Online Ethics Center
FOR ENGINEERING AND SCIENCE

Emerging Biotechnologies: Class Plan (75 minutes)

Author(s)

Valerie Racine

Description

This class plan gives a selection exercises out of which an instructor may build a class session around the Emerging Biotechnology case on Genome Editing and the Ethics of CRISPR-Cas9. The materials are suitable for upper division undergraduate courses in bioethics or the life and environmental sciences.

Body

1. Introduction

Genome Editing and the Ethics of CRISPR-Cas9 — Case Discussion

The ethics of emerging biotechnologies is an important topic for both undergraduate and graduate students in the life sciences. This class plan is designed to facilitate discussion of one of these technologies--a genome-editing tool. The case study at the center of the class plan reviews a scientific article describing experiments in which researchers edited the genomes of non-viable human embryos using an engineered enzyme complex called CRISPR-Cas9. The goal of this session is to raise and discuss issues in research ethics, science communication, and the broader

ethical, social, political, and legal implications of emerging technologies.

---

2. Assigned Readings

- Marchant, Gary, Ann Meyer, and Megan Scanlon. "Integrating social and ethical concerns into regulatory decision-making for emerging technologies." *Minn. JL Sci. & Tech.* 11 (2010): 345.
  The authors argue that social and ethical concerns about emerging technologies are often best addressed between the research and commercialization stages of development. However, federal regulatory agencies are kept from properly addressing these concerns because of legal and practical constraints. The authors then consider whether and how these agencies could give greater weight to social and ethical concerns in their decision-making processes, and consider some potential drawbacks of doing so. They end by suggesting two ways in which these concerns can be successfully incorporated into the deliberations and decisions of regulatory agencies. The first model suggests that regulatory agencies ought to provide an ethical impact statement with the stated regulations. The second model calls for the creation of an ethics review board to review decisions made by regulatory agencies.

- Baltimore, B. D., Paul Berg, Michael Botchan, Dana Carroll, R. Alta Charo, George Church, Jacob E. Corn, et al. "A prudent path forward for genomic engineering and germline gene modification." *Science* 348, no. 6230 (2015): 36-38.
  The authors discuss the science and ethics of new genome editing technologies, with a focus on the use of CRISPR-Cas9, and offer a set of recommendations to ensure the ethical use of this technology. The authors argue that germline gene modification is controversial because it invokes the fear of a slippery slope from medical interventions designed to eradicate diseases to other non-medical uses. They also stress that the long-term consequences of these interventions remain unknown. The authors recommend an open dialogue about the benefits and the risks of this new technology to ensure the public’s trust in science.

- Jasanoff, Sheila, J. Benjamin Hurlbut, and Krishanu Saha. “Human genetic engineering demands more than a moratorium.” *The Guardian*, 7 April 2015.
  The authors claim that the suggested moratorium on emerging genome editing technologies, such as CRISPR-Cas9, is a relic from the 1975 Asilomar conference; a meeting which addressed public concerns about the safety of recombinant DNA technology. They argue that there are limitations to the Asilomar approach to discussing social and ethical issues arising from emerging biotechnologies, and that perhaps the Asilomar conference is not the best model by which scientists can engage the broader public about emerging biotechnologies. Instead, the authors suggest that more efforts are needed by leaders and scientists to engage citizens within a deliberative democracy, such as building a more complex architecture that enables public participation, as well as investing in education in science, technology, and society studies, in addition to STEM education.

- Ledford, Heidi. “CRISPR, the disruptor.” *Nature* 522 (2015).
  The author presents an historical analysis of the development of the CRISPR gene-editing technology. She first describes how CRISPR differs from other gene/genome-editing technologies and explains how it is being compared to the development of PCR in the 1980s as having a similarly profound impact on the development of genetic research. She then outlines the safety and ethical concerns that have been raised with respect to proposed applications of the technology in different contexts, including gene therapy, agriculture, and engineered ecosystems.

