
Contemporary Ethical Issues in Stem Cell Research

Valerie Gutmann Koch, Beth E. Roxland,
Barbara Pohl, and Sarah K. Keech

Introduction

Recent developments in stem cell technologies hold out the promise of finding treatments and cures to a wide range of conditions and diseases. With these advancements, however, come ethical concerns. Some ethical issues have been the focus of extensive commentary and analysis since the derivation of human embryonic stem cells (hESCs) in 1998 [1]. In particular, literature and policy debate have focused on the ethical appropriateness of using human embryos for stem cell research [2, 3]. As research in the field of hESCs has advanced, the debate evolved from focusing solely on the propriety of destroying embryos for research purposes to a broader discussion of appropriate methods of creating embryos for research [4–6]. Much attention has been generated in response to the technique of somatic cell nuclear transfer (SCNT)—in which the nucleus of a somatic, or differentiated, cell is placed into an oocyte, usually after the oocyte’s nucleus has been removed, thereby creating a type of cloned cell [7]—including whether SCNT will encourage

human cloning for reproductive purposes [8, 9]. Additionally, ethicists and policy-makers have endeavored to address the development of human-animal chimeras [10], by focusing on the normative concerns related to animal welfare and questions about whether the creation of chimeras implicates notions of human dignity and the moral acceptability of crossing the “species barrier.”

In light of the substantial literature on these topics, this chapter will focus on more contemporary bioethical issues central to individuals’ participation in stem cell research as “human subjects”—both in the initial stages of research (as donors of gametes, somatic cells, or embryos) and, as the research progresses from bench to bedside, where humans may be participants in stem cell clinical trials or patients receiving innovative therapies. Both the acts of donation to stem cell research and participation in stem cell clinical trials are considered human subjects research, and protocols must adhere to the core principles of research: beneficence, respect for persons, and justice [11, 12]. Beneficence and its corollary, non-maleficence, place responsibility on researchers and research institutions to maximize the benefits and minimize the harm to subjects [11]. Respect for persons requires recognition of the importance of individual autonomy and personal decision-making [11]. Finally, justice dictates the fair distribution of the risks and benefits of research, as well as availability of the products of research, across individuals and populations [11].

This chapter explores how these core ethical principles may be implicated in research requiring donations of gametes, embryos, and somatic cells and in clinical trials of stem cell therapies. The first section of this chapter addresses certain rights of individuals who donate biological materials for the purposes of hESC research, including the necessity of providing voluntary informed consent and how compensation for participation may affect the voluntariness of such consent. The second section will evaluate ethical issues relating to the study of stem cell-based therapies in humans.

V.G. Koch, J.D. (✉)
New York State Task Force on Life and the Law,
Chicago Kent College of Law, 90 Church Street, 4th Floor,
New York, NY 10007, USA
e-mail: valeriegkoch@gmail.com; vgk01@health.state.ny.us

B.E. Roxland, J.D.
NYU School of Law, 40 Washington Sq., S., New York, NY, USA
e-mail: broxland@alumni.law.upenn.edu

B. Pohl, M.A.
New York University, Center for Bioethics, 285 Mercer Street,
9th Floor, New York, NY 10003, USA

S.K. Keech, J.D.
Columbia University Mailman School of Public Health,
722 West 168th Street, New York, NY 10032, USA

Issues Arising from Donations of Biological Materials to Human Embryonic Stem Cell Research

Autonomous decision-making about donating biological materials for stem cell research requires the provision of fully informed, voluntary authorization or agreement [11]. It obligates institutions and researchers to disclose the nature and purpose of the research, as well as the potential risks and benefits of participation, in a manner that promotes true comprehension of the information provided.

