BOOKS

An Elusive Consensus

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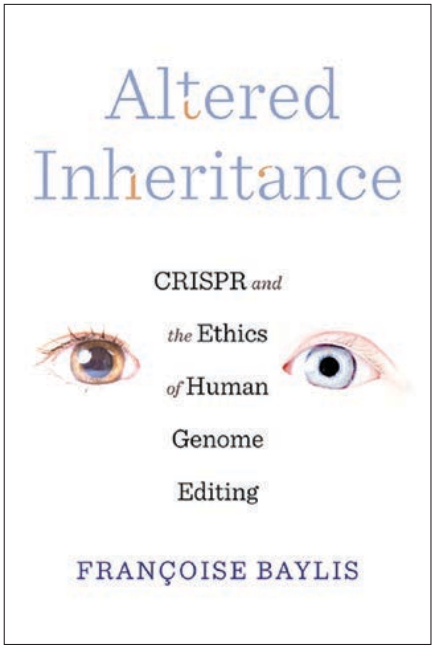
A few months into my medical training, I heard Fred Sanger, the Nobel prize-winning biochemist, describe a miracle—DNA sequencing in his lab—and Ray White, a pioneer in human genetics, excitedly reveal the first genetic markers that would grow into a human genetic linkage map. I also encountered two infant children with Leigh syndrome, a rare metabolic disorder of the central nervous system that usually leads to death within a few years, inherited from their mother's mitochondrial mutation. The wonder of science was palpable in the lectures by Sanger and White, but the parents' agony facing the relentless progression of a childhood genetic disease is the strongest memory I retain.

These events did not seem to fit together at the time, but technological convergence has brought them together decades later. Methods for deciphering the genome have matured, and ways to alter the human genome have followed in their wake. Public debate about who should control those technologies has intensified.

CRISPR genome editing, a recent breakthrough in molecular biology that allows for the precision editing of genes, is governed by several public policies about research funding, regulation, and intellectual property. For instance, the National Institutes of Health can fund research to use and advance the technology, so long as the agency does not fund work to alter embryos. The Food and Drug Administration cannot acknowledge receipt of or review protocols for research that would involve heritable change in human embryos.



Altered Inheritance: CRISPR and the Ethics of Human Genome Editing
by Francoise Baylis. Cambridge, MA: Harvard University Press, 2019, 304 pp.

Both of those policies result from riders to appropriations bills that have been updated annually. The Dickey-Wicker Amendment has restricted embryo research since 1996, and an amendment initiated by Representative Robert B. Aderholt (R-AL) has since fiscal year 2016 barred FDA research on editing the genes of human embryos. Both laws were attached to must-pass annual funding bills, inserted quietly with little debate. They are constitutionally suspect because they are statutory mandates embodied in funding bills, but they remain the closest things the United States has to a "policy"; this, in the largest biomedical research enterprise the world has ever known.

Meanwhile, the US Patent and Trademark Office has granted patents on gene editing technologies, but is now—eight years after the critical science was conducted—reviewing a possible "interference," an administrative procedure to sort out competing patent claims on related inventions. The dispute concerns patents sought by two clusters of academic research institutions, one led by the University of California, Berkeley, and the other by the Broad Institute of MIT and Harvard. This pits leaders in the field against one another for control of patent rights: Jennifer Doudna of UC Berkeley and Emmanuelle Charpentier (who conducted her seminal research at the University of Vienna, and now is at the Max Planck Institute) against Feng Zhang and his colleagues at the Broad Institute and their collaborators.

This is the second round after a previous interference proceeding concluded two years ago in Zhang's favor. The US patent status contrasts starkly with that of the European Patent Office, which has revoked some Broad patents and confirmed dominant UC Berkeley patents. To oversimplify this battle of academic titans, the Broad Institute got the initial upper hand in the United States, and UC Berkeley in Europe. And both academic clusters have outsourced licensing authority to competing start-up firms, further compounding the complexity and putting more fingers in the pie.

