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comment

Human germline genome editing and broad societal consensus

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Should human genome editing be limited to somatic cells, or should germline genome editing also be permitted? Should (apparently) permissible human genome editing be limited to therapeutic purposes, or should enhancement purposes also be permitted? Who decides, and on what basis?

Everyone who has heard of CRISPR–Cas9 gene editing probably has an opinion about whether (and if so, how) this technology should be used in humans. "If you have the skills and the knowledge to fix these diseases, then frickin' do it", said one patient advocate[1]. Others, including scientists, are more cautious. For example, Eric Lander, head of the Broad Institute, writes, "It has been only about a decade since we first read the human genome. We should exercise great caution before we begin to rewrite it … authorizing scientists to make permanent changes to the DNA of our species is a decision that should require broad societal understanding and consent."[2]

No one discounts the scientific and therapeutic promise of human gene editing[2]. The technology could be used to treat sickle cell anaemia, metabolic liver disease, human immunodeficiency virus (HIV) infection, progressive blindness, heart disease, cancer, Alzheimer's disease, Huntington's disease, and so on. Many, however, including myself, worry about the hubris and the potential negative consequences of the discrete goal of trying to take over the evolutionary story. Those who share this worry about the introduction of heritable genetic modifications typically draw a clear demarcation between somatic cell gene editing to hopefully cure individual patients, and germline gene editing to hopefully create genetically healthy individuals capable of having genetically healthy offspring[3]. Another worry concerns the use of human gene editing not merely to treat or eliminate hereditary illnesses, but also to enhance non-medical physical and mental characteristics (for example, to improve athletic abilities).

Heritable genetic modifications

With CRISPR–Cas9 gene editing, the ethics of creating 'designer babies' has taken on a certain urgency as the prospect of creating generations of genetically modified humans now seems within reach. In the past couple of years, three studies involving genome editing of human embryos have been published. In addition, the goal of editing the genomes of the sperm and egg (and the progenitors of those cells) prior to *in vitro* fertilization has been identified.

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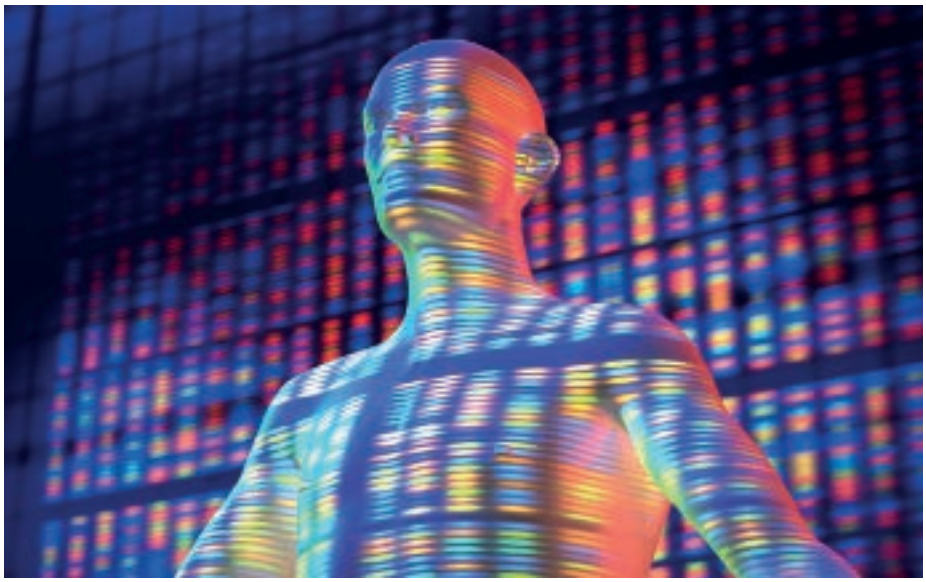
In very general terms, there are urgent research ethics concerns about the safety of the technology (resulting from incomplete editing, inaccurate editing, off-target mutations, on-target mutations with unintended consequences, and mosaicism), the unlikely prospect of a favourable harm/benefit ratio (where potential medical benefit outweighs research risks), and the inability to obtain consent from those who would be born following genetic modification. There are also more complex ethical concerns about opportunity costs and the proper balance between increasing reproductive options and promoting social justice, the commodification of children, the exacerbation of existing inequalities, the rebirth of eugenics, and the introduction of new forms of discrimination and stigmatization resulting from the medicalizing and pathologizing of difference.

