

# **The Ethics of Genetic Engineering**

**Roberta M. Berry**

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Human genetic engineering may soon be possible. The gathering debate about this prospect already threatens to become mired in irresolvable disagreement. After surveying the scientific and technological developments that have brought us to this pass, *The Ethics of Genetic Engineering* focuses on the ethical and policy debate, noting the deep divide that separates proponents and opponents. The book locates the source of this divide in differing framing assumptions: reductionist pluralist on one side, holist communitarian on the other. The book argues that we must bridge this divide, drawing on the resources from both encampments, if we are to understand and cope with the distinctive problems posed by genetic engineering. These problems, termed “fractious problems,” are novel, complex, ethically fraught, unavoidably of public concern, and unavoidably divisive. Berry examines three prominent ethical and political theories—utilitarianism, deontology, and virtue ethics—to consider their competency in bridging the divide and addressing these fractious problems.

The book concludes that virtue ethics can best guide parental decision-making and that a new policy-making approach sketched here, a “navigational approach,” can best guide policy-making. These approaches enable us to gain a rich understanding of the problems posed and to craft resolutions adequate to their challenges.

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**Roberta M. Berry**

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**To my wonderful husband Bill  
With love and thanks for endless support and encouragement.**



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# Preface

Advances in bioscience and biotechnology now enable parents to use in vitro fertilization to create embryos that might become their future children, and then to screen those embryos for a variety of genetically influenced diseases. Parents then can select only non-affected embryos for transfer to the womb. Other advances have enabled researchers to create “transgenic” nonhuman animals—animals genetically engineered for selected genetically influenced features—by incorporating genetic material into the developing embryos of these animals. Continuing advances might make it possible for future parents to create transgenic children—the product not only of screening but of genetic engineering for selected genetically influenced features.

As I contemplate the prospect of “designer babies” and follow the emerging debate, I worry more about how we decide than what we decide. I have confidence in our capacity as practical reasoners to solve ethical and public policy problems around the kitchen table and at the town hall. We have long experience and considerable expertise in solving these problems—they are as much a part of human life as gathering our daily bread and we would not have survived to ponder the prospect of genetic engineering if we were not skilled in both these practical arts. But just as we cannot put bread on the table without the necessary tools for the harvest, neither can we solve the ethical and policy problems posed by genetic engineering without suitable methods for addressing them.

I see the greatest threat to our problem-solving capacity in too-ready deference to and reliance on inapt methods drawn from the disciplines of philosophy, law, and policy. The powerful tools of welfare economics can be very helpful in addressing policy questions that elude our understanding in the absence of data gathering and analysis—about contributions to economic efficiency, for example. And establishing duties and rights can be very effective in preserving and enforcing the practical knowledge we have gained through historical experience of wrongful social conduct—as with treating individuals on the basis of membership in racial groups, for example. But it does not follow that a utilitarian calculus of welfare maximization or a deontological assessment of duties or rights is well-suited to parental or policy decision-making about revising the genomes of our future children.

As the problem of harvesting the field leads us to tools that suit, so the problems of parental and policy decision-making instruct us about apt methods for addressing them. The advent of genetic engineering poses what I call “fractious problems”—novel problems thrown off by advances in bioscientific knowledge and biotechnological know-how that are complex, ethically fraught, unavoidably of public concern, and unavoidably divisive given their ethically fraught nature. The features of these problems pack powerful challenges to our problem-solving capacity.

The primary challenge, I believe, arises in understanding these problems—gaining an epistemological grip on them. I observe, in the gathering debate, that we often disagree about their most basic contours and, in consequence, we argue past each other. This is unfortunate both in fostering an atmosphere of mutual incomprehension or worse and in disabling one of the most important benefits of life in community—the opportunity to engage multiple reasoners in the shared effort to solve practical problems.

While commentators generally argue that the fruitless and often acrimonious debates surrounding issues such as genetic engineering are due to irreconcilable disagreement about religious versus secular values or social versus scientific and technological values or both, I see the matter somewhat differently. These features of fractious problems evoke different and potentially incommensurate ways of understanding our lives as individuals and as members of society, but ways of understanding that are not necessarily irreconcilable. With the advent of the modern scientific and technological enterprise—its enormous success owing in large part to the power of its reductionist methods—most of us understand ourselves, in part, as Darwinian and molecular beings, reducible to our functional and material components, and see our practical choices as amenable to guidance through reduction to risks and benefits, rights and duties. Yet, we remain the holist beings who populate Platonic dialogues, religious texts, the plays of Shakespeare, and the literature of psychoanalysis. With the advent of the modern, pluralistic, democratic state—its enormous success owing in large part to the power of freedom and tolerance in enabling individual flourishing—we are all pluralists now, pursuing our diverse goals pursuant to our diverse commitments. Yet, we remain communitarian in our aspirations as social beings for shared commitments that bind us together.

I observe in the emerging debate surrounding genetic engineering a tendency for debaters to cleave to one pair or another of these ways of understanding the problems: reductionist pluralist versus holist communitarian. Apt methods for addressing these problems, I argue, will cross these divides and integrate these ways of understanding. If we are to understand the problems posed by genetic engineering, we must fully appreciate that we are evolved beings reducible to our genomes and other biological components and that we are also more than and different from that. We must not only respect but honor our pluralistic pursuit of diverse means and goals in procreation and parenting as in all else, and at the same time recognize that

not everything goes when it comes to practices that vitally affect future human beings and members of the political community.

I argue that, in the context of parental decision-making, an ethics of virtue is competent to integrate these diverse ways of understanding and that utilitarian and deontological approaches are not. In the context of policy-making, I sketch and argue for the merits of a “navigational approach” to decision-making as competent to the task, and I argue that other approaches are not. The reason why these methods are best suited to these problems brings us back to our capacity as practical decision-makers. A virtue-based approach to individual decision-making and a navigational approach to policy-making ask us to immerse ourselves in the problems in concrete, contextualized detail, resisting the allure of pruning the problems to fit decision-making principles that may appeal in the abstract but only “work” to the extent we blinker ourselves to the multi-dimensional complexity of the problems before us and these different ways of understanding them.

In individual decision-making about procreation and parenting, we have long experience in confronting practical problems in the rich and untidy detail in which they present themselves to us. We can and do find guidance, I argue, in age-old virtues that have guided decision-makers through these thickets in the past. In policy-making, a navigational approach best captures the methodological merits most perspicuous in common-law decision-making, in which judicial decision-makers navigate from past historical experience of problems with similar features to interim, tentative solutions that carry forward past wisdom tailored to the distinctive features of the problems before them. On a navigational approach, genetic-engineering policy-makers will immerse themselves in the concrete, contextualized details of parental decision-making about genetic engineering and look to our past historical experience of policy-making concerning problems with like features—problems that have arisen at the intersection of bioscience and biotechnology with the practices of procreation and parenting.

