Main Submission

Heritable Genome Editing: Technological Innovation for Future Perspectives in Healthcare

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The year is 2017. Western civilization has become the epitome of a technology-driven era, with advances in medical science revolutionizing our treatment of disease. In 2011, genome editing was named "Method of the Year" by *Nature Methods,* and harnessing the CRISPR/Cas9 system to bring precision to this practice earned it the title of "Breakthrough of the Year" by *Science* in 2015 (1). However, legislations and policymaking have struggled to keep up with the rapid expansion of genomic diagnostics and treatment in clinical practice, and the growing disconnect between these two fundamental aspects of our healthcare system creates a barrier to translating knowledge into tangible health benefits for patients. As with any approach to a complex problem, there lies a challenge in defining a particular need. What aspect holds most promise to facilitate the application of our knowledge?

I believe that prevailing ethical issues are the foundation of this disconnect. Arguments on procreative liberty, public health benefit, and disability rights are nothing new to bioethical literature in this realm, though they have been left largely unexplored past the hypothetical. Now, with the tangible benefit of genomic interventions gaining increasing attention from successful *in vitro* studies, what was once hypothetical has become reality. Challenging public, clinical, and political populations alike to explore this potential is a much-needed influence to promote future health perspectives and human well-being in an emerging era of precision medicine.

In February 2017, the United States National Academy of Sciences (NAS) and National Academy of Medicine (NAM) released a report titled "Human Genome Editing: Science, Ethics and Governance" that supports this notion. An international panel of experts addressed the need to explore current capabilities of human genome editing and propose updated regulations that advocate for careful consideration over total prohibition (1). Recommendations on topics of heritable changes and where to draw the line on what would be considered enhancement invite the most scrutiny. The concept of gene editing that radiates beyond an individual in their lifetime to a whole future lineage has been a longstanding qualm

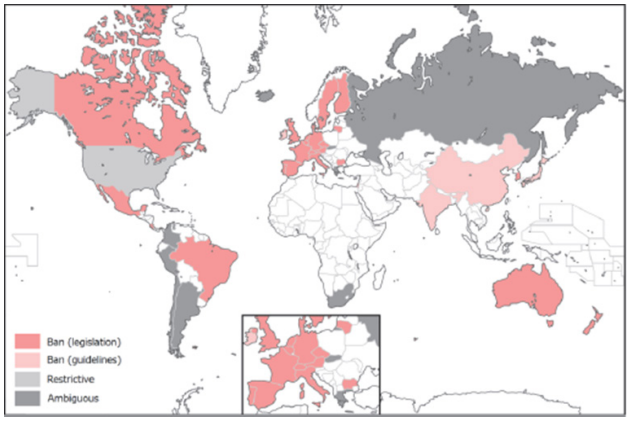

Figure 1: The regulation of heritable human genome editing varies extensively worldwide. Red represents countries with strict legal prohibition, while dark grey represents those that are ambiguous in their policies (2).

for regulatory legislations and, as such, has considerable international variation (Figure 1) (1,2).

Take, for example, the widely popularized news story in mid-2016 about the first live-born "three-parent baby." The eye-catching title describes a 36-year-old woman who carries a mutation in some of her mitochondrial DNA (mtDNA), an independent genome exclusive to these tiny organelles, inherited through the maternal cell line (1,3). Though unaffected herself, the mutations manifested into a lethal form of Leigh syndrome in all of her six naturally conceived children (3). Mitochondrial replacement therapy (MRT), a form of *in vitro* fertilization, allowed healthy mtDNA from a donor "third parent" to replace mutated mitochondria in the mother's oocyte, resulting in a healthy pregnancy and birth with no complications (3).

However, because this technique is not approved in the United States, and would violate Canadian laws, the MRT procedure took place in Mexico, where regulations are more accommodating (3,4). Cases like this exemplify the need to establish international norms; MRT does not alter the nuclear genome, but does create a new set of heritable genetic material that would never occur naturally, hence designating it to be classified as a heri-

table genetic change. If a lengthy, legal process could be streamlined both with updated legislation and state of the art technology like CRISPR/Cas9, it would diminish a monumental barrier to accessible healthcare for similar patients who are quasi-eligible for life-changing genetic treatments, yet unable to afford international intervention.

Varying barriers to MRT and other types of germline gene therapy stem from regulations addressing the sensitive topic of genetic ailments debilitating enough to warrant their elimination in the cell line of an individual – an unsavory concept for many ethicists and rights activists in the disability community (5). Disability rights have seen milestone successes, and concerns of a slippery slope to past eugenic practices arise from the idea of heritable genome editing providing a "cure" for disability (6). The logic behind each opposing side is sound, though I argue that these ideas of social acceptance regarding disease or disability and social acceptance of heritable genome editing do not have to be mutually exclusive. Advanced technology can now provide the possibility to prevent an outcome parents might reasonably want to avoid, and it does not follow that these individuals would value the lives of existing people with disability or disease to a lesser extent (7).

Changing any standard of care in medicine is a multidimensional, carefully dissected process – and for good reason. This being said, many norms in our society today were at one point inconceivable ideas. The Human Genome Editing (2017) report gives explicit recognition to how human genome editing can effectively transform the treatment of disease. These discussions are needed to facilitate the next step: inviting international governing bodies and jurisdictions to embrace an attitude of forward-motion thinking for future perspectives that will most benefit the evolution of medical treatment. ■

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