HUMAN GENOME EDITING

FRAMING OUR BIOLOGICAL FUTURES

BACKGROUND INFORMATION

PGET
PREPARING FOR HUMAN GENOME EDITING TECHNOLOGIES

Baylor College of Medicine

ASU

Museum of Science

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INTRODUCTION

Welcome to *Human Genome Editing: Framing Our Biological Futures*!

We have invited you to take part in this forum to help us learn about your views on the use of human genome editing technologies and how decisions around them should be made. Human genome editing technologies are able to make changes to genes. Genes are small parts of your DNA that determine different characteristics or traits and may cause disease.

Supporters of human genome editing technologies hope to develop therapies for diseases controlled by genes that have no cure. However, others are concerned that these technologies could be used for purposes besides curing diseases and could have unintended effects that could be passed on to future generations.

At the forum, you will share your views with fellow community members. This booklet provides basic information about genes, genome editing technologies, and their possible uses and drawbacks. It also contains four possible versions of the future in which human genome editing technologies have been implemented. At the forum, you will deeply explore one of these possible futures and think about whether it is desirable. This will help you decide what parts of that future you might want society to work towards or to prevent.

Human genome editing technologies are still early in development. Now is the perfect time to share your voice about their potential future use! What kinds of uses of human genome editing technologies do you want? Who should make decisions and policies about these technologies? We look forward to hearing your opinions and making your views known to decision makers.

These forums are part of "Preparing for Human Gene Editing (PGET)"–a three-year research project funded by the National Institutes of Health and led by researchers at the Baylor College of Medicine and Arizona State University in partnership with the Museum of Science. PGET seeks to respond to the call for forward-looking policy development and deliberative public engagement to guide the future of human genome editing.

HOW TO READ THE BOOKLET

This booklet contains three main sections to give you background information for your conversations during the forum:

1. The first section is a brief explanation of what genes are, what human genome editing technologies are, and a history of the development of these technologies.
2. The second section is a discussion of what human genome editing can do and some considerations to take into account when making decisions about what, if anything, human genome editing should be used for.
3. The third section is an introduction to the four possible futures that participants will be discussing during the forum. It explains how these versions of the future were developed and how they can be used to make decisions in the present.

HOW THE FORUM WILL WORK

The forum consists of 5 sessions plus a short introduction at the beginning and evaluation at the end of the day. Each session focuses on a different topic related to human genome editing. The sessions build on each other throughout the day, as you begin to piece together your hopes and fears for human genome editing.

Part 1: Open Framing
What is your current experience with health and healthcare?

Part 2: Human Genome Editing
What is human genome editing and how do you think it should be used?

Part 3: Possible Futures
What might a world with human genome editing look like in 2040? How does that affect what you would like to see in the future?

Part 4: How Should We Make Decisions About Human Genome Editing?
What values should scientists and policymakers consider when making decisions about human genome editing technologies and their use? Who should have access to these technologies? Who should fund them?

Part 5: Hopes and Concerns
When thinking about human genome editing after all you've learned, what are your hopes and fears for the technology?

During the forum, you will be seated at a table with other community members and a trained facilitator. Some sessions will include a short video or briefing that will be read by the facilitator to review information in this booklet. You will then have the opportunity to discuss a variety of issues, weigh different options, and develop your ideas about the future of human genome editing technologies individually and as a group.

HOW THIS DOCUMENT WAS PRODUCED:

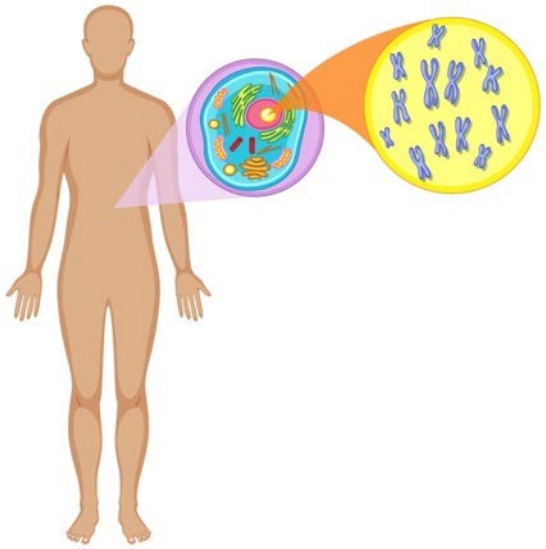
The booklet was written by the research team. An External Advisory Committee reviewed the information to determine that it is accurate, sufficient, and balanced, based on the issues that you will discuss during the forum.