Suggested Readings:

- Jonas, Hans. "Technology and responsibility: Reflections on the new tasks of ethics." *Social Research* (1973): 31-54.
  For excerpts, see: Jonas, H. “Technology and Responsibility: Reflections on the New Tasks of Ethics,” in R.L. Sandler (ed.). *Ethics and Emerging Technologies*. Palgrave Macmillan, 2014, 37-47.
- Cressey, David, and David Cyranoski. “Human-embryo editing poses challenges for journals.” *Nature* (2015).
- Lanphier, Edward, Fyodor Urnov, Sarah Ehlen Haecker, Michael Werner, and Joanna Smolenski. "Don't edit the human germ line." *Nature* 519, no. 7544 (2015): 410.

- Sarewitz, Daniel. “CRISPR: Science can’t solve it.” *Nature* 522 (2015).
- Vogel, Gretchen. "Embryo engineering alarm." *Science* 347, no. 6228 (2015): 1301.

---

3. Case Description Handout

In April 2015, scientists in China published a paper in an online journal, Proteins & Cells, about experiments editing the genomes of non-viable human embryos (Liang et al. 2015). The research team, led by Junjiu Huang, used an engineered enzyme complex, called CRISPR-Cas9, to target and edit the HBB gene that codes for human β-globin protein. Defects in that gene can lead to β-thalassaemia, a heritable blood disorder that can be fatal.

In 2012, scientists Jennifer Doudna and Emmanelle Charpentier developed the CRISPR-Cas9 bioengineered complex that was used by the researchers in China. The technology has been used in previous research on animal and adult human cells. The technology allows researchers to target a specific gene by binding and splicing the DNA at specific locations, and replacing or repairing the segment by inserting other molecules (Cyranoski & Reardon 2015).

In their research, Huang and his team used non-viable, single-cell human embryos, which they obtained from a fertility clinic. The embryos possessed an extra set of chromosomes because they had been fertilized by two sperm and thus could not develop beyond the first stages of development. Huang and colleagues’ aim was to test whether the technology could reliably target defective genes and replace these genes with repaired sequences. Their results showed that only a small fraction of the 86 embryos used in the study had the replaced genetic material at the targeted gene. The researchers also found that there were many “off-target” mutations that might have been introduced in the genome as a by-product of the technological intervention (Cyranoski & Reardon 2015). These results led the researchers to conclude that clinical applications of the technology to human embryos were still premature.

The authors of the paper also claimed that the prestigious journals, Science and Nature, rejected their paper because of ethical objections to their research on human embryos, and specifically, because of ethical objections to any kind of germ

line genetic modification. The editors at the journal, Proteins & Cells, justified publishing the paper by claiming that they verified the researchers' institutional approval and the consent forms from the embryo donors, and confirmed that the study was compliant with Chinese laws and the Declaration of Helsinki's set of ethical principles on human experimentation (Cressey & Cyranoski 2015).

---

4. Case Discussion & Analysis

Leading scientists called for a moratorium on research on human embryos using genome-editing technologies, like CRISPR. What are the likely outcomes or consequences of a moratorium? What ethical goals could be achieved?

- In response to the call for a moratorium on CRISPR, the US National Academy of Sciences (NAS) and the National Academy of Medicine (NAM) have launched an initiative to develop new guidelines to address the use of technology which makes germ line genetic modification possible, and called for members of the scientific community to attend an international summit on the topic set for autumn 2015.
- The call for a moratorium invoked comparisons to technological innovations that led to recombinant DNA in the 1970s and the meeting at Asilomar in 1975, where molecular biologists met to discuss and set guidelines to ensure that genetic research would develop in a safe manner (Vogel 2015).
- Comparison with Asilomar 1975:
    - 1972/73 – concerns emerge about recombinant DNA technology
    - 1974 – "Berg letter" calls for a moratorium & entails a strong reaction from the scientific community
    - 1975 – international meeting at Asilomar, CA; 4 days; included leading molecular biologists, select members of the press, 3 lawyers; goal was to consensus statement; claimed that if they (the scientists) did not reach a consensus, then Congress would impose their regulations; fear of compromising the autonomy/freedom of scientific research
    - Major issues: biosafety, known and unknown risks, liability
    - Explicitly excluded: social and ethical concerns; biowarfare, environmental issues

- UPDATE: In response to calls for a moratorium, the US National Academy of Sciences (NAS) and the National Academy of Medicine (NAM) have launched an initiative to develop new guidelines to address the use of technology which makes germ line genetic modification possible, and called for members of the scientific community to attend an international summit on the topic set in December 2015 (Reardon 2015b).
- The International Summit on Human Gene Editing held in Washington, D.C., in December 2015, was hosted by the National Academy of Sciences, the National Academy of Medicine, the Chinese Academy of Sciences, and the U.K.'s Royal Society. (See “Content Commentary” below for more details on the result of this summit.)

