AUTONOMY AND INFORMED CONSENT IN NONTHERAPEUTIC BIOMEDICAL RESEARCH

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The common law and federal regulations create overlapping legal regimes that require researchers to obtain the informed consent of most human subjects of medical research. The fast-growing field of biomedical research generally, and stem cell research in particular, gives rise to a range of unresolved and contested legal issues concerning the extent and implementation of the informed consent requirement. This Article identifies and assesses a series of these: (1) Must researchers obtain the informed consent of participants in nontherapeutic research not covered by federal research regulations? (2) As part of the process, must researchers disclose their financial interests in their projects? (3) Must informed consent be obtained before researchers use tissues stored in tissue banks? (4) Must informed consent be obtained from both gamete donors before research use may be made of a stored human embryo? The Article argues that these questions can be best resolved by focusing the analysis on the core value of subject autonomy that underlies the principle of informed consent.

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INTRODUCTION

Stan suffers from a chronic illness with a genetic component. Peter is a research scientist who wants to harvest stem cells from Stan's blood, use those cells to study the progression of the disease, and hopefully create a treatment for that disease. Does Peter have an obligation to obtain Stan's informed consent before extracting the blood? Does that requirement, if it exists, require Peter to reveal that he hopes to patent his discoveries and license the patent for millions of dollars?

David and Eliza went to an in vitro fertilization (IVF) clinic for help conceiving a baby. The clinic produced ten embryos with David's sperm and Eliza's eggs, three of which were implanted into Eliza and seven of which were frozen. Eliza gave birth to twin boys, and the couple does not want additional children. When they began their treatment, they signed a consent form that said excess embryos could be donated by the clinic for "research" but did not specify what type of research. Peter wants to use their embryos to create human embryonic stem cell lines, a practice that is controversial because it requires destroying the embryos. Must he go back to Eliza and David to obtain more specific informed consent? May he use the embryos if Eliza and David have gotten a divorce, and Eliza gives consent but David does not?

All of these questions have two things in common: (1) Their answers are unclear, at least in some circumstances, because they fall outside the two overlapping legal regimes that govern informed consent in the context of biomedical research; and (2) their answers will become increasingly important as biomedical research advances in the twenty-first century.

This Article provides answers to these questions by emphasizing the core value of autonomy that underlies the principle of informed consent.¹ Part I

^{1.} See, e.g., Tom L. Beauchamp & Ruth R. Faden, Informed Consent: Meaning and Elements, in 3 ENCYCLOPEDIA OF BIOETHICS 1277, 1279 (3d ed. 2004); Daniel Strouse, Informed Consent to Genetic Research on Banked Human Tissue, 45 JURIMETRICS J. 135 (2005). Although commentators sometimes claim that the concept of informed consent embodies other principles in addition to the promotion of autonomy, see, e.g., Peter H. Schuck, Rethinking Informed Consent, 103 YALE L.J. 899, 921 (1994) (claiming that its purpose is to "provide information to empower the patient to protect her own interests" and to cause physicians to place the patient's interests above their own), and many complain that remedies for legal violations of this principle are not well tailored to protecting autonomy interests alone, see, e.g., Richard S. Saver, Medical Research and Intangible Harm, 74 U. CIN. L. REV. 941,

explains why the donation of large quantities of human tissues is necessary for stem cell research to fulfill its scientific potential. Part II describes the two bodies of law relevant to tissue donations—the federal regulations concerning research involving human subjects and the common law doctrine of informed consent—and explains why they do not provide adequate guidance for answering the questions posed above.

The following four Parts identify and analyze unique informed consent issues raised in the context of nontherapeutic biomedical research, of which stem cell research is the most prominent example. Part III considers the fact that a substantial amount of stem cell research could fall outside the boundaries of both the federal regulations and the common law doctrine of informed consent as it is usually understood. It argues that the law nonetheless requires that researchers obtain specific informed consent from tissue donors. Part IV analyzes whether the informed consent principle requires that researchers divulge their financial interests in the research to stem cell research donors. and concludes that it does. Part V argues that tissues stored in tissue banks may be used for stem cell research when obtaining specific informed consent for stem cell research use from their donors is not feasible. Part VI contends that, in the case of embryo donation, the autonomy principle requires that both gamete donors (that is, the donor of the sperm and the donor of the egg used to create the embryo) provide informed consent before the embryo may be used for stem cell research, even when one of those parties has exclusive dispositional control over the embryo.

I. THE NEED FOR TISSUE DONORS FOR STEM CELL RESEARCH

Cells, the basic building blocks of organisms, each contain a complete copy of the organism's DNA. The DNA contains the organism's entire genome—that is, every one of the organism's genes. According to the findings of the Human Genome Project, the genome of each human consists of about 25,000 genes. These genes are found spread across forty-six chromosomes, half of which are inherited from the person's mother and half from the person's father. Different types of human cells (skin cells, blood cells, bone cells, and brain cells, for example) have different characteristics and different functions. In order to be able to serve such different functions, different genes are activated, or "expressed," in different types of cells, while the vast majority of genes in any particular type of cell lie dormant. Through "gene expression,"

^{964 (2006) (}claiming that injuries to interests in "autonomy and self-determination [alone] rarely become cognizable and therefore compensable"), the centrality of autonomy is rarely questioned.

the cell creates particular proteins that, working together with proteins created by other cells, build and maintain the organism and enable it to function.

When a specialized cell is created, its function is decided and is fixed. In the lingo of cell biology, such a specialized cell is "fully differentiated." The genes that are expressed will remain expressed, while the others will lie dormant. A stem cell, in contrast, is one that is not fully differentiated. It can divide into two identical copies of itself, as many types of specialized cells can, but it also can divide into one copy of itself and one different, more specialized cell, with a different gene expression pattern (differentiation).

Research involving stem cells can help lead to cures for a wide range of diseases in three different ways. First, by studying the ways that stem cells differentiate and create specialized cells, researchers hope to better understand the causes and development of a range of diseases that result from abnormal cell division or differentiation, or from cell injury or death.

Second, if scientists can prompt stem cells to differentiate and develop in ways that mimic the progression of diseases, researchers can then use them to test the efficacy and toxicity of pharmaceuticals and other medical treatments. For example, stem cells could be prompted to differentiate into large quantities of heart cells, and new chemical compounds could be applied to those cells to see if the compound was dangerous to them.

Third, and most significant, researchers may be able to use stem cells to directly cure diseases. Currently, disease usually is treated with efforts to remove, destroy, or fix errant or damaged cells with surgery, chemical compounds, or radiation. In theory, stem cells, prompted to differentiate into healthy mature cells, can be used to replace diseased or dead cells. In other words, medical science can harness the body's natural healing powers to cure disease rather than relying on blunt, external force that fights against the body's biology. One approach is to inject stem cells into the diseased area of the body and to allow them to regenerate healthy cells inside the body. Another is to prompt stem cells to grow replacement cells or tissues outside of the diseased body, and then to surgically replace the diseased tissues with the specially constructed replacements.²

The stem cells that are a necessary condition for achieving these lofty objectives come in two basic varieties: human embryonic stem cells (hESCs) and human adult stem cells (hASCs).

^{2.} See, e.g., John C. Fletcher, Deliberating Incrementally on Human Pluripotential Stem Cell Research, in 2 NAT'L BIOETHICS ADVISORY COMM'N, ETHICAL ISSUES IN HUMAN STEM CELL RESEARCH, at E-6 to E-7 (2000); National Institutes of Health, Stem Cell Basics, http://stemcells.nih.gov/ info/basics (last visited Dec. 18, 2006).

hESCs are harvested from embryos approximately five days after fertilization, when the embryo is at a stage of development called the blastocyst. To date, the source of hESCs has been exclusively blastocysts created as part of IVF treatment but not implanted in the womb of the patient. The necessary blastocysts could also be created by using sperm and eggs donated specifically for research purposes and fertilizing the eggs in vitro for that purpose.