BACKGROUND INFORMATION ON HUMAN GENOME EDITING

These materials are intended to introduce you to what human genome editing is, describe different types of human genome editing, explain what it may be able to do in the near future, and summarize some concerns that experts and previous public engagements have raised about human genome editing.

WHAT ARE GENES?

Every living thing on Earth is made up of cells. Cells are tiny, biological mechanisms that, collectively, make up the overall shape and activities of an organism—like the bricks of a building, the pieces of an airplane, or the individual people who make up an organization. Each cell in your body is a tiny engine that contains a blueprint describing the structure and operation of the entire body and tells the cell how to do its job within it. In most large organisms, including humans, this "blueprint" is a long string of *deoxyribonucleic acid,* or DNA, that the cell "reads" to perform its work. *Genes* are small components of DNA that provide instructions for various structures (e.g., eyes, muscles) and functions (e.g., sight, digestion) of the body. The term *genome* refers to the collection of all the genes in an organism. Genes come in many different versions, and the combination of these variations means that everyone has a unique "blueprint." When two people have a child, that child develops with a new blueprint provided by combining components of each parent's blueprints.



Zooming in on a human body to a cell and then the chromosomes inside. Chromosomes are made up of DNA *(brgfx / Freepik)*

Although DNA is the "blueprint" of an organism, it does not entirely determine the characteristics of that organism. The characteristics of a building depend not only on its blueprint, but on the building site and the effects of sun, weather, and maintenance. The outcome of a football play depends not only on arrows and circles drawn on a whiteboard, but on the specific players who execute it, the choices they make, and what the other team does—as well as the terrain and temperature. Similarly, there are many and variable processes that translate DNA, along with many environmental and situational factors that impact an organism. These processes never occur in exactly the same way twice. This is why "identical" twins still have minor differences in appearance and may have major differences in personality and behavior. In short, bodies are not wholly the products of "nature" or of "nurture," but of both.

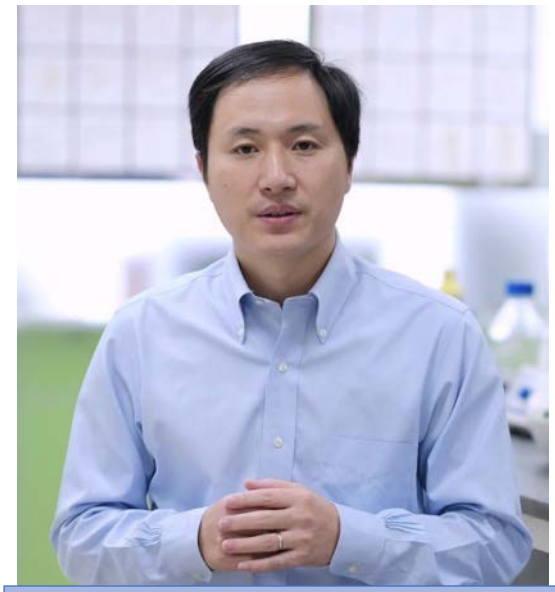
Because the processes that produce, sustain, and change bodies are many, variable, and complex, it is difficult to understand or describe the specific roles or effects of most genes. Most genes are believed to affect many bodily traits in combination with many other genes, and the functions of many genes are currently unknown. There are a few genes, however, that seem to reliably determine certain bodily features. These are called *monogenic traits*, traits caused by a certain version of a single gene. Sometimes, when an essential gene is not working normally, it can cause diseases like cystic fibrosis, sickle-cell anemia, Huntington's disease, and Type 1 muscular dystrophy.

WHAT IS HUMAN GENOME EDITING?

Since the 1970s, scientists have been developing ways to change genes, or modify the "blueprints" of cells. This process is referred to as *genetic engineering*. Some early experiments were performed on bacteria, which are small and easy to modify – it's even possible to do simple modifications in a classroom. Gene editing tools became well known primarily through applications to animal and plant agriculture, in genetic testing tools, and in the production of certain medical products, including artificial insulin. These genetically modified (GMO) crops and animals are subjects of significant controversy, and some nations have labeling requirements or restrictions against them. GMO crops are, however, widespread in the United States.

In the past, researchers generally agreed that modification of human genes was too difficult and dangerous to attempt. Exceptions have included "gene therapy" trials intended to develop therapies for persons with inherited diseases like the ones mentioned above. However, a new generation of tools developed over the 2010s, often referred to as *CRISPR*, has made genome editing significantly easier, faster, and cheaper. Genome editing research is now quicker and easier, and many researchers who could not edit genes before now have the capability to do so.

