The Genetic Frontier

Some scientists say human engineering is possible, and imminent. But is it a good idea?

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"No one really has the guts to say it." James Watson, codiscoverer of the structure of DNA, tells a panel of the world's leading molecular biologists in 1998, before putting the lie to his own statement by bluntly asking *the* question: "If we can make better human beings by adding new genes, why shouldn't we?"

It's typical Watson rhetoric, reported by Gregory Stock in his book *Redesigning Humans: Our Inevitable Genetic Future*. All the same, as our information technologies are increasingly turned upon the data in our own genes, humans who would be longer-lived and smarter—and perhaps saner—seem a feasible, attractive project to many people besides simply Dr. Watson. Conversely, for many other observers, the notion of a self-designed human species is disquieting. For some, it's loathsome. Playing God, losing our humanity, employing Nazi-style eugenic programs, and instating genetic apartheid: foes of human genetic enhancement darkly recite a standard litany of such charges.

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Amid the tizzy on both sides, how likely is it that we will manipulate human genes in any meaningful way within the next two decades? After all, serious practical obstacles exist. Critically, many traits we might desire to upgrade—for instance, intelligence and aging—appear not to correlate to single genes, but to be caused by large numbers of them and regulated by networks of other genes and poorly understood loops of RNA, transcription factors, and, surely, undiscovered mechanisms.

Hence, our scope for genetic engineering through single-gene fixes may be severely limited, as are our current abilities to fix single genes. Besides, talk of designer babies and "posthumans" reeks of both science fiction and self-improvement cultism.

History suggests that predictions of millenarian transformation based on a single technology are reliably wrong: today, for example, society enjoys neither the nuclear-powered vacuum cleaners nor the domed cities that 1950s pundits forecast, nor even the commuter moon shuttles and artificially intelligent androids of Stanley Kubrick's 1968 futurist film classic, *2001: A Space Odyssey*. So a hefty dose of skepticism might be mandatory in examining genetic engineering's current claims about the not-so-distant future.

Still, as *The Genomic Revolution: Unveiling the Unity of Life* attests, substantial developments are already under way.

This book, edited by Michael Yudell and Robert DeSalle, began as a collection of 17 papers written by various life sciences luminaries for a fall 2000 conference hosted by the American Museum of Natural History. Contributors include Craig Venter, who led Celera Genomics to produce a usable sequence of the human genome years ahead of schedule, and Leroy Hood, who pioneered the technology for rapid automated DNA sequencing. [Disclosure: Dr. Hood sits on the scientific advisory board of Acumen Sciences, which publishes this journal.]

These figures were asked to speak about the nascent technologies on the frontier of biological science. Ironically, in trying to maintain the nonspeculative, sometimes bland tone that most scientists regard as responsible (Dr. Watson is notably absent from the book, and Dr. Venter is on his best behavior), they effectively underscore the idea that we are in fact closer to a new scientific dawn than many people, especially nonscientists, may realize.

The majority of researchers and clinicians in this book express themselves in the sober, circumscribed terms of their technical expertise. Specialists in *in vitro* fertilization talk about specific issues related to the conception, handling, screening, and implantation of human embryos—not about how such techniques might allow intervention in embryonic genes. Likewise, researchers trying to solve the problems that impede hundreds of ongoing gene-therapy programs worldwide discuss cures for particular diseases that real people suffer, not how such genetic interventions could be applied in embryos.

Nevertheless, as Mr. Yudell and Dr. DeSalle's introduction notes, their contributors' restrained discussions of "genetic enhancement technologies, gene therapy, [and] genetically modified organisms…consistently conjure up visions of Aldous Huxley's *Brave New World*."

All in all, *The Genomic Revolution* makes clear that a great deal of human genetic alteration could be done by simply using reproductive and therapeutic technologies we already possess. Somatic gene therapy, which affects a patient's body cells, except for those destined to become sperm or eggs, has already yielded some success with certain immunodeficiency diseases and genetic disorders like cystic fibrosis. Germ-line intervention, which would alter the genes in an embryo's inaugural cells, thereby modifying those of the resulting adult, would sidestep the myriad difficulties that somatic gene therapy confronts in ferrying therapeutic genes to specific targets within a patient's tissues; therefore, germ-line intervention would probably be simpler to manage than similar therapy in whole organisms.