These questions about genetic engineering, what and how parents and policy-makers should choose, have asserted their own grip on me over the past several years—riveting my attention in a way that demanded that I attempt to address them. This book is my effort to do so. I wish to acknowledge the people who have contributed to bringing this project to fruition, while noting my ownership of its shortcomings.

I first became keenly interested in the ethical, legal, and policy consequences of the Human Genome Project then underway while on the faculty at Drake University Law School. I am especially grateful to Dean David Walker, who was most helpful in supporting and encouraging my scholarship in this area. While a visiting faculty member at the Notre Dame Law School, I had the good fortune to make the acquaintance of Professor John Robinson, now Executive Associate Dean of the Law School, whose knowledge and insight into issues at the intersection of philosophy and law stimulated and significantly influenced my study of and reflection on the

issues addressed in this book. Professor David Solomon, W.P. and H.B. White Director, Notre Dame Center for Ethics and Culture, encouraged my ambition to develop a philosophical “toolkit” adequate to my research program; his graduate course in ethics and penetrating commentary on the works we studied continue to resonate and influence my work. Harvey Bender, Professor of Biological Sciences and Director of the Human Genetics Program at Notre Dame, introduced me to the wonders of human genetics and graciously invited me to observe his clinical practice, both of which have been key to the development of this project. Professor Kevin McDonnell, Edna and George McMahon Chair in Philosophy at Saint Mary’s College, Notre Dame, became a prized source of knowledge and wisdom about biomedical ethics—in particular on the importance of connecting study, reflection, and practice through engaging concrete problems.

Phillip Sloan, Professor and former Chair of the Program of Liberal Studies and a Professor in the Program in History and Philosophy of Science at Notre Dame, had the most direct influence on this project. Professor Sloan served as my advisor and dissertation director in my Ph.D. program in the history and philosophy of science at Notre Dame. But these labels do not adequately capture the breadth and depth of his intellectual influence and professional and personal support, including the extraordinary effort and care with which he guided, critiqued, and encouraged my Ph.D. dissertation. I continue to try to show my gratitude and appreciation by measuring my interactions with students on his model.

When I joined the faculty of the School of Public Policy at the Georgia Institute of Technology, Professor Susan Cozzens, who was then Chair of the School of Public Policy, was wonderfully supportive of my interdisciplinary research program and drew me into the organization of a trans-Atlantic interdisciplinary workshop on issues in biopolitics, broadening my appreciation of the scope of these issues. The philosophy faculty within the School of Public Policy has provided both warm collegial support and very helpful critiques of a portion of this project. I am especially grateful for the stimulating series of philosophical conversations about works-in-progress hosted by Professor Bryan Norton on his back porch and organized by Professor Michael Hoffmann. I thank in particular the Georgia Tech philosophy faculty and graduate student in public policy and the Agnes Scott College philosophy faculty who participated in critiquing a portion of this work: Jason Borenstein, Lara Denis, Paul Hirsch, Michael Hoffmann, Jon Johnston, Robert Kirkman, Lee McBride, Bryan Norton, and Roger Wertheimer.

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- Berry, Roberta M., "Can Bioethics Speak to Politics about the Prospect of Inheritable Genetic Modification? If So, What Might it Say?" in *The Ethics of Inheritable Genetic Modification*, ed. John E. J. Rasko, Gabrielle O'Sullivan, and Rachel A. Ankeny (Cambridge: Cambridge University Press, 2006), 243–77.
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# **1 Genetic engineering: Past and present as prelude to the future**

## **A. Fractious problems and ethical and policy decision-making**

It might become possible in the not-too-distant future to revise the genome of a child before birth by genetic engineering. If this technology becomes feasible, should parents use it? If so, what features should they strive to influence? What should be the stance of the political community to the possible advent of genetic engineering: should policy-makers aim to promote, prohibit, or regulate its development, provision, or use?

Debate about these questions is well underway and disagreement runs deep. Some envision a future humankind—or successor species—transformed and improved by genetic engineering to reduce suffering and disability, extend life, and enhance our abilities and appearance. For others, there is a sense of foreboding: this new biotechnology threatens radical revision of our practices of procreation and parenting and the social and political fabric in which they are embedded, perhaps undermining our capacity to love and accept children as they are and to accommodate without resentment those with disabilities. Still other debaters hope for and fear less.

To a significant degree, I will argue, debaters frame the issues differently and speak past one another, employing concepts and arguments that do not engage one another. In this respect, the emerging debate seems familiar, like debates about other issues—embryonic stem cell research and end-of-life technologies, for example—that both bedevil the present-day policy-making process and also frustrate individuals concerned to do the right thing but unable to step inside the framing assumptions and embrace with confidence the resolutions proposed by opposed camps.

The issues that generate these debates pose what I call “fractious problems.” These problems share five salient characteristics: (1) They are generated by advances in science or technology that pose novel ethical and policy challenges. In the case of genetic engineering, the challenges arise in the realm of human procreation and parenting. (2) The problems are complex, challenging our capacity to understand and cope with them. In the case of genetic engineering, the complexity inheres both in the science and technology and in their application to the most complex of subjects: developing

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human life in all its interactive dimensions—biological, psychological or “intentional,” and social. (3) They are ethically fraught in that they tap deep secular or religious foundational beliefs—in the case of genetic engineering, beliefs about procreation and parenting. (4) The problems posed are of unavoidable public concern. Procreational and parenting practices involve choices that are intensely personal and private, and recognized as such in law and social practice, and, at the same time, of significant public concern because they affect future members of society. (5) And, in modern, pluralistic, democratic political communities, these problems are unavoidably divisive; the foundational beliefs tapped will be diverse and, in some cases, conflicting in their implications for individual and policy choice.