With increased ease comes increased interest by researchers and funders in investigating and pursuing human genome editing. This could involve biomedical research in the pursuit of therapies, cures, or knowledge expansion, and, eventually, application of genome editing treatments to humans or embryos. These possibilities have concerned and even alarmed many scientists, bioethicists, policymakers, and civil leaders. Such concerns were worsened by the 2018 revelation that U.S.-trained Chinese researcher, He Jiankui, had, without the knowledge of the scientific community, edited the genomes of two embryos in an effort to make them resistant to HIV. This eventually resulted in the birth of twin girls. The international scientific and ethics communities condemned He's actions but suggested that human genome editing should still be pursued in a slower and more deliberate fashion. Human genome editing has been debated at many expert meetings and summits and in the pages of scholarly publications. Experts hold many different opinions on whether human genome editing should be pursued, and—if so—how, where, and for what purposes.

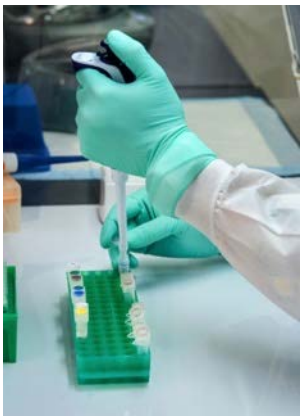


U.S.-trained Chinese researcher He Jiankui conducted his research without the knowledge or approval of the international scientific community. *(The He Lab)*

Many scientists and bioethicists draw distinctions between different types of human genome editing, which they view as carrying different potential scientific, ethical and social problems. You may find these distinctions useful, so we have summarized them below. You do not have to frame your opinions only within these categories.

BASIC RESEARCH, CLINICAL RESEARCH, AND APPLICATION

Scientists tend to draw sharp lines between *basic research*, intended to build general knowledge and understanding and conducted in petri dishes and test tubes; *clinical research*, intended to investigate the effectiveness of particular treatments and conducted on human test subjects; and *application*, the widespread release of treatments for general use. Scientists tend to think basic research as separate from clinical research and application. However, the knowledge and techniques developed in basic research affect what clinical research can and will be done. Both then affect potential applications.