Who should be included in decisions about whether or not this research should be restricted? On what basis should participation be decided?

- Critics of 1975Asilomar conference claim that the meeting was not inclusive, which resulted in a very myopic discussion centered on biosafety issues.
- Asilomar left out ethicists, politicians, religious groups, and representatives of human-rights organizations or patient-interest groups (Reardon 2015).
- They also included only very specific kind of scientists, molecular biologists.
- Critics thus argue that Asilomar was merely an effort by scientists to resist government restrictions / and interference from non-specialist and a PR campaign to promote public trust in scientists.
- Sarewitz argues for the importance of a democratic deliberative process when identifying and addressing the ethical issues about emerging technologies.
- Jasanoff *et al.* (2015) argue that more efforts are needed by leaders and scientists to engage citizens and ensure their participation in these deliberations, such as building a more complex architecture that enables public participation, as well as investing in education in science, technology, and society studies, in addition to STEM education.

How should academic journals and other scientific institutions deal with this kind of research? What are their ethical responsibilities?

- *Science* and *Nature’s* decision to decline to publish the research paper was due to “undisclosed ethical objections.”
- Their decision raised further ethical issues about the dissemination of that scientific research.

- Managing editor of *Protein & Cells*, Xiaoxue Zhang, claimed that their editorial board was not blind to the potential ethical objections to the research, but decided to publish the article as a way to “sound an alarm” to begin discussions about the future direction of genome editing technologies (Cressey & Cyranoski 2015).
- There remain questions about whether discussion of social and ethical concerns should come before or after the scientific research is conducted or published/disseminated.
- UPDATE: For more substantial discussion on this topic, consult: Resnik, David B. "H5N1 Avian Flu Research and the Ethics of Knowledge." *The Hastings Center Report* 43, no. 2 (2013): 22.

What are the roles and responsibilities of the individual scientists involved in the research?

- As the case description highlights, the editors of the journal and the authors of the article followed existing regulatory guidelines within their institution and country. The researchers had obtained institutional approval and consent from the embryo donors. The editors also confirmed that the study was compliant with Chinese laws and the Declaration of Helsinki’s set of ethical principles on human experimentation.
- UPDATE: For a more in-depth discussion on this topic, consult: Resnik, David and Adil E. Shamoo. "Bioterrorism and the Responsible Conduct of Biomedical Research." *Drug Development Research* 63, no. 3 (2005): 121-133.

---

5. General Themes in the CRISPR case

What are some of the general / crosscutting themes in the ethics of emerging biotechnologies which are reflected in this case?

- Ethical issues with human germline genetic modifications (uncertainty of long-term effects, concern about “designer babies,” concern about justice; i.e. fair distribution of costs and benefits)
- Ethical issues with moratorium and self-regulation of science (comparisons with recombinant DNA & Asilomar in 1970s)
- Ethical issues about governance and public participation/representation

- Ethical Issues about scientific research communication and dissemination
- Scientific self-regulation vs. Governmental Oversight
- Assessing and managing risks (problem of uncertainty)
- Interfering in “natural” processes – e.g. procreation, ecosystems / humans’ relationship with the natural world
- Global and national bio-security issues
- Bio-safety

---

6. Workshop/General Discussion

Given our case analysis and our discussion about some of the general themes in the ethics of emerging technologies, how should we tackle an ethical analysis of CRISPR-Cas9? (In other words, what are the questions that are being asked? What questions should be asked?)