If these fractious problems seem particularly likely to give rise to unfruitful debate, how might we hope to bridge the divides, foster productive engagement of the issues, and advance the debate in ways that can help individuals and the political community understand and cope with them? For help with this question, we might consider the observations and analyses of philosopher Alasdair MacIntyre and historian of science Thomas Kuhn regarding debates across divides generated by other sorts of problems.<sup>1</sup> MacIntyre claims that modern moral debate is characterized by interminable and irresolvable debate. Partisans argue past each other rather than acknowledging one another’s arguments as worthwhile and engaging them in fruitful ways. Comparing these problems to those identified by Kuhn and others with respect to rival scientific programs, MacIntyre writes of the challenges in resolving disagreement across opposed systems of thought and practice:

[T]here is and can be no independent standard or measure by appeal to which their rival claims can be adjudicated, since each has internal to itself its own fundamental standard of judgment. Such systems are incommensurable, and the terms in and by means of which judgment is delivered in each are so specific and idiosyncratic to each that they cannot be translated into the terms of the other without gross distortion.<sup>2</sup>

Debate across incommensurable systems need not be endlessly fruitless, MacIntyre argues. As in science, tension between opposed systems can yield productive change: debate may reveal that “one of the contending standpoints fails in its own terms and by its own standards.”<sup>3</sup> To this end, MacIntyre identifies and compares three systems of moral inquiry—the Thomist tradition to which he is committed, an “encyclopaedist” tradition encompassing modern moral philosophies such as utilitarianism and Kantianism, and a Nietzschean approach.<sup>4</sup> MacIntyre argues that reconciliation across such systems of thought is possible, citing the example of Aquinas, who stood outside the Augustinian and Aristotelian systems and invited participants from both to make the imaginative leap to a system that

transcended both, drawing on arguments from within both systems to demonstrate their mutual need for the resources of the other.<sup>5</sup>

Kuhn, characterizing theory choice across rival programs in science, describes a “conversion” experience that may follow upon the experience of failure of one’s own system and that is accompanied by an imaginative leap of the sort MacIntyre describes.<sup>6</sup> Defending his characterization of the process against charges of subjectivity in theory choice, he protests:

Nothing . . . implies either that there are no good reasons for being persuaded or that those reasons are not ultimately decisive for the group. Nor does it even imply that the reasons for choice are different from those usually listed by philosophers of science: accuracy, simplicity, fruitfulness, and the like. What it should suggest, however, is that such reasons function as values and that they can thus be differently applied, individually and collectively, by men who concur in honoring them.<sup>7</sup>

So, on Kuhn’s account, there is an independent set of values—even if not a shared standard of judgment based on criteria that can be applied in an algorithmic way—to which rival programs in the domain of science can and do appeal to advance the conversion process.

The debate surrounding genetic engineering involves incommensurability issues more limited in scope and different in kind from those considered by MacIntyre and Kuhn. But if their observations and analyses capture common features of a social dynamic of debates across incommensurability divides, then we might hope that fruitless debate can turn productive across divides of the sort that fractious problems can generate. We might find opportunities for reconciliation or conversion drawing on resources from opposed frameworks or common values or both.

The thesis of this book is that we can best understand and cope with the fractious problems posed by genetic engineering for individual and policy decision-making by methods suited to their characteristics. At the level of individual decision-making, I will argue that virtue ethics provides the best epistemological grip on these problems and the most apt approach for coping with their characteristics. I support this argument by seeking to show the incapacity of the two main competing ethical approaches, utilitarian and other consequentialist approaches, and Kantian and other deontological approaches, and the relative capacity of virtue ethics. At the level of policy-making, I will argue that what I call “a navigational approach” provides a similarly superior epistemological grip and problem-solving capacity when compared to public utilitarianism and public deontology. The epistemological virtues of these methods help us draw on resources that span the divides, united by common values—even if not shared criteria for problem resolution—to advance our individual flourishing and the flourishing of the political community. They hold promise for

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helping us understand and cope with these problems by stepwise, incremental, iterative efforts that cumulatively add to our store of practical knowledge.

The most problematic divide reflected in the debate surrounding genetic engineering, I conclude, is not traceable to opposed foundational beliefs of the sort often cited as the source of irreconcilable individual disagreement and social conflict in debates surrounding fractious problems—beliefs about when life begins, what particular religious or secular tenets require, the nature of scientific discovery and knowledge, the place of technology in society, the proper scope of individual liberty vis-à-vis the state, the preservation of social values. Rather, the most problematic divide arises from divergent ways of understanding the issues posed by novel, complex, and ethically fraught problems that tap into sometimes conflicting foundational beliefs and that unavoidably require some sort of public resolution.

On one side of this divide are “reductionist pluralists.” For the reductionist pluralist, the vast successes of the bioscientific and biotechnological enterprise are primarily owing to the penetrating power of reductionist methodologies in revealing the mysteries of life and enabling the development of biotechnologies that promise benefits inconceivable before the modern era. The reductionist pluralist sees the problems of individual and policy decision-making as amenable to similar methods of reduction and resolution, by calculation of risks and benefits or by application of principles establishing rights and duties. Also key to advancing the frontier of bioscientific knowledge and biotechnological know-how is another methodological approach associated with modernity: the creative, unfettered, pursuit of knowledge and know-how, unconstrained by externally imposed or predetermined goals. A methodological pluralism—in which the decisions of investigators and innovators are propelled by initiative, curiosity, and a willingness to follow the possibilities revealed in the pursuit wherever they might lead—succeeds in advancing knowledge and unleashes the possibilities for beneficial technique. Similarly, for the reductionist pluralist, honoring free choice is the preferred method for coping with problems of individual and policy decision-making.

On the other side of the divide are “holist communitarians.” For the holist communitarian, the reductionist methodologies of the bioscientific and biotechnological enterprise might be recognized as useful but not sufficient in understanding life or in guiding individual and policy decision-making. The results of inquiry and innovation founded solely or primarily on reductionist methodologies will be inadequate because they cannot fully comprehend the subject of study and of the application of technique. Similarly, methods that strive to reduce the issues posed for individual and policy choice to categories of risks and benefits or rights and duties will be inadequate in their comprehension of what is at stake. The pursuit of bioscientific knowledge and biotechnological know-how should be understood as social activities embedded in the ongoing life of the community rather

than independent activities answerable only to the demands of their practice. While day-to-day activities might proceed in a manner best suited to the nature of these activities as unconstrained and freewheeling, the bioscientific and biotechnological enterprise ultimately is answerable to community norms.

This divide between reductionist pluralists and holist communitarians in framing the problems posed by the prospect of genetic engineering is discernable, I will point out, in much of the debate to date. Proponents of genetic engineering tend to draw on reductionist pluralist arguments influenced by one or both of the two dominant ethical theories of modernity: utilitarian and other consequentialist approaches, or Kantian and other deontological approaches. Opponents sometimes draw on deontological approaches but primarily invoke holist communitarian concepts and arguments influenced by a variety of religious, environmental, naturalistic, and other approaches.

I will argue that a virtue-based ethics for individual decision-making and a navigational approach for policy-making offer the most promise for bridging the divide between reductionist pluralists and holist communitarians, drawing on the resources—the different ways of understanding—from across the divide and our common values. My method of argumentation is meant to illustrate my argument: that it will be through immersion in the problems, in concrete, contextualized detail—their historical antecedents and their future instantiations—that we can bridge divides and make incremental, cumulative advances in understanding and coping with the problems posed by the advent of genetic engineering.