Basic research is conducted in lab conditions. *(CDC / Unsplash)*

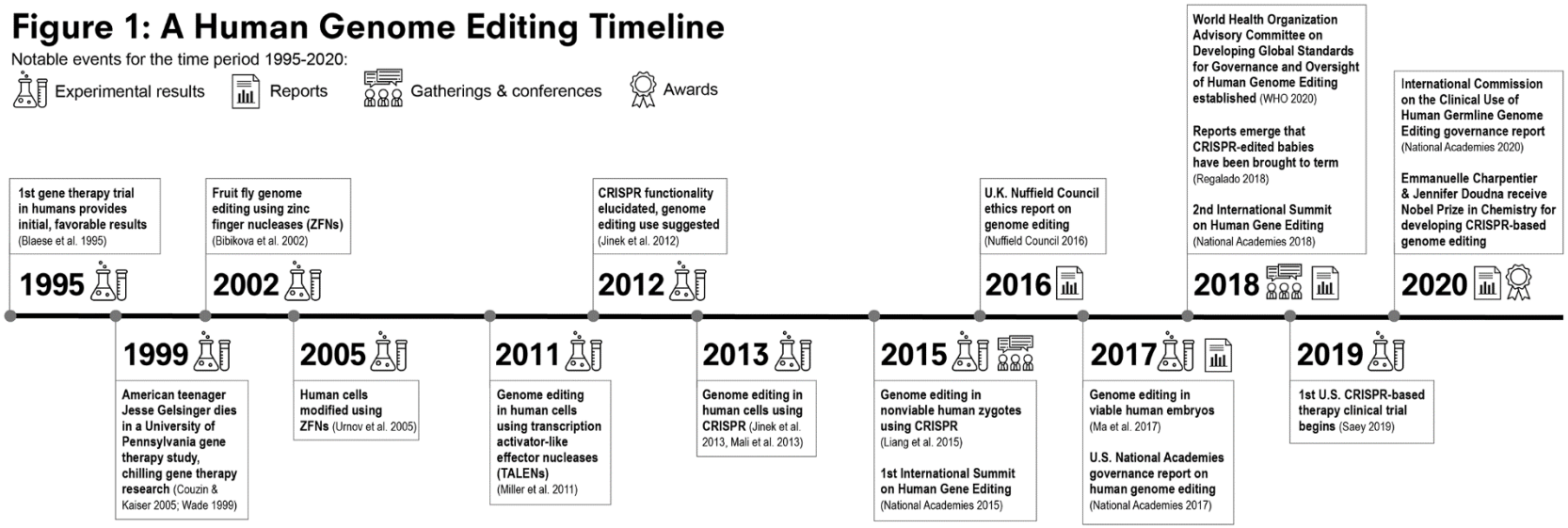
SOMATIC VS. GERMLINE INTERVENTION

Somatic editing is a genome editing intervention that can be used on a child or adult to modify specific cells and only affects the individual treated. Alternatively, *germline* editing can occur at a very early stage in human development, shortly after fertilization of the egg, to modify all cells. These changes would be carried through into every cell in the body and be passed on to the treated individual's descendants. As further discussed below, experts tend to regard somatic editing as ethically similar to existing biomedical research and treatments using gene therapy, as it only affects one person. Scientists tend to view germline editing as something new and potentially problematic, as it affects all of a treated person's descendants.

THERAPY VS. ENHANCEMENT

Some commentators on human genome editing draw a distinction between *therapeutic* uses, which would aim to treat or prevent disease, and *enhancement* uses, which would aim to alter the physical or mental characteristics of healthy humans. Bioethicists and researchers tend to feel that therapeutic uses are more acceptable than enhancement uses and enhancement efforts should be prohibited. The line can be hard to draw in practice because some hypothetical treatments which could be used as therapy for ill persons might also be usable as enhancements in healthy persons. For example, a modification intended to treat muscular dystrophy could be applied to healthy persons to enhance muscle growth. Some experts have even voiced concerns that underground enhancement markets could develop among elite athletes seeking extra advantages. This could also lead to a shift in standards for "normal health," including life expectancy and what physical capabilities are appropriate for certain ages.

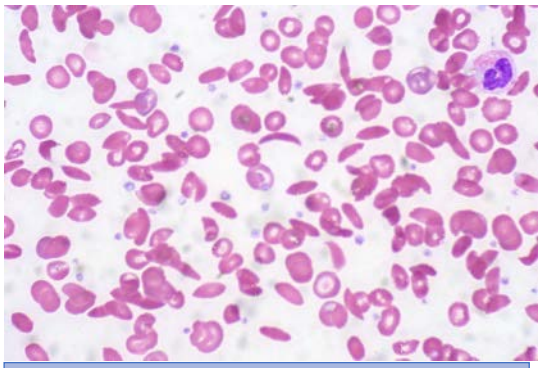
While the therapy/enhancement distinction is fuzzy at best, most human traits of potential interest for enhancement - intelligence, athleticism, and resistance to infectious disease—result not from individual genes, but from complex interactions of many genes, environment, personal history, and lifestyle. Genuine genomic enhancement of these traits may be very difficult.



Source: Nelson, J.P., C.L. Selin, & C.T. Scott (2021). Toward anticipatory governance of human genome editing: A critical review of scholarly governance discourse. *Journal of Responsible Innovation* (online first). doi: 10.1080/23299460.2021.1957579.

WHAT CAN HUMAN GENOME EDITING DO?

Although the language of "genome editing" may evoke science fiction movies with bioengineered organisms, present capabilities in human genome editing are relatively limited. Experts suggest that preventative therapies or treatments for *monogenic* genetic diseases—inherited genetic disorders caused by a single gene, including muscular dystrophy and sickle-cell anemia—are plausible if research continues. Treatments for the diseases sickle cell anemia, beta thalassemia, and transthyretin amyloidosis are currently in trials with promising results. However, most human traits of interest are *polygenic*—caused by complex and poorly-understood interactions between many genes, as well as lifestyle, upbringing, nutrition, and environment. Polygenic traits can cause other diseases and conditions, such as predispositions to certain cancers, diabetes, coronary heart disease, and schizophrenia. They also include non-disease characteristics like intelligence, athleticism, physical appearance, height, longevity, resistance to infectious disease, and appetite. It is unclear whether human genome editing would ever be able to significantly and reliably affect polygenic traits, though some genome editing research investors hope that it will.



Sickle Cell Anemia, which makes red blood cells develop a sickle shape, is a monogenic disease, meaning it is caused by a single gene. *(CDC / Unsplash)*

Near-term, practical uses of human genome editing would likely be limited to therapy or prevention for certain relatively rare and deadly monogenic disorders, such as Tay-Sach's or Huntington's disease. Longer-term capabilities might be broader, but cannot be predicted or guaranteed in any detail.

BROADER CONSIDERATIONS ABOUT HUMAN GENOME EDITING RESEARCH

The purpose of these forums is to learn what you think about human genome editing, including whether and how it is relevant to your own life. In developing and articulating your opinion, you may find it useful to learn what issues have been raised by experts, policymakers, and previous public engagements about human genome editing in society. This is not a comprehensive list. It is a list of some things that have come up in previous discussions with the public and experts around human genome editing. We encourage you to be vocal about whether and how your own opinions, hopes, and concerns are reflected in these topics, and especially about what you feel is missing from the conversation.