While ensuring that fully informed, voluntary consent can be challenging to all forms of stem cell research and human subjects research generally, it may be more complicated in the hESC research context due to the complexity of the research, the potentially wide distribution of stem cell lines derived from donated biological materials, the downstream potential of this research, and the provision of compensation for participating in research through acts of donating. Donations to stem cell research also challenge the central notion of what it means to “participate” in research, particularly when examining various stakeholders’ rights to control, direct, or financially benefit from stem cell lines and other derivative products that have been substantially altered from the original donated material.

Consent to Donation of Clinically Excess Gametes and Embryos for Research Purposes

Gametes and embryos typically are donated to stem cell research after they have been harvested in the context of reproductive treatment (i.e., in vitro fertilization (IVF)) but are no longer considered clinically necessary. Analyzing the adequacy of informed consent for donation of clinically excess gametes and embryos requires an examination of (1) whether the donor was apprised of all alternatives to participating in the research by donating, (2) the timing of the consent in relation to the transfer of the materials to the research protocol, (3) the specificity of the consent to research, and (4) from whom consent was obtained.

First, in order for an individual to make a fully informed decision to participate in research, he or she must understand the alternatives to participation. In the case of donating clinically excess gametes and embryos to stem cell research, donors should be apprised, at a minimum, that these materials may be (1) provided to others for procreative purposes, (2) donated for research, or (3) destroyed [5, 13].

Second, at the initiation of the reproductive treatment, those undergoing IVF are often offered the option of providing clinically excess gametes and embryos to research after the treatment is either successful or halted for other reasons.

The timing and nature of this initial consent raise ethical issues when it is relied on as the sole consent to donation to stem cell research. It is unlikely that a general consent to research at the beginning of a reproductive process would include specific information regarding the nature and type of research that would occur if the excess biological materials were donated to research. Individuals also may not be fully aware of the consequences of their decision to participate in a specific research project or the implications of allowing derivation of stem cell lines from excess materials. Individuals also likely would not be apprised of any new information generated after the time of the initial consent, including possible advances in research techniques or additional alternatives to donation. Obtaining re-consent—particularly where such re-consent is more specific to the research study and the potential risks and benefits of participating in the research—closer to the time of transfer to the research facility may help obviate concerns that the individual did not make a fully informed choice about participating in research. However, because of the difficulties in tracking down individuals for re-consent after significant time has elapsed, many commentators have asserted that it may also be ethically acceptable to use gametes and embryos in stem cell research if general consent to research was provided at the time gametes or embryos were harvested for IVF purposes [6] and re-consent is prohibitively difficult [4].

Third, when considering the donation of clinically excess embryos to research, determining which parties should provide consent research is a contentious issue. In other research contexts, informed consent need only be provided by a singular person who may become a research participant. In contrast, to procure an embryonic stem cell line, multiple parties’ autonomy rights may be implicated—including those who have control or custody of embryos (who may or may not be biologically linked to the embryos) and third-party donors of gametes (who may have intended those gametes to be used only for reproductive purposes) [4, 6, 13]. Because the parties who have dispositional authority over the embryos may not be the same individuals whose biological materials comprise the embryo, significant privacy and autonomy concerns arise [14, 15].

Ethical Issues Arising from Stem Cell Line Banking and Wide Distribution of Lines

Once stem cell lines are derived, they are commonly deposited in stem cell banks for storage and distribution. These repositories maintain records of donor information, such as ethnic background, infectious disease screening results, and medical history, so that proper lines will be disseminated to researchers seeking to study certain traits or diseases [16]. These repositories facilitate information sharing among

researchers regarding stem cell lines available to the scientific community and promote efficient domestic and international transfer of lines [16]. But while banking and registries help facilitate research, they also raise a host of autonomy issues for donors.

Consent to Future Research

As a basic aspect of informed consent, a participant should comprehend the nature and type of research in which they may participate. However, while researchers may be able to disclose and describe to gamete, embryo, or tissue donors the types of research they intend to conduct with any stem cell lines derived from their biological materials, the eventual banking and wide distribution of the lines makes it a near impossibility either for the researcher to disclose or the participant to consent to all types of future research. This particularly applies once stem cell lines are transferred internationally, where research rules may differ substantially from those in the donors' home countries.