I proceed next to a contextualizing discussion of historical advances in bioscience and biotechnology and their ethical and policy implications, followed by a discussion of the present-day state of the bioscience and biotechnology of genetic engineering and the surrounding ethical and policy debate. Then, in Chapters 2–4, I turn to the future to test three philosophical approaches against an imagined future context of individual decision-making by prospective parents. In these chapters, I present dialogues between couples contemplating engineering their future children and “reproductive counselors” (RCs) who bring utilitarian, Kantian, and virtue-based approaches to their counseling. Finally, in Chapter 5, I compare utilitarian, deontological, and virtue-liberal, communitarian, and non-liberal approaches to the policy issues posed by the possible advent of genetic engineering. I then sketch what I call a “navigational approach,” and argue for its epistemological and problem-solving merits, akin to those of a virtue-based approach to individual decision-making.

## **B. Past: Genetic medicine, eugenics, reproductive medicine and counseling**

Beginning in the mid-nineteenth century, modern bioscience advanced rapidly and began to influence the practice of medicine and, by the mid-twentieth

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century, modern biotechnology asserted significant influence on the practice as well. Before the mid-nineteenth century, medicine could offer patients little beyond comfort. By the mid-twentieth century, patients turned to medicine with realistic hope of being cured. And, by the late twentieth century, sophisticated medical interventions routinely saved lives for those who would have had no prospect of survival decades earlier. The empowerment of medicine over the course of a century and a half is largely the story of the infusion of bioscience and biotechnology into the practice.<sup>8</sup> The story of the infusion of genetic bioscience and biotechnology is largely told through three overlapping programs, in genetic medicine, eugenics, and reproductive medicine and counseling.

### *1. Genetic medicine*

While “scientific medicine” began in early modern times, as historian of science Roy Porter writes, “In the short run, the anatomically based scientific medicine which emerged from Renaissance universities and the Scientific Revolution contributed more to knowledge than to health.”<sup>9</sup> In the nineteenth century, Claude Bernard pioneered the use of experimental method in medicine and Louis Pasteur and Robert Koch pursued the relationship between microorganisms and diseases.<sup>10</sup> And the roots of modern research programs in organic chemistry, physiology, cell biology, and, eventually, molecular biology—all with important implications for medicine—are traceable to novel ways of understanding life systems developed by nineteenth-century researchers including Justus von Liebig, Carl Ludwig, and Rudolf Virchow.<sup>11</sup> It was only in the mid-nineteenth century that understanding of infectious diseases, thanks to the work of Pasteur, Koch, and others, led to the ability to operate under antiseptic conditions. And only in the twentieth century were effective cures—sulfa drugs and antibiotics—developed for combating infectious disease.<sup>12</sup>

If effective scientific medicine began in earnest in the mid-nineteenth century, “technological medicine” began in the mid-twentieth, with the advent of sophisticated diagnostic equipment as well as life support, organ transplantation, and other medical technologies aimed at improving or saving lives. Physician Lewis Thomas, reflecting on his life in medicine begun in the 1930s, remarked on the nature of the doctor-patient relationship before the advent of technological medicine: “In my father’s time, talking with the patient was the biggest part of medicine, for it was almost all there was to do. The doctor-patient relationship was, for better or worse, a long conversation in which the patient was at the epicenter of concern and knew it.”<sup>13</sup> Technological medicine transformed this relationship—as well as the expected outcome for the patient:

[With] the advance of medicine’s various and complicated new technologies, the ward rounds now at the foot of the bed, the drawing of blood samples

for automated assessment of every known (or suggested) biochemical abnormality, the rolling of wheelchairs and litters down through the corridors to the X-ray department, there is less time for talking. . . . The hospitalized patient feels, for a time, like a working part of an immense, automated apparatus. . . . The difference can be strange and vaguely dismaying for patients. But there is another difference, worth emphasis. Many patients go home speedily, in good health, cured of their diseases. In my father's day this happened much less often, and when it did, it was a matter of good luck or a strong constitution. When it happens today, it is more frequently due to technology.<sup>14</sup>

The advent of bioscientific and biotechnological medicine introduced ethical and policy issues that persist to the present day. As medicine has grown more effective, access to its benefits has become a significant concern and the contribution of new technologies to escalating healthcare costs, with implications for access, has been noted.<sup>15</sup> And particular questions of fair distribution have arisen with respect, for example, to the allocation of scarce organs for transplantation to patients in need.<sup>16</sup> New technologies have introduced concerns surrounding the loss of doctor-patient intimacy and the implications for the practice of medicine, as noted by Thomas. In addition, these technologies have posed novel questions, for example, about determinations of death and about the circumstances under which life support should be withheld or withdrawn from the gravely ill—and about whether patient care is driven by the demands of technologies rather than the best interests of patients.<sup>17</sup>

While genetic medicine has come to prominence only recently—clinical applications of genetic medicine appear only in the mid-twentieth century—its roots extend into nineteenth-century advances in bioscience as well. Its clinical presence has expanded rapidly with the advent of genetic biotechnologies in the late twentieth century and these technologies have generated their own additional set of ethical and policy issues, many of them arising at the intersection with programs in eugenics and reproductive medicine and counseling.

Research programs in evolutionary science and in genetics were initiated in the nineteenth century with Charles Darwin's theory of evolution and Gregor Mendel's "laws" predicting the transmission of characters from generation to generation. Early-twentieth-century research programs forged a "synthesis" explaining how natural selection might operate in ways consistent with both. In the closing decades of the twentieth century, dissenting theories challenged aspects of the "received view" of evolution founded in this synthesis, and vibrant research programs in sociobiology, evolutionary biology, and evolutionary psychology emerged from the debate, pursuing the implications of evolutionary theory for human behavior, ethics, and policy.<sup>18</sup>

Beginning in the twentieth century, a cross-fertilization of biochemistry and genetics opened up a new field of inquiry as researchers pursued the

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molecular basis of Mendelian genetics. In 1953, James Watson and Francis Crick announced their discovery of the structure of DNA, and a research program investigating how Mendelian characters were related to underlying molecular structures followed in the wake.<sup>19</sup>

With the 1973 discovery by Stanley Cohen and Herbert Boyer of a recombinant DNA technique—allowing a section of DNA to be snipped from one organism and inserted into the DNA of another—new opportunities for research and clinical applications emerged. And new ethical and policy concerns were raised: would recombinant organisms devastate the natural environment? Might this technology open the door to genetic engineering of human beings? In response to these concerns, bioscientists assembled in Asilomar, California, in February 1975, and agreed on a voluntary 16-month moratorium on use of the technique until a governmental regulatory system could be implemented. Thereafter, the National Institutes of Health (NIH) established an advisory committee—the Recombinant DNA Advisory Committee (RAC)—and issued guidelines, pursuant to the advice of the RAC, permitting the use of the technique.<sup>20</sup> From the mid-1970s through the early 1980s, a wide-ranging public debate about safety and broader ethical issues was carried on in a variety of forums, including the National Academy of Sciences, the U.S. Congress, and the federal Office of Technology Assessment.<sup>21</sup>