Scientists hope also to be able to create blastocysts for research through a process known as "somatic cell nuclear transfer" (SCNT), also called "therapeutic cloning." This process, demonstrated in animals but not yet in humans, requires taking the nucleus from a fully differentiated cell of a person (a "somatic" cell), injecting it into an enucleated egg cell, and stimulating the egg to begin development as if it had been fertilized by a sperm cell. When the resulting embryo reaches the blastocyst stage, the stem cells would be harvested just as if the blastocyst had been created through fertilization. The advantage of creating hESC using SCNT is that the resulting stem cells would have the same genetic makeup as the donor of the adult cell. Thus, they could potentially be used to create cell therapies for the donor without the serious problem of immune system rejection that plagues recipients of tissue transplants.

hASCs are found in small quantities in the tissues of fetuses and fully gestated persons. They have less potency than hESCs—meaning each type can differentiate into only a limited number of specialized cells—and they do not proliferate as well in an undifferentiated state as do hESCs. Nonetheless, hASCs have already proven useful for some therapies—bone marrow transplants as part of leukemia treatment is the leading example—and have the potential to provide cures for other types of diseases and injuries.

In the case of both hESCs and hASCs, scientific progress depends not only on the skill of scientists and the availability of funding, but also on the ability of researchers to procure large quantities of human tissues. Obtaining hESCs requires the donation of embryos or, alternatively, sperm and eggs. Perfecting SCNT will require the donation of a large number of eggs, as well as somatic cells. hASC research relies on the availability of tissues from human donors.

II. REGULATIONS AND THE COMMON LAW

A set of federal regulations known as the "common rule" (because seventeen different federal agencies have adopted them),³ as well as closely

^{3.} See generally 45 C.F.R. pt. 46 (2005). The common rule has been adopted verbatim by seventeen federal government agencies responsible for the federal funding or regulation of research.

related regulations of the Food and Drug Administration (FDA),⁴ require that research using federal funds (or being prepared for FDA review) and involving human subjects be approved by an Institutional Review Board (IRB).⁵ Among other responsibilities, the IRB must determine that the risks of the research are reasonable in relationship to anticipated benefits and are minimized.⁶ The IRB also must ensure that appropriate informed consent is obtained from each research subject.⁷

The common rule's informed consent requirement is designed to supply research subjects with all the information they need to perform an autonomous risk-benefit analysis.⁸ It states that researchers *must* disclose the following information: the description, purpose, duration, and experimental nature of the study; any reasonably foreseeable risks or discomforts to the subject; any reasonably expected benefits to the subject or to others; appropriate alternative procedures or treatments that might be advantageous to the subject; the extent of privacy and confidentiality of records identifying the subject; the availability of compensation or treatment for possible injuries; contact information in case the subject has questions or concerns; and the right to withdraw from the study at any time without penalty.⁹ In addition, an IRB *may* require that other information be given to the subjects when "the information would meaningfully add to the protection of the rights and welfare of subjects."¹⁰

Independently of the common rule, a requirement of physicians to obtain the informed consent of their patients in therapeutic settings became firmly ensconced in American tort law over the course of the twentieth century. The idea that patients have a right to accept or decline medical intervention dates back at least to Justice Cardozo's pronouncement in *Schloendorff v. Society of New York Hospital*¹¹ that "[e]very human being . . . has a right to determine what shall be done with his own body."¹² The 1957 case of *Salgo v. Leland Stanford Jr. University Board of Trustees*¹³ introduced the term "informed consent" into the legal lexicon. In that case, concerning an invasive radiological study of a patient's aorta that left him paralyzed, the court held that the

^{4. 21} C.F.R. § 56.109 (2005).

^{5. 45} C.F.R. §§ 46.103(b), 46.109, 46.119.

^{6.} *Id.* § 46.111(a)(1)–(2).

^{7.} Id. § 46.111(a)(4)–(5).

^{8.} Id. § 46.116; see also Strouse, supra note 1, at 138 ("The cardinal value advanced by informed consent to research is regard for autonomy.").

^{9. 45} C.F.R. § 46.116(a).

^{10.} Id. § 46.109(b).

^{11. 105} N.E. 92 (N.Y. 1914).

^{12.} Id. at 93.

^{13. 317} P.2d 170 (Cal. Dist. Ct. App. 1957).

physician was obligated to disclose the risks of the procedure "necessary to an informed consent."¹⁴

Today, depending on the jurisdiction, physicians may face lawsuits for damages if they fail to provide a patient with the information that a reasonable physician would provide in recognition of the patient's right to make an autonomous treatment decision,¹⁵ or if they fail to provide the information that a reasonable patient would have wanted in order to make an informed treatment decision.¹⁶ Generally speaking, the subjects of mandatory disclosure include the nature of the treatment, the likelihood of success, the reasonably foreseeable risks, any alternative treatments, and the clinical prognosis if the patient declines treatment.¹⁷

The common rule and the informed consent doctrine—two distinct but overlapping bodies of law—create a regime designed to protect the autonomous decisionmaking of participants in medical research. In the most common medical research setting—the clinical trial—researchers provide treatment to patients while simultaneously collecting clinical data. In such cases, both sets of rules concerning informed consent usually apply. Federal regulations will apply when the research receives federal funding, the results of the research will require FDA approval, or both; and courts have held that physicians owe a duty to patients to whom they are providing treatment to obtain informed consent regardless of whether that patient is enrolled in a clinical trial that specifies a precise treatment protocol.¹⁸

The advent of biotechnology and the rise of biomedical research has challenged the doctrine of informed consent to adapt to the context in which medical treatment and scientific research are decoupled, such that subjects

^{14.} *Id.* at 181 (quoting jury instructions).

^{15.} See, e.g., Natanson v. Kline, 350 P.2d 1093, 1106 (Kan. 1960).

^{16.} See, e.g., Canterbury v. Spence, 464 F.2d 772, 786-87 (D.C. Cir. 1972).

^{17.} See Schuck, supra note 1, at 916–17.

^{18.} See Jesse A. Goldner, An Overview of Legal Controls on Human Experimentation and the Regulatory Implications of Taking Professor Katz Seriously, 38 ST. LOUIS U. L.J. 63, 80–87 (1993) (reviewing cases in the context of "Therapeutic' Clinical Research"). Although some courts and commentators have argued over whether physician-researchers should have the same duties to patients participating in controlled clinical trials as they do in the context of individual treatment, none, of which I am aware, contend that the duty to obtain informed consent should be abolished in the former case. See, e.g., E. Haavi Morreim, The Clinical Investigator as Fiduciary: Discarding a Misguided Idea, 33 J.L. MED. & ETHICS 586, 586, 594 (2005) (criticizing the "Common View" that physicians owe the same fiduciary duties to research subjects as they do to patients but emphasizing the fundamental importance of informed consent even in the research context). Cases in which courts have ruled that researchers do not have the same duties to clinical research subjects as to patients usually concern malpractice claims, not informed consent claims. See, e.g., Payette v. Rockefeller Univ., 643 N.Y.S.2d 79 (N.Y. App. Div. 1996); Craft v. Vanderbilt Univ., 18 F. Supp. 2d 786 (M.D. Tenn. 1998).

participate in research without becoming objects of experimentation. The growing field of stem cell research presents a prominent example of this set of circumstances, although certainly not the only one. Scientific progress in the field will require the procurement of various bodily tissues and early-stage embryos from individuals who are not receiving any treatment or themselves being studied as part of the research.

