Published in final edited form as:
Am J Bioeth. 2005 ; 5(3): 21–W9.

Evaluation of Genetic Enhancement: Will Human Wisdom Properly Acknowledge the Value of Evolution?

Marilyn E. Coors and **Lawrence Hunter**
University of Colorado School of Medicine

Sandel's condemnation of any technology for human genetic enhancement as ungrateful for the "gift" that is our genetic heritage fails to properly engage with the process that shaped that heritage (Sandel 2004, 55). By attending carefully to what evolution tells us about the nature of human biology, it becomes possible to acknowledge the profound challenges of properly managing the risks inherent in genetic enhancement, while granting that there may be potential benefits to a technology that is nearly inevitable. Rather than simply reject enhancement because it interferes with our relationship to nature as Sandel does (humans interfere with nature every day in both beneficial and harmful ways; Sandel 2004, 62), we propose that there is a non-obvious value in our genetic heritage (as a product of evolution) that should be balanced against the sometimes-competing values embodied in human desires. Furthermore, this balancing provides a reasoned approach to the evaluation of proposed genetic enhancements that is applicable to the practical cases that are likely to confront us shortly.

The rapid adoption of related biomedical interventions such as cosmetic surgery and performance-enhancing drugs suggest that human genetic enhancement will likely happen as soon as it appears safe and "effective." However, enhancing genetic interventions will be particularly difficult to evaluate, for reasons beyond the uncertainty surrounding what should count as an "effective" enhancement. An appreciation of how our genetic heritage arose, and of how it unfolds in the life of an organism, should give pause to those who would advocate treating genetic enhancements as just another instance of the kinds of enhancements alluded to above. In addition to concerns raised elsewhere about, for example, deleterious social consequences of individually beneficial genetic modifications, we wish to emphasize the difficulty of making safe and effective enhancements to evolved systems in the first place. In order to design safe and effective departures from naturally occurring genomes (i.e., enhancements), biomedical researchers must correctly predict the phenotypic consequences of previously unobserved genetic combinations. There are two related aspects of our genetic heritage that make this task particularly difficult. First, the process of evolution does not prefer modular designs; instead, biomolecular systems are densely interdependent. Second, most genes appear to be pleiotropic, meaning that they have multiple functions, which further complicates the understanding of the system as a whole. These characteristics of evolved systems suggest that the challenge of discovering genuinely enhancing genetic alterations will be much more difficult than designing therapeutic ones.

While the insertion of foreign genes into laboratory animals (and some agricultural organisms) has sometimes succeeded in creating the desired function, there is no way to assess how often such attempted interventions have failed. Furthermore, the potential dependence of the response to a foreign gene to the entire genetic background (i.e., every specific detail of the genome) of the host means that interventions that appear to function as predicted in one organism may have a completely different effect in another, even if the two organisms are closely related. It is for this reason that a genetic change can have radically different consequences among people; what is safe for one may not be safe for another. An illustrative example can be drawn from the recent molecular biology literature. p53 is a well-studied gene that has been highly conserved throughout the evolution of animals. p53 is so well studied primarily because damage to it is observed in a very large number of human cancers (DePinho 2000). Our current understanding of its function is that it detects damage to DNA, triggering either repairs or, in the case of damage that cannot be repaired, causing cells with damaged DNA to stop replicating or even die (Itahana et al. 2001; Ryan et al. 2001).

One might therefore imagine (as some have) that an increase in p53 activity would be protective against cancer. Such a vision would be typical of the idea behind many potential genetic enhancements: If gene X plays an important role in valuable process Y, making more of X will lead to more Y, which would be a good thing. Yet our genomes are not so easy to understand, and the balancing act achieved by evolution may be more delicate than we imagine. In 2002, an accidental error in an attempt to modify to the p53 gene created a line of mice that overexpressed the gene, (i.e., those mice created much more p53 in their cells than normal mice do; Tyner et al. 2002). These mice developed normally and did, in fact, have a reduced incidence of tumors. However, despite their resistance to cancer, the altered mice died younger than their normal counterparts. Furthermore, the altered mice appeared to age at an accelerated rate, showing such symptoms as osterporosis, atrophy of muscle and skin, weight loss, and depletion of hematopoietic stem cells (Campisi 2002). Increasing p53 production beyond its normal level did prevent cancer, but it also caused premature aging.

