POLICY FORUM

BIOSCIENCE AND LAW

Biotechnologies nibbling at the legal "human"

Recent advances in the biosciences invite reconsideration of fundamental legal concepts such as the definition of "human"

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The law has always viewed living human beings—and the tissues, organs, and other body parts derived from them—as special and different from the nonliving, nonhuman. But bioscientific advances are nibbling away at classical legal boundaries that form the bedrock of the normative structures on which societies are based. Recent developments such as in human genetics, neuroscience, and cell and tissue research pose qualitatively different challenges than what has come before, seeming to blur legal distinctions between human beings and other living organisms, between living human beings and dead ones, and between human tissues and cells and nonhuman ones. Although cognizant of the important bioethical and philosophical debates surrounding the issues raised, we focus on how legal systems may respond to these bioscience challenges to traditional binary, legal classifications. Determining whether some "thing" is now some "one" carries with it profound implications for the rights and obligations the law recognizes for "humans." Although it may be tempting to think that these new developments require us to reconsider the time-honored legal definitions of humans, living humans, or human tissue, we suggest that current legal dualisms can be applied in ways that provide adequate flexibility to allow weighing the many issues that surround developments in genetics, neurosciences, and cellular bioengineering and challenge how we legally define what is "human."

Recent advancements in the neurosciences, such as the possible revival of "dead" pig brains, pose issues for our understanding of both cognition-based conceptions of identity and even death itself. In the context of cell and tissue research, the creation of synthetic human entities with embryo-like features (SHEEFs) and human-animal chimeras create penumbras in our accepted legal taxonomies of organisms. CRISPR technologies may lead to likely widely acceptable somatic gene therapies for serious inheritable conditions while also leading to germline editing that affects future "humans," to say nothing of possible frivolous genetic enhancement.

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CLASSICAL DUALISMS

The classical dualisms found in legal systems around the world—whether animal versus human, person versus thing ("property"), living versus dead, drug versus device, or enhancement versus therapy—are already in the process of being "retranslated" under specific legislation or by the courts, creating new terms such as human genetic identity or integrity (*1*), common heritage of humanity (*2*), human species, crimes against humanity (*3*), and membership in the human family (*4*). Being "human" is the legal starting point for these concepts. But is the definition of "human" in the legal sense understood? Is it under threat?

As stated in Article 1 of the Universal Declaration of Human Rights, all human beings are "born free and equal in dignity and rights" (*4*). Predicated on the inherent dignity of human beings, human rights and their correlative obligations find their basis in legally recognized personhood. With their framing and internal normative hierarchy, laws provide security and certainty for human interactions in society and in the world. Any proposals for the reclassification of legal and regulatory boundaries surrounding the definition of "human" generally could do well to first understand the complexity and plasticity of the classical dualisms, of the biotechnologies, and of the regulatory ecosystem.

Reference to the inherent dignity of humans as "members of the human family" (*4*) may serve as the legal filter for degrees of protection before birth and after death. The law starts with the position that any living organism born from a person is a natural person from at least the time of birth until the time of death, but things quickly become more complicated.

The special treatment of "humanness" does not apply only in that period or to legal persons. All countries provide some protection for the embryo or fetus through abortion laws, fetal protection laws, limits on embryo research, and other ways. The approaches range from constitutional recognition of legal personhood at conception [for example, (*5*)] to the 14-day rule regarding research on embryos [for example, (*6*)].

Similarly, legal systems use different ways of defining the end of personhood through death. Most jurisdictions declare death, and end rights, when there is either irreversible cessation of cardiopulmonary functions or of all brain functions. But missing persons can, in many jurisdictions, be declared legally dead after a long period when they are not seen. Even after death, the tissues of (former) humans are legally entitled to special treatment; some countries provide distinct treatment to human remains from particular populations, such as with the Native American Graves Protection and Repatriation Act in the United States. Sometimes legal natural persons will lose the benefits of data protection legislation if their data are "anonymized," making them, for that purpose, a kind of "nonperson."

Some are tempted to consider consciousness or self-consciousness, or the likely resumption of either, as a crucial legal criterion for membership in the human family, as a definition of the end of life or possibly of its beginning (*2*).