III. NONTHERAPEUTIC RESEARCH OUTSIDE OF THE COMMON RULE

A. The Gap in the Law

The common rule does not apply to all scientific research that requires the participation of human subjects. It applies only if the research is funded with federal money or if the institution conducting research has given "assurances" to the federal government that the research will comply with the common rule.¹⁹ In many areas of scientific inquiry, the finite scope of the common rule is of little practical import, because most research is supported by federal funds, or is conducted at research institutions that receive federal funds and have agreed to comply with the common rule in all of their research endeavors.²⁰ A large amount of research that falls outside of this framework involves drugs, biologics, or devices for which FDA approval will be sought, subjecting the research to virtually identical FDA requirements.²¹

Current restrictions on federal funding of hESC research, however, make stem cell science unusual in this respect. Legislation prohibits federal funding of any research that destroys embryos.²² In addition, President Bush

^{19.} See 46 C.F.R. § 46.101 (2005); see also Jocelyn Kaiser, Broader Oversight for Research on Humans?, 275 SCIENCE 605 (1997) (noting that the common rule simply does not apply to "state-funded studies or research by private institutions not receiving federal funds"). See generally 21 C.F.R. pt. 50 (2005).

^{20.} See Strouse, supra note 1, at 136 n.2.

^{21. 21} C.F.R. §§ 56.109, 312.66.

^{22.} The U.S. Congress first enacted this limitation in 1996 and has renewed it as an amendment to appropriations bills every year since. For example:

None of the funds made available by Public Law 104-91 may be used for-

⁽¹⁾ the creation of a human embryo or embryos for research purposes; or for any other God forsaken thing;

⁽²⁾ research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 CFR 46.208(a)(2) and 42 U.S.C. 289g(b).

For purposes of this section, the phrase "human embryo or embryos" shall include any organism, not protected as a human subject under 45 CFR 46 as of the date of enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes.

Balanced Budget Downpayment Act, Pub. L. No. 104-99, § 128, 110 Stat. 26, 34 (1996).

refuses to allocate any federal funds for research using any hESC lines derived after August 2001.²¹ This limits federal funding in this area to research using twenty-two cell lines²⁴ that possess limited genetic diversity and are unsuitable for clinical use because of contamination with mouse cells.²⁵ Alternative funding sources, including states (led by, but not limited to, California's initiative authorizing \$3 billion of spending on stem cell research), foundations, individual philanthropists, and, to a lesser extent, private firms, have stepped into the resulting vacuum. The result is that a nontrivial amount of stem cell research in the United States in the coming years might be conducted in laboratories not subject to the requirements of the common rule.

Many of these funding sources nevertheless are likely to require that researchers follow the precepts of the common rule—in fact, California's stem cell agency has already issued proposed regulations that would do precisely this²⁶—but there is no legal requirement that they do so. If research not subject to the common rule is conducted by physician-researchers within the context of clinical treatment, the common law requirements of informed consent would apply. But a potentially important issue in stem cell research is whether scientists conducting research not covered by the common rule and outside

^{23.} President George W. Bush, President Discusses Stem Cell Research (Aug. 9, 2001), http://www.whitehouse.gov/news/releases/2001/08/20010809-2.html. In July 2006, the U.S. Senate joined the U.S. House of Representatives in enacting a law that would have overruled the president and increased federal funding for hESC research. Stem Cell Research Enhancement Act of 2005, H.R. 810, 109th Cong. (2005). President Bush immediately vetoed the bill, and a House vote to override the veto fell far short of achieving the necessary two-thirds. See Sheryl Gay Stolberg, First Bush Veto Maintains Limits of Stem Cell Use, N.Y. TIMES, July 20, 2006, at A1. Even taking into account the results of the November 2006 congressional election, it is extremely unlikely that the House could pass a stem cell funding bill with a veto-proof majority in the 110th Congress (although the Senate could probably muster the necessary sixty-seven votes).

^{24.} The National Institutes of Health maintains a registry that identifies lines eligible for federal funding and identifies which ones are actually available for use. *See* National Institutes of Health, NIH Human Embryonic Stem Cell Registry, http://stemcells.nih.gov/research/registry (last visited Dec. 18, 2006).

^{25.} See Exploring the Promise of Embryonic Stem Cell Research: Hearing Before the S. Special Comm. on Aging, 109th Cong. 42, 44 (2005) (prepared statement of John D. Gearhart, Professor, Johns Hopkins University, Department of Medicine) ("The 22 lines now eligible for federally funded research are contaminated with animal cells, lack genetic diversity, are not disease-specific, and are not adequate for researchers to apply to a wide variety of diseases."); see also PRESIDENT'S COUNCIL ON BIOETHICS, MONITORING STEM CELL RESEARCH 5 (2004); COMM. ON GUIDELINES FOR HUMAN EMBRYONIC STEM CELL RESEARCH, NAT'L RESEARCH COUNCIL, GUIDELINES FOR HUMAN EMBRYONIC STEM CELL RESEARCH 15 (2005) [hereinafter NRC GUIDELINES].

^{26.} See California Institute for Regenerative Medicine, Third Revised Medical and Ethical Standards Regulations, http://www.cirm.ca.gov/laws/nopc_stds.asp (last visited Dec. 18, 2006).

the context of clinical treatment are under a legal obligation to obtain the informed consent of human tissue donors. 27

B. Filling the Gap

Because most scientific research involving human subjects is carried out subject to the common rule, in the context of a therapeutic relationship, or both, the issue of informed consent in nontherapeutic research rarely appears in judicial opinions. However, there is some, although admittedly weak, authority for the proposition that, even if the common rule does not apply, stem cell researchers would have a legal obligation to obtain informed consent from human tissue donors.

In Whitlock v. Duke University,²⁸ a federal district court considered a claim brought by a diver who had participated in a Duke University study of the effect of deep underwater pressure on the human nervous system.²⁹ The diver sustained an injury and claimed that he had not been fully informed of the study's risks.³⁰ The court observed that North Carolina's informed consent statute covers only therapeutic interactions.³¹ It then concluded that it was "self-evident" that the state's courts would find that informed consent is also required in the nontherapeutic research context where "the researcher does not have as an objective to benefit the subject."³²

The Whitlock analysis is problematic precedent for the case of tissue donors, however, on two levels. First, the court's claim that its conclusion was self-evident is undermined by contrary dicta in *Grimes v. Kennedy Krieger Institute, Inc.*³³ In that case, Maryland's high court found that researchers owed duties to subjects in a research project it found to be nontherapeutic (probably incorrectly³⁴) only because federal funding triggered the common rule, determining that "there is no duty of which we are aware prescribed by the Maryland Code in respect to scientific research of the nature here present."³⁵

34. See Lainie Friedman Ross, In Defense of the Hopkins Lead Abatement Studies, 30 J.L. MED. & ETHICS 50, 51 (explaining how the particular research study in question was, in fact, therapeutic).

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^{27.} Over the past decade, bills have been introduced in Congress that would effectively apply the common rule to all research, not just research sponsored by the federal government, but none have made it to the floor for a vote. *See, e.g.*, Human Research Subject Protections Act of 1997, S. 193, 105th Cong. (1997); Human Research Subject Protections Act of 2002, H.R. 4697, 107th Cong. (2002).

^{28. 637} F. Supp. 1463 (M.D.N.C. 1986), aff d, 829 F. 2d 1340 (4th Cir. 1987).

^{29.} Id.

^{30.} Id. at 1466.

^{31.} Id. at 1467–68.