DIRECT EFFECTS ON RESEARCH SUBJECTS AND PATIENTS

Relevant for: human genome editing research and applications in humans

All biomedical research on humans involves some inconvenience and danger to research subjects from side effects. Research subjects are typically paid for taking on those dangers. Regulations and oversight bodies work to minimize risks to research subjects, prevent exploitation, and ensure that research subjects know what they're signing up for. Nonetheless, risks and unforeseen consequences do remain when testing new and unproven medical interventions. In 2020, three patients died in a gene therapy trial for myotubular myopathy conducted by U.S. pharmaceutical company Astellas Gene Therapies (known as Audentes Therapeutics at the time). Financial incentives for clinical trials mean that often disease sufferers who are less well-off take on more of the dangers of testing.

CONSENT FOR RESEARCH OR TREATMENT

Relevant for: germline (heritable) human genome editing

Biomedical research ethics are built around the principle of *informed consent*. Research subjects and patients must understand and freely accept the potential risks, benefits, and uncertainties of research conducted upon their bodies. *Germline* editing could be used to modify embryonic cells early in prenatal development. Because this person's cells were edited as an embryo, there was no option of refusal for that person. That person's descendants would also be affected by the intervention and they would not have the opportunity to consent to modification either. However, in some cases, early intervention could be the easiest or the only way to prevent certain inherited diseases.

In germline (heritable) editing, the person whose cells are edited cannot provide informed consent. *(Ernesto del Aguila III, NHGRI)*

PROLIFERATION OF TOOLS

Relevant for: all human genome editing

New genome editing techniques make genome editing research and application less expensive and lower technical barriers to entry. This has already increased the number and spread of researchers working on genome editing, for better or worse. It could speed and distribute innovation, making new developments harder to observe or control. Some worry that human genome editing could be practiced in unregulated jurisdictions with less oversight and fewer safeguards to protect research subjects and patients. Restrictions on genome editing research or application may be difficult to enforce due to the widespread distribution of genome editing tools.

MULTIGENERATIONAL EFFECTS

Relevant for: germline (heritable) human genome editing

In germline (heritable) editing, changes would not only effect one individual, but also their descendants. *(57Andrew/flickr)*

Germline human genome editing would introduce changes affecting not only one treated individual, but many or all of their descendants. Long-term effects of genome editing interventions on treated persons' children, grandchildren, and great-grandchildren could not be determined without long-term observation of those descendants. Biomedical research institutions have rarely conducted such multigenerational observation, and research designs would be complicated by the fact that future descendants cannot consent to observation at the time experimentation began. This makes understanding and controlling the long-term effects of germline human genome editing complicated and difficult.

RESEARCH ON EMBRYOS OR EMBRYONIC TISSUE

Relevant for: some genome editing research

Human genome editing research does not have to, but could make use of embryos or embryonically derived tissues.

The 1990s and 2000s saw significant controversy about the laboratory use of human embryos or tissues derived from embryos for biomedical research. The definition of "embryo" has been subject to significant debate, but here it is used to refer to a microscopic collection of cells which could, if placed into a womb, develop into a baby. Critics of such research argued that each embryo is a potential human life and that creation or use of embryos for research violated the rights of such potential humans. Research advocates argued that embryos used in research were left over from in-vitro fertilization (assisted reproduction) services which would never be implanted into a womb, and they were too early in development to be treated as potential individuals or persons. Other critics raised concerns about the potential exploitation of young women to harvest eggs for research. Currently, U.S. federal law prohibits use of federal funds for creation of embryos for research purposes, and U.S. states possess a wide variety of restrictions and rules for research involving embryos or embryo-derived cells.

INCREASING HEALTH INEQUITIES

Relevant for: all human genome editing research

New, high-tech medical treatments tend to be expensive, and prices do not reliably decrease over time. It is likely that any new treatments emerging from human genome editing would follow this pattern as biomedical corporations look to recoup their investments and turn a profit. In nations without public healthcare, like the United States, this would limit access to only the wealthy. In nations with public healthcare, treatments could give

providers large amounts of taxpayer funds and place additional strain on the public healthcare system. In any case, it is likely that the wealthiest members of society would be the greatest, and perhaps the only, beneficiaries of human genome editing, increasing differences in healthcare quality between the rich and everyone else.