GENETIC IDENTITY

It could be argued that the human genome defines "human." The definition of the human genome adopted by the United Nations (UN) Educational, Scientific and Cultural Organization (UNESCO) in 1997 was that it "includes both the genetic makeup of humanity as a whole and of the individual genes in their tangible form (genetic material) and genes in their intangible forms (genetic information)." Thus, UNESCO maintained that it is the human genome that "underlies the fundamental unity of all members of the human family as well as the recognition of their inherent dignity and diversity" (*7*). References to human dignity, genetic identity, or genetic integrity are used to prohibit human reproductive cloning (*7*, *8*), human germline intervention (*9*), and eugenics (*8*). For example, human reproductive cloning is deemed to be incompatible with human dignity under the 2005 UN Declaration on Human Cloning (*10*) or even as a crime against the human species (*3*).

The vast diversity of human genomes means there is no single "human genome" but billions of them, to say nothing of the billions belonging to the deceased. Their overlap with the genomes of clearly nonhuman organisms creates another problem, as does their vast overlap with, and substantial contribution from, our extinct cousins, Neanderthals and Denisovans. "The human genome" is made still more problematic by the possibility of humans carrying genetic variations never before seen in our species, either from editing or from natural mutation. Genomes change with every human generation. In short, there is no defined "human genome" that can be used as an easy way to determine humanity.

SPECIES IDENTITY

Humans are biological organisms on an evolutionary continuum, in the same biological kingdom as other animals, and science shows that we share the vast majority of the human genome with other clearly nonhuman species. But new research techniques, such as xenotransplantation and human/nonhuman chimeras, challenge the animal-human species divide and that of "human life" with its broad spectrum as opposed to living, natural persons with legally recognized rights and obligations. The creation of chimeric embryos by introducing human stem cells to animal embryos often falls between the gaps of the relevant human and animal legislation (*11*). The status, and rights, of some nonhuman animals with no human cells continues to be contested. A U.S. court recently rejected an effort to extend the writ of habeas corpus to chimpanzees, thus allowing for their continued imprisonment, although not without an interesting separate opinion discussing their "human" qualities (*12*). Merely considering animals "things" in law may be falling out of favor [for example, (*13*)].

NEURO IDENTITY

Is it the brain then that defines "human"? The size and complexity of the human brain distinguishes it from those of other species. However, similar to the case of consciousness, we include individuals with cephalic disorders, including anencephaly, in the human family. Initial legal recognition of brain death allowed the law to keep pace with accepted medical standards. Now, there is evidence of some false positives, in which "noncritical" brain functions continue despite the individual being considered dead. We may have gone from a situation before the adoption of the brain death standards in which it was possible to be biologically dead but legally alive, to one of being biologically alive but legally dead. And what should we do with human neural organoids or large portions of ex vivo human brains that are kept "active"? What about the great apes, dolphins, and other nonhumans with impressive cognitive capacities?

The boundaries between enhancement and therapy, of human and cyborg, also present legal issues. Freedom of conscience and of thought, some of the oldest concepts to be protected through human rights, may need to be reworked in response to neuroenhancements. The right to self-determination may need to be extended and articulated through a right to use, or to refuse, neuroenhancements (*14*).

CELLS AND TISSUES

Whereas regulatory oversight and approvals govern the classification and distribution of drugs and devices and provide transparent public gateways to the market, the demarcations regarding human tissues and cells are increasingly fluid, and public safety is at stake. The United States, Europe, and Japan all take importantly different approaches to medical uses of cell therapies. In order to exercise jurisdiction over and regulate autologous stem cells therapies and their use in rogue clinics, the U.S. Food and Drug Administration classified such cells as "drugs" (*15*). Similar legal contortions will no doubt occur in the future as bioengineered therapies will be considered products or devices, depending on their inclusion of human cells.

Parties the world over also continue to dispute questions of rights in cells or tissues that clearly were once part of a legal person or—in the case of frozen embryos, sperm, or eggs—things that might in the future give rise to a legally recognized person. To date, court decisions hover between classifying such cells and tissues as either property or potential persons, often looking to how the parties themselves understood the cells and tissues. Sometimes, the disputes are determined through the law of persons, seeing the tissues and cells as an extension of the (human) self. Or yet still, destruction of stored cells and tissues may be required under environmental protection law because they are considered to be medical waste.

MOVING FORWARD

Against this movable feast of "human" rights and biological developments, do the classical legal boundaries still matter, and if so, why? Altering the legal meaning of "human" ultimately affects the foundation for all human rights. Between legal classifications of biomedical waste and legal obligations to future generations, both the certainty that law provides in human interaction and the content of the concomitant duties and freedoms it accords are at stake.

