With global gene editing slow down, what's the future of 'designer babies?'

Our genome is one of the most precious aspects of being human. Its similarity to all other living organisms is what connects us to nature, but its inherent differences are what defines our uniqueness as both a species and as individuals.

So in April of 2015, when scientists in China revealed that they had successfully edited a human embryo it was met by understandable concern in some circles.

It also reignited the century-old debate over the ethics of manipulating human genetics in order to improve a population — a practice known as eugenics.

The Nazis attempted to make a 'master race' of Arayns through the use of social policies, instituting what is known as negative eugenics — eliminating those who they believed were inferior, such as Jews, gypsies and other minorities. These practices led to the death or sterilization of hundreds of thousands of people who possessed many traits — homosexual, weak, feebleminded — the Nazis considered undesirable. By using institutionalized selective breeding, the Nazis believed they could eliminate any deleterious genes and each subsequent generations would become stronger and stronger, until their master race was complete.

The Nazis believed they could create 'designer babies' — removing undesirable traits from the gene pool. For the Nazis this meant the removal of the intellectually and physically weak, but others saw designer babies in what they believed was a more constructive light. Margaret Sanger, the founder of Planned Parenthood, and many early 20th century progressives were strong advocates in America for so called positive eugenics, which sought to promote childbearing by those who were deemed most "fit" — the healthiest, those with the "best genes".

In the time of Sanger, defining "fit" versus "unfit" got lost in a shuffle of anti-immigration and racially motivated policies and thus the question still lingers today: How do you define "fit"? Where do we draw the line between "fit" and "unfit"? Designer babies don't have to mean culling out "defective" humans and creating superior ones in a petri dish. There are some 25,000 human genes, and each play an important but unique part in creating a person. Targeting some of these could end a great deal of human suffering, what matters most is how we define "fit".

Designer babies redux

Concerns about ‘designer babies’ bubbled to the surface during the international conference on human gene editing, which concluded in early December 2015 in Washington. It featured leaders from America, China, the United Kingdom and elsewhere. The impetus for the gathering was the significant advances made with the genome editing technique known as CRISPR-Cas9, which can very precisely makespecific, targeted changes to an organism’s genes. At the end of the conference the leaders released astatement describing what they believed should be the future of gene editing in humans, including geneediting on human embryos and germline cells.

There is an important distinction to be made here as there are essentially two types of human cells, both of which can have their genetic makeup edited exogenously. *Germline cells* are the sperm and eggs that are involved in reproduction. *Somatic cells* are the rest of the cells — neurons, skin, liver immune, etc. Editing a sperm cell has a much different effect than editing a stomach cell. An edit to a sperm or egg cell can lead to a heritable change that may be passed to offspring and result in permanent changes to the human gene pool — perhaps, say critics, creating new “breeds” of humans. The same is true of an edit to a human embryo. Gene therapy is the technique used to make changes to the genome an adult’s somatic cells, this has been used to treat conditions in which a somatic cell has a faulty gene which happens in cancer and genetic diseases. Gene therapy creates genetic changes that are confined to a single individual and they do not affect our collective gene pool. The conference members addressed that specifically in its wrap up statement, which urged caution in this area:

> It would be irresponsible to proceed with any clinical use of germline editing unless and until (i) the relevant safety and efficacy issues have been resolved, based on appropriate understanding and balancing of risks, potential benefits, and alternatives, and (ii) there is broad societal consensus about the appropriateness of the proposed application. Moreover, any clinical use should proceed only under appropriate regulatory oversight. At present, these criteria have not been met for any proposed clinical use: the safety issues have not yet been adequately explored; the cases of most compelling benefit are limited; and many nations have legislative or regulatory bans on germline modification. However, as scientific knowledge advances and societal views evolve, the clinical use of germline editing should be revisited on a regular basis.

But the very discussion of germline changes set off alarm bells among some and generated scary articles and headlines around the world. *Washington Post* writer Joel Achenbach conjured up images of war and violence by noting that some now want to call the genome editing technique CRISPR a “gene-sniper.” Other reactions were no less measured:

- “Would you date someone whose genes had been tweaked?” read one headline.
- “No designer babies, but summit calls for cautious research.” read another.
- Designer babies are inevitable claimed another journalist: “Here’s Why We’ll Eventually Have to Accept Designer Babies“.