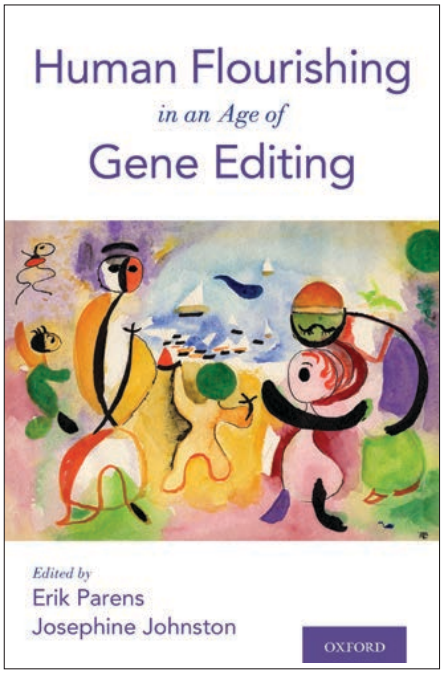
While the US Congress passes secretive, sloppy funding legislation and patent offices in different jurisdictions craft incoherent policies, a hot debate plays out about whether, when, and under what conditions it might make sense to introduce heritable forms of genome editing into human beings. Welcome to science policy in 2020.

Bioethics has come to this game with a profusion of policy statements, guidelines, and suggestions. Three books have come out in close succession that deal with different aspects of reproductive technologies and

genetic methods, or "reprogenetic" technologies. The books are completely different in intended audience and method. All are valuable additions to the literature and build on other excellent books, such as Henry T. Greely's *The End of Sex and the Future of Human Reproduction* (2016), which was written just as the CRISPR debate was gathering steam.

The Canadian bioethicist Françoise Baylis has attended closely to the debate about genomic editing. She attended many of the early meetings, helped plan the famous 2015 International Summit on Human Gene Editing in Washington, DC, and coauthored the March 2019 call for a moratorium on heritable genome editing in *Nature* with lead author Eric Lander from the Broad Institute. The 2015 summit produced a statement that concluded: "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 an appropriate understanding and balancing of risks, potential benefits and alternatives, and (ii) there is a broad societal consensus about the appropriateness of the proposed application."

Baylis's book, *Altered Inheritance,* is a plea for broadening the debate beyond a case-by-case technical assessment of risk and potential benefit. She takes seriously the second criterion for moving ahead: societal consensus. Her approach is philosophical and historical. It is a blow-by-blow account of some of the seminal events, and Baylis marshals her arguments effectively. That is not a backhanded compliment, but rather a real expression of pleasure at her passion and presentation. But one caveat: the volume could have been more tightly edited. The trip would be more pleasant and shorter if it were nonstop, instead of the takeoff and landing for each chapter. The story of how the Chinese researcher He Jiankui used CRISPR to edit the genome of twin girls born in 2018 is told many times in different ways. By consolidating the chronology and avoiding repetition, the book could have been shortened by a quarter.



Human Flourishing in an Age of Genome Editing
edited by Erik Parens and Josephine Johnston. New York, NY: Oxford University Press, 2019, 288 pp.

Baylis takes direct aim at experts who would restrict the debate to technical considerations, and at genome-editing advocates such as the psychologist and science writer Steven Pinker, who in a *Boston Globe* op-ed called on bioethicists to "get out of the way" and stop blocking progress with speculative fears. Baylis rightly points out that, in fact, bioethicists have not slowed progress in genome editing technologies and research, given that clinical trials are underway for many uses that do not entail heritable change. What's more—despite He Jiankui's conspicuous misadventure that made him a convicted criminal in China—there is overwhelming technical agreement that genome editing of human embryos is premature.

Genome editing has captured the public imagination. It has, inevitably, spawned science fiction, copious social commentary, and a messy and protracted process seeking the elusive "broad societal consensus." Baylis argues that such a consensus is not a unicorn. It can be achieved, but not through a restricted technical debate dominated by a technoscientific elite.

Baylis is not alone in calling for broader constituencies to have a direct say in decisions about moving forward with genome editing technology. The science and technology studies professors Sheila Jasanoff and Ben Hurlbut have called for a "global observatory" that would make accessible a range of responses to genome editing, track developments in the various technologies, and convene public discussions of the issue. The underlying arguments are compelling. But whether, when, and how to proceed in the face of real disagreement remains. The choice of "observatory" is itself something of a contradiction, since the overt purpose is to exert some control over the technological trajectory of a human endeavor, not merely to observe stars.