Several possible explanations for this counterintuitive observation have been suggested (Campisis 2002), but what is relevant to the idea of genetic enhancement is that even modest alterations in the best studied genes can, by virtue of their position in densely interdependent biomolecular systems, have completely unexpected consequences for aspects of the organism that were not at all suspected to be related to the function of the gene. Another concern raised by the dense interconnectedness of living systems and illustrated by this example is the possibility of harms to the host from putatively enhancing genetic interventions which take a long time to become apparent, and occur in systems that were not *a priori* thought to be related to the intervention.

While evolution does not produce optimal or perfect organisms, it has explored a very large number of genetic variants that were not as successful as the organisms that exist in the present day. While not impossible, it is awfully hard to do better than evolution; any modest genetic alteration that would increase our reproductive fitness even by a tiny amount would have been rapidly distributed throughout the human population. The idea that human minds, with our newfound (and still quite basic) understanding of molecular biology could design genuine improvements over our evolved genetic heritage is an idea bristling with hubris.

Kamm (2005) worries “whether we have the ability to alter ourselves without making things worse”; we clearly share this concern. The desire for enhancements by a public ill-equipped to understand the molecular biological detail of any proposed intervention, coupled with the financial incentives on the part of promoters of the technology, have the potential to lead to grievous and potentially irremediable harms to many individuals. It is this potential that drives us to recommend that any proposed somatic cell genetic intervention for purposes of

enhancement be tightly regulated by a body of experts without financial conflicts of interest, much as therapeutic interventions are. Germ line genetic enhancements raise distinct intergenerational ethical issues that are outside the scope of this response (Coors 2003).

A thorough analysis of each intervention should weigh the anticipated beneficial consequences against the anticipated harmful consequences including an evaluation of the state of existing knowledge and possible unanticipated consequences both for the individual and society, now and in the future. The consequentialist weighing of harms and benefits is necessary but not sufficient to assess proposed genetic enhancements. It is the exercise of human wisdom that empowers us to choose a mean between imprudent experimentation and outright rejection of potentially desirable technology when assessing enhancement. Wisdom is linked to truth, knowledge, and reason; it is the disposition to deliberate correctly on what is good or bad, and to consider how to act well in order to live well. The goal of enhancement is living well, and we contend wise choices in its pursuit will be difficult. Wisdom requires the use and extension of our knowledge of the evolutionary processes that created our genetic heritage, and the humility to recognize and appreciate the importance of aspects of that heritage that are not yet fully understood. Public opinion or sentiment based on shallow values, ephemeral fads, and market demand cannot substitute for this wisdom if we are to assuage Kamm's concerns.

Hans Jonas, a twentieth-century philosopher who proposed an ethic that emphasizes the role of wisdom in the genetic age, stressed predictive wisdom, which is the ability to recognize the limitations of scientific knowledge and the confines of human ability to predict the ramifications of that knowledge. Predictive wisdom acknowledges that it is not possible to know with certainty the future results of present actions (Jonas 1984). As such, it encompasses the virtue of humility, revived by Jonas to correlate with the magnitude of human control over our genome. Humility in this new role emphasizes the "excess of our power to act over our power to foresee and our power to evaluate and to judge" (Jonas 1984). Our impending power to alter our genetic heritage, which arose as a result of billions of years of hard-won experience, coupled with a limited ability to predict the consequences of alterations to an evolved system, cries out for a cautious and humble approach. Wisdom requires nothing less.

References

Campisi J. Between Scylla and Charybdus: p53 links tumor suppression and aging. Mechanisms of Ageing and Development 2002;123:567–573. [PubMed: 11850020]

Coors, ME. The matrix: Charting an ethics of inheritable genetic modification. New York: Roman & Littlefield; 2003.

DePinho RA. The age of cancer. Nature 2000;408:248–254. [PubMed: 11089982]

Itahana K, Dimri G, Campisi J. Regulation of cellular senescence by p53. European Journal of Biochemistry 2001;268:2784–2791. [PubMed: 11358493]

Jonas, H. The imperative of responsibility: In search of an ethics for the technological age. Chicago: University of Chicago Press; 1984.

Kamm. Is There a Problem With Enhancement? The American Journal of Bioethics 2005;5(3):5–14. [PubMed: 16006376]

Ryan KM, Phillips AC, Voudsen KH. Regulation and function of the p53 tumor suppressor protein. Current Opinions in Cell Biology 2001;13:332–337.

Sandel M. The case against perfection. The Atlantic Monthly 2004;293(3):51–62.

Tyner SD, Venkatachalam S, Chol J, et al. p53 mutant mice that display early ageing-associated phenotypes. Nature 415:45–50. [PubMed: 11780111]