Concerns unite political opposites

A slew of advocacy groups attended and presented at the conference, with many far left and far right organizations expressing their opposition to germline editing. Pro-life groups, like The Ethics and Religious Liberty Commission believe that designer babies are an infringement on the sanctity of human life. British fertility expert Gillian Lockwood described designer baby services as "turning babies into commodities you buy off the shelf." The popular Christian website Beginning and End called designer babies "playing god in the womb."

The Center for Genetics and Society (CGS), which lies on the other side of the political spectrum, insisted there exists "no medical justification" for the editing of human germline embryos. It also notes that any medical necessity for making these changes can be done through other means (i.e. screening embryos and abortions). CGS also advocates for the application of the precautionary principle for designer babies on the grounds that because we don't understand the consequences of germline genome editing, we should not proceed with any aspect of it. Executive Director Marcy Darnovsky outlined these risks in a New York Times Op-Ed in 2014:

> Will the child be born healthy, or will the cellular disruptions created by this eggs-as-Lego-pieces approach lead to problems later on? What about subsequent generations? And how far will we go in our efforts to engineer humans?

Germline editing also raises a swarm of other ethical concerns. For example, Luke Robert Mason the executive director of HumanityPlus — a nonprofit dedicated to advocating for the ethical use of technology to expand human capacities — saw a civil liberties issue brewing when he posited "will it be legally enforceable that you'll have to disclose to a partner if you have had your germline edited?"

Yet many of these fears and objections to germline editing attack the process at steps much further down the debate than we currently find ourselves. Darnovsky and Mason pose intriguing questions and concerns, that while legitimate, have fallen so far down the slippery slope, they have missed discussing the first incremental question: where do we draw the line between what is a "fit" modification and what is an "unfit" modification.

Should we fear germline editing?

To begin discussing the line, its important to understand what kind of edits can be made and what kind cannot be made. In fact, many of the fears in society are predicated on a misunderstanding of this distinction. One of the reasons for this knowledge gap has been the many advances in CRISPR, a genome editing technique which frequently dominates headlines which describe its effectiveness, accuracy, and precision. CRISPR was discovered just a few short years ago in bacteria as a defence mechanism against DNA from invading viruses. During infection, a virus will insert its DNA into a bacteria, the CRISPR sequences in the genome of the bacteria recognize and bind to the viral DNA, and an associated enzyme (often Cas9) cuts up and inactivates the DNA. Recently, scientists realized that these CRISPR sequences can be manufactured to match and recognize any genetic sequence and the

associated enzymes could cut human DNA. Later changes would allow for the insertion of new genes into the cut regions of the DNA.

The advances of CRISPR were the impetus to this latest conference on human genome editing. However, gene editing techniques are not the aspect of creating a designer baby that will dictate how far or how fast we can go. Genetic Literacy Project's sister site GENeS, carried a comment from Paul Root Wolpe a Professor of Bioethics and the Director of the Center for Ethics at Emory University, explained as much:

> *At this point in our understanding of the dynamics of human development, we can send in one or a small number of genes to correct or modify single traits. However, our understanding of the genetics of complex traits like intelligence, or musical ability, or athleticism is still rudimentary, and no one would know how to create a more intelligent child, for example.*

Take for example, the process that would need to be undertaken to design a great athlete using gene editing of an embryo. A geneticist may have an idea of what sequences are necessary to design an embryo with the capacity to produce a baby with exceptional physical size. One example could be a version of a gene that codes for a growth factor with higher than average potency. However, great athletes are so much more than a herculean frame. Hand eye coordination, confidence under pressure, and intelligence, all have poorly understood genetic basis. In fact each of these traits may may have significant environmental (i.e. nutrition) aspects and most likely involve a large number of genes.

In short, scientists cannot simply "edit in" *the athlete gene* to an embryo and voila the next Carli Lloyd is designed. The commodity fear that many on the far right have does not exist because we simply will never be able to reduce these abstract characteristics to a few pieces of genetic code.

