Intersect, Vol 10, No 2 (2017)

CRISPR in Popular Media: Sensationalism of Germline Editing in Human Embryos

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Abstract

In this paper, I investigate popular media's framing of CRISPR and its involvement in germline gene therapy. I examine the depiction of a single controversial event regarding CRIPSR from many popular news sources. Each news article critiques Junjiu Huang's use of CRISPR to genetically modify human embryos. Though these articles demonstrate some real dangers of CRISPR's use, many news articles exaggerate the dangers of CRISPR's use by Huang. Such articles bias readers with one-sided quotes from respected scientists and overly dramatic language that unfairly criticizes the ethicality and safety of Huang's experiment. Popular media fails to distinguish Huang's specific experiment from critiques of clinical germline therapy and to accurately portray CRISPR's dangaers. These irresponsible actions are ultimately to the detriment of the readers.

Introduction

What Is CRISPR/Cas9 and Why Is It Suddenly Everywhere? (Yin, 2015). This headline is particularly perceptive at grasping the question in the minds of the public as they witness the explosion of CRISPR in the news. CRISPR is an acronym for Clustered Regularly Interspaced Short Palindromic Repeats, which originated as a bacterial defense system against viruses. "CRISPR" is used to refer to all of CRISPR/Cas9, a system capable of making sequence-specific DNA edits. CRISPR allows for a cure for monogenetic disorders, those caused by single gene defects (Xiao-Jie et al., 2015). CRISPR has the potential to cure a wide range of disorders because its specificity hinges on the sequence of a single guide RNA, called an sgRNA. The CRISPR/Cas9 system is able to modify a new DNA sequence by changing only the sgRNA sequence that guides the CRISPR-associated Cas9 nuclease (a protein that can cleave the bonds of DNA). This Cas9 nuclease is unique because its action is directed by the chosen sgRNA sequence (while the Cas9 protein stays the same). This differs from other nucleases, which require the synthesis of a new protein in order to edit a new sequence of DNA.

CRISPR technologies can be implemented in two different ways that directly edit the human genome. The first of these is somatic therapy, a technique that uses CRISPR only in non-reproductive cells. Disease-causing mutations could be repaired in these non-reproductive cells (but not in egg or sperm cells), eliminating the disease in the individual. (Lanphier et al., 2015). Though offspring of patients treated with somatic therapy would still be afflicted with the disorder caused by the mutation, there is no chance of offspring inheriting other mutations caused by CRISPR. The alternative use of CRISPR to directly edit the human genome is germline therapy. In this method, CRISPR modifies DNA in reproductive cells. Consequently, genetic modifications would be passed on through generations if the resulting embryo were implanted (Lanphier et al., 2015). However, scientists also use germline techniques to perform basic research—research meant to improve scientific theories—in order to better understand human development (Callaway, 2016).

Whether the research on human germline cells is intended for clinical purposes or for basic research, the ethical considerations of altering human embryos are important. It is essential that the embryos used are non-viable, meaning that they are unable to grow or develop due to a genetic or metabolic disorder causing development failure. Particularly, non-viable embryos are defined by their inability to survive past the twenty-week minimum necessary for development. Tripronuclear embryos (embryos containing three pronuclei—separate nuclei from egg and sperm cells that have not yet fused together to form a single nucleus in the embryo) arising from polyspermic zygotes (fertilized by multiple sperm and so resulting in excess pronuclei) are unable to survive past the minimum period for viability (Baylis, 2005). Polyspermic zygotes therefore lack "intrinsic potential for ongoing development" (Baylis, 2005) and are consequently

inherently non-viable. When performing germline gene therapy research with CRISPR, this distinction between non-viable and viable embryos is important.