---

7. In-Class Activity – City Hall Meeting in 2015

Separate class into five groups (works best with a class of ~20-30 students):

- Senior research scientists (the Principle Investigators in the lab)
- Graduate Students/Post-Docs (working under the PI)
- Maintenance personnel who take care of the lab or work in building
- People who live in community
- Policy-Makers

Instructions for the class:

Pretend it’s 2015, right after the call for a moratorium on gene-editing research with CRISPR, and you’re participating in a town hall meeting in Tempe, AZ, to discuss the ethical concerns about this technology, and also to inform the general audience about what sorts of research at Arizona State University might use this technology and why.

Come up with a list of interests/concerns/worries, which represent members of your assigned groups.

State and defend your concerns and your recommendations. What should be done? How should it be implemented?

Should the “public” be involved? If so, how? What is the most effective way to ensure public participation and representation in these discussions?

---

8. Content Commentary

The publication of Huang and colleagues’ research caused a stir in the scientific community and generated many editorials and opinion pieces in scientific publications warning about the ethical issues that must be addressed before this research is pursued any further.

Scientists were quick to call for a moratorium on all genome editing of human embryos, and invoked similarities to the technological innovation that led to recombinant DNA in the 1970s and the meeting at Asilomar in 1975, where molecular biologists met to discuss and set guidelines to ensure that genetic research would develop in a safe and ethical manner (Vogel 2015).

However, many are critical of the comparisons with the Asilomar meeting and the attempt to use that conference as a model on which to build bioethical guidelines for future research with genome editing technologies (Jasanoff et al. 2015). Critics claim that the 1975 Asilomar conference was not an inclusive meeting because many of the stakeholders were not invited, such as ethicists, politicians, religious groups, and representatives of human-rights organizations or patient-interest groups (Reardon 2015b). Because of the lack of representation from non-scientists in the discussions, critics claim that Asilomar was merely an effort by scientists to resist government restrictions and promote public trust in the idea that scientists are able to regulate themselves (Reardon 2015b).

In response to calls for a moratorium, the US National Academy of Sciences (NAS) and the National Academy of Medicine (NAM) have launched an initiative to develop new guidelines to address the use of technology which makes germ line genetic modification possible, and called for members of the scientific community to attend

an international summit on the topic set in December 2015 (Reardon 2015b).

The International Summit on Human Gene Editing held in Washington, D.C., in December 2015, was hosted by the National Academy of Sciences, the National Academy of Medicine, the Chinese Academy of Sciences, and the U.K.'s Royal Society. Members of the Summit's organizing committee submitted a public statement shortly after the meeting, outlining four recommendations. First, basic and preclinical research on gene-editing technologies is needed and should proceed. Second, clinical use of the technologies on somatic cells should be explored. Third, it is irresponsible to pursue clinical applications of gene-editing technologies on germline cells at this time. And, fourth, there is a need for ongoing discussions regarding the clinical use of germline gene editing, so the national academies should create a forum to allow for discussions which are inclusive and which engage with a variety of perspectives and expertise.

Some science policy experts have argued that the complexity of the issues surrounding germ line genetic modification cannot be adequately addressed from a scientific perspective. For example, Daniel Sarewitz, co-director of Arizona State University's Consortium for Science, Policy, and Outcomes, argues:

The idea that the risks, benefits and ethical challenges of these emerging technologies are something to be decided by experts is wrong-headed, futile and self-defeating. It misunderstands the role of science in public discussions about technological risk. It seriously underestimates the democratic sources of science's vitality and the capacities of democratic deliberation. And it will further delegitimize and politicize science in modern societies (Sarewitz 2015).

Sarewitz's comment signifies the importance of a democratic deliberative process when identifying and addressing the ethical issues about emerging technologies, as well as developing guidelines that will help to decide how these technologies will be further developed and used. In this particular case, there is worry that germ line genetic modification on human embryos to replace defective genes may lead to a slippery slope to eugenics, or attempts to create perfect designer babies.