At a minimum, an effective informed consent process should make donors aware of whether they will be able to place restrictions on immediate or future uses of their donated tissues. In order to allow for future research using donated biological materials, it is necessary for potential donors to understand that derived stem cell lines may be kept and stored for many years and used in future studies and that future research protocols may use the lines in ways that are currently not known or unforeseeable. Although the option of allowing donors to consent to certain types of research but not others has been considered [6], doing so would arguably impede research and may be practically unenforceable. Some jurisdictions have dealt with this issue by ensuring that donor consent forms clearly state that if the individual is uncomfortable with the idea that stem cell lines derived from their biological materials may be used in ways that are unknown at the current time, they should abstain from donating [13].

Withdrawal of Donated Materials from Research

Stem cell research challenges traditional notions of research "participation" and its attendant rights—including the right to withdraw from the research. According to generally accepted principles of human subjects research, any participant who enrolls in a research protocol has the right to withdraw from the study at any time without prejudice [17].

The issue of withdrawal arises on two levels in stem cell research: the right to withdraw the originally donated biological materials and the right to withdraw the stem cell lines derived from these materials. It is generally accepted that a donor has the right to withdraw his or her biological sample until the time the sample has itself been used in the research [5]. A donor arguably has the ethical right to withdraw consent to the usage or storage of any tissue that has not been

used in the research. Currently, most ethical guidelines include the opportunity to withdraw consent up until an individual's gametes or embryos are used in cell line derivation and/or when identifying information has been stripped from the donated sample [4, 15].

However, the issue of withdrawal becomes more challenging once stem cell lines have been derived, manipulated, and combined with other biological materials, implicating a key concern: at what point—if any—is the original donor no longer considered a participant in research?

For those who believe that these downstream products are tied inextricably to the original donor (regardless of the degree of derivation and manipulation), the donor arguably should have the right to withdraw not only his or her actual biological sample but also the stem cell lines derived therefrom. Others counter that the protections contained in human subjects research laws and regulations were originally conceived in order to prevent involuntary participation in research [18], particularly protocols involving physical harm or bodily violations. Depending on how one defines "research participant," it may follow that once derivations and manipulations of stem cell lines have proceeded, the original donor does not have the same rights and is not entitled to the same degree of protection as other research participants. Notably, however, existing policy and current academic literature appear to acknowledge that the US federal rules and regulations governing informed consent for research with human subjects also apply to most research with biospecimens, except in some limited conditions [19–21].

Drawing a line after which withdrawal is prohibited—regardless of where that line is drawn—calls into question donors' continued status as a research participant and implicates their autonomy interests and privacy rights [22, 23]. It also gives rise to concerns related to bodily integrity and property rights in the tissue [24].

Importantly, even if the right to withdraw downstream stem cell products is ethically appropriate, its practical unenforceability could render the right moot. More specifically, worldwide distribution of stem cell lines—which are almost universally coded or otherwise de-identified—may severely limit the ability to trace or identify the lines a donor wishes to withdraw [23]. Accordingly, it is essential to inform a potential participant of the extent to which he or she may be able to withdraw consent to usage of the donated biological materials as well as the stem cell lines and other products derived therefrom.

Return of Research Results

Another fundamental question relating to the donation of biological materials is whether there is an ethical duty to return research findings—whether the results are directly

related to the research (“individual research results”) or not directly related to the central research question (“incidental” findings)—to research participants [25]. Stem cell research raises particular challenges to result verification. For example, induced pluripotent stem cells (iPSCs) may have been genetically modified, or embryos derived from donor gametes may not be identical to donor genomes. Thus, it may be uncertain whether a presumed finding is valid unless it can be replicated with a fresh specimen from the donor.