Beyond ethical considerations, there are also certain dangers associated with gene therapy. As noted above, CRISPR can cause unwanted mutations, since CRISPR may target unintended DNA sequences. Genomes contain many identical DNA sequences, so CRISPR may target similar, but unintended sequences in addition to the intended gene (Rodriguez, 2016; Otieno, 2015). Known as off-target effects, these mutations pose a risk especially when considering that these unwanted, potentially harmful changes are hereditable (Rodriguez, 2016; Otieno, 2015). Such mutations are present in both germline and somatic therapies; however, the danger is significantly greater for germline therapy. When mutations arise in reproductive cells, the off-target effects can be inherited by the next generation. The potential harm of these dangerous mutations may outweigh any potential benefits of the therapy itself. This is especially true considering other problems CRISPR poses. The guiding mechanism of sgRNA as well as the Cas9 protein's editing capabilities do not act with perfect efficiency (Peng et al., 2015). Moreover, cell division may sometimes occur before genetic modification is complete (Sharma and Scott, 2005). As a result of these factors, not all cells may receive the copy of the edited gene. This causes genetic mosaicism, a condition in which all cells in an embryo do not have the same genotype (a person's specific genetic code). Genetic mosaicism generates problems when testing if germline therapy was successful—if cells have varying genotypes, then a good outcome in one cell does not mean the therapy as a whole was successful (Feltman, 2015).

CRISPR's controversies, particularly regarding its use for germline therapy in human embryos, feature prominently in popular news media. I will specifically analyze the portrayal of this debate in the news through the lens of Junjiu Huang's attempt to alter the gene causing the blood disorder β-thalassaemia in human embryos. Huang, a Chinese scientist at Sun Yat-sen University, was the world's first researcher to publish a report of gene-edited embryos. Though Huang's research was stopped early because only a small percentage of the genomic edits were successful, the results were published in Protein & Cell (Cyranoski and Reardon, 2015; Otieno, 2015; Rodriguez, 2016). I constrain my discussion of this event to written news articles intended for a general audience. I intend to demonstrate that the news media has been irresponsible in its framing of CRISPR; its extreme portrayal of the dangers of germline therapy provides readers with an overly negative view of CRISPR technologies.

Extreme Framing of Germline Therapy

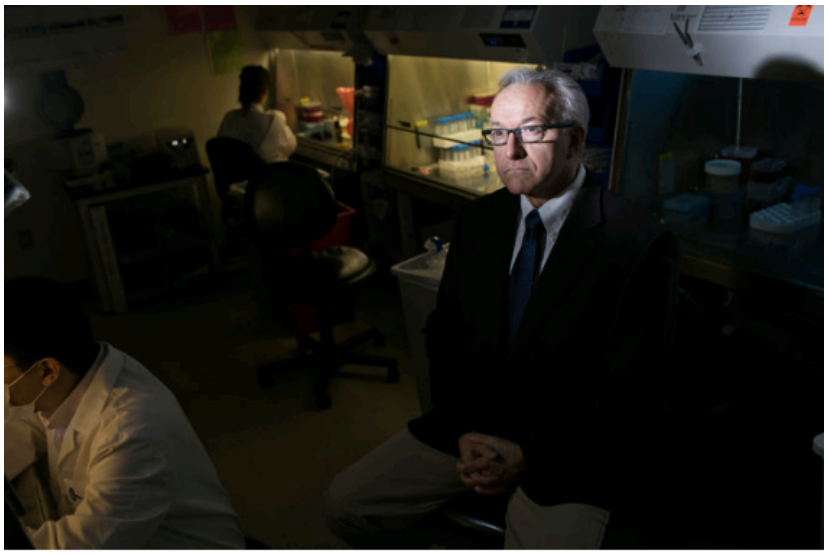
They're going to CRISPR people. What could possibly go wrong? (Begley, 2016). This very insightful headline from STAT news captures how newspapers recounted Huang's experiment by framing CRISPR as

entirely dangerous. By only mentioning dangers (particularly when these included dangers are unfounded or described using sensational language), readers are unable to form their own opinion about the ethicality and safety of germline therapy and of specifically Huang's experiment. This situation is exacerbated by the quotes from reputable scientists chosen to substantiate this one-sided portrayal. Moreover, the readers of these popular news articles will often have no prior background on the subject, which intensifies the effect of the news media's overly negative portrayal of CRISPR.