Lastly, the decision by Science and Nature to decline to publish the research paper because of undisclosed ethical objections raised further ethical issues about the dissemination of scientific research within a global context. The managing editor of Protein & Cells, Xiaoxue Zhang, has claimed that their editorial board was not blind

to the potential ethical objections to the research, but decided to publish the article as a way to “sound an alarm” to begin discussions about the future direction of genome editing technologies (Cressey & Cyranoski 2015). Whether these discussions should come before or after the scientific research is conducted or published raises important questions about how best to regulate innovative scientific research with uncertain outcomes or potential dual-use applications.

---

9. Bibliography

Baltimore, B. D., Paul Berg, Michael Botchan, Dana Carroll, R. Alta Charo, George Church, Jacob E. Corn, et al. "A prudent path forward for genomic engineering and germline gene modification." *Science* 348, no. 6230 (2015): 36-38. doi: 10.1126/science.aab1028

Cressey, David, and David Cyranoski. “Human-embryo editing poses challenges for journals.” *Nature*. April 25, 2015. Accessed December 10, 2015. http://www.nature.com/news/human-embryo-editing-poses-challenges-for-journals-1.17429

Cyranoski, David, and Sara Reardon. "Chinese scientists genetically modify human embryos." *Nature.* April 22, 2015. Accessed December 10, 2015. http://www.nature.com/news/chinese-scientists-genetically-modify-human-embryos-1.17378

Doudna, Jennifer A., and Emmanuelle Charpentier. "The new frontier of genome engineering with CRISPR-Cas9." *Science* 346, no. 6213 (2014): 1258096. doi: 10.1126/science.1258096

Jasanoff, Sheila, J. Benjamin Hurlbut, and Krishanu Saha. “Human genetic engineering demands more than a moratorium.” *The Guardian*. April 7, 2015. Accessed December 10, 2015. http://www.theguardian.com/science/political-science/2015/apr/07/human-genetic-engineering-demands-more-than-a-moratorium

Lanphier, Edward, Fyodor Urnov, Sarah Ehlen Haecker, Michael Werner, and Joanna Smolenski. "Don't edit the human germ line." *Nature* 519, no. 7544 (2015): 410. Accessed December 10, 2015. http://www.nature.com/news/don-t-edit-the-human-germ-line-1.17111

Ledford, Heidi. “CRISPR, the disruptor.” *Nature* 522. June 8, 2015. Accessed December 10, 2015. http://www.nature.com/news/crispr-the-disruptor-1.17673

Liang, Puping, Yanwen Xu, Xiya Zhang, Chenhui Ding, Rui Huang, Zhen Zhang, Jie Lv et al. "CRISPR/Cas9-mediated gene editing in human tripronuclear zygotes." *Protein & cell* (2015): 1-10. doi: 10.1007/s13238-015-0153-5

Reardon, Sara. “Ethics of Embryo Editing Paper Divides Scientists.” Nature. April 24, 2015a. Accessed December 10, 2015. http://www.nature.com/news/ethics-of-embryo-editing-paper-divides-scientists-1.17410

Reardon, Sara. “US science academies take on human-genome editing.” Nature. May 18, 2015b. Accessed December 10, 2015. http://www.nature.com/news/us-science-academies-take-on-human-genome-editing-1.17581

Sarewitz, Daniel. “CRISPR: Science can’t solve it.” *Nature* 522. June 23, 2015. Accessed December 10, 2015. http://www.nature.com/news/crispr-science-can-t-solve-it-1.17806

Vogel, Gretchen. "Embryo engineering alarm." *Science* 347, no. 6228 (2015): 1301-1301. doi: 10.1126/science.347.6228.1301

Links:

Embryo-Editing: The Ethics of CRISPR on Flipboard: https://flipboard.com/@naturenewsteam/embryo-editing%3A-the-ethics-of-crispr-27j1164kz

The National Academies of Sciences, Engineering, and Medicine – *On Human Gene Editing: International Summit Statement*: http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=12032015a

Contributor(s)

Valerie Racine
Karin Ellison
Joseph Herkert

Rights

Resource Type

Instructor Materials

Parent Collection

Ethics of Emerging Technologies in the Life Sciences

Topics

Controversies
Embryo Research
Emerging Technologies

Discipline(s)

Genetics and Genomics
Life and Environmental Sciences