The ethical implications of requiring return of research results may be intensified as the discovery of clinically relevant and scientifically valid information becomes more frequent and donors increasingly express a desire to receive these findings. Supporters of a duty to return results rely upon the principles of respect for persons and autonomy, as well as the notion that individuals have an interest in obtaining personally relevant results and information about the research in which they participated. Among other factors, the nature and duration of the relationship between the research participant and the researcher may be the most important in determining whether a duty to return results exists [26]. A duty to return may also hinge on considerations related to ownership, property rights, autonomy, and an individual’s status as a “research participant.”

There are also practical considerations in considering the return of results to donors. First, the obligation to return results may strain already limited resources and delay research—particularly in jurisdictions that require that any discussion of genetic information be conducted by a clinician with particular expertise. Second, where samples are de-identified, locating the individual who donated the sample may be practically impossible. Third, if, during the consent process, researchers tell potential participants that research results may be returned, some donors may not seek medical treatment or undergo testing that they otherwise would have because of a misunderstanding that researchers would notify them of any and all negative findings.

Compensation of Oocyte Donors for hESC Research

Encouraging involvement in scientifically valuable research by providing compensation to research subjects is the subject of much ethical discussion [27]. In the context of stem cell research, it is well settled that no compensation should be provided to those who donate clinically excess gametes and embryos because these donors have not expended any additional time or been subject to additional risk, and compensation could be construed as purchasing the bodily materials themselves. However, the issue of whether or not and to what extent women who donate their oocytes directly and solely for stem cell research should be compensated has been the subject of much debate [9]. While direct reimbursements for

the costs associated with the donation process, such as travel costs or time taken out of work, are relatively commonplace [6], some commentators and policy-makers assert that women should be compensated beyond direct expenses for the substantial time, burden, and discomfort associated with the donation process [15].

The process of undergoing hormonal stimulation for egg harvesting can be a lengthy and potentially risky process. Although it appears that serious complications rarely accompany the egg harvesting process, some uncertainty remains regarding the frequency and severity of such risks, due to the dearth of long-term studies of risk conducted on donors [28–30]. Some scholars assert that compensation for donation fairly promotes a mutual benefit for both the researcher and the donor [31] and appropriately acknowledges the woman’s contribution and effort.

Others have argued that justice demands that compensation beyond direct expenses should be provided to women who donate their oocytes directly to research, as women in the USA have historically been allowed such compensation for the parallel act of donating oocytes for reproductive purposes [9]. Indeed, the medical procedures and risks associated with oocyte donation are the same, regardless of the purpose for which the eggs are intended.

However, some commentators have asserted that compensation of oocyte donors may compromise a potential donor’s ability to provide free and voluntary informed consent. Compensation may become coercive if it blinds a person to the risks involved in the research or if it leads a person to conceal or misrepresent information that would disqualify his or her from being eligible to participate [32]. Few studies have been conducted that support the argument that reasonable compensation affects a person’s perception of risk presented by a protocol [33, 34]. Exactly what may constitute an undue inducement to participate in hESC research is unclear, as it must be determined on a case-by-case basis. In determining whether compensation qualifies as undue inducement, ethicists and policy-makers may consider whether the financial incentive serves as the primary or sole reason for an individual to donate oocytes for research [35, 36].

Further, it has been asserted that compensation of oocyte donors may not protect donors from exploitation or appropriately respect the integrity of their biological materials. Compensating oocyte donors may exploit underprivileged populations who would not otherwise choose to engage in research. Scholars also worry that compensation of oocyte donors may lead to the “commodification” of human biological materials, undermining the dignity or meaning of human life. These concerns may lead to prohibitions on compensation for the number or quality of eggs donated [15, 32, 37]. Whether or not compensation for oocyte donation is analogous to purchasing biological materials or providing an incentive commensurate with the risk undertaken by the provider is still a topic of great debate [38–40].

