

CRISPR: Science and Ethical Misconduct

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At the end of 2018, a Chinese researcher, He Jiankui, announced that he had edited human germline genes using CRISPR-Cas9 (CRISPR) technology. Jiankui claimed he had implanted the embryo, which had been carried to term and birthed. This news came as a shock to the world, especially the scientific and bioethics community. The technology, CRISPR, allows for precise gene editing. This means that gene sequences that have been identified to be either beneficial or harmful can be carefully extracted and replaced where they are intended to go. Jiankui's team targeted a particular gene, CCR5, to manipulate as way to protect against HIV. The father-to-be was HIV-positive, so the manipulation was purportedly to protect the offspring from an increased risk from the disease. The gene is also a germline gene, which means the manipulations will also affect future generations, as opposed to a somatic gene, where manipulations will only affect the particular organism. The embryo was then implanted in the woman, allowed to grow to term, and twin girls were born.

The use of the CRISPR technology to manipulate germline cells in an embryo that was then allowed to develop into a human highlights some of the ethical concerns with that technology. Manipulation of genes has the ability to alter any organism in fundamental ways. While much of the intent of this technology is to protect humans from disease, there is concern about the use of genetic manipulation. Some of these concerns include using the technology to select and modify embryos for certain traits, such as height, eye color, or intelligence, in a way that might take away natural diversity or create a genetic elitism. Other concerns are around safety in the application of some of these manipulations, as there has not been sufficient study to know how the manipulations will affect humans. The specific concerns around germline manipulation focus on whether it is appropriate to create alterations that will affect multiple generations. Jiankui and his researchers took a bold step into the realm of ethically sensitive research seemingly irrespective of these concerns.

Jiankui's actions were not necessarily revolutionary in terms of the scientific techniques employed, but how they stepped outside the norms established in the scientific field regarding the use of such technology. The National Academy of Sciences and the National Academy of Medicine put out a joint statement in 2017, outlining three main areas of

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The Ethicist Is In

BY D. ELIZABETH SHEFFIELD, J.D., DNAP, M.A.



The Case:

Betty, a 50-year-old woman, was found unconscious on a park bench. Upon admission to the hospital, Betty was found to have pneumonia that quickly spread to both lungs and she needed a breathing machine to keep her alive. After a month and despite multiple life-support treatments being used, it became evident that Betty would most likely never improve. Betty was in multi-system organ failure and her body was being supported by a surgically attached breathing machine, continuous dialysis to replace the function of her kidneys and medicines to raise her blood pressure. Unfortunately, Betty never regained consciousness to communicate with the medical team. The social worker was unable to find any family or friends. Betty had been homeless for some time. Her attending physician called for an ethics consultation asking, “What is ethically appropriate for this patient who is getting worse and has no one to speak for her?”

The Ethicist:

Betty’s medical team was grappling with what to do with a patient who could not speak for herself, and who did not have a surrogate to speak for her with regards to treatment decision-making. For homeless patients who do not have families or friends, an important question is: “Who speaks for these individuals?” Traditionally, family members guide the medical treatments for such patients by using substituted judgment. Substituted judgment is when an individual who knows the patient’s values and wishes regarding medical treatments, informs the medical team of those wishes in order to guide medical treatment choices. When a patient is unrepresented, the medical team uses the best interest standard, i.e., what would be in the best interests of a particular patient with regards to medical treatments with particular attention to the relief of suffering and the restoration of function. There are two issues in this case:

- 1. Medical treatments for an unrepresented patient and**
- 2. The appropriateness of aggressive medical treatments in a patient with a poor prognosis.**

Most patients in Betty’s condition have someone who can share their values and preferences with the medical team. While the social worker did not find a relative or friend of Betty, he did find a community case manager named Erik. Erik had known Betty for years. He told the medical team that Betty had struggled for years with substance use, mental illness, and chronic homelessness.



Erik confirmed that Betty had neither spoken about family nor did he know of any family. What Erik did know was Betty and her preferences. Erik shared with the medical team that the patient had been a loner and found joy being outside and walking. She did not like hospitals and always talked about being “a free bird.” When Erik would try to make her doctors’ appointments, she told him that she did not want doctors and medicines to control her life. In the past when

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use for this technology. They “identify basic research..., clinical applications to treat or prevent disease or disability in somatic cells, and clinical applications to treat or prevent disease in germline cells.” (NAS/NAM 2017). The recommendations emphasized that basic research with this technology is important in order to push scientific process. However, the guidelines cautioned against utilizing the technology for clinical trials in somatic cells, citing the need to use existing regulatory processes. It concluded with notes of further caution when dealing with germline cells, establishing a set of criteria for such research. This criteria for permissible research included “absence of reasonable alternatives,” “availability of credible pre-clinical and/or clinical data on risks and potential health benefits of the procedures,” “during the trial, ongoing, rigorous oversight of the effects of the procedure on the health and safety of research participants,” “maximum transparency consistent with patient privacy,” and “reliable oversight mechanisms to prevent extension to uses other than preventing a serious disease or condition.”

Objective assessments of Jiankui’s research have argued that he violated, in spirit if not letter, each of these conventions, particularly that there were other ways of addressing the problem and that there were inadequate safeguards in place. Jiankui has stated that his research addressed a terrible disease and that, as a father, he very much cared about the safety of the twin girls who were born from his research.

China’s Communist Party and the State Council has developed a new body, Ministry of Science and Technology (MOST) to oversee research done in the country. Under a new policy, MOST will oversee a blacklist for researchers found to engage in scientific misconduct, as well as a blacklist for poor quality journals. Being blacklisted could

disqualify researchers from getting funding, doing research, and perhaps even finding other jobs.