And so, despite their restrained tone, papers in *The Genomic Revolution* bear titles like "Mapping Morality: The Rights and Wrongs of Genomics" and "Redesigning the Self: The Promise and Perils of Genetic Enhancement."

One set of chapter coauthors pauses to predict candidly: "There will be winners and there will be losers." If habitually restrained scientists feel compelled to write such things, it's hard not to speculate that, as progress in genomics and molecular biology accelerates, some limitations hitherto seen as immutably part of human life may not survive the next hundred years. Nobody in the past, for instance, thought we could introduce the firefly's luciferase gene into plants to make them glow.

One could argue that the thrust of biological development has been headed toward human self-design ever since gene lines produced the first animals that beyond executing inherited behaviors, learned new ones. But as the late Harvard University biologist

REDESIGNING HUMANS: OUR INEVITABLE GENETIC FUTURE
By Gregory Stock
Houghton Mifflin, 288 pages, $24

THE GENOMIC REVOLUTION: UNVEILING THE UNITY OF LIFE
Edited by Michael Yudell and Robert DeSalle
Joseph Henry Press, 249 pages, $28

OUR POSTHUMAN FUTURE: CONSEQUENCES OF THE BIOTECHNOLOGY REVOLUTION
By Francis Fukuyama
Farrar, Straus and Giroux, 272 pages, $25

TOMORROW NOW: ENVISIONING THE NEXT FIFTY YEARS
By Bruce Sterling
Random House, 224 pages, $25

Stephen Jay Gould delighted in explaining, evolution doesn't favor complex, intelligent organisms; viewed statistically, most successful life remains in the bacterial mode, even though the drive toward adaptation and variation has, over time, produced organisms of greater complexity (like us) at the far end of evolution's simplicity-skewed bell curve.

Any argument for human genetic self-design as evolution's inevitable continuation consequently derives, Gould would have stressed, from an anthropocentric view of evolution. Such an argument would be essentially teleological, based on explaining material phenomena by the higher purposes they're presumed to serve, rather than their actual causes.

Ironically, little would separate the notion that there is an imperative to human self-design from Francis Fukuyama's opposing, but equally teleological, arguments in *Our Posthuman Future: Consequences of the Biotechnology Revolution* (see "Closer to God," page 83); both assume an ultimate purpose to human evolution.

A decade ago, Dr. Fukuyama, now a professor of political economy at Johns Hopkins University, argued in his book *The End of History and the Last Man* (Avon Books, 1993) that history was over, in a qualified sense. Henceforth, U.S.-style democracy and free markets would provide the format for all future human societies. Now, in *Our Posthuman Future*, Dr. Fukuyama sticks to that thesis but allows himself the wiggle room provided by biotechnology.

A posthuman species, he writes, could signify "the recommencement of history." That would be a Bad Thing, by the professor's estimation. Dr. Fukuyama is disturbed by what he calls "speciesization," or the forking of the race into two families: one genetically enhanced to be swift, clever, memorious, altruistic, and long-lived; the other ... less so.

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Even if a genetic elite didn't lord over an underclass of unmodified humans, the emergence of a genetically bifurcated society would be the end of our universally shared human nature. This would be a Very Bad Thing, in Dr. Fukuyama's teleological view of matters: the creation of human beings as they now exist has been evolution's whole purpose.

An argument could be made that a posthuman world in which the verities of human nature amounted to no more than chaff in the breeze—where another Auschwitz was inconceivable, but also in which the sad, beautiful insights of Sophocles and Shakespeare were about as meaningful as birdsong—would be an unbearable price to pay for genetically engineered transcendence. Dr. Fukuyama doesn't make that argument; instead, he meanders through European philosophy's greatest hits, emphasizing thinkers—Aristotle, Locke, Rousseau, Mill, and the like—who promoted notions about "natural rights" derived from human nature.

Again, one might construct a persuasive argument that those thinkers provided civilizational software, laying the groundwork for a society in which humans are as coöperative, logical, and humane as human nature allows. The author doesn't put forth that argument either.

