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Managing Cell and Human Identity

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Emerging scientific discoveries and new technologies that aim to improve human health challenge our understanding of what it means to be human, with individuality and personal will, among other traits. Perceptions of being and the boundaries between us and other species may be disrupted by our potential to manipulate genes and their expression, regulate cellular functions, and replace tissues for interventions to improve the quality of life as a result of trauma, disease, and aging. As we gain a greater understanding of genetic complexity, molecular mechanisms, and cellular and tissue functions, enabling technologies aimed at modifications could, in theory, also be applied to enhance our physical and cognitive abilities. In this Perspective and during an upcoming Symposium at the Institute for Regenerative Medicine at the University of Pennsylvania (1), we consider how the normative and historical discourse about human identity may help us decide if, how, and when to use genetic, stem cell, and reproductive technologies that may change characteristics of our cells and thus, perhaps, our individual and human identities. Just as challenging ethical questions and deliberative reflection occurred when whole organ or tissue donations were first established, such questions have been raised again about new advances in altering genes and gene functions, replacing cells, and engineering tissues for regenerative medicine.

For example, the ability to isolate blood forming stem cells from a person with sickle cell anemia to correct the underlying gene mutation (2) can allow the corrected stem cells to be returned back to the person to prevent, ameliorate, or cure the disease (3). Blood cell gene repair is an extension of existing technologies such as bone marrow transplants. Diseases may directly or indirectly affect human behavior and therefore correcting harmful mutations could impact one's sense of personal identity. In theory, but genes in central nervous system cells could also be modified, which may affect functions that influence mentation or affect. This is not new in medical history, as curing or alleviating suffering, altering mental states,

and establishing new capacities has long been associated with radically new ideas about the self and its limits.

Gametes, which carry deep religious and philosophical importance, might be altered to avoid specific mutational errors. Indeed, skin biopsy cells from a mouse can now be reprogrammed genetically to the pluripotent stem cell state and then directed into functional oocytes (4). Currently, unresolved technical barriers prevent this from being done with human cells and ethical issues would have to be resolved as well. Clinical application could be problematic in proving its worth, when other options exist to address infertility and the risks of hereditary disorders. But the concept raises the question of control over human destiny.

We suggest that classic discourses about personal identity are relevant to current ethical debates about whether and when to apply such technologies. Moral appeals to beneficence have long driven arguments on behalf of technological progress, and long-standing human yearnings potentiate the calls for radical biological interventions. Such appeals are countered by competing appeals that challenge this drive and raise questions about the ethical, social and legal implications of such technologies. We believe that we will be better able to make decisions enabling or restraining complex and morally vexed medical research if we begin with a better understanding of historical narratives about embodiment and will.

Philosophical and theological discussions about the nature and meaning of personal human identity have stimulated debate since at least the 5th century CE. They have animated the philosophy and theology of the Middle Ages, and have informed early modern thought. John Locke argued that mere physical identity, the persistence of the body over time, is insufficient to capture the meaning of selfhood, which must rather be associated with consciousness and moral sentiments. Rene Descartes employed methodological doubt, noting that the very act of being in error about his own existence ensures that, at a minimum, he must exist even if only as an entity that is in error. In the course of examining mind-body duality, David Hume argued that, upon introspection, he was unable to identify a “self,” only a perpetual bundle of perceptions. The same is true of our perceptions of what we take to be the external world, Hume contended, so that we not only attribute the idea of selfhood to our internal perceptions, but ideas like causation to our experience of the external world. In response, Immanuel Kant developed a complex account of the rational subject that self-legislates the regularities that govern the external world, making experience possible. William James produced an account of the self within the framework of the nascent science of psychology that utilized both introspection and the results emerging from 19th century physiological laboratories. His position, neutral monism, viewed the mental and the physical as two ways of describing the same entity. For some analytic philosophers, the “mind-body” problem is altered by scientific disciplines such as neuroscience, which has made new claims about the fragility of perception. Some philosophers argue that consciousness itself is simply a construct of a wholly material brain (5). However, phenomenologists and many theologians have focused on the stability of perception as central to the idea of the self and the irreducibility of consciousness.