While donors of oocytes for hESC research in the USA have historically not been compensated beyond reimbursement for out-of-pocket costs and medical expenses related to the donation [6, 7], New York State has adopted policies that permit capped compensation of women for the time, burden, and discomfort associated with the donation process, so long as the donor also has been fully apprised of—and comprehends—the risks associated with donation [41]. This policy reflects how compensation for donation of oocytes for hESC research may promote a balance between the individual and societal benefits of the research and the risks posed to research participants.

Ethical Issues Involving Translational Stem Cell Research

Clinical stem cell research has the potential to expand the range of therapies available for neurological or other kinds of disease and may be progressing more rapidly than the normative considerations applying to these research practices [42, 43]. While some cell-based therapies are already the standard of care for certain medical conditions, many other types of stem cell products may soon have clinical value. The increased focus on moving stem cell science from bench to bedside makes the need for ethical guidance for testing and using novel stem cell therapies in humans particularly acute [44]. The following section will focus on the ethical considerations associated with clinical application of stem cell products.

Challenges to the Already Fluid Boundary Between Medical Practice and Scientific Research

Translational stem cell research involves the close—and often overlapping—connection between research and medical practice. Indeed, stem cell-based clinical research involves the shared interests of the two enterprises, as researchers and medical practitioners alike employ novel therapies and scientific theories. However, prevailing ethical principles distinguish scientific research from medical treatment. It is commonly accepted that scientific research promotes “generalizable knowledge” for the entire population, whereas medical treatment focuses on the well-being of the individual patient [11].

Clinical Research Paradigm and Medical Innovation Model

Clinical application of cell-based therapies may fall within the traditional research paradigm. Typically, research proceeds in three sequential stages, in which researchers conduct experiments *in vitro*, then *in vivo*, and finally in human

subjects. Clinical research, defined as any trial to evaluate the effectiveness and safety of medications or medical devices by monitoring their effects on large groups of individuals, represents the commonly recognized model for human subjects research [12]. These trials aim to produce generalizable knowledge that will yield benefits to a wider population or society at large. A number of clinical trials involving stem cell-based therapies for a variety of different diseases are currently underway [45].

Where trials of stem cell-based therapies are presented as an alternative to existing treatment options, researchers and oversight committees should consider the principle of clinical equipoise—i.e., the genuine uncertainty among expert clinicians about the relative merits of an investigational intervention and the available alternatives—when deciding which model to pursue [46]. In doing so, researchers should address whether a protocol or intervention is designed solely to deal with the research question or if it may have potential therapeutic benefit [47]. Clinical equipoise assessments are based on the expected benefits and burdens of the interventions for the overall patient population rather than on particular individuals’ unique characteristics. When an intervention is known to be particularly risky, or individuals are randomly assigned to an inferior therapy, clinical equipoise does not exist [48, 49].

The medical innovation model may offer clinicians the opportunity to provide potentially beneficial stem cell-based therapies outside the context of a formal clinical trial. Innovative therapies should (1) have an appropriate scientific rationale, (2) provide an explicit explanation for why the researchers need to pursue a more experimental option, and (3) include a well-articulated characterization of the treatment regimen as well as a sufficient data reporting plan, particularly for adverse events [50]. This model is distinguishable from the clinical research model in that the former concentrates on the welfare of the individual patient, while the latter focuses on scientific results that can be applied to a broader patient population [51, 52]. Although a sufficient evidentiary base is necessary for using medical innovations, medical innovation is not standardized to a point where a trial is appropriate.

Notably, although the clinical research model and the medical innovation model differ, the two paradigms are not incompatible. In some cases, medical innovation (with adequate preclinical evidence to support the intervention and appropriate ethical oversight) [51] may be an important alternative to the slower-moving clinical research process for individuals with serious illnesses and limited treatment options [53].

