technology. Peters proposes that we proceed with caution in using CRISPR, constantly assessing the risks and benefits of various CRISPR applications as time progresses. Peters's complete argument and insights on this CRISPR revolution can be found in several articles in *Zygon: Journal of Religion and Science* (e.g., Peters 2019). This yellow light proposed by Peters was well received by virtually every speaker at IRAS.

Lisa Fullam, a feminist Catholic ethicist from Santa Clara University, reframed the ethical discussion around Catholic and social justice frameworks. Fullam argued that the magisterium of the Catholic Church technically does not say anything about CRISPR. The definition of personhood from the Church gives room for even abortion, some might argue. This is because strictly speaking, only persons have rights but not clump of cells. Personhood at conception only became the magisterial position in 1869, following the discovery of mammalian ovulation in 1827. Interestingly, this also explained the formulation of the doctrine of the immaculate conception of Mary in 1859 (Cumming 1861). On the other hand, Fullam noted that the *Laudato si'* (Francis and Catholic Church. Pope (2013-: Francis) 2015) seemed to argue that CRISPR is playing God. This is a point that Hurlbut strongly supports.

However, the Declaration on Procured Abortion footnote 19 argues that ensoulment is a philosophical definition, and not a scientific one. This means that personhood is not necessarily bestowed at the point of conception. The clump of cells calling for a soul was presented as a possibility in 1974. Taken together, the diverse Catholic magisterial documents suggest room for Catholic theologians of various positions on the use of CRISPR.

Fullam further argued that this discussion can be framed as a social justice issue. The Dignitas *Personae* (Catholic Church. *Congregatio pro Doctrina Fidei.* 2009) would support the argument that CRISPR therapy would be promoted if beneficence would overcome the risks. Similar to many scientific association guidelines, enhancement is a problem (Gouw 2018a). Enhancement leads to concerns about eugenics, social injustice, and lack of self-love. Taken to an extreme, CRISPR enhancement could lead to the commodification of "designer" children. On the other hand, Pope Francis has argued that we should not develop a throwaway culture (McElwee and Wooden 2018). CRISPR IVF could actually be used to modify embryos with genetic problems to give parents an alternative to throwing them away. This would be one creative way to get Catholic magisterium to positively accept CRISPR technology.

Fullam presented both the Catholic position as well as her novel approaches to this problem. I just would like to highlight the last pointed question that she raised as a feminist scholar. There are multiple feminisms: womanist, Latina, African American and many others. All of them would remind us that CRISPR tinkering will be done to women's bodies. Even current IVF already has side-effects that are harmful to women. Thus in discussing the use of CRISPR, we should not only calculate risk benefit outcomes, but also bear in mind the women who oftentimes have to bear these various treatments (Fullam 1999).

Arthur Sutherland, theologian at Loyola University Maryland, presented a very interesting perspective on CRISPR. Sutherland began with two fundamental presuppositions. First, he defined theology as reflection of content, thus forcing us to constantly check our own background and biases. Second, he assumed that genetic manipulation is here to stay, not whether it should be done or not. Given these two fundamental presuppositions, he proceeded to explore how in ethics we always create boundaries. There are many different kinds of boundaries: superimposed, geometric, fortified, physical, relic, frontier, political, and many others. After having defined the various boundaries that we have created artificially in various scenarios, Sutherland proceeded to explore the implications of having boundaries in general. First, we need to evaluate who we define as strangers and why. Second, we need to understand that diversity is not difference, and it is boundaries that turn differences into out-of-group strangers or in-group diversity. In other words, differences that are found within our boundaries are called diversity, while differences that are found beyond our boundaries constitutes our definition of a stranger. Third, Sutherland noted that boundaries reflect limited resources and zones of obligation: family, kin, village, country. Thus how we define our boundaries will define how we prioritize the use of our resources, and vice versa (Sutherland 2006).

I think the advent of CRISPR demands the analysis of a new kind of boundary: genetic boundaries. Genetic boundaries will differentiate the GenRich from the GenPoor (Gouw 2018a). This new distinction will arise due to differences in access to the technology. Moreover, novel, more specific boundaries may arise depending on specific traits that are modified. Overall, technologies always create boundaries, and CRISPR boundaries are more subtle because one may look externally identical, such that differences that are needed to identify the "other" are invisible.

Understanding that genetic boundaries could be a subset of "invisible" boundaries, we need to explore how in the past we have struggled with other invisible boundaries, such as political boundaries.

In summary, the ethicist speakers at the conference agreed that CRISPR technology has such great potential to alleviate suffering that it would be immoral to simply prohibit the use of this technology. However, discernment of which cases or scenarios warrant the use of CRISPR technology will depend on the various parties involved and the circumstances presented. Social justice and religious concerns should not be left behind in assessing this novel technology.

CRISPR and Religion

Though the ethical discussions presented by the main speakers involved religion, I would like to bring three of our speakers into dialogue in this segment of the article, specifically on the role of religion in facing this CRISPR revolution.