Central to our concerns is considering whether new technologies in gene editing and regenerative medicine will affect the above historical arguments and our perception of self-identity. If the self is partly but not wholly body, then does it matter if we edit a gene, replace cells, or change an organ? Since our body is part of, or contributes significantly to, our identity and how we see ourselves, any alterations in its structure or function impacts that identity. Alterations of brain cells or grafting cells into the brain, where personal identity is formed, maintained, and changed over time with new experiences is obviously of greater concern. At the other end of the spectrum of continuity throughout biologic life, commonplace measures of identity, such as fingerprints, iris patterns, and digital vein branching are unlikely to be altered by any intervention during life. Yet if the self is partly but not wholly continuity of memory, then does it matter if the change in memory is due to traumatic brain injury or a neural implant? Indeed, there are manifold characteristics over which an individual can exert a degree of control. Learning from experience can result in rewiring of the brain, which many would argue alters identity.

There are wide variations in genomes and epigenomic states, as well as life experience and learning among humans, and each parameter significantly impacts human identity. Nonetheless, alterations in even a single gene, either in the germ line or in somatic cells, may have a profound affect on a person's identity. In the former case, a mutation causing a severe Mendelian disease greatly affects many, if not most, aspects of life. Similarly, a somatic mutation leading to a malignancy can profoundly alter a person's sense of self. Such a genetic change could be as important for one's sense of self as a debilitating injury. While manipulation of the human genome has the potential to modify one's self-identity, as we learn about the complexity of the gene regulatory networks, currently it is risky to predict how any manipulation may ultimately affect all aspects of our phenotype. Yet as the power of bioinformatics grows and researchers learn more about human genomes and epigenome dynamics, we may learn more about the underpinnings of any human moral gesture.

Though they are related, questions about what can be considered a human being can be distinct from those of selfhood. For example, if non-human cells contribute to cell replacement, forming an interspecific chimera, is the patient rendered other than human? Is this a matter of degree (i.e., how many cells are replaced) or of kind (which cells and organs are affected), or both? People who receive xenotransplants (e.g., porcine heart valves) are not generally considered less than or other than human, but that view might not apply to, say, neural regeneration. While it is now possible to grow human organs in animals for transplantation (6, 7), in practice, outside of the CNS, most concerns with grafts between species deal with the passage of viruses to the human patients and outlawing the grafting of human 'reproductive' cells into animals. In the end, human beings may be forced to answer the question whether being human is what is important or rather continuing to be a person possessed of certain morally valuable traits, such as the ability to love and to be compassionate – recognizing that some humans can lack these traits as well.

Perhaps in a century, the term "human being" will be an object of nostalgia rather than a single moral category. Technologies for enhancing cognitive, psychological, and physical abilities could initiate a supra-human or "transhuman" phase of our evolution, with unknown long term consequences (8,9). We have emphasized to this point the implications of direct

interventions for therapies and enhancement. Perhaps just as important is how new technologies will shape our expectation of what it is to be, or remain, human, considering our personal desires to improve ourselves beyond a given normal human capability. For example, there is a major emphasis on research to enable us to slow the aging process and live longer. If these efforts are successful, we and our culture could be transformed. Along with the power to alter our own life form, we have increasing power to alter the life forms around us, which will also modify how we view ourselves. While it would seem that our place in world would be considered differently if human hands at the lab bench fundamentally change animal and plant life, humans have performed agriculture for millennia.

Despite all of the aforementioned considerations, the urgency to rebuild ourselves following disease and injuries impels many patients to want therapies now, without a concern for how the technologies being used on our cells or bodies may impact human identity. How will the imperatives of such patients influence the future goals of realizing therapies and enhancements? We suggest that by considering the complex question of what it is to be an embodied human, we will be better able to make decisions not only about ethically defensible medical research for therapies, but also whether we should progress toward a supra-human future.

References

1. Symposium on Managing Cell and Human Identity, Institute for Regenerative Medicine, University of Pennsylvania; April 26, 2017;
2. Dever DP, et al. *Nature*. 2016; 539:384. [PubMed: 27820943]
3. Ribeil JA, et al. *N Engl J Med*. 2017; 376:848. [PubMed: 28249145]
4. Hikabe O. *Nature*. 2016; 539:299. [PubMed: 27750280]
5. Dennett, D. *From Bacteria to Bach and Back*. W.W. Norton; 2017.
6. Wu J, et al. *Reprod Domest Anim*. 2016; 51(Suppl2):18.
7. Yamaguchi T, et al. *Nature*. 2017; 542:191. [PubMed: 28117444]
8. Harris, J. *Enhancing Evolution: The Ethical Case for Making Better People*. Princeton University Press; 2007.
9. Church, G., Regis, E. *Regenesis. How Synthetic Biology will reinvent nature and ourselves*. Basic Books; New York: 2012.