^{32.} Id. at 1468.

^{33. 782} A.2d 807, 846 (Md. 2001).

^{35.} Grimes, 782 A.2d at 846-47.

Second, the court's conclusion that the research in question was nontherapeutic—although accurate in the sense that the subjects did not hope to receive direct health benefits from the study³⁶—obscures an important difference in the relationship between the researcher and the subject than the one that exists in the tissue donation context. In *Whitlock*, the experimental design called for the exposure of subjects to a stimulus in order to test its effect. As in clinical trials and individual treatment situations, where the duty to obtain informed consent most clearly applies, the researchers were experimenting on the subject. In the type of biomedical research with which this Article is concerned, the research "subjects" are not the object of experimental treatment or manipulation; they are donors of raw materials that, once separated from the donor, will be studied or manipulated. Any contact between the researcher and the donor is incidental to the purpose of the research itself.

In Greenberg v. Miami Children's Hospital Research Institute, Inc.,³⁷ a federal district court in Florida faced the issue of informed consent in precisely the type of nontherapeutic research that is of interest here.³⁶ The plaintiffs in *Greenberg* were the parents of, and organizations that work with, children afflicted with Canavan disease, a rare and fatal genetic disorder that occurs mainly in Ashkenazi Jews.³⁹ The plaintiffs made initial contact with defendant Dr. Reuben Matalon in 1987 and requested his help in searching for the gene or genes that cause Canavan disease.⁴⁰ To assist Dr. Matalon in his research, the Canavan families supplied him with epidemiological information from a confidential Canavan registry, as well as blood, urine, and autopsy samples from Canavan patients.⁴¹ In 1993, Dr. Matalon successfully isolated the gene responsible for Canavan disease and proceeded to submit a patent applications.⁴² The patent was issued in 1997 and assigned to Miami Children's Hospital (MCH), Dr. Matalon's employer.⁴³ A year later, MCH informed the plaintiffs

^{36.} See, e.g., Leonardo D. De Castro, Ethical Issues in Human Experimentation, in A COMPANION TO BIOETHICS 379, 380 (Helga Kuhse & Peter Singer eds., 2001) (defining therapeutic and nontherapeutic experiments).

^{37. 264} F. Supp. 2d 1064 (S.D. Fla. 2003).

^{38.} Id.

^{39.} Id. at 1066.

^{40.} Id.

^{41.} Id. at 1067.

^{42.} Id.

^{43.} U.S. Patent No. 5,679,635 (filed Sept. 9, 1994) (issued Oct. 21, 1997).

of its intention to enforce its patent rights and to limit Canavan disease testing through a campaign of restrictive licensing of the patent.⁴⁴

The plaintiffs sued Dr. Matalon and MCH alleging, among other charges, that they failed to obtain the plaintiffs' informed consent.⁴⁵ Responding to a motion by the hospital to dismiss the lawsuit, the court struggled with the question of whether tort law requires informed consent when researchers were neither treating nor experimenting on their subjects, but merely using the subjects' tissues and medical data. It regarded the question as a "novel one in Florida."⁴⁶ Eventually, the court determined that the researchers did have a duty to the plaintiffs to obtain their informed consent, but it based its conclusion only on the ground that the defendant had conceded the point in oral argument.⁴⁷ This justification hardly makes the holding a ringing endorsement of a broad legal principle.

Despite their limitations as precedent, Whitlock and Greenberg suggest that researchers procuring tissues for biomedical research have a legal obligation to obtain the informed consent of the tissue donors even if the research program falls outside the regulatory scope of the common rule. This conclusion seems clearly correct when the research requires a physical intrusion into the person of the donor, whether the intrusion is major (for example, the harvesting of eggs for SCNT), or minor (for example, the collection of a blood sample). The participation decision cannot be made consistent with the core value of autonomy unless the participant is sufficiently informed of the costs and benefits involved. The usual disparity of information between researcher and research subject justifies the imposition of a duty on the former to obtain informed consent. If this reasoning is enforced under the common law in the context of therapeutic research, it ought also to be enforced when the subject in question is the object of nontherapeutic research or a donor of biomedical material for nontherapeutic research, where both the importance of subject autonomy and the expected disparity of information between researcher and subject is no different.

The conclusion is also correct, although perhaps not as obviously so, when a subject's participation in the research requires no physical intrusion at all, such as if the subject is asked to provide a previously drawn blood sample. In this circumstance, informed consent is just as necessary to protect the subject's

^{44.} Greenberg, 264 F. Supp. 2d at 1067.

^{45.} Id. at 1068.

^{46.} Id. at 1069.

^{47.} Id. at 1070.

decisional autonomy, although admittedly it is not necessary to protect the subject's control over his or her body, viewed more narrowly.

IV. DISCLOSURE OF FINANCIAL INTERESTS

A. The Moore Precedent

A more difficult issue to resolve is whether the doctrine of informed consent requires researchers to disclose not only the possible harms that the subject might suffer as a result of his participation in the research project, but also the financial benefits potentially available to the researchers. This question is likely to be particularly important in the context of stem cell research, and more so as the basic science advances and gives way to the development of marketable tests and treatments. Of course, the possibility of scientists benefiting financially from the fruits of their research is hardly unique to the stem cell research revolution, so it would seem likely that courts would be quite familiar with the question. Surprisingly, the issue arises in published judicial opinions quite rarely.

The landmark case on the topic is *Moore v. Regents of the University of California.*⁴⁸ UCLA physician Dr. David Golde obtained consent from his patient, John Moore, who suffered from hairy cell leukemia, for the removal of his blood, bone marrow, and spleen.⁴⁹ The consent form, however, failed to mention that Dr. Golde and others intended to use the excised tissues for research purposes.⁵⁰ Within a few years of Moore's treatment, Dr. Golde established a cell line from Moore's T-lymphocytes,⁵¹ for which the Regents of the University of California obtained a patent.⁵² Moore sued Dr. Golde, the Regents, and two pharmaceutical firms that obtained licenses from the university to use the "Mo" cell line, claiming among other things a "lack of informed consent.⁵³

The California Supreme Court held that Moore's treating physicians had a duty to disclose any commercial research interest they might have in the patient's biological tissue before removing the tissue.⁵⁴ The court's reasoning was that patients expect their doctors' therapeutic recommendations to be based entirely on their professional judgment of the patients' best interests,

^{48. 793} P.2d 479 (Cal. 1990), cert. denied, 499 U.S. 936 (1991).

^{49.} Id. at 481.

^{50.} Id.

^{51.} Id.

^{52.} U.S. Patent No. 4,438,032 (filed Jan. 6, 1983) (issued Mar. 20, 1984).

^{53.} Moore, 793 P.2d at 483 n.4.

^{54.} Id. at 485.

and that they are entitled to know of any information that might undermine the physicians' apparent motive of beneficence.⁵⁵ In contrast, the court found that the Regents and the pharmaceutical firms had no fiduciary duty to Moore, and thus owed him no duty to disclose their commercial interests.⁵⁶

B. Extending Moore to the Nontherapeutic Context

Because the defendants in Moore either had a therapeutic relationship with the plaintiff or no direct relationship at all, the decision in that case does not squarely address the disclosure responsibilities of researchers who collect tissues directly from donors in a nontherapeutic research setting, as is likely to be the case when stem cell researchers wish to biopsy tissue or harvest eggs. Invasive procedures carried out by a researcher with no therapeutic relationship to tissue donors was precisely the context of the Greenberg case, however.