The revocation of funding and shunning the researcher, are not too far from what a similar researcher may face in the United States. Charges of financial fraud and the loss of position could certainly be expected. Indeed, there are punishments for those who step far outside accepted boundaries, even if they are tied to other laws rather than ethical position statements.

Perhaps more to the point, though, what does it mean when someone steps outside the bounds? Certainly ethical guidelines are there to provide direction. But they are also there to outline some form of moral consensus. Thus someone who steps outside either states they do not agree with the boundaries or they state they do not wish to be part of the group who set the bounds.

How ought we respond to those who choose to step out? If we are serious about the boundaries, serious about moral consensus, certainly there must be a defense of the boundaries themselves. We must assert why we think the consensus is right and why the action in question is wrong. This should be both reasoned and clear, for if we are to have any authority, it must be made clear why it is not permissible. But we must also decide what those boundaries are worth. Is it more important to recognize the bad actions, throw a flag and explain the infraction? Or should we exclude the players from participating again? If we are serious about moral consensus, there must be something. Without responding to the major exceptions, we risk the meaning of having boundaries at all. It’s time that the scientific, bioethics, and research communities came together to address these questions and clearly outline the consequences for members who choose not to follow the guidelines.

i (NAS/NAM 2017, recap of major recommendations).

ii (David Cyranoski, *Nature*, China introduces sweeping reforms to crack down on academic misconduct, June 08 2018).

3 Reasons to Come to Paris This Summer!

Neuroethics Network

PMHV is working with the ICM, Institut du Cerveau et de la Moelle Épinère (Brain & Spine Institute), to coordinate the 6th Neuroethics Network meeting, **June 19-21, 2019 in Paris**. The theme for 2019 is *Going Global and Facing the Future*. Keeping in mind that the foremost goal of techniques and technologies is to improve patient care, brain scientists, clinicians, ethicists and legal scholars will address the newest developments and application in Neuroethics.

International Bioethics Retreat

The International Bioethics Retreat will be held **June 26-28 at Reid Hall, Paris**. The Retreat is unique among bioethics meetings in that experts in medicine, philosophy, law, and health policy are invited from around the world to present their current research projects.

Cambridge Consortium for Bioethics Education

The 9th Cambridge Consortium for Bioethics Education will be held **July 3-5 at Reid Hall, Paris**. Practical Problems and Shared Solutions is the theme of this year's conference. Tackling the hard questions and finding practical answers in teaching bioethics is the aim of the Cambridge Consortium for Bioethics Education. The meeting brings together international leaders in bioethics education and focuses on "how to" methods of teaching bioethics.

For details, visit icmbioethics.com. Please contact us if you would like further information about these conferences or have an interest in presenting at a future conference.



Save the Date: Summer Workshop

CALIFORNIA PACIFIC MEDICAL CENTER
PROGRAM IN MEDICINE & HUMAN VALUES

Challenging Patients: New Solutions to Recurring Problems in Ethics Consultation

SATURDAY, JUNE 8, 2019
8:30 a.m. – 4:45 p.m.

More details will follow.

REGISTRATION OPENS APRIL 1.

Registration will close when the workshop is full.

Clinical Ethics Service

PMHV will offer Clinical Bioethics Services to Alta Bates Summit Medical Center



PMHV is delighted to announce that our program will be expanding clinical bioethics services to Sutter Health's Alta Bates Summit Medical Center (ABSMC) in 2019. To date, PMHV has provided clinical bioethics services to all Sutter Health affiliates in the Bay Area except ABSMC, thus this is an exciting opportunity for our program to serve all Bay Area affiliates. Over the past year, ABSMC hospital ethics committees have expressed increasing interest in gaining the assistance and support from our team of professional bioethicists. PMHV will be providing clinical ethics consultations, education, policy development and expertise in organizational ethics issues at this East Bay hospital. The leadership team at ABSMC is enthusiastic about teaming up with our program to provide bioethics services and we are eager to include them in our PMHV family.

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she had been admitted to the hospital, she had told Erik that she didn't want to go back to the hospital again. She liked eating and walking the streets of San Francisco. What Erik had done in this case was remarkable: he was able to share details about Betty that made the team aware of who she was as a person.

Many hospitals struggle with patients like Betty and the question of how to decide what medical treatments are ethically appropriate for an unrepresented patient. Some hospitals have policies that outline the process for medical decision-making in such cases. In Betty's case, hospital policy required that the case be discussed by the Ethics Committee. An Ethics subcommittee was convened to evaluate the situation and provide recommendations. In order to ascertain what would be in Betty's best interests, the Ethics subcommittee spoke with the medical team involved in her care, discussed her prognosis and medical recommendations by the treating team. The subcommittee also spoke with Erik, who gave a much valued perspective of Betty. The subcommittee members heard what Betty enjoyed and valued the most in her life: her autonomy and freedom. The medical team felt that no matter what the

interventions, Betty's course would be dismal with a poor prognosis for any meaningful recovery. The medical team explained to the Ethics subcommittee that if Betty were to survive, the remainder of her life would most likely be spent inside institutional walls on life support. The question became: Would this existence be an acceptable way of life for Betty? The breathing machine and dialysis were life-sustaining treatments but, as per Erik, who had known the patient better than anyone else, she would not have wanted her life to be in the intensive care unit of the hospital or to linger on machines unable to eat, talk, or walk.

After listening to Erik speak about Betty and her life, and what she may have wanted with regards to medical treatments, the members of the Ethics subcommittee agreed that removing the painful burden of life-sustaining medical treatments and shifting the goals of care to focus on the patient's comfort were in her best interest. Betty passed away peacefully a few days later. This case illustrates that, like most of life, nothing is black and white. While Erik was not Betty's designated health care decision-maker or surrogate, at the end of her life, he gave Betty a voice.

References:

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