Moreover, the distinctions between the protections offered by the clinical research model and the medical innovation model may be mitigated by encouraging physician-scientists who provide innovative therapies to share any relevant information with other researchers and to move therapies that are

successful for critically ill individuals into large-scale clinical trials when possible [54]. In addition, by applying the criteria of medical innovation in surgical procedures to stem cell interventions, the medical innovation model could further approach the level of ethical oversight and protection ensured under the clinical research paradigm [51, 55]. In the case of studies of cell-based therapies, particularly those that deviate from the standard of care, the two models at issue—clinical research and medical innovation—should emphasize the scientific validity of the intervention. Both models also require intensive follow-up and evaluation.

Clinical Use of Unproven Medical Interventions

In contrast to the clinical research and medical innovation models, an ethically unacceptable approach to translational stem cell research is the clinical use of unproven medical interventions that do not have sufficient previous research or demonstrable evidence that the procedures are safe and effective in the target population. This model, often referred to as the unproven intervention model, is distinguishable from the medical innovation model by its failure to support its interventions with adequate preclinical evidence [56]. As a result, although the medical innovation model and the clinical research paradigm may be able to coexist within a single ethical and research framework, the use of unproven stem cell interventions may not meet the ethical standards established and expected by the research community and beyond.

As noted above, a sufficient evidentiary base is one of the core ethical requirements for using medical innovations [53]. Unlike medical innovations, unproven interventions generally do not include objective follow-up of patients and independent evaluation. The ability to differentiate objectionable unproven treatments from valid medical innovations is one of the key challenges facing those concerned with the integrity of stem cell treatments.

Some commentators have maintained that people should be permitted to select medical treatment based on their personal level of risk tolerance, but respect for patient autonomy may not always justify softening basic ethical protections. On the contrary, it may be imperative to ensure that appropriate safeguards apply to procedures offered to the desperately ill, as they may be particularly vulnerable to abuse or coercion.

In the absence of regulatory oversight, patients and clinicians are often left to weigh the risks and benefits of a particular stem cell therapy, despite a lack of equipment to successfully perform this task. However, physicians can still provide invaluable protection against ethically unsupportable unproven interventions. The professional obligations of physicians, as exemplified by the duty to minimize harm, may prohibit them from providing these therapies to patients. Empirical evidence suggests that many novel stem cell-based therapies are not effective or safe enough at this time to war-

rant distribution in the clinic [54, 57]. Recent deaths or severe physiological responses of patients who received unproven medical treatments have raised concerns about the stem cell clinics that have delivered these treatments [58].

Patients seeking stem cell interventions frequently travel—sometimes abroad to foreign countries—giving rise to what is commonly referred to as “stem cell tourism” [59]. Although not all travel for innovative therapies is ethically problematic, many in the scientific community have expressed concern that lucrative stem cell treatments are being aggressively marketed to desperate patients without appropriate safeguards to ensure the safety and potential effectiveness of the advertised interventions and without a mechanism to prevent misleading or fraudulent claims [60–62]. Approved stem cell therapies remain rare, and clinics offering unapproved stem cell treatments are frequently, though not exclusively, located in countries that are not known for their biomedical research [60]. In such cases, the jurisdiction in which an advertised procedure is offered does not indicate the extent to which such treatment “adheres to the widely accepted translational pathway from basic science to clinical application” [61].

In response to the explosion of stem cell-related marketing and tourism, efforts should be made to promote safe and effective treatments and prevent misleading or fraudulent advertising through demands for improved transparency of the methods, results, expertise, and oversight of clinics offering stem cell interventions [61].

Challenges to the Ethical Principles Central to Human Subjects Research

As with other first-in-human clinical trials, translational stem cell research may require adopting and altering existing research oversight procedures in order to uphold the core ethical principles of human subjects research [54, 55, 63]. The clinical application of novel stem cell therapies may present unforeseeable risks and benefits to subjects and therefore require additional or different forms of oversight [64]. Research oversight committees, including institutional review boards (IRBs) and, in some instances, Embryonic Stem Cell Research Oversight Committees (ESCROs) or Stem Cell Research Oversight Committees (SCROs), must carefully weigh the risks and benefits to participants and monitor them over the course of the trial and consider study design issues (e.g., the potential harms, benefits, and safety of different clinical trials) [6, 54].