After finding that medical researchers must obtain informed consent from their subjects, the Greenberg court decided that this principle did not require the researchers to disclose their potential economic interests in the research. The Greenberg judge distinguished Moore on the basis of the difference between a therapeutic and a nontherapeutic relationship with the subiect.⁵⁷ The court defended a more limited disclosure requirement in the nontherapeutic context by claiming that extending Moore-type duties to medical researchers would be "unworkable and would chill medical research."⁵⁸ The judge also distinguished the situation of research subjects in the two cases by describing subjects in nontherapeutic settings as "donors rather than objects of human experimentation" who participate voluntarily and thus should be accorded different treatment from that given to a patient seeking a therapeutic benefit.⁵⁹

The first of these justifications is inapt and the second exactly backward. As to the first, there is no reason why disclosure of financial interests would have a differentially chilling effect on nontherapeutic research. It is a small burden for researchers who hope to patent biotechnological products or processes and profit from doing so to disclose this possibility to donors as part of the process of obtaining informed consent, which they must follow anyway. Research progress would be impeded only if subjects do not wish to donate

^{55.} Id. at 483-84.

Id. at 486. 56.

Greenberg v. Miami Children's Hosp. Research Inst., Inc., 264 F. Supp. 2d 1064, 1070 57. (S.D. Fla. 2003). Id.

^{58.}

^{59.} Id. at 1070-71.

tissues to researchers who seek personal profits, and promoting research by disguising this fact clearly undermines the principle of informed consent.⁶⁰

The second justification is backward because, if anything, research subjects in nontherapeutic settings should be given more, not less, information.⁶¹ The informed consent doctrine exists to protect the autonomy of patients and research subjects. The principle that should therefore guide disclosure is materiality. That is, patients and research subjects should be given all information likely to be material to their decision as to whether to participate in research. Possible risks to subjects' health are clearly material, so they must be disclosed. The researcher's favorite color is not material, so there is no need to disclose this information and, in fact, disclosure of immaterial facts should be discouraged because it can often create confusion.

It is probably correct, as the Moore court claimed, that most patients would want to know if their physician had economic interests in their treatment in order to identify if there might be a lurking conflict of interest that would call into question the objectivity of the physician's recommendation. All other things being equal, however, we would expect subjects who hope to obtain a therapeutic benefit from participation in medical research to consider the scientists' economic incentives less material because the potential benefits to the subjects from participation are clear and often potentially very valuable. Patients often seek treatment through a research protocol because they are seriously ill and the conventional alternatives have proven ineffective.⁶² In contrast, subjects who stand to gain no health benefits from research participation are more likely to find the financial interests of the researchers material to their decision as to whether to participate in the study.⁶³ The primary benefit for such subjects is likely to be contributing to the social benefit of the research, and a researcher's pecuniary interest might affect the subject's evaluation of the expected social benefit.

Financial incentives seem especially likely to be material when the request for research participation comes from a medical professional who has

^{60.} See Grimes v. Kennedy Krieger Inst., Inc., 782 A.2d 807, 844 (Md. 2001) (holding that the duty to disclose material information to subjects is not affected by "[t]he fact that if such information was furnished, it might be difficult to obtain human subjects for the research").

^{61.} Cf. NAT'L COMM'N FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL & BEHAVIORAL RESEARCH, THE BELMONT REPORT: ETHICAL PRINCIPLES AND GUIDELINES FOR THE PROTECTION OF HUMAN SUBJECTS OF RESEARCH 11 (1978) [hereinafter BELMONT REPORT] ("[T]]he research subject, being in essence a volunteer, may wish to know considerably more about risks gratuitously undertaken than do patients who deliver themselves into the hands of a clinician for needed care.").

^{62.} See, e.g., Saver, supra note 1, at 965.

^{63.} See Strouse, supra note 1, at 141 n.28.

an independent treatment relationship with a potential subject unrelated to the research project. Scientists often pay clinicians for each subject the clinician enrolls in a research study.⁶⁴ This arrangement is likely to be particularly common in the context of stem cell research because it will often be efficient for scientists to rely on physicians who treat specific genetic diseases to recruit somatic cell donors with those diseases and to rely on infertility specialists to recruit egg or embryo donors.

Some medical organizations believe that it is improper for treating physicians to make such requests under any circumstances.⁶⁵ Others believe that it is unethical for treating physicians to receive compensation for such efforts.⁶⁶ Both of these positions are unrealistic and unreasonable. It is clearly cost effective for scientists to use medical personnel who have clinical contact with particular populations to recruit research study participants from those populations. An offer of compensation for successful recruitment no doubt encourages clinicians' cooperation in these efforts, and such an offer is not at all illicit. Explaining research protocols to potential participants and enrolling them can be a time-consuming activity. Physicians usually are not expected to work for free in other contexts, and there is no particular reason why ethics would demand that they do so in the recruitment context.

A treating physician's compensation for recruitment, however, probably would be material to many potential subjects because the financial incentive casts doubt, at a minimum, on the physician's apparent altruistic motivations on which the patient might otherwise rely. A patient who believes his physician is requesting a donation of tissue for research without financial inducement is likely to interpret the request as a signal that his physician believes the research in question is scientifically important. In contrast, a patient who knows his physician is being paid for procuring donations is less likely to

^{64.} See OFFICE OF INSPECTOR GENERAL, DEP'T OF HEALTH & HUMAN SERVS., RECRUITING HUMAN SUBJECTS: PRESSURES IN INDUSTRY SPONSORED CLINICAL RESEARCH 17–20 (2000), reprinted in CARL H. COLEMAN ET AL., THE ETHICS AND REGULATION OF RESEARCH WITH HUMAN SUBJECTS 371–75 (2005).

^{65.} See Ethics Comm., Am. Soc'y for Reproductive Med., Donating Spare Embryos for Embryonic Stem Cell Research, 78 FERTILITY & STERILITY 957, 960 (2002) (calling for "someone other than the treating infertility specialist [to] make requests for embryos for research purposes"); cf. Bernard Lo et al., Informed Consent in Human Oocyte, Embryo, and Embryonic Stem Cell Research, 82 FERTILITY & STERILITY 559, 562 (2004) (claiming there is no reason for concern if the treating physician is not involved in the research project).

^{66.} See COLEMAN ET AL., supra note 64, at 376 (citing the opposition of "[s]everal professional organizations" including the American College of Physicians).

make such an inference. A proper application of the autonomy principle underlying the doctrine of informed consent thus requires disclosure.⁶⁷

V. TISSUES PREVIOUSLY PROVIDED FOR OTHER PURPOSES

A clinical trial or other medical experiment with a therapeutic component requires, by its very nature, interaction between research subjects and the researchers. This is not always the case when the subject's participation consists of providing tissue on which the researcher will then experiment. For experiments on tissues, interaction between the researcher and the subject occurs only if the project requires the extraction of new tissues. A major potential source of the raw material needed for stem cell research, however, is preexisting tissue collections. These include sperm or ova originally donated for IVF purposes, somatic cells collected in the therapeutic context and stored in tissue banks, and embryos cryopreserved in IVF clinics. In some instances, no consent was ever given to use these tissues for research purposes. In others, consent was obtained to use the tissues for a specific research project for which the tissue is no longer needed, or for research generally, without specific mention of stem cell research. Whether and what type of consent is required for use of preexisting tissues for research is an important and unsettled issue for stem cell science.

A. The Role of Identifiability Under the Common Rule

The relevant legal regime concerning informed consent for the use of preexisting tissue is complex. The common rule applies only to "human subjects," whom it describes as "living individual[s]."⁶⁶ However, the common rule's definition of human subjects includes not only living individuals from whom the researcher directly obtains "data through intervention or interaction," but also living individuals about whom a researcher obtains "identifiable private information."⁶⁹ This definition clarifies that the original donors of preexisting tissues constitute "human subjects" covered by the rule, but it then raises the question as to what constitutes "identifiable" information.