During this period of public concern and controversy, the emerging biotechnology industry focused on producing products with marketable clinical applications. Recombinant DNA techniques allowed human DNA fragments to be inserted into bacteria to turn the bacteria into manufacturing centers for the biochemical products of the human DNA.<sup>22</sup> By 1978, a small biotechnology company, Genentech, had succeeded in turning bacteria to the production of human insulin. More biotechnology companies joined the race to produce both pharmaceuticals and diagnostic tests, and larger pharmaceutical companies began to turn their attention to the potential of new biotechnological techniques.<sup>23</sup> In the 1980s, a new biochemical technique for replicating pieces of DNA—polymerase chain reaction (PCR)—expanded the range of practical applications. Other techniques were developed and deployed as the numbers of biotechnology firms grew rapidly.<sup>24</sup>

New techniques enabled the creation of an expanding array of transgenic animals for use in further research on genetic engineering, in industrial applications, and as models for the study of disease. Doubts as to the commercial value of these biotechnologies were resolved by a series of court cases establishing the patentability of man-made life forms. In the 1980 decision *Diamond v. Chakrabarty*,<sup>25</sup> the U.S. Supreme Court interpreted the U.S. Patent Act to permit the patenting of genetically engineered life forms—in this case, a bacterium for industrial application in the dissipation of oil spills. In 1988, the first patent for a multi-cellular animal, the “Harvard onco-mouse”—a mouse engineered to be a useful model in the study of cancer—was

issued, prompting a series of unsuccessful court challenges. By the close of the twentieth century, patents for hundreds of transgenic animals had been issued.<sup>26</sup>

Programs in human genetics and clinical genetics initiated in the mid-twentieth century also contributed to the emerging field of genetic medicine. James Neel brought a wide-ranging background in genetics, medicine, and statistical methods to the study of the effects of radiation exposure on the residents of Hiroshima and Nagasaki and their descendants in post-War Japan.<sup>27</sup> Neel's research later expanded to include the study of sickle-cell anemia and other hereditary diseases in various groups. His 1949 research results showed a pattern of recessive inheritance in sickle-cell anemia—those children who inherited recessive genes from both parents suffered the disease. These results coincided with the conclusion reached the same year by Linus Pauling and others based on their study of underlying molecular processes—evidence of the potential for fruitful integration of the ongoing molecular research program with the developing program in human genetics. Neel also was a pioneer in obtaining funding for genetic research both through private foundation support and, increasingly, from federal agencies, including the NIH.<sup>28</sup>

The first clinical genetics department in the United States was established by Victor McKusick, a member of the medical faculty of Johns Hopkins University, in 1957. McKusick's department, connected by research ties with Neel's human genetics department at the University of Michigan, developed an expansive clinical research program investigating genetic disorders of all sorts.<sup>29</sup> Interest in the practical implications of research in clinical genetics grew as breakthroughs in the study of chromosomes—cytogenetics—revealed the cause of Down syndrome and other chromosomal disorders. Physicians increasingly referred patients with family histories of these disorders to clinical geneticists.<sup>30</sup>

By the end of the 1950s, human and clinical genetics were well-established research programs. As historian Daniel Kevles concludes, "Neel's and McKusick's laboratories loomed particularly large on the landscape, but peaks of quality could be seen in most regions of the country."<sup>31</sup>

In the 1960s and 1970s, human and clinical genetics became institutionalized in American medical education, the knowledge base regarding genetic contributions to disorders grew rapidly, and the possibility of screening for a genetic disorder and then treating it became real. In 1960, McKusick initiated a program to teach genetics to medical school faculty during a summer institute; by 1972, "courses in genetics were required in half of all American medical schools and offered in more than three-quarters."<sup>32</sup> By 1971, almost 900 diseases caused by a single gene had been identified, and the effectiveness of screening for a genetic condition, and then treating those affected, was demonstrated in a newborn screening program for phenylketonuria (PKU) conducted between 1966 and 1974.<sup>33</sup>

Advances in the molecular and human and clinical genetics research programs of the mid-twentieth century—and the hope that much more might be achieved—supplied impetus to a new research initiative in genomics.

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Formally begun in 1991, the Human Genome Project (HGP) brought “big science” to the realm of bioscience and biotechnology, with its massive ambition to map and sequence the human genome, multi-year funding, international reach, and involvement of partners in academia, industry, and government.<sup>34</sup> The successful effort to win Congressional support for the HGP evidenced growing confidence in the power of bioscientific and technological advance to generate medical benefits:

[The HGP] was created not by citizens concerned about cancer or heart disease or even genetic disorders, but rather by scientists who argued that a concerted research program was an expeditious way to improve research on all diseases. This was a subtle departure from traditional biomedical politics, in which those affected by a disorder generally lobbied for funds to stop their suffering. The rationale was still ultimately linked, and legitimately so, to preventing the suffering caused by disease. The genome project was initially presented by scientists, however, not disease-group advocates.<sup>35</sup>

Fifty years after Watson and Crick first laid bare the structure of DNA, the mapping and sequencing of the human genome was completed,<sup>36</sup> with the expectation that benefits generated by the HGP and related research programs, eventually, would justify the significant public and private investment.<sup>37</sup>

As the HGP effort was underway, a separate research program in somatic-cell gene therapy pursued clinical application of the knowledge and know-how gained from the medical genetics research programs of the late twentieth century. Gene therapy, generally, entails introducing genetic material into human cells in the hope of compensating for the deficient functioning of genes in those cells or of repairing those genes. Initially envisioned as a possibility in the 1970s, the first approved gene therapy experiment was conducted in 1990. More than 400 clinical trials were conducted over the course of the 1990s. Results were mixed, and less promising than had been hoped at the outset.<sup>38</sup> And the death in 1999 of an 18-year-old experimental subject raised serious concerns about the adequacy of the existing regulatory apparatus, involving the U.S. Food and Drug Administration (FDA) as well as NIH and the RAC;<sup>39</sup> regulatory reform measures were initiated shortly after the subject’s death.<sup>40</sup> Despite setbacks, in the early twenty-first century, researchers continued to pursue the prospect of gene therapy with the hope for eventual clinical success as well as improved understanding of disease processes that could yield other medical benefits.<sup>41</sup>

By the late twentieth century, these interdisciplinary and inter-institutional medical genetics research programs, organized around projects and problem solving, spanned the private and public, the national and international, and industry and academia.<sup>42</sup> This integration yielded an enterprise well equipped to carry its projects from conceptualization to solution, pursuing new opportunities and retreating from dead ends, adding capacities as needed and

dropping outmoded capacities along the way.<sup>43</sup> Reductionist understanding of the evolved, molecular being and a robust pluralism in the pursuit of new knowledge and technique have been central to its success. But the enterprise has also been tethered to the purposes of medicine—curing and relieving the suffering of the whole being—and to the shared social commitment to advancing these goals. Its cumulative accomplishments have brought us to the threshold of human genetic engineering. But before turning to consideration of this future possibility, I return to the past, to examine the historical ties of genetic medicine to programs in eugenics and reproductive medicine and counseling—and to survey the ethical and policy issues generated by these programs.