In the final analysis, he fails to explain how human nature inevitably produces human rights, why those human rights automatically mandate against human genetic enhancement (rather than for it), and how he defines human nature (except that it shouldn't be genetically enhanced). Finally, he illustrates the inherent error of discussing the ethics of genetic enhancement without understanding the emerging technologies for its implementation.

Like most opponents of human genetic engineering, Dr. Fukuyama posits "superbabies" as the central abomination that we must prevent. But why would anybody attempt a highly problematic human germ-line intervention with permanent consequences when any of the desired genes could be much more precisely targeted, and made to express themselves as and when they were wanted? For an idea of how this alternative could work and how much better and tidier it could be, consider Gregory Stock's *Redesigning Humans.*

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This book is an encyclopedia of fascinating possibilities. In particular, one genetic technology that the author describes is the use of human artificial chromosomes—or HACs—which are auxiliary chromosomes that could be introduced to supplement a patient's regular genome or, eventually, inserted into the first cells of human embryos.

In either case, since they would come without functional human genes of their own, any HAC would thus comprise a kind of inert scaffolding or harness into which medical geneticists could plug whatever genetic modules a subject might want: genes for HIV resistance, for instance, or for more efficient muscles. Furthermore, any genetic module within a person could be turned off or deleted, say, when an upgrade became available.

The beauty of this scheme, as Dr. Stock points out, is that HACs do not alter genes on the natural chromosomes and, theoretically, circumvent the customary argument against genetic modification—that it risks passing harmful traits permanently into the human germ line.

"Imagine that a future father gives his baby daughter chromosome 47, version 2.0," Dr. Stock writes. "By the time she has a child herself, she finds 2.0 downright primitive. . . . She may be too sensible to opt for some of the more experimental modules for her son, but she cannot imagine giving him her antique chromosome." Sound like science fiction? Think again. Artificial bacterial chromosomes have existed for years.

The pioneering work on an artificial human chromosome was done at Case Western Reserve University in 1997 and was much more simple than everyone thought it would be. Researchers added the separate components of chromosomes into a nucleus, and these components essentially self-assembled into a smaller chromosome that cellular machinery replicated and distributed to daughter cells, though not as accurately as it did natural chromosomes.

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At least two companies, Athersys in Cleveland and Chromos Molecular Systems in Burnaby, British Columbia, plus the Murdoch Children's Research Institute in Parkville, Australia, are developing the technology.

In short, as the science fiction writer and journalist Bruce Sterling puts it in *Tomorrow Now: Envisioning the Next Fifty Years*, "Corny ideas about the ubermensch are . . . outdated Victorian and Nazi kitsch from the 19TH and 20TH centuries. They are not realistic concepts about the true potential of DNA."

While merely appropriated by folks like Dr. Fukuyama, the term *posthuman* was coined 20 years ago by Mr. Sterling, who has been ruminating about the subject ever since—most notably, in his famous novel *Schismatrix*. His first nonfiction book in a decade, *Tomorrow Now*, is equal parts contemporary cultural analysis, futurism, and a bracing history of science.

Here, for example, is Mr. Sterling on the practical problems of designer babies: "First, logically and necessarily, must come the *alpha-rollout* of a superbaby."

In other words, in the real world there must be a beta-release superhuman, which is really no kind of superhuman at all, as Mr. Sterling clarifies when he further addresses that prototype's predicament. "When you finally become 21 years old, genetic understanding is 21 years deeper and broader than it was when you were first put into production. So you're not only a hack job—you're also an antique."

Moreover, Mr. Sterling continues, "There are already better, faster, and cheaper ways of doing whatever it was you were genetically altered to do. And these are probably not inscribed within human eggs, the way your alterations were. ... Normal humans [have] advanced genetics they can plug and play."

Unfortunately, the importance or even the benignity of human germ-line intervention will not silence the opponents of human genetic enhancement. "Darwin's *Origin of Species* is the inspiration of genetics," Mr. Sterling writes. "Darwin's book was written way back in 1859. In 2059 people will still be in frank denial about its revelations."