^{67.} A quite different issue is whether nontherapeutic research subjects should be offered financial incentives. See, e.g., James A. Anderson & Charles Weijer, The Research Subject as Wage Earner, 23 THEORETICAL MED. 359 (2002); Neal Dickert, Ezekiel Emanuel & Christine Grady, Paying Research Subjects: An Analysis of Current Policies, 136 ANNALS INTERNAL MED. 368 (2002); Ethics Comm., Am. Soc'y for Reproductive Med., Financial Incentives in Recruitment of Oocyte Donors, 74 FERTILITY & STERILITY 216 (2000).

^{68. 45} C.F.R. § 46.102(f) (2005).

^{69.} Id.

The common rule provides that information is identifiable if "the identity of the subject is or may readily be ascertained by the investigator or associated with the information."⁷⁰ According to a policy statement issued by the federal government's Office for Human Research Protections (OHRP), the agency responsible for guaranteeing compliance with the common rule, biological samples do not count as being identifiable under the regulations if the researchers cannot link the samples to specific individuals, even if the samples are coded and someone else possesses the key to the code.⁷¹ So, for example, according to the OHRP's interpretation, if a fertility clinic were to provide stem cell researchers with excess eggs, the common rule would apply and informed consent would thus be required if the individually identifying information was provided along with the eggs. But the common rule would not apply if the eggs were first anonymized (that is, stripped of all individually identifying information), or if they were given a code in place of individually identifying information, as long as the clinic agrees never to provide the key to the researchers.

Further, the common rule itself exempts from IRB review research involving the "study of existing... pathological specimens or diagnostic specimens, if ... the information is recorded by the investigator in such a manner that subjects cannot be identified."⁷² This provision suggests that researchers legally can use, without first obtaining informed consent, tissues provided by third parties that come with identifying information so long as the researchers do not record the identifying information themselves.⁷³

There is an even broader loophole in the common rule as well. IRBs may waive the informed consent requirement if they determine that the proposed research poses "no more than minimal risk to the subjects" and that the research "could not practicably be carried out without the waiver."⁴ Because the use of tissues that already exist outside of the donors' bodies would pose no physical risk to subjects, this provision clearly suggests that if a study's purposes require the use of identified tissues and if going back to donors for specific informed consent is impractical, researchers can (with IRB approval) proceed without informed consent.⁷⁵

- 73. See COLEMAN ET AL., supra note 64, at 707.
- 74. 45 C.F.R. § 46.116(d).

^{70.} Id. § 46.102(f)(2).

^{71.} Office for Human Research Protections, Dep't of Health & Human Servs., Guidance on Research Involving Coded Private Information or Biological Specimens 3 (Aug. 10, 2004), *available at* http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf.

^{72. 45} C.F.R. § 46.101(b)(4).

^{75.} Institutional Review Boards (IRBs) could, of course, deny the waiver on the ground that even research that is not physically intrusive could cause "psychosocial" types of harm. See infra text accompanying note 77.

Human embryos are capable of developing into living individuals given the proper conditions, yet the common rule appears to exclude embryos themselves from coverage.⁷⁶ However, the common rule would appear to classify both donors of gametes that formed an embryo as human subjects, subject to IRB oversight and informed consent requirements, at least for research that makes use of federal funds or is conducted by an institution that has pledged to follow the common rule in all research. As is the case for gametes and other tissues, there appears to be no federal bar to researchers using "deidentified" embryos for stem cell research without the specific informed consent of the gamete donors.

B. Autonomy, Not Privacy

Both the common rule's distinction between identifiable and nonidentifiable tissues, and the common rule's waiver provision, are inappropriate because they lose sight of the core value of autonomy that underlies the principle of informed consent. The identifiability rule protects donors' privacy and the possibility of discrimination or other consequences that the revelation of sensitive medical information might cause—sometimes called "psychosocial harms."⁷⁷ The waiver rule turns on the presence or absence of risk to subjects. Neither of these rules, however, makes any attempt to protect the rights of the donors as autonomous actors to decline to participate in research studies for any reason or for no reason at all. A further problem is that it is unclear the extent to which, as genetic technology advances, tissues can be deidentified and the protection of donors from psychosocial harms be completely guaranteed.

Perhaps for these reasons (although its reasons are not clearly delineated), the National Research Council's recently published *Guidelines for Human Embryonic Stem Cell Research* (*NRC Guidelines*) propose that informed consent be required, with no possibility of waiver, before any gametes, somatic cells, or embryos are used for stem cell research.⁷⁸ The approach of the *NRC Guidelines*, however, also fails to take seriously the core value of autonomy. When researchers must collect tissue specimens from donors, requiring the

^{76. 45} C.F.R. § 46.102(f) (defining "[h]uman subject" as "a living individual").

^{77.} See Strouse, supra note 1, at 140. When unusual genetic material is tied to demographic information, it would often be possible for a persistent researcher to identify an individual even if the data is technically deidentified. See Isaac S. Kohane & Russ B. Altman, *Health-Information Altruists*—A *Potentially Critical Resource*, 353 NEW ENG. J. MED. 2074, 2074–75 (2005) (describing the ease of reidentifying deidentified data).

^{78.} See NRC GUIDELINES, supra note 25, at 54.

scientists to obtain informed consent protects the ability of all potential human subjects to exercise self-determination over the use of their tissues: those who consider all relevant information and subsequently agree to participate in the research endeavor, and those who consider the information and decide not to participate. When researchers wish to make use of preexisting tissues originally collected for other purposes, however, it will often be too costly or too burdensome to trace the original donors, such that requiring specific informed consent for use of the tissue for the research project in question will effectively preclude the conduct of the research.⁷⁹ The NRC Guidelines' approach would protect the autonomy of those who would have declined to participate, but it would undermine the autonomy of those who would have agreed to participate but are effectively prohibited from making that choice.

How to balance the needs of both groups requires a subtle analysis, not the blunt prohibition proposed by the NRC Guidelines. The proper question to ask is whether the use of preexisting tissues for stem cell research without consent will facilitate or undermine what would have been the autonomous choice of most tissue providers had it been feasible to make research-specific, individual requests. Answering this question requires consideration of the circumstances under which the tissue was collected, whether the tissue is identified or deidentified (because privacy concerns would affect the participation decisions of many subjects), and the type of tissue involved (because this also might affect donor preferences).

If the donor provided consent to general research use of the tissue at the time of the donation, often called "blanket consent," it is appropriate to use the tissues for stem cell research. If the consent given was limited to the use of deidentified tissue, then it obviously should only be used if deidentified. If the original consent had no such limitation, no such limitation should be necessary when it is used in stem cell research.

A plausible argument can be made that blanket consent is never truly informed consent, because the tissue donor lacked all of the information necessary to make an informed decision about whether to permit the use of his or her tissue in the research at issue.⁸⁰ The problem with this argument, however, is that it loses sight of the fact that informed consent is not an end in itself, but

^{79.} See, e.g., Henry T. Greely, Breaking the Stalemate: A Prospective Regulatory Framework for Unforeseen Research Uses of Human Tissue Samples and Health Information, 34 WAKE FOREST L. REV. 737, 758 (1999); Strouse, supra note 1, at 142–43.