"Hominum causa omne jus constitutum est" ("All law is created for the sake of men") is a maxim from Roman law and is the origin of most legal systems the world over. It epitomizes the relationship between "man" and law. Uncertain boundaries can lead to unintended and untoward legal consequences, which only intensify when one considers the effect of judicial decisions. A new classification has the potential to affect and bind all future parties while unsettling the past. Irrespective, classical dualisms continue to serve as frameworks for legal determinations in most specific contexts. Courts, scientists, and physicians continue to be creative in their interpretations of emerging biotechnologies and in the imposition of necessary limits across the dualisms. Regions of the world with different cultural values concerning the beginning or end of life or on the use of tissues and cells still remain subject to the international umbrella filter of "human" rights. Our traditional approaches to this may not be badly out of date, but they need to be applied flexibly. So, what can we suggest as a way forward?

We care about living organisms that are human in their characteristics, but they do not always need to have exactly human characteristics. "Human beings" typically have two arms and two legs, but we recognize as human those without all those limbs, through amputation or congenital condition, as well as people with artificial limbs. Possession of a "human genome" is part of being a legal natural person, but we need to recognize both that a genome is neither in itself sufficient (a human lymphocyte is not a legal person) nor, in exact detail, necessary. Like the body, the genome needs only to be "substantially" human. Unusual or rare variations are not disqualifying in themselves but form part of the decision. The same is true of humans with some tissue from nonhuman organisms or some mechanical implants. It is also true of nonhuman organisms with some human tissues or DNA; a mouse with a human immune system should not be seen as substantially human or a natural legal person. Similarly, some version of "substantially" could be applied to definitions of brain death, not to require some kind of "higher brain death" rule but to avoid complexity when small bits of living brain, either in vivo or in vitro, are used to assert that the legal natural person still lives.

What constitutes "substantially" in these contexts will not be measurable by percentages or similar specific tests but will be a judgment call—like many such legal terms, such as "unreasonable" or "best interests." Using "substantially" will not provide an exact answer but will give the decision-maker (judge, jury, or other) some guidance, just

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as "beyond a reasonable doubt" says something more than "preponderance of the evidence" when considering the burden of proof and "reckless" means something beyond "negligent" when considering culpability for injuries. For the most part, this should be possible in the interpretation of the meaning of the word "human," without requiring new legislation. As a result, its application may vary from judge to judge and culture to culture while still, as a concept, providing some useful guidance.

The other big question is when we treat molecules, cells, tissues, organs, or bodies as "human" in terms of deserving respect. Again, "substantially" might be a useful part of the definition. Additional consideration may include whether the body part was ever a part of a natural legal person. If a kidney grew in a natural legal person, that argues for it being "human" even if it had a very odd morphology, function, or even genome. A kidney grown totally in a laboratory, even if a fully human kidney, may not deserve respect if it was never inside or "part of" a natural legal person. But a kidney from a pig, genetically modified to function in a human, might not be viewed as "human tissue" while in the pig but be so viewed if it had functioned inside a natural legal person for years.

We have attempted to address the classical legal dualisms defining "human," an approach that may be useful to the law, at least until our cultures arrive at better ways of understanding and approaching these new realities. Rules that include the word "substantially" are never fully satisfying. Nevertheless, in a universe where things blend into each other and living organisms are not cleanly divided into Platonic natural kinds, they may be the best filter we can apply: a malleable term for contextual and proportionate evaluation. "Substantial" is already a term in, inter alia, copyright and data protection law and therefore is an analytic tool the law already possesses. Such rules here will no doubt still lead to close or contested decisions—how to treat a SHEEF for example—but we believe that more frequently they can lead to results that we are (substantially) comfortable with while still preserving the core of our legal dualisms. In practice, our human families do not always meet exact definitions with perfect edges, but we can see substantial connections among them. On the spectrum from living cell to organism to human being, with all their new biotechnological variations, to a natural, legal person (alive or dead), perhaps the concept of membership in the hazily bordered human family can serve as a useful source for the delimitation of the "human." ■

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ACKNOWLEDGMENTS

The authors thank M. Beauvais for his invaluable editorial and research assistance. The article was made possible by a grant from the WYNG Foundation. The article is the joint contribution of B.M.K. and H.T.G. It was inspired by an international think tank on the topic (Montreal, 9 to 11 June 2019). The authors declare no competing interests.

10.1126/science.aaz5221

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Science **366** (6472), 1455-1457.
DOI: 10.1126/science.aaz5221