But this does not mean gene editing has no role for humans, instead the technique holds an immense amount of promise in treating genetic diseases, for example conditions like cystic fibrosis, sickle cell disease, and Huntington's disease. These afflictions arise because of mutations at specific locations in genes that scientists are very familiar with. For example, sickle cell disease is caused by an error in just one single letter of genetic code.

Some may still question the ethics of whether we should do this type of editing. However, it is justifiable that using CRISPR — or another technique — to edit out these types of mutations would merely be consistent with what physicians and researchers have been doing for centuries: treating diseases. The difference today is that we have the tools to eliminate these conditions and their origin something we are also already doing this with gene therapy. Next year, the FDA is expected to approve the first gene therapy, but it won't be long until these drugs are ubiquitous as right now there are about 2,000 ongoing clinical trials for gene therapy in America.

One way to get around all of the ethics but still ensure these diseases are treated is to just focus resources on gene therapy. Even CGS gave gene therapy an endorsement in their statement response to the conference. At face value, this would seem to be a fair compromise. Don't edit embryos, but treat the new born who has a genetic condition with the appropriate gene therapy. However, there are key

advantages to using gene editing on an embryo, as opposed to gene therapy on an adult. Gene therapy techniques must target thousands or even millions of cells and replace a faulty gene in each one of them to have a therapeutic affect. But an embryo only has a few cells which give rise to a whole adult, thus the problem is cut off at its source by using gene editing.

Furthermore, editing out heritable defects stops the problem from infecting future generations. One change to an embryo or a germline cell and an entire lineage is saved from the devastating affects of one of these genetic diseases. One single edited embryo results in the same end point as having everyone of that embryo's descendent who inherits the faulty trait undergo a gene therapy. By doing the genome editing just once, as is the case with editing an embryo or germline cell, we minimize any risk from the procedure over what could arise from having to preform gene therapy in each successive generation.

What might change because of this conference?

The conference was important in advancing the two decade old discussion on where we draw the line for manipulating our genetic code, even for life improving reasons. The leaders gave the go-ahead for many other types of gene editing like gene therapy**,** but were more cautious on germline editing. They go on to list six justifiable objections including fears of off-target edits, increases in social class divide, and the difficulty in removing such edits once they have been made and they go on to conclude that "It would be irresponsible to proceed with any clinical use of germline editing."

This sounds like a ban, and it was reported as such by outlets like the *New York Times* which outright initially said the meeting led to a moratorium on germline gene edits. It took them a few days to get it right . In reality though, no moratorium could have ever been placed on any aspect of gene editing as a result of this conference, primarily because the conference's leaders have no regulatory authority anywhere in the world.

So, lacking any real regulatory authority anywhere, the real impact of the decision on the permissibility for this type of gene editing is similar to their decision on both basic research and gene therapy: follow the existing and evolving regulations of a region. In fact, despite the confusion, many lab and clinical uses of gene editing around the world will continue because the countries where this type of research can take place have very loose laws about gene editing.

Many countries around the world do have laws restricting gene editing on humans, however, several of these laws are not very cut and dry and the line is therefore not clearly draw. Tetsuya Ishii, a bioethicist at Hokkaido University in Sapporo, Japan, read through the relevant legislation of 39 countries and found that 29 of them have laws that could be interpreted as banning germline editing. However, these "bans" in some places — China, India and Japan — read more like suggestions than laws. In Russia, Ishii deemed the laws were too ambiguous to interpret. In the United States, laws only prohibit federal funding for research on human embryos, but no law explicitly codifies a ban on germline editing.

Scientists in some of these places where the bans read more like suggestions may push the envelope on editing the genomes of embryos, like what already happened in China. This is why it is vital that the conference's leaders also made it clear in their statement that everyone needed to reconvene regularly to

discuss where to draw this line. Frequent discussions on these topics is the best way to ensure that society and science harmoniously progress together. But for these subsequent meeting to lead to successful policy that draws a clear but realistic ethical line we all need to be more realistic about what we can actually accomplish via gene editing on humans, ending human suffering, and not on how to recreate the X-men *in vitro.*

Nicholas Staropoli is a research associate for the American Council on Science and Health. He has an M.A. in biology from DePaul University and a B.S. in biomedical sciences from Marist College. Follow him on twitter @NickfrmBoston.