Michael Ruse, a philosopher, educator, and public thinker, argued that religion was useful in the past, but has always been problematic in dealing with ethical dilemmas. Ruse specifically points to doctrine of original sin of St. Augustine, which pushed Christians to say that war is bad but inevitable due to original sin. Ruse used the ethical discussion of war in light of original sin to discuss why religion is not always a good companion in ethical discussions, including genetic engineering. Ruse argued that due to original sin, Christian theologians such as Peters claim that we need God to save us. The problem here is that we pass the responsibility back to God, according to Ruse. On the other hand, Ruse argues that Darwinians like himself would accept that at some point in evolution, as a species we thought war was good to propel evolution and survival of select groups. However, Darwinians never thought that war was inevitable. Furthermore, Ruse argues that as evolution progressed, Darwinians now understand that altruism is a better way to survive; thus we can stop war now. Ruse argues the solution to advance evolution without war is to educate ourselves on the impact of war and why it is bad. Then we'll stop war and move on to improve society in a constructive way (Ruse 2019).

Similarly, when it comes to CRISPR, Ruse found the argument of the inevitability of evil in human nature as a hindrance to the use of CRISPR, and not helpful. This argument always puts Christian ethicists in a dilemma that is unnecessary. It would be better to simply acknowledge that we want good outcomes from CRISPR, and we need to educate ourselves about CRISPR so that we can use it wisely. The solution to ethical problems is learning from our mistakes, which is all part of education. Vicenten agreed on the necessity of education. Katz disagreed with Ruse that religion is a hurdle in ethics; Katz argued that religion is a resource that can unite multiple parties to cooperate and discuss how to best utilize scientific discoveries.

Peters disagreed strongly on several points, but mainly that the notion of progress through evolution is legitimate, because "progress" itself is a subjective moral concept. Ruse argued that the notion of progress is not contradictory to evolution. Ruse replied that though he could understand the argument that evolution does not have progress because it is a random process without a natural teleology or purpose, historically it has indeed shown progress. Peters then asked Ruse if he was a Pelagian. Ruse, of course, refused to be labeled with any Christian label because he is not Christian. However, if being Pelagian meant believing in humanism, so that through education we can improve ourselves, Ruse says, then so be it! Otherwise why do we teach at all?

Within the context of this Peters–Ruse argument, I would like to highlight Mladen Turk's talk. Turk is a philosopher and faculty member of the Elmhurst College. While Ruse is less enthused about having religion influence decisions on how to regulate CRISPR, Turk argues that CRISPR could inspire a new religion. CRISPR can perhaps even alter evolution by editing genes to make us more virtuous. This is a point that Peters, Gouw, Washington, Vicenten, and Fullam all disagreed on (Peters 1995, Gouw 2018b).

I would present Turk's argument in a Tillichian framework of method of correlation. Turk identified that there is a universal problem. This universal problem is that the human condition is full of death, groundlessness, insatiability, and belittlement. Such universal problems call for solutions. In the past the solution has been religion. Religion has been able to provide worldviews or narratives that help us deal with death, insatiability, and all the aforementioned problems (Turk 2013). However, Turk noted that CRISPR may prove to be a better solution than religion. In the past, religion was the answer to intractable life problems, but now CRISPR may actually be able to fix all these issues. CRISPR will replace religion because not only does it impose logical order to this world, but CRISPR can also bring physical order through genetic modification.

It is very interesting to highlight how Ruse's argument that religion is useless received these two different responses. Peters's response is that Ruse's argument is false due to the assumption of progress in evolution. Turk's response is that Ruse's argument is false simply because we have had the wrong religions in the past, and that CRISPR will be the better upcoming religion.

Having highlighted Ruse, Peters, and Turk in the relationship between religion and CRISPR, I would like to present an interesting approach by Constance Bertka, our chaplain during the conference. Bertka argued that religion has been used to exclude others, thus we have to be very cautious. On this point, Sutherland and Fullam would agree. Bertka expanded the horizon of CRISPR beyond its interactions with ethics and religion. Bertka further elaborates in her article in this issue of *Zygon: Journal of Religion and Science* that there are factors playing key roles in CRISPR ethics other than just science, ethics and religion: legal systems, economic battles, and even racism. Thus, Bertka disagrees with Ruse and Turk that religion should not be part of CRISPR discussions or that CRISPR could be the next religion. However, Bertka agrees with Ruse and Vicenten that education is important, based on her experience as a Broader Social Impacts Committee (BSIC) member of the Smithsonian National Museum of Natural History, and agrees with Turk that CRISPR goes beyond just scientific applications because it addresses broad human conditions, unlike most other science technology.

Concluding Remarks

The speakers and participants at the conference inspired very fruitful discussions. There are some take home lessons that we can learn from CRISPR in science, ethics and religion. In science, CRISPR technology keeps moving forward in its precision, applications, and de-risking efforts. Scientists are constantly seeking guidance on how technology can be applied, but that cannot happen until the public is aware of what CRISPR is and what it can do. Education is critical to keep the public engaged and informed. In ethics, CRISPR technology revives some older unresolved debates from previous scientific discoveries, such as cloning and stem cell research. There are also new issues specific to CRISPR due to the broadness of its applications. Therefore, we will need to find resources in other branches of ethics. In religion, CRISPR science demands the need to expand the discussion beyond Judeo-Christian frameworks. We need to hear more voices from other religions. Last but not least, religious and secular movements need to find ways to communicate and work together in facing this CRISPR revolution.

This thematic section of *Zygon: Journal of Religion and Science* brings together a selection of contributions from participants to the IRAS Conference. I wrote an overview article about the science of CRISPR. This is followed by two articles, on respectively ethics and religion of CRISPR, by Roger Adams (based on his poster presentation) and Constance Bertka (who was the conference chaplain). The final contribution is a poem by Linda Groff (written and circulated during the conference).

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