Newspapers do examine some real threats. Gina Kolata's article in *The New York Times*, "Chinese Scientists Edit Genes of Human Embryos, Raising Concerns," mentions some of the dangers discussed above: "the experiment resulted in many off target effects and in genetic mosaicism" (Kolata, 2015). *The Washington Post*'s article, titled "The rumors were true: Scientists edited the genomes of human embryos for the first time" (Feltman, 2015), also describes genetic mosaicism, stating that all embryos will not obtain the new gene. These real dangers, however, do not excuse the exaggerated negative portrayal of CRISPR by the news media.

For instance, many news articles present Huang's experiment as crossing a clear ethical line. Andrew Griffin's article "Fears arise as Chinese modify human embryo genes" in *USA Today* presents a one-sided negative portrayal of CRISPR. Griffin uses the position of power of a renowned scientist to make provocative arguments. Griffin introduces Edward Lanphier by citing his titles as both president of the biopharmaceutical firm Sangamo BioSciences and chairman of the Alliance of Regenerative Medicine (Griffin, 2015). Griffin proceeds to quote Lanphier as dramatically stating, "We are humans, not transgenic rats" (2015). Griffin (2015) includes this vivid comparison to demonstrate what Lanphier labels as the "fundamental ethical issue" against using CRISPR in human germline cells. Consequently, Griffin seems to present the unethicality of Huang's experiment as a foregone conclusion. The otherwise uninformed readers will believe this notion because of the ethos granted to Lanphier as a distinguished scientist.

Meanwhile, Griffin excludes from his article arguments that could allow readers to determine their own stance on human germline editing. For instance, John Harris, a bioethicist at the University of Manchester, makes the argument that research like Huang's is no worse ethically than the common practice of discarding non-viable human embryos used for *in vitro* fertilization (Cyranoski and Reardon, 2015). Presenting opposing arguments would provide readers with the chance to decide for themselves their position on the ethics of Huang's experiment. Instead, such news articles utilize quotes from scientists to validate a single side of the CRISPR debate, ultimately leaving readers with a skewed understanding of the debate itself.



"This is an unsafe procedure and should not be practiced at this time, and perhaps never," Dr. George Q. Daley of Children's Hospital in Boston said of the genetic editing experiment.
Dominick Reuter for The New York Times

FIGURE 1. Photograph from Gina Kolata's (2015) article "Chinese Scientists Edit Genes of Human Embryos, Raising Concerns" in the *New York Times*.

Gina Kolata's (2015) *New York Times* article "Chinese Scientists Edit Genes of Human Embryos, Raising Concerns" likewise capitalizes on the reputation of a respected scientist to validate a singular, negative perspective. Readers will first notice the caption beneath a picture (see Figure 1) of a doctor sitting pensively in a dark medical facility, in which "Dr. George Q. Daley of Children's Hospital in Boston" states that the procedure is unsafe, and "should not be practiced at this time, and perhaps never" (Kolata, 2015). The setting of the picture reinforces that this advice comes from a reputable doctor, someone whose safety warnings are typically accepted without question. Meanwhile, the menacing darkness of the image promotes a visceral feeling of danger to readers. Kolata proceeds to use the position of power of a scientist to ascribe ethos both to the quote and ultimately to the idea that CRISPR therapies should not yet or perhaps ever be practiced in humans.

Kolata's critique seems to criticize the safety of Huang's experiment itself (a concern I will demonstrate later to be unfounded). While criticisms of the safety of clinical germline therapy at the moment are valid, the critique is not obviously directly at clinical germline therapy specifically. Instead, it focuses on Huang's specific experiment, while ignoring that the experiment is not necessarily intended for clinical use (and certainly is not intended for clinical use in the near future). Huang's experiment demonstrates the potential of germline editing for use in basic research, where any changes made by CRIPSR would not enter the gene pool. Robin Lovell-Badge, a geneticist renowned for the discovery of the

SRY (sex-determining) gene ("Robin Lovell-Badge"), argues that germline editing will be valuable in understanding embryonic development. Much of our current understanding originates from studying mice, but this is inadequate as the developments of mice and humans quickly diverge after the earliest stages (Hawkes, 2015). Performing more basic research is therefore imperative, and consequently the safety of germline genetic therapy in general should not be condemned.