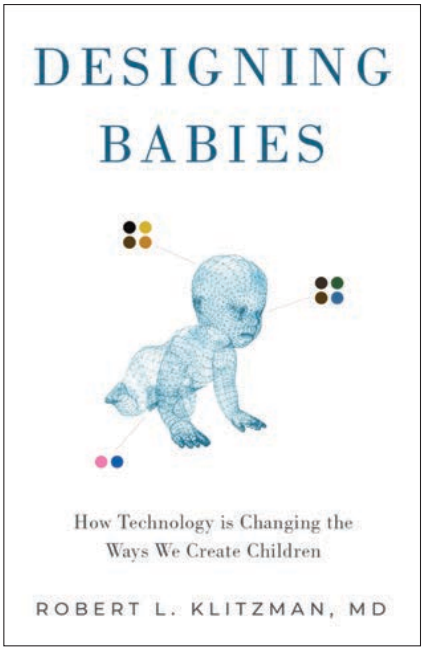
Baylis devotes an entire chapter to "slow science." Proponents of that movement maintain that science is distorted by short-term publication and career goals, and they argue for careful, reproducible, responsible science. All to the good. But they are marching under a banner that will command scant support for slow science in the era of coronavirus and a race for COVID-19 treatments and vaccines. This rhetorical framing is also unlikely to prove persuasive to parents wanting a treatment for Leigh syndrome. To be fair, the argument is not really about speed, but about due diligence and openness, and incorporating the views of those who will be affected by what science and technology come up with. The foreseeable dynamics are confrontations between people primarily concerned about urgent medical problems and those concerned about long-term social consequences. There is strong consensus for careful, transparent, reproducible science, which is the main

point; calling it "slow science" may prove an unfortunate rhetorical choice.

Looming in the background of this debate is how to connect diverse ethical, religious, and political perspectives into policies that govern genome-editing technology. Baylis's book is an important contribution, but its central premise that consensus is achievable is only one possibility, and maybe not the most likely one. Support for the emergence of an eventual societal consensus is provided by in vitro fertilization, which has become widely accepted after vigorous initial debate; recombinant DNA (shuttling DNA among organisms by deliberate engineering); and—more controversially—genetically modified organisms. But there are also examples where societal consensus has remained elusive—embryo research, fetal tissue research, and abortion—despite many decades of intense debate.

At the center of the debate about genome editing is an ongoing cultural dialogue about intervening in the human genome. The Hastings Center, a bioethics research institute, enters this dialogue with a volume that directly addresses human flourishing: what does it mean for a human being to have a fulfilling life? This debate is not unique to genome editing, although that is the context the book explores.

The Templeton Foundation, a philanthropy focused on projects at the intersection of religion and science, funded the Hasting Center's scholars Erik Parens and Josephine Johnston to convene a group of contributors who ultimately produced *Human Flourishing in an Age of Gene Editing.* The collected essays inject a group of voices, augmenting the central arguments in Baylis. The book starts with a bang, an impassioned and beautifully written essay by Rosemarie Garland-Thompson, the disability studies pioneer, who tells her tale of flourishing despite—indeed in part because of—the genetic condition with which she was born and has lived. It is a compelling first-person narrative. Other essays address



Designing Babies: How Technology is Changing the Ways We Create Children
by Robert L. Klitzman. New York, NY: Oxford University Press, 2020, 360 pp.

the role of human dignity and social determinants of health. As a collection, the essays aim to move beyond technical genetic fixes to the human genome, and examine whether interventions at the genetic, individual, or social levels are most appropriate for enabling human flourishing. They address "how should we think about it," rather than prescribe policy solutions.

The book is intended to address issues that the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research "dismissed," in the words of Parens and Johnston, in *Splicing Life*, the commission's 1982 report on the social and ethical issues involved with recombinant DNA. I don't read *Splicing Life* in that way, since it took the Frankenstein myth and religious concerns seriously; but *Splicing Life* did indeed focus on near-term practical decisions that particular government organizations would face. It was a policy report, after all, that focused on immediate policy decisions that both needed to be made and could be made without resolving the broader and longer-term social issues.