## 2. Eugenics

Modern eugenics programs, initiated in the late nineteenth century by “founder of the faith” Francis Galton, were incorporated into a broad-based social movement by the early twentieth century. The shared aim of eugenicists was to improve what they believed to be the heritable characteristics of human beings. Some eugenicists, in addition, championed reform measures aimed at improving social influences on human characteristics.<sup>44</sup> Eugenicists in the United States and in Europe advocated both “positive” eugenic efforts, such as encouraging “healthy” parents to have many children, and “negative” eugenic measures, including involuntary sterilization of the “feeble-minded” and others who were “unfit.” The movement engaged activists from across the political spectrum who found common cause in their enthusiasm for the exercise of influence over the human genetic endowment to achieve their goals.<sup>45</sup>

The eugenic movement of the pre-World War II period began in earnest in the United States with Justice Oliver Wendell Holmes’s opinion in the 1927 U.S. Supreme Court case *Buck v. Bell*.<sup>46</sup> That decision authorized the involuntary sterilization of a young woman, Carrie Buck, who was believed—incorrectly, we now know<sup>47</sup>—to be mentally disabled. Holmes wrote:

We have seen more than once that the public welfare may call upon the best citizens for their lives. It would be strange if it could not call upon those who already sap the strength of the State for these lesser sacrifices, often not felt to be such by those concerned, in order to prevent our being swamped with incompetence. It is better for all the world, if instead of waiting to execute degenerate offspring for crime, or to let them starve for their imbecility, society can prevent those who are manifestly unfit from continuing their kind. The principle that sustains compulsory vaccination is broad enough to cover cutting the Fallopian tubes. . . . Three generations of imbeciles are enough.<sup>48</sup>

Holmes was an enthusiast for science and social science and their application in all realms of life, including the law, and a social Darwinian, persuaded of the necessity of weeding out the unfit through reformist social policies. In a

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letter to his British socialist and eugenicist friend Harold Laski, Holmes wrote of his satisfaction in uniting these commitments through his sanction of involuntary sterilization in *Buck v. Bell*:

I wrote and delivered a decision upholding the constitutionality of a state law for sterilizing imbeciles the other day—and felt that I was getting near to the first principle of real reform. I say merely getting near. I don't mean that the surgeon's knife is the ultimate symbol.<sup>49</sup>

The decision in *Buck v. Bell* resolved the question of the constitutionality of state involuntary sterilization measures; by the 1930s, most states had enacted such laws. Tens of thousands of Americans determined to be “unfit” were sterilized involuntarily in the following decades before the repeal of these laws in the 1960s.<sup>50</sup> In 1933, the German Nazi regime, drawing on American experience with eugenic sterilization, enacted an involuntary sterilization law<sup>51</sup> authorizing sterilizations, as Kevles recounts, for:

feeble-mindedness, schizophrenia, epilepsy, blindness, severe drug or alcohol addiction, and physical deformities that seriously interfered with locomotion or were grossly offensive. . . . Within three years, German authorities had sterilized some two hundred and twenty-five thousand people. . . . About half were reported to be feeble-minded.<sup>52</sup>

“Mainline” eugenicists, who advocated policies including involuntary sterilization, were opposed by religious and secular critics, including a number of scientists, who accused them variously of violating human dignity by these coercive measures, unwarranted biological reductionism, excessive focus on bodily perfection, and racism and classism.<sup>53</sup> Opponents also included “reform” eugenicists, who believed the mainline program was fundamentally flawed in its foundation in unsound science and its race- and class-based prejudice; most reformists also opposed involuntary sterilization.<sup>54</sup> Reformists believed that genetic endowments influencing the development of undesirable qualities, such as low intelligence and “anti-social character,” as well as desirable qualities, such as high intelligence and high “levels of activity,” were distributed evenly throughout the population. Any apparent clustering by race or class was owing to unjust social conditions that should be remedied.<sup>55</sup> Some reformists urged that a scientifically sound eugenics that recognized these facts and pursued a mix of social reform and other measures, on the other hand, could supply new meaning to human existence in a post-Darwinian world.<sup>56</sup>

Pre-War reformists, including British scientists J. B. S. Haldane and Julian Huxley, and Americans Hermann Muller and Theodosius Dobzhansky, forged connections aimed at advancing a reform eugenics program and distancing it from mainline eugenics. They sought alliance with the emerging fields of human and clinical genetics and, often, with social reform efforts as

well.<sup>57</sup> To forge connections with human and clinical genetics, reformists prepared books for general practice physicians setting forth information on human genetics and the known inheritance patterns of genetic diseases in hopes that physicians would advise their patients about any risks to their potential offspring. Prominent physicians, such as Lionel Penrose, who were not affiliated with mainline or reform eugenics but who were interested in seeking cures for genetic conditions, sometimes worked in cooperation with reformists in advancing understanding of and the dissemination of knowledge about heritable diseases.<sup>58</sup>

Other reformists promoted efforts to integrate knowledge of human genetics with reproductive medicine and social reform measures. Haldane, for example, in his 1924 utopian novel that inspired Aldous Huxley's *Brave New World*, urged the separation of procreation and sexual bonding; Muller attempted to advance a program to accomplish this, as Kevles writes:

To Hermann Muller, and to twenty-two British and American Scientists who signed his "Geneticists' Manifesto," in 1939, the course was obvious: for the sake of eugenics, replace "the superstitious attitude toward sex and reproduction now prevalent" with "a scientific and social attitude." Render it "an honor and a privilege, if not a duty, for a mother, married or unmarried, or for a couple, to have the best children possible, both in respect of their upbringing and of their genetic endowment."<sup>59</sup>

Both mainline eugenics and reform eugenics faced a far less receptive public in the wake of World War II with the realization of the full extent of the Nazi horror. Mainline eugenics was thoroughly discredited and the reform eugenics program lost many adherents—but far from all.<sup>60</sup> Reformists of the post-War period labored to distance themselves from mainline eugenics and to establish a reform eugenics program founded on sound science and with greater penetration into the practice of medicine. As Diane Paul notes, five of the first six presidents of the American Society of Human Genetics, founded in 1948, were also directors of the American Eugenics Society, a reform eugenics organization.<sup>61</sup> Muller, a Nobel Prize winner in 1946 for his work showing that X-rays could cause genetic mutations in fruit flies,<sup>62</sup> worked to foster the relationship between genetics and the practice of medicine with the founding of the *American Journal of Human Genetics*, writing in the preface to volume 1, number 1, in September 1949:

[A]n unfortunate compartmentalism has for many years hindered persons in medicine and in the other specifically human disciplines from attaining the necessary knowledge of genetics and, *mutatis mutandis*, has hindered geneticists from mastering the more special human subjects. Although this situation has prevailed for over a generation, we believe that the time is now ripe for a fertile liaison, and it is the purpose of the present society and journal to subserve it.<sup>63</sup>

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In the same preface, Muller reflects on the recent past and future of eugenics. In reaffirming the goals of the pre-War reform eugenics movement, he finds fault in the crank science and ill-conceived social measures of the Nazi regime as well as the Soviet regime, which had suppressed genetic science that did not comport with regnant social theory:

There remains, not least, the question of the guidance of reproduction away from genetically less favorable and in the direction of more favorable paths, in other words, the question of eugenics. As we have pointed out above, this whole subject has fallen into disrepute because it has been so perverted by unscientific propagandists and cranks, with hastily conceived remedies which they desired to foist upon the community as substitutes for social measures with which they did not agree. We do not wish this kind of eugenics. . . .

At the same time, we must be careful not to be panicked into throwing away the wheat with the chaff. It is the present writer's considered opinion that eugenics, in the better sense of the term, "the social direction of human evolution," is a most profound and important subject and that it will in due time be worked on seriously, not in a spirit of ill-considered partisanship and prejudice, but in one of scientific objectivity combined with social consciousness.<sup>64</sup>

Muller and other eugenicists pursued the revival of eugenic proposals in subsequent decades, to a mixed reception. In 1949, Muller warned of the "genetic load" caused by retention of mutations due to improved living conditions and medical care that allowed those with mutations to survive to reproduce, and accelerated by man-made radiation in the nuclear age.<sup>65</sup> He predicted a future in which everyone would be an "invalid" surviving only thanks to enormous efforts to "prop up their own feebleesses."<sup>66</sup> And he urged voluntary measures to encourage the healthy to reproduce and those with high genetic loads to refrain.<sup>67</sup> Muller also revived, beginning in 1959, his advocacy of a program of eugenic artificial insemination, now labeled "germinal choice," in an era in which the new technological capacity to freeze sperm made the program more feasible. Enthusiasts included Ernst Mayr of Harvard University, James F. Crow of the University of Wisconsin, and Francis Crick, Nobel Prize winner for his co-discovery of the structure of DNA. But the plan foundered, as Muller and a former collaborator disagreed about what characteristics should be selected for in inviting the deposit of samples from sperm donors—and critics noted that Muller's own views continued to shift over time.<sup>68</sup>

The new generation of post-War researchers in human and clinical genetics showed diminishing interest in the reform eugenics program. Kevles claims that these increasingly sophisticated research programs revealed a complexity that was fundamentally inconsistent with the underlying assumptions of the reform eugenics program, and this drove the new generation away:

"Human genetic research may have been spurred in part by reform-eugenic goals, but the more that was revealed about the complexity of heredity in human beings, the less did eugenics—even much of the reform variety—appear defensible in principle, or even scientifically within reach."<sup>69</sup>

The indifference of bioscientists was matched by active opposition from prominent commentators, including theologian Paul Ramsey and biochemist and physician Leon Kass.<sup>70</sup> As in the pre-War period, religious and secular opponents challenged the eugenic focus on bodily perfection and reductionist assumptions about the nature of human life. Opponents also pointed to practical and ethical questions introduced by the new reproductive technologies of artificial insemination and in vitro fertilization (IVF), such as determining the ownership of embryos and questions of legitimacy and obligations to pay child support for children conceived with donated gametes.<sup>71</sup>

Despite decreasing interest and increasing opposition among the new generation of human and clinical geneticists and the public, the post-War eugenics program continued to exert an influence. Its legacy is discernable in some of the historical practices in reproductive medicine and counseling.

### **3. Reproductive medicine and counseling**

Beginning in the mid-twentieth century, new techniques for screening prospective parents, their early-stage embryos created in IVF procedures, and their fetuses *in utero*, along with the constitutionally mandated legalization of early-term abortions in the U.S. and the development of new assisted reproductive technologies enabled prospective parents to exercise far more procreative control than ever before. These new powers generated new ethical and policy issues as well.<sup>72</sup>

Beginning in the 1950s, clinical geneticists could inform prospective parents of the likelihood that a future child might suffer from the same genetic condition as an earlier born child.<sup>73</sup> By the 1970s, screening tests were widely employed to test members of high-risk groups for carrier status for diseases including sickle cell, Tay-Sachs, cystic fibrosis, and muscular dystrophy.<sup>74</sup> These screening technologies enabled prospective parents to make choices, including forgoing procreation, adopting, or attempting artificial insemination with donated sperm.

By the 1960s, the sex of a fetus could be determined by amniocentesis, revealing the risk of sex-linked diseases such as hemophilia for those with a family history of these diseases. Also in the 1960s, Down syndrome could be diagnosed and, in the 1970s, neural tube defects such as spina bifida.<sup>75</sup> In response to this information, parents could prepare themselves for the arrival of these children or women could choose to obtain abortions—legally available throughout the U.S. after the 1973 U.S. Supreme Court decision in *Roe v. Wade*.<sup>76</sup> Prenatal diagnostic genetic testing increased dramatically in the wake of *Roe v. Wade* and was typically offered to pregnant women "at-risk" due to advanced age or carrier status.<sup>77</sup>

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With the birth of the first “test tube” baby, Louise Brown, in 1978, assisted reproduction moved beyond insemination by use of donor sperm to the creation of embryos by IVF with gametes obtained from social parents, donors, or any combination.<sup>78</sup> Beginning in the 1990s, pre-implantation genetic diagnosis in conjunction with an IVF procedure permitted prospective parents to select only “healthy” embryos for transfer to a woman’s uterus.<sup>79</sup> And, beginning in 2006, by the technique of pre-implantation genetic haplotyping, embryos could be screened for a greatly expanded array of genetic conditions.<sup>80</sup>