^{80.} Henry Greely calls such blanket consent for future research "permission" rather than "informed consent" since such broad consent cannot be fully informed. See Greely, supra note 79, at 754, 758–59.

rather a means to satisfying the ultimate goal of protecting research participants' ability to exercise control over the uses to which their body is put. The vast majority of the people who provided blanket consent probably would have provided consent, even for controversial hESC research, if researchers had been able to make the specific request at the time of tissue collection. The autonomy of these individuals is enhanced by a less restrictive rule. There is little doubt that some prior tissue donors who provided blanket consent to research use would object to their tissues aiding stem cell research, especially hESC research. The less restrictive rule admittedly compromises their autonomy, although it does not undermine it completely. Individuals who have made earlier tissue donations accompanied by blanket consent to research who object to the use of their tissue for stem cell research should be permitted to contact the repository of their tissue and withdraw or amend their consent for future uses.

The problem is more difficult when no consent to research use was requested or provided at the time of tissue procurement: for example, if somatic tissue was retained after treatment for potential therapeutic purposes, or if in vitro embryos were cryopreserved for possible future IVF use and then abandoned by the gamete donors. For most tissues, the identifiable/deidentifiable distinction made by the common rule is appropriate when it is impractical to seek informed consent retrospectively. As long as privacy is protected, it is likely that most individuals would not object to the research use of their banked tissues, but this presumption seems far less likely to be correct if the tissue can be traced to the donor.

In contrast, the use of embryos for stem cell research should never be permitted without consent, even if the embryos are deidentified. Empirical research shows that, when given the choice, remarkably few couples—fewer than 3 percent according to one study—choose to donate their excess IVF embryos to research.⁸¹ It is not well understood why most IVF patients apparently would prefer to see their excess embryos destroyed than used for medical research, and it doubtlessly would benefit society if these doomed embryos were put to scientific use. It is clear, however, that the principle of supporting autonomy requires the opposite presumption.

^{81.} See David I. Hoffman et al., Cryopreserved Embryos in the United States and Their Availability for Research, 79 FERTILITY & STERILITY 1063, 1068 (2003).

VI. SPECIAL EMBRYO CONSENT ISSUES

A. The Dual Donor Problem

Informed consent is more complicated in the case of embryos than it is for somatic cells or gametes, because there are two individuals from whom consent potentially could be obtained. Imagine that a married couple that created embryos for IVF gets divorced, and that one spouse wants to donate the cryopreserved embryos for research and one does not. Who has the authority to determine the use to which the embryos are put? This issue could prove quite important in the future if certain embryos—for example, those with rare genetic mutations—have unique value to researchers.

This precise issue arose in Kass v. Kass,⁸² in which the parties earlier had agreed that if they could not decide how to dispose of their frozen embryos, the unused embryos would be donated to research.⁸³ Upon divorce, Mrs. Kass sought possession of the embryos for implantation.⁸⁴ The New York Court of Appeals relied on contractual principles to uphold the parties' contingent agreement to donate the spare embryos to research.⁸⁵ In other cases in different jurisdictions, courts have been called upon to resolve disputes in which one spouse wished to use existing embryos for procreation (for his or her own use or for donation to another couple) and the other objected. In all of these cases to date, courts have ruled that the interests of the spouse seeking to avoid procreation outweighed the interests of the spouse seeking procreation, whatever the content of prior agreements.⁸⁶

The judicial decisions concerning disposition of stored embryos have appropriately recognized both the foundational principle of freedom of contract and the limitation of that principle when constitutional values are implicated. Contracts to procreate should be unenforceable on public policy grounds because of a constitutionally recognized interest in avoiding procreation.⁸⁷

86. See Davis v. Davis, 842 S.W.2d 588 (Tenn. 1992) (finding no preexisting agreement); A.Z. v. B.Z., 725 N.E.2d 1051 (Mass. 2000) (holding that preexisting agreement to donate was of uncertain duration and was outweighed by public policy supporting woman's desire not to become a parent); J.B. v. M.B., 783 A.2d 707 (N.J. 2001) (holding that preexisting agreement is unenforceable if one party changes his or her mind before donation is made).

87. See Eisenstadt v. Baird, 405 U.S. 438, 453 (1972) ("If the right of privacy means anything, it is the right of the *individual*, married or single, to be free from unwarranted governmental intrusion into matters so fundamentally affecting a person as the decision whether to bear or beget a child.").

^{82. 696} N.E.2d 174 (N.Y. 1998).

^{83.} Id. at 176-77.

^{84.} Id.

^{85.} Id. at 180-82; see also Litowitz v. Litowitz, 48 P.3d 261 (Wash. 2002) (relying on predivorce contract to dispose of embryos maintained for five years when both spouses later sought sole possession).

When procreation is not at issue, however, a couple's pre-IVF decision about the future disposition of excess embryos should bind them unless they mutually agree to change their instructions. This means that if the Kasses entered into an agreement at the outset of their IVF treatment that excess embryos would be donated to research, Mr. Kass should be permitted to direct the disposition of the embryos in that way.

It is important to recognize, however, that the issue of control over disposition is distinct from the question of whether scientists may use embryos directed to them for research purposes. Just because Mr. Kass is entitled to turn the Kasses' embryos over to scientists, it does not necessarily follow that those scientists should be permitted to use them for research purposes. Similarly, if a couple legally abandons their excess embryos, thus giving the IVF clinic the right to dispose of them, this does not necessarily mean that scientists should be allowed to conduct research on those embryos. The issue of control over the embryos needs to be separated from the question of whether research use should be permitted, which, as we have seen, properly turns on autonomy concerns.

Federal law is clear on this point, at least for research that falls under the common rule. Because the embryo is not implanted, it lacks standing as a "human subject" under the federal regulations. The two gamete donors (assuming that they are still alive) would both be considered human subjects if the embryos are not deidentified, and the consent of both would be required before the excess embryos could be used for research purposes. As argued in detail in the previous Part, the need for informed consent should not turn on whether embryos are identifiable because this distinction confuses privacy and autonomy interests. However, to the extent that dual consent is required, the law resolves the issue appropriately.

The autonomy principle that underlies the concept of informed consent requires dual consent, whether or not the common rule applies to the research in question, and whether or not the gamete donors are identifiable to the researchers. In this instance, my analysis is consistent with the positions taken by the *NRC Guidelines* and the guidelines promulgated by the American Society of Reproductive Medicine's ethics committee (*ASRM Guidelines*).⁸⁸ If one gamete donor would like to see excess embryos used for stem cell research and the other objects, protecting the autonomy of one party requires compromising the autonomy of the other. This issue obviously

^{88.} See NRC GUIDELINES, supra note 25, § 3.2, at 83; Ethics Comm., Am. Soc'y for Reproductive Med., Donating Spare Embryos for Embryonic Stem-Cell Research, 82 FERTILITY & STERILITY S224 (Supp. 1, 2004) [hereinafter ASRM Guidelines].

cannot be resolved by asking which outcome would protect the autonomy of more individuals, because the scorecard is even at one to one.

In this situation, the relevant question is whose autonomy would be compromised to a greater extent by protecting the autonomy of the other donor. The answer is that allowing the use of the excess embryos for research would cause more damage. Permitting the use would completely sacrifice the autonomy interest of the opposing donor in refusing to have his or her tissues employed in stem cell research. Not permitting the use would burden the other donor's autonomy interest, but to a far lesser degree: He or she could still choose to participate in stem cell research by donating other gametes.

Even more complex problems would arise if one or both gamete donors are not the same individuals who created the embryos at issue. Assume, for example, that an infertile couple uses donor eggs and sperm to create a number of embryos for implantation into the wife's uterus, the first implantation cycle is successful, and the parents want only one child, making excess embryos available for other purposes. Whose consent is needed before the excess embryos could be used for stem cell research? The courts would almost certainly find that the infertile couple has dispositional control over the embryos. Under the common rule, however, the consent of the gamete donors and not the infertile couple would be necessary before scientists could use the embryos for research purposes.