Public attention was drawn to these issues in 2015 when researchers at Sun Yat-sen University in Guangzhou, China, published a paper reporting the genetic manipulation of non-viable human embryos using CRISPR–Cas9[4]. This publication prompted the US National Academy of Sciences — in coordination with the US National Academy of Medicine, the Chinese Academy of Sciences, and the UK's Royal Society — to co-host an International Summit on Human Gene Editing. The overarching goal of the summit was to "explore the many questions surrounding the use of gene editing tools in humans"[5]. To quote the opening remarks of David Baltimore, Chair of the Organizing Committee, "Today, we sense that we are close to being able to alter human heredity. Now we must face the questions that arise. How, if at all, do we as a society want to use this capability?"[5].

I was a member of the 12-person Organizing Committee of the International Summit on Human Gene Editing. In that role, I was a signatory to the *On Human Gene Editing: International Summit Statement* issued in December 2015 at the close of the summit[5]. The statement included four conclusions, one of which outlined an apparently simple, yet exquisitely complex, two-part ethical framework for evaluating human germline gene editing. That conclusion stipulated that "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". Another conclusion stressed the need for ongoing international conversation to continue to explore contentious issues surrounding human gene editing. In response to the statement, the presidents of the four co-hosting organizations agreed that they would work with other academies around the world to continue the conversation[5].

The conclusions on germline gene editing and on the need for ongoing discussion



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demonstrated a clear (if unwitting) commitment to 'slow science' — to resisting fast, competitive, benchmarked science divorced from social and cultural concerns (http://slow-science.org). It signalled the need for time to carefully and conscientiously reflect on whether we (humans) should attempt to take over the human evolutionary story by introducing heritable genetic modifications. To quote Baltimore again, "This summit will not be the last word on human gene editing. Rather, we hope that our discussion here will serve as a foundation for a meaningful and ongoing global dialogue."[5]

The irresponsible becomes permissible

Fourteen months later, I was surprised to read that a committee established by two of the four co-hosts of the international summit — the US National Academy of Sciences and US National Academy of Medicine — had done an about-face and, in so doing, set aside sociologist Ruha Benjamin's admonition that process and policy should go hand in hand[5]. In their February 2017 report *Human Genome Editing: Science, Ethics, and Governance*, the academies concluded that "clinical trials using heritable germline genome editing should be permitted"[6] provided the research is only for compelling reasons and under strict oversight limiting uses of the technology to specified criteria. The first of these criteria is "the absence of reasonable alternatives"[6].

An obvious question that follows from this about-face is why eschew the commitment to broad societal consensus and embrace germline gene editing for therapeutic purposes? Before I address this question, however, a few comments about the downstream questions of the 'who' and the 'what' of broad societal consensus are in order.

In the 2015 statement, the 'who' was to be "inclusive among nations and engage a wide range of perspectives and expertise — including from biomedical scientists, social scientists, ethicists, health care providers, patients and their families, people with disabilities, policymakers, regulators, research funders, faith leaders, public interest advocates, industry representatives, and members of the general public"[5]. The 'what' was to be a discussion of "acceptable uses [if any] of human germline editing"[5]. In the 2017 report, the 'who' is the public (which is not defined anywhere in the report) and the 'what' is no longer whether (and if so when) human germline gene editing should be permitted, but whether germline gene editing, which is (apparently) permissible for therapeutic purposes, should also be permissible for enhancement purposes[6].