This rapidly expanding set of options was accompanied by rapid growth in genetic counseling. The ethos of genetic counseling from its inception in the 1940s through the 1960s, on Diane Paul’s account, was that “the heredity of the population should be a matter of public concern.”<sup>81</sup> In the 1970s, the U.S. Department of Health, Education, and Welfare encouraged prenatal testing, explicitly embracing the policy goal of preventing disability through abortion.<sup>82</sup> During that decade, however, this approach was gradually supplanted by a new ethos of client autonomy and choice according to their own values.<sup>83</sup> By the late 1970s, there was near consensus that genetic counseling should be non-directive and client centered. The goal of the profession was to inform and support clients in their reproductive choices, not to attempt to advance any public interest in the heredity of children.<sup>84</sup>

Despite the apparent neutrality of the non-directive approach, the selective transfer of embryos and the abortion of fetuses on the basis of genetic condition or gender have generated complaints that the healthcare system effectively encourages “eugenic” choices.<sup>85</sup> Regarding abortion to avoid having children with disabilities, Diane Paul writes:

Policy makers generally assume that individual and social interests are congruent, that families will act “rationally.” . . . [T]he assumption that normal people will do what they can to avoid the birth of children with disabilities has a long history. . . . By the 1960s, it seemed politic to drop the old label for this program. As Frederick Osborn wrote in 1968, “Eugenic goals are most likely to be attained under a name other than eugenics.” Of course eugenics and reproductive choice are congruent only if families ordinarily make the “right” decisions.<sup>86</sup>

Paul identifies “subtle pressures” to make the “right” choice: women may “feel pressured to be tested and avoid having children with disabilities—by their doctors, who fear being sued if the child is born with a genetic disorder, by anxiety over the potential loss of health or life insurance, by their inability to bear the enormous financial costs of caring for a severely disabled child, or by the lack of social services . . . for handicapped children.”<sup>87</sup>

Even if reproductive counseling does generate subtle pressures of this sort, a return to the coercive eugenics of the past seems very unlikely. On Kevles’s account, while new genetic technologies may open new possibilities for troublesome consequences, we have effectively turned the corner on coercive

eugenic policies. Any proposal for coercive negative eugenics would face widespread public opposition and a coalition of powerful partners—consisting of newly empowered former target groups for eugenics—spearheading the opposition. The regime of constitutionally protected reproductive rights developed in the last quarter of the twentieth century serves as an additional bulwark against any attempt by a majority to impose a coercive eugenic plan on an embattled minority group.<sup>88</sup>

The ethical and policy issues raised by the application of new knowledge and technique in the realm of reproductive medicine—and associated counseling—have ranged from safety issues, to issues surrounding claimed eugenic aims, assumptions about the value of human life, and subtle coercion. Defenders of new reproductive technologies have pointed to their contributions to reducing the incidence of genetic disease, with its associated suffering and other costs, and to enabling more individuals to experience the joys of procreation and parenting.<sup>89</sup>

Critics of eugenics programs noted its reductionist understanding of human life—both in the insistence of mainline eugenicists on the genetic basis of disfavored human features and in the assumption of mainline and reform eugenicists that the sum of human features constituted the value of human beings. This reductionism was combined with a communitarian commitment to a “fitter” population, whether pursued by voluntary or coercive eugenic practices. The distinction—challenged by some—between eugenics and latter-day reproductive medicine and counseling, then, lies in the latter’s embrace of the medical conception of the whole person—albeit informed by a reductionist understanding of the basis of heritable disease—and in its rejection of the communitarian goal of fitness in favor of the plural goals of clients. This brings us to consideration of the prospect of genetic engineering and the gathering ethical and policy debate.

## **C. Present: The prospect of genetic engineering, the gathering debate, fractious problems and decision-making**

### **1. The prospect of genetic engineering**

Although the possibility of engineering the human germ line began to be widely discussed in the period following World War II, the state of bioscientific knowledge, medical reproductive art, and biotechnological technique was clearly inadequate to the task.<sup>90</sup> Now, at the beginning of the twenty-first century, there is growing confidence, at least among its proponents, that human genetic engineering will one day be feasible.<sup>91</sup>

LeRoy Walters and Julie Gage Palmer, in their 1997 book, *The Ethics of Human Gene Therapy*, survey the range of potentially feasible and desirable interventions based on then-current understandings of genetic contributions to various phenotypic features—and on successes to that point with engineering transgenic animals.<sup>92</sup> Although they acknowledge serious “techni-

cal” challenges, in particular with enhancement of complex polygenic features such as intelligence, they express optimism that at some point engineering for a number of features will be possible. In an appendix to the book, Mario R. Capecchi discusses the state of the art for engineering transgenic nonhuman animals: targeted gene replacement.<sup>93</sup> As he explains, techniques have advanced from the crude injection of genetic material into the nucleus of a fertilized ovum—in hopes that some would be incorporated at some point on a chromosome and would become functional—to the more sophisticated technique of homologous recombination.<sup>94</sup>

Homologous recombination involves extracting embryonic stem (ES) cells from an early embryo and injecting them with genetic material. The genetic material is spliced into the correct position on a chromosome, replacing the existing homologous material, by a natural repair mechanism within the cell. These revised ES cells are then reinserted into the embryo; some of the cells of the animal that develops from this embryo—those descended from the revised ES cells—will contain the substituted genetic material.<sup>95</sup> This technique can be used to “knock out” certain stretches of genetic material so that the resulting animals can be studied and inferences drawn about the developmental influences of the deleted material.<sup>96</sup>

While applying a similar technique in humans has been contemplated,<sup>97</sup> Lee Silver, in his 1998 book, *Remaking Eden*, notes that the risks of unintended harm—now experienced in the production of transgenic animals—would be unacceptably high. He predicts that by the middle of the twenty-first century, however, safe and effective human genetic engineering might be accomplished by another technique—perhaps by inserting artificial human chromosomes into fertilized human ova.<sup>98</sup>

Gregory Stock, in his 2002 book, *Redesigning Humans*, also is optimistic that genetic engineering technology eventually will be developed and deployed.<sup>99</sup> He too discusses the use of artificial human chromosomes—referring to techniques developed by John Harrington and Huntington Willard in 1997. He notes that as of the late 1990s, biotechnology companies, pursuing the use of artificial chromosomes for other purposes, had succeeded in achieving replications through multiple divisions of human cells in culture and multiple generations *in vivo* in mice.<sup>100</sup>

Stock envisions that gene modules and their regulatory sequences might be inserted on artificial “auxiliary” chromosomes for use in human genetic engineering.<sup>101</sup> Initially, Stock proposes, the modules would be based on beneficial gene variants copied from nature; this would enable us to proceed even without comprehensive understanding of their workings. As a precaution against unintended and unanticipated negative consequences, a mechanism for turning off the activity of these gene modules might be included. Also, in conjunction with genetic engineering, genes on the original natural chromosomes could be “silenced”—preventing their expression—to avoid harmful consequences from the presence of both original and new versions of the genes.<sup>102</sup> On the accounts of Stock and Campbell, artificial chromosomes

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