Here, the common rule's identified/deidentified distinction is a sensible proxy for the hypothetical choices of gamete donors when it is impractical to seek their actual choices. If the embryos are deidentified, research use should be permitted. Most individuals willing to allow their gametes to be used for another couple's reproductive purposes would not object to the use of embryos created from those gametes for research, so long as there is no risk that this use would violate their privacy (although, to be sure, not all gamete donors would feel this way). Such a prediction is far less likely to be accurate, however, if the genetic information contained in the embryo could be traced back to the donors.

B. The Timing of the Informed Consent Process

An unsettled question in the context of excess embryo disposition is when it is proper to obtain informed consent for research use. The ASRM *Guidelines* provide that the process should take place only after a couple attempting IVF has decided to discontinue storing their excess embryos.⁸⁹ The justification is that postponing a discussion of research use until that time protects couples just beginning the IVF process from facing any pressures to donate.⁹⁰ The assumption is that patients will believe the physician seeking informed consent would prefer to see excess embryos donated to research or to another couple rather than destroyed, and that patients will hesitate to choose an alternative option that risks disappointing their physician. The law in some jurisdictions, however, requires earlier presentation of all options for disposition. The California Health and Safety Code, for example, requires that fertility treatment providers obtain advanced written directives from patients concerning the disposition of excess embryos and that one option offered must be donation for research.⁹¹

In this dispute, it is an easy call to side with California and against the ASRM. The approach of the former reinforces the autonomy principle underlying informed consent by protecting the patients' decisional autonomy, and that of the latter undermines that principle. In addition, being informed about the possible uses of excess embryos—including but not limited to research—and being able to direct their disposition prior to the beginning of IVF might make some couples more comfortable with the IVF process. Pre-IVF choice reduces the costs of obtaining informed consent for donation by saving the patients and the clinic staff from having to arrange a meeting after treatment has ended. For all these reasons, it is unsurprising that the vast majority of IVF clinics ask their patients to designate prior to treatment what should be done with their excess embryos.⁹²

The ASRM's concern with the possibility of patients expressing choices that do not reflect their true preferences can be addressed by insuring that the informed consent process includes an explanation that the couple is free to change its decision at any time. This requirement is already found, in fact, in the common rule.⁹³ So long as the donors can notify their IVF clinic at any time after they are finished using its services that they have changed their mind and no longer wish to have excess embryos donated to research, any fears of subtle pressure to donate at the beginning of the process are alleviated. Couples who

^{89.} ASRM Guidelines, supra note 88, at S226. The American Academy of Pediatrics is in agreement. See Comm. on Pediatric Research & Comm. on Bioethics, Am. Acad. of Pediatrics, Human Embryo Research, 108 PEDIATRICS 813, 815 (2001).

^{90.} ASRM Guidelines, supra note 88, at S226.

^{91.} CAL. HEALTH & SAFETY CODE § 125315(b) (West 2006).

^{92.} See Andrea D. Gurmankin et al., Embryo Disposal Practices in IVF Clinics in the United States, POL. & LIFE SCI., Aug. 9, 2004, at 4, 6.

^{93. 45} C.F.R. § 46.116(a)(8) (2005).

feel pressured to give the "right answer" prior to receiving treatment can simply notify the treating clinic of a change in their preference when treatment ends.

CONCLUSION

The burgeoning field of stem cell research raises a number of complicated questions about the application of the informed consent principle to nontherapeutic research that rarely appeared in days before the explosion of biomedical research. Four have been addressed in this Article: (1) whether informed consent is required in nontherapeutic research not governed by the common rule; (2) whether informed consent in the nontherapeutic context requires informing tissue donors of the researchers' financial incentives; (3) whether specific informed consent must be obtained before new types of research may be conducted on banked tissues; and (4) when and from whom informed consent must be obtained before excess IVF embryos are used for research. In each case, the issues are best resolved by keeping an unwavering eye on the core value that underlies informed consent: facilitating the autonomous choice of research subjects. Requiring informed consent for its own sake, or confusing autonomy with privacy, can lead judges, regulators, and researchers astray.

FRIENDSHIP & THE LAW

Ethan J. Leib

This Article's central argument is that the law needs to do a better job of recognizing, protecting, respecting, and promoting friendships. The law gives pride of place to other statuses—family and special professional relationships are obvious ones—but the status of the friend is rarely relevant to legal decisionmaking and public policymaking in a consistent way. After defining the concept of the friend, I offer a normative argument for why the law should promote a public policy of friendship facilitation and for why the law ignores friendships only at its peril. I highlight how the law already finds friendship relevant in certain issue areas without any self-conscious or systematic understanding of it, and I recommend other issue areas where friendships without even recognizing that we are doing so, and friendship commands more attention from legal scholars and legal decisionmakers. I offer a framework to show how the law could exact certain duties from friends and confer certain privileges upon them as well.

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INTRODUCTION

The lawyer may have to utter with Montaigne (himself once a lawmaker), "O my friends, there is no friend."¹ To be sure, there are lawyers who advocate for their clients as friends.² There are those who sue as "next friends" on behalf of incompetents with whom there is no real or current friendship.³ And lawyers sometimes submit amicus briefs, as "friends" of the court.⁴ Countries even enter "friendship" treaties with one another.⁵ Yet, the status of the friend—the true friend that is not merely a friend by analogy—seems nearly absent from the law. We build within our legal system all sorts of preferences for family members—for example, the recognition of marriage in our tax law, spousal

^{1.} MICHEL DE MONTAIGNE, Of Friendship, in THE COMPLETE ESSAYS OF MONTAIGNE 140 (Donald M. Frame trans., 1958). This aphorism is attributed to Aristotle and is the source of a long set of reflections by Jacques Derrida. See JACQUES DERRIDA, POLITICS OF FRIENDSHIP (George Collins trans., Verso 1997) (1994); Jacques Derrida, The Politics of Friendship, 85 J. PHIL. 632 (Gabriel Motzkin trans., 1988). My own take on Aristotle and Montaigne's theories of friendship can be found in Ethan J. Leib, The Politics of Family and Friends in Aristotle and Montaigne, 31 INTERPRETATION 165 (2004).

^{2.} See Charles Fried, The Lawyer as Friend: The Moral Foundations of the Lawyer-Client Relation, 85 YALE L.J. 1060 (1976). But Fried acknowledges that "the ordinary concept of friendship provides only an analogy." Id. at 1071. For thoughtful discussions of Fried's thesis, see DANIEL MARKOVITS, TRAGIC VILLAINS ch. 3 (forthcoming 2007); Stephen R. Morris, The Lawyer as Friend: An Aristotelian Inquiry, 26 J. LEGAL PROF. 55 (2002).

^{3. &}quot;Next friend' status is a jurisdictional grant of standing to a third party. The third party is allowed to pursue the legal rights of the real party-in-interest. The grant of next friend status historically has been limited to cases where, because of incapacity, incompetence or unavailability, the real party in interest is unable to advocate his or her position." Paul F. Brown, *Third Party Standing—"Next Friends" as Enemies: Third Party Petitions for Capital Defendants Wishing To Waive Appeal:* Whitmore v. Arkansas, 110 S. Ct. 1717 (1990), 81 J. CRIM. L. & CRIMINOLOGY 981, 981 n.3 (1991). I discuss more about next friend standing infra Part III.B.4.

^{4.} See David Gossett, Friendship: Amicus Briefs in the Supreme Court, 8 GREEN BAG 2d 363 (2005).

^{5.} See, e.g., Treaty of Peace and Friendship, U.S.-Morocco, Jan. 1787, 8 Stat. 100.