LACK OF TRANSPARENCY AND OVERSIGHT

Relevant for: research by private corporations and unconventional players

Human genome editing research has been a largely niche and academic enterprise up until recently. Researchers have publicly reported their activities in academic literature. However, as private industry has invested in and deployed genome editing techniques, and as easy-to-use genome editing tools have become accessible to unconventional players such as "biohacker" communities, some experts have voiced concerns that it is becoming increasingly difficult for scientists, publics, regulators, or policymakers to stay aware of what is being done and whether it may be a matter for concern.

FAKE TREATMENTS AND HYPE

Relevant for: supposed and actual human genome editing applications

Many experts have voiced significant concerns that hype around human genome editing could lead fraudulent or ill-informed medical practitioners to offer ineffective or dangerous treatments under false promises. Right now, hundreds of clinics around the U.S. offer supposed "stem cell" treatments which are, at best, useless. Effective stem cell treatments are still years to decades away. These clinics have been able to spread because the Food and Drug Administration has not been given the resources or political backing to shut them down. Some observers fear a similar wave of potentially dangerous clinics offering supposed genome editing treatments, and voice a need for stronger oversight to prevent abuses.

Many experts worry that fake treatments promising results could be sold, like snake oil and other treatments that weren't regulated in the 19th and 20th centuries *("North Carolina Christian advocate [serial]" (1894))*

INTELLECTUAL PROPERTY AND PRIVATIZATION OF GOODS

Relevant for: all human genome editing research

Over the last 40 years, patent protections have been extended to research tools, including many of the new genome editing techniques. Strong patent protections are profitable and encourage innovation in pursuit of those profits. However, some advocates of research fear that competition for patent priority leads to secrecy and wasteful duplication of effort between different research groups. Others are concerned that patents on important research tools, like genome editing techniques, may price many researchers out and slow the development of the field.

COST VS BENEFITS

Relevant for: all human genome editing research

Developing human genome editing technologies for public use will likely cost a lot of money and take a long time. This money could be invested in other things. *(Nick Youngson/Alpha Stock Images)*

Development, safety and efficacy testing, and approval of human genome editing would cost significant amounts of money and take a long time. Gene therapy treatments based on genome editing technologies developed in the early 2000s are only now nearing approval for public use. It is likely that in the near-term, human genome editing can only expect to be useful for a small set of relatively rare and simple genetic diseases. This may also be true in the long-term. Particularly in the case of public funding, investment in human genome editing would take funds that could have been used in other ways, including investment in public health, infrastructure, education, or defense, and other topics of scientific research. There are thus legitimate questions to be asked about the potential costs and benefits of human genome editing development weighed against other potential investments.

SOCIAL MARGINALIZATION AND PRESSURE TO MODIFY

Relevant for: all genome editing research

Disability advocates have spent decades fighting for recognition of the rights and dignity of disabled persons, including persons with genetic disabilities which genome editing might be able to prevent or treat. Some advocates are concerned that the possibility of such prevention or treatment could amplify views of disabled people as “mistakes” who should be “edited away” and place pressure on disabled parents to edit their children. In the case of certain disabled groups, for example, the Deaf community, this could increase stigma against disabled persons and create societal pressure to eliminate their distinct subcultures and ways of life. In a more general sense, it is possible that publicity around genome editing could revive ideas of genetic determinism or eugenics, which have in the United States and elsewhere been historically integrated into programs of oppression, sterilization, and even genocide of minority racial groups, disabled persons, and people who are low income.

MULTI-USE KNOWLEDGE

Relevant for: all genome editing research

Genome editing is a broad tool that can be used for many purposes, in the same way that the same knowledge can be used to build both civilian airliners and military jets and missiles. Developing and spreading the generic base of knowledge and technique makes it easier to pursue any of those purposes, even ones which may be undesirable or dangerous. It is possible that knowledge and tools developed in the process of pursuing therapies in adults could also be used for applications like prenatal modification or bioweapon development. While investing in developing basic knowledge and techniques around genome editing for desirable uses, the possibility this knowledge could be used for undesirable or dangerous purposes must also be considered.

The same knowledge can be used to build planes for commercial airlines and to build this SR-71 Blackbird. *(Adam Reeder/flickr)*

TECHNOLOGICAL MOMENTUM

Relevant for: all genome editing research

Scientific research and technological development can be difficult to redirect or stop once they get rolling, simply because they build coalitions of researchers, investors, politicians, and public groups with established interests in further development. Some human genome editing commentators suggest that research should proceed freely but that widespread application of human genome editing should not occur without general public approval. Nonetheless, more research makes widespread application more likely regardless of public views or preferences.