Splicing Life's value as a policy document was to address pressing concerns about whether, when, and how to introduce genetic engineering technologies, with implicit faith that the slope was not so slippery that introducing DNA into bone marrow cells to treat inherited immune deficiency, thalassemia, or sickle cell disease would ineluctably slide all the way into *Brave New World* territory. The prospect of treating severe diseases without producing inherited genetic changes required an oversight mechanism, which the National Institutes of Health and the Food and Drug Administration then proceeded to develop between the report's release in 1982 and the first review of gene transfer protocols in 1988. But Parens and Johnston are right that the President's Commission left fallow ground that needed to be plowed. CRISPR technology now rekindles concerns about deliberately altering humans, and the Hastings volume should be part of that debate.

The Hastings volume directly confronts some of the broader issues—particularly limitations of genetic "fixes" to human conditions—that were deferred by the Commission in 1982. It is worth noting, however, that the letter from religious authorities that prompted the *Splicing Life* report was not, first and foremost, about what Parens and Johnston assert: the potential hazards of recombinant DNA. The clerical letter to President Carter did indeed raise that question, and it also raised questions about human flourishing now addressed in the Hastings volume. The immediate precipitant of the clerical letter, however, was the June 1980 Supreme Court decision allowing patents on engineered life forms in *Diamond v. Chakrabarty.* Concerns about commercial biotechnology exercised the clerics most—yet the Hastings Center volume and the Bayliss book only glancingly address the business incentives that religious leaders

worried would lead American culture astray. This is not a bug but a feature of these books. They choose to address the long-term and moral implications of powerful new technologies for changing human DNA. This leaves open the moral, legal, and policy questions raised about commercialization pressures that most worried clerics in 1980. Those pressures have only intensified since 1980 for genome editing and reproductive technologies. Probing the financial incentives and the priorities of the technoscientific institutions engaged in this work is at least as morally fraught as the themes explored in the Hastings essays and Bayliss book, and a challenge for future scholars.

The final book in this triad is Robert Klitzman's *Designing Babies*. Don't let the book's title mislead you: it's about the process of having kids much more than about editing their genomes. Although the book does touch on genome editing, it's primarily based on extensive interviews with people who have experienced technologically assisted reproduction and adoption. Klitzman and his interviewees lay out the real-world choices that people make—surrogacy, in vitro fertilization, preimplantation genetic testing, adoption—in practical detail.

His subjects talk explicitly about costs and trade-offs. Choices that are often posed as alternatives are directly challenged by real-world considerations. Preimplantation diagnosis followed by embryo selection, or adoption, are often posited as two alternatives to genome editing in the bioethics literature, for example, yet both "alternatives" are more likely to fail than succeed. Klitzman explains how and why. Many couples (and most individuals) are ineligible for adoption, and the adoption process can be even more expensive than assisted reproduction. The complexities of domestic adoption are considerable, and international adoption adds even more layers. And the other option—assisted reproduction involving embryo selection—often fails, meaning it's also not a genuine alternative in many cases. Klitzman's book amply illustrates the supremely difficult choices that prospective parents can face, using their own voices, leavened with his review of relevant background facts.

Klitzman's book is organized according to types of decisions facing prospective parents. It's a great title to recommend to those who are contemplating or undergoing medically assisted reproduction or using adoption. But it's a difficult book to read cover to cover because so much work is done by the interview quotes, which are necessarily repetitive and overlap from chapter to chapter.

All three of these books are possible tools for teaching. The volumes by Baylis and the Hastings editors are designed and well suited for academic coursework. Baylis writes with a single voice with a central theme, making for a coherent, in-depth reading experience. The Hastings volume is unlikely to be read straight through, but it's useful as a collection from which teachers can make selections. The Klitzman book is intended for potential parents considering assisted reproduction or people interested in the technologies—not quite a "how to," but rather a "what to think about" book.

Each of these books adresses the arguments that are likely to be raised in policy debates, and each has obvious implications for which constituencies should be involved. None, however, directly grapples with the knotty question of how policy decisions should get made. These books are inputs into, rather than solutions for, the political process of sifting arguments, juggling constituencies, and making decisions about the future of human genome editing and human reproductive technologies.

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