Sarah Knapton's article "China shocks world by genetically engineering human embryos" in *The Telegraph* similarly exploits the position of a scientist to further a false assumption about the ethicality of research with CRISPR. Knapton's article harnesses the esteem of "Prof Shirley Hodgson, Professor of Cancer Genetics, St. George's University" to pose an untenable question, an accusation that hardly merits a response: "I think that this is a significant departure from currently accepted research practice. Can we be certain that the embryos that the researchers were working on were indeed non-viable?" (Knapton, 2015). However, Huang's experiment used polyspermic zygotes (zygotes fertilized by multiple sperm and as explained above are consequently inherently non-viable). It is well established that such zygotes cannot result in live birth and thus provide an ideal mechanism for human embryo research (Bredenoord et al., 2008). Huang's experiment, which utilized tripronuclear embryos (embryos with three pronuclei due to polyspermy), therefore followed appropriate research practice (Huang et al., 2015). Huang's research article also details his methods: he only selected tripronuclear embryos with three clear pronuclei (Huang et al., 2015). Huang's study also notably "conformed to ethical standards of Helsinki Declaration and national legislation and was approved by the Medical Ethical Committee of the First Affiliated Hospital, Sun Yat-sen University" (Huang et al., 2015), which would certainly ensure the discussed methods were appropriately followed.

Therefore, Hodgson must not be disputing whether appropriate measures were taken to ensure the zygotes were polyspermic. Rather, Hodgson must be questioning Huang's honesty about truly using polyspermic zygotes. Professor Hodgson's reputation is the sole validation for this unsubstantiated claim. By including these accusations from Hodgson without any of the above counterpoints, Knapton's inquiry has no basis and merely represents a crude attack of Huang's morality. Unfortunately, readers will believe this unwarranted criticism when presented in this context and thus will come away with an unfairly negative view of germline therapy.

Popular news media also presents a one-sided perspective through the use of sensational language. Kolata (2015) presents a skewed view of the ethics and impact of Huang's experiment by incorporating dramatic language in her *New York Times* article. Kolata quotes Edward Lanphier as stating, "It literally boils down to, How do you feel about the human race and the human species?" (Kolata, 2015). Such a question, especially

when framed by someone with the influence of Lanphier, leaves room for only one response from readers: the use of CRISPR must cease in order to save the human race. The phrasing of Lanphier's question necessitates this response; anyone who feels differently about the ethicality and safety of the use of CRISPR suddenly must be against the protection of the human race. This language therefore prevents readers from reaching their own conclusions about the ethical use of CRISPR. Furthermore, such language overstates the potential impact of Huang's experiment. Performed on embryos that will never be implanted, this research actually has no direct effect on the human gene pool (Huang et al., 2015). Yet, readers may see this exaggerated question and wonder why Huang was allowed to perform his research if there was such grave potential to harm the human race. Readers could assume Huang's research was reckless or that Huang did not properly address safety concerns.

In Knapton's (2015) article in *The Telegraph*, the author uses dramatized language to describe Huang's experiment, portraying CRISPR's use as uncontrolled. Knapton frames Huang as ignoring safety, ethicality, and the impact of his actions. She begins her article "China shocks world by genetically engineering human embryos" in *The Telegraph* by condemning China for becoming the "'Wild West' of genetic research" (Knapton, 2015). The "Wild West" has connotations of being an uncontrollable, reckless territory, in which the people have no regard for law and order. This comparison, therefore, suggests that Huang acted without restraint. Furthermore, for China to be the "Wild West," there is an insinuation that Huang must have ignored a global consensus on basic research involving genetically modified human embryos. Not only did no moratorium on germline editing exist prior to his research, it was Huang's research itself that sparked a renewed international call for such a moratorium. Additionally, there is a difference between clinical application of embryo research and use for basic research (Kaiser and Normile, 2015). While the former is completely irresponsible at the moment, the latter can provide important findings as long as its consequences are controlled (Kaiser and Normile, 2015). For this reason, Knapton's (2015) assertion that Huang needs to be "reined in" is problematic. This implies that there was something inherently wrong with Huang performing this basic research. Furthermore, I have established above that Huang's research should not be definitively declared as unethical or unsafe. As a result, news articles should avoid insinuations of improper experimental conduct. Consequently, Knapton's language further presents a distorted view of Huang's research and of CRISPR's use for germline therapy.