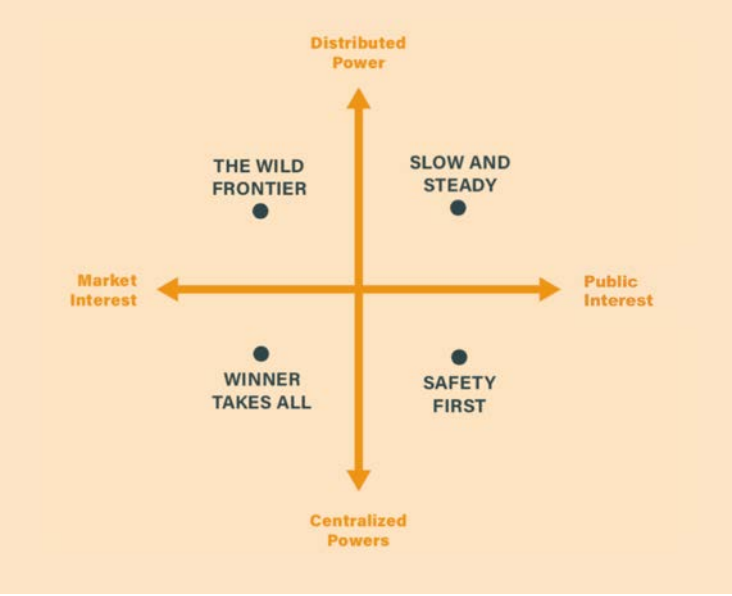
POSSIBLE FUTURES WITH HUMAN GENOME EDITING

One key feature of both emerging technologies and social action is *uncertainty*. No person or group, lay or expert, private or public, knows exactly what will come of technological development, policymaking, or group action, and no one even knows what all of the possibilities are. The further into the future we think, the more uncertain things are. In such complex systems as human bodies, economies, and nations, accurate prediction is impossible.

Scenarios, or "possible futures" as we call them throughout our forum, are a tool for managing uncertainty. Rather than trying to predict what *will* happen, they try to describe a variety of things that *could* happen, organized into a few plausible, hypothetical future situations. Thinking about multiple possible futures in this way can reveal previously unseen trends, potential dangers and opportunities, relationships, and ways in which people and organizations can promote desirable outcomes and work against undesirable ones. It can also help people to make plans or build capabilities that will serve them well across a wide variety of possible futures, rather than only one version of the future.

Earlier in this project, a multidisciplinary group of experts developed four possible futures for human genome editing technologies. The purpose of looking at these possible futures is to help you to think about not only the many different ways in which human genome editing could develop, but the different ways in which it could fit into society and support or harm things and people you care about. During the forum, you will discuss one of these four possible futures, pre-assigned to your group, in depth. Then you will hear from other groups about the possible future they discussed. All four scenarios are described in some detail below. While reading each, consider the following:

- What would it be like for you to live in this future world?
- What opportunities, dangers, and consequences would you, your loved ones, and others face in this world?
- Would you, your loved ones, or others find this future desirable?



The four possible futures can be roughly categorized along two axes: human genome editing as controlled by market or public interests, and with power that is centralized or distributed.

THE WILD FRONTIER

In a world of rapid innovation, questioned expertise, and powerful market incentives, profitable technologies advance along with an explosion in human gene editing experimentation under highly variable rules.

What do people know about genome editing? People disagree about what counts as "science" and "knowledge". They also have differing views about human genome editing. Most people don't know how human genome editing works, or the types of things it can – and cannot – do. Marketing shapes the majority of what people think about human genome editing.

Who is in charge? National and sometimes local governments make laws about human genome editing, though wealthy business leaders command a lot of informal authority. Oversight is spotty and local.

Who has access? Many people have access to the technology to develop human genome editing treatments, but there is little guarantee that the treatments are real or effective. The most effective treatments are extremely expensive.

How is it used and who can provide it? Real and fake applications are widely marketed for purposes of enhancement. Real treatments tend to be provided by clinics connected to biotech groups that are barely regulated, while fake treatments are provided by clinics connected to unregulated, questionably certified, small-time medical professionals.

SLOW AND STEADY

This is a world where science and technology are more open and governed democratically, rather than by those who have the most expertise or resources, and social values guide new innovations.

What do people know about genome editing? There's increased public interest in, and knowledge of, science, in particular in human genome editing, as a result of widespread engagement between the public and experts in academia, industry, and government. However, some discontent people intentionally confuse people with false information.

Who is in charge? There is formal cross-national governance in the form of a temporary ban on germline editing until it is proven safe and effective, a stated focus on eliminating diseases caused by one gene, and agreed upon

standards for approving gene therapies. There is also an advisory and oversight network for research and development made up of international, national, and local agencies, as well as citizen and patient advocacy groups.