In this way, the answer to the original question of 'who' has been made opaque and the original question of 'what' has been transformed from a question about the moral demarcation line between somatic gene editing and germline gene editing to a question about the moral demarcation line between germline gene editing for therapeutic purposes and germline gene editing for enhancement purposes. This is problematic, to say the least.

The importance of public consultation

Why, at a time when even conservative organizations like the World Economic Forum explicitly recognize the importance of engaging the public in discussions about governance, would the US National Academy of Sciences and US National Academy of Medicine decide to 'go it alone' and affirm the permissibility of germline gene editing for therapeutic purposes? Two likely motivational drivers are "the pursuit of scientific prestige and capturing a highly lucrative commercial market"[7].

Meanwhile, in this time of social and political unrest, there is increasing awareness of the importance of quality governance both in terms of process and substance. In democratic countries, an important facet of quality governance is dialogue among those who are likely to be affected by the norms, standards, policies, guidelines, laws, and regulations. On this very point, the World Economic Forum counsels informed public consultation across borders. In the *Global Risks 2015* report, we learn that effectively balancing the potential benefits and the risks of emerging technologies depends on stable governance[8]. Governance will be more stable "if the various stakeholders likely to be affected are involved in the thinking about potential regulatory regimes and given the knowledge to enable them to make informed decisions"[8]. The so-called stakeholders are not the only ones to be consulted, however: "given that risks tend to cross borders, so must the dialogue on how to respond … [and] given the power of public opinion to shape regulatory responses, the general public must also be included in an open dialogue about the risks and opportunities of emerging technologies through carefully-managed communication strategies"[8].

So, at a time when the increasingly international and participatory nature of governance is being acknowledged and promoted, why would the US National Academy of Sciences and US National Academy of Medicine dismiss these commitments to democratic process and endorse manipulating the genomes of future generations? Given the state of the science, it can hardly be said that there was a need for swift policy deliberations and conclusions.

Broad societal consensus

I think it is possible (perhaps even likely) that the authors of the 2017 report (a majority of whom were not signatories to the 2015 statement) preferred to set aside the daunting challenge of working towards a broad societal consensus. I imagine that while they would have been sanguine about the prospect of eventually satisfying the safety and efficacy requirements (with or without understanding the need for debate about where to set the thresholds for acceptability), they would have been

dismissive of the prospect of achieving broad societal consensus. What is this[9]? And, more specifically, how would we know it if we saw it?

These are good questions to which I don't have a complete answer. With the benefits of 'slow science' and 'slow ethics', however, I am confident we could figure this out. We might, for example, begin with a critical review of strategies for decision-making by consensus that have been developed over time by various discrete communities. Of particular interest here might be strategies that involve what the philosopher John Beatty describes as "no-objection" and "let-stand" decision-making[10]. For illustrative purposes, Beatty highlights the Navaho way of discussing an issue "until there is unanimity of opinion or until the opposition feels it is no longer worthwhile to urge its point of view"[10]. Another strategy, one employed by Quakers, rests on the view that "Unity is not to be confused with unanimity. It is not necessary for every member to fully agree with a decision, but rather for Friends to discern that as a body they are called in a particular direction."[10] Yet another perspective is offered to us by the Women's Encampment for a Future of Peace and Justice; they suggest that consensus means that in reaching a decision "no one felt that her position on the matter was misunderstood or that it wasn't given a proper hearing"[11]. How is this goal to be achieved? By observing the principles of responsibility, self-discipline, respect, cooperation, and recognizing that this will inevitably involve struggle[11].

Why struggle? Because although all humans have a common interest in the human genome, much work is needed to identify other common interests that might rightfully guide policy deliberations. Hence, there is merit in setting aside the conclusion of the 2017 report on the permissibility of germline gene editing for therapeutic purposes, and embracing the challenge of seeking broad societal consensus on this ethically controversial issue. ❐

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Competing interests

The author declares no competing interests.

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