Not only do these news articles present CRISPR's use as heedless of safety or ethicality, they portray Huang's experiment as unnecessary, and consequently demonize the researchers who performed the experiment. Knapton (2015) quotes Human Genetics Alert Director Dr. David King, who claims Huang's experiment had no purpose, given that there are other

"ethical ways" to prevent the inheritance of the disorder β-thalassaemia. King states that the research was therefore an example of "scientific careerism," where researchers attempt to assure their place in history regardless of the necessity of their work (Knapton, 2015). If the research is presented as pointless to readers, they will wonder why Huang wasted the potential of the human embryos, a concern which would be exacerbated should readers not know that these embryos were nonviable and would have no potential for further development. As such, newspapers present the researchers as villains, particularly considering that no benefits of the use of CRISPR, even for somatic therapy, are listed in the news articles. Even accepting that germline therapy may be pointless for curing β-thalassaemia, Huang's research still carries great importance. There are disorders like cystic fibrosis that manifest themselves systematically throughout the body, disorders like muscular dystrophy that reside in a single, but pervasive tissue, and disorders like Huntington's disease that are realized in difficult to access places like the basal ganglia; these problematic conditions will restrict the application of other clinical therapies (Porteus and Dann, 2015). Therefore, given that clinical germline therapy will be important to conduct at some point in time, microbiologist Guo-Qiang Chen admits that it takes research that evaluates the current progress of embryo editing in order to eventually see positive outcomes (Kaiser and Normille, 2015). Yet, the potential necessity of germline therapy clinically or of basic research into embryo editing is never expressed in popular news media. Consequently, readers are left believing that the scientists must have, in the words of Dr. Daley, a "deranged motivation" (Kolata, 2015) in order to consider undertaking this research. This dramatic language highlights the extreme portrayal of the dangers of germline therapy. This framing demonstrates a lack of responsible reporting, since readers are not given the chance to personally weigh the ethical and safety concerns of CRISPR or to reach their own conclusions.

Discussion

In examining the popular media's portrayal of Junjiu Huang's germline therapy of human embryos, a pattern of recurring misrepresentations and exaggerations emerges. Primarily, the media critiqued Huang's experiment as if he altered human embryos with the intention of implantation. Yet, this is not the case. Such insinuations can be avoided by keeping separate discussions of the ethicality and safety of germline therapy from any critiques of Huang's experiment itself. Discussions of germline therapy's safety and ethicality should also be fairly reported. Dangers should be presented sensibly, with attempts made to demonstrate the extent to which the dangers can be overcome in the future. Ethical considerations made during research, like using non-viable embryos, should also be properly addressed in any discussions. Additionally, debates on germline editing should distinguish between use for basic

research and use clinically. Critiques of clinical use (where edited cells are implanted) should articulate that clinical use is not actionable in the immediate future. News media often fail to specify any time frame for clinical use (and will even directly imply that clinical therapies are currently taking place). Given the current dangers involved in implanting an edited embryo, this causes clinical use to be unfairly depicted as reckless. Moreover, any debate on clinical use should include why germline therapy may be the only therapeutic option for certain disorders. Otherwise, it may be believed that the potential dangers always outweigh the clinical benefit.

To properly portray this debate, articles should avoid sensationalizing the described dangers and include a balance of scientific perspectives. This is especially true when considering including quotes from scientists used to validate a single perspective that may otherwise have no basis. Readers will benefit more from a constructive dialogue of the current status of germline editing than from a mere dramatization of Huang's experiment. In accomplishing this, news articles will be able to better educate their audiences on necessary debates on safety and ethicality. Only then can popular media promote important dialogue on CRISPR's controversies.

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