Who has access? Globally, countries work together to make sure there is equitable access to human genome editing technologies in the broadest possible scale to everyone who follows the rules in government, industry, and academia. However, outside of the agreed upon standards and areas of focus, access is severely restricted.

How is it used and who can provide it? Application areas are matched with the highest public needs, at the level of nation states as well as the level of genetic diseases affecting the most vulnerable populations. Providers are different in different countries, depending on the applications and patient groups.

SAFETY FIRST

Moral and safety concerns result in more rules and governmental oversight, leading to a few globally dispersed and uncoordinated centers of excellence.

What do people know about genome editing? People know different amounts about human genome editing depending on each country's values. How much the public knows does not necessarily correspond to how much human genome editing is permitted.

Who is in charge? There is no global system of governance. However, some countries work together in groups to align resources around shared goals and priorities. Systems of governance vary depending on country's permissibility of human genome editing. Those who break the rules are severely punished.

Who has access? Access to human genome editing treatments is limited to those with health conditions that align with their country's prioritized applications of human genome editing technology or to those who have the money and ability to travel to countries where other human genome editing uses are allowed.

How is it used and who can provide it? Applications vary depending on the country. Some countries ban human genome editing, some permit some applications of it, and some permit all applications of it. These applications are a mix of national and/or local public health priorities and military-driven enhancement-focused applications. The relatively few providers of human genome editing either have institutional prestige or relationships to prestigious institutions.

WINNER TAKES ALL

Never before seen corporate consolidation between information technology, biomedicine, and genomics firms leads to a rapid market and profit driven development of genome editing.

What do people know about genome editing? Because research and information are closely guarded, the public has limited belief in and understanding of scientific enterprise. Human genome editing is understood mainly as a tool of the rich. The majority of people around the world only know about human genome editing via social media and popular new outlets, which focus on extremes in enhancement and terrible legal debates among wealthy entrepreneurs.

Who is in charge? There are no global governance agreements about the development of human genome editing technologies. Instead extreme nationalism, which is heavily influenced by biotech corporate interests, rules.

Who has access? Access to gene editing technology is limited to those rich enough. Advances occur, but are not part of a larger public health care system and remain only accessible to a select few. As time goes on, more and more people are left out.

How is it used and who can provide it? The main application areas for human genome editing are hereditary germline editing, and a proliferation of somatic gene therapies. These are both used for treatment and enhancement. Treatment is provided only by a few of these consolidated global companies. No independent entrepreneurs or universities have access to human genome editing technology.

Publication

This information booklet was made to serve the specific purpose of informing participants in Human Genome Editing: Framing Our Biological Futures public forums. The publication is provided by the Preparing for Human Gene Editing (PGET) project team to its forum host partners and the forum participants.

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APPENDIX

Content from Figure 1: A Human Genome Editing Timeline

Notable events for the time period 1995-2020:

- 1995:
  - 1st gene therapy trial in humans provides initial, favorable results (Blaese et al. 1995)
- 1999:
  - American teenager Jesse Gelsinger dies in a University of Pennsylvania gene therapy study, chilling gene therapy research (Couzin & Kaiser 2005; Wade 1999)
- 2002:
  - Fruit fly genome editing using zinc finger nucleases (ZFNs) (Bibikova et al. 2002)
- 2005:
  - Human cells modified using ZFNs (Umov et al. 2005)
- 2011:
  - Genome editing in human cells using transcription activator-like effector nucleases (TALENs) (Miller et al. 2011)
- 2012:
  - CRISPR functionality elucidated, genome editing use suggested (Jinek et al. 2012)
- 2013:
  - Genome editing in human cells using CRISPR (Jinek et al. 2013, Mali et al. 2013)
- 2015:
  - Genome editing in nonviable human zygotes using CRISPR (Lian et al. 2015)
  - 1st International Summit on Human Gene Editing (National Academies 2015)
- 2016:
  - U.K. Nuffield Council ethics report on genome editing (Nuffield Council 2016)
- 2017:
  - Genome editing in viable human embryos (Ma et al. 2017)
  - U.S. National Academies governance report on human genome editing (National Academies 2017)
- 2018
  - World Health Organization Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing established (WHO 2020)
  - Reports emerge that CRISPR-edited babies have been brought to term (Regalado 2018)
  - 2nd International Summit on Human Gene Editing (National Academies 2018)
- 2019
  - 1st U.S. CRISPR-based therapy clinical trial begins (Saey 2019)
- 2020
  - International Commission on the Clinical Use of Human Germline Genome Editing governance report (National Academies 2020)
  - Emmanuelle Charpentier & Jennifer Doudna receive Nobel Prize in Chemistry for developing CRISPR-based genome editing

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