While IRBs and ESCROs or SCROs are traditionally based in a single institution, effectively overseeing complex translational stem cell research may require expertise from more than one type of institution [65]. Relying on a more centralized strategy could encourage a “higher-level” review

process [51, 65, 66]. By promulgating ethical standards pertaining to risks and benefits, a central committee could also facilitate information sharing among different research institutions that are using the same stem cell lines to produce and test their potential therapies [2].

In addition to differing oversight procedures, the informed consent process must also account for the complex risks and the potential for unknown complications necessitating periodic health assessments or withdrawal from a study [63, 67]. Ensuring that participants provide fully informed consent to participate in stem cell clinical trials is particularly challenging in light of the unique level of publicity surrounding this area of research. Stem cell research also may exacerbate the therapeutic misconception, which arises when research participants do not understand the distinction between treatment and research [68, 69]. Individuals participating in novel stem cell trials may believe that their participation will necessarily include a therapeutic benefit. When the therapeutic misconception is coupled with the promises of commercial stem cell therapies that have not been substantiated by scientific evidence, participants may become further confused or misled as to the benefits of participation. Thus, a particularly rigorous informed consent process is essential to ensure that potential participants are fully informed of the risks and benefits of participating in stem cell research and understand the distinction between research and clinical care.

Additionally, where stem cell therapies seek to treat or cure conditions that impair cognitive function, such as Alzheimer's disease, clinical trials will, by necessity, need to enroll individuals suffering from those conditions [43]. Because these individuals may lack the capacity to provide first-person consent, special procedures should be in place to ensure that these clinical trials are conducted according to stringent ethical standards. Institutional oversight committees should consider additional protections for vulnerable populations, methods of communicating the risks and benefits to individuals that will maximize their comprehension and foster individual's assent or dissent to participation, and rules for appointing surrogate decision-makers in the event that the individual is incapable of providing fully informed, valid consent.

Finally, once therapies become widely available, the principle of distributive justice may mandate affordable access to resulting therapies and treatments for those who participate in publicly funded translational stem cell research. It may be advisable that relevant stakeholders—including researchers in academic and private companies, government funding organizations, patients, and providers—consider, in advance, how to ensure the fair and transparent distribution of stem cell therapies and products. Providing access to the benefits of translational stem cell research for the broader community may ameliorate increasing societal concern about health disparities.

Conclusion

Applying well-established ethical frameworks to the design and conduct of stem cell research involves recognition of the varied ways individuals can contribute to or participate in stem cell research—as donors of gametes, cells, or embryos for hESC research, as participants in clinical trials, or as recipients of innovative stem cell-based therapies. Acquiring the biological materials to perform stem cell-based research should abide by norms that recognize donors' rights. Additionally, the biological nature of stem cells may make it difficult for research institutions to abide by the three main principles governing human subjects research in testing novel stem cell-based therapies: beneficence, respect for persons, and justice. Finally, experiments studying the clinical application of stem cells continue to blur the distinction between research and medical treatment. The three approaches to introducing stem cell-based therapies in humans—the clinical research paradigm, the medical innovation model, and the clinical use of unproven interventions—are not always adequately protective of participants nor are they necessarily compatible.

Despite the continuing need to address ethical questions central to stem cell research involving human subjects, it is clear that stem cell research will continue to advance. As it does, policy-makers, ethicists, researchers, and oversight bodies should consider how best to ensure that donors' rights are respected and research participants are adequately protected.

Disclaimer The views expressed in this chapter are solely those of the authors and do not necessarily represent those of the Empire State Stem Cell Board, the New York State Task Force on Life and the Law, the New York State Department of Health, Health Research, Inc., or the New York State Government.

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