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CHAPTER 1 *Summary of the Science of Stem Cell Research*

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Both the goals and methods of scientific research are rooted in the historical and social terrain in which science seeks answers to its questions. This is true as well for the specific fields of science relevant to stem cell research, including molecular biology, genetics, and clinical medicine. Because scientific research is by definition an inquiry at the frontiers of the known world, its questions are often destabilizing ones. The researchers, then, are often brought into conflict with those aspects of human culture that express the traditional and familiar, including political structures, law, and religions. In such cases science represents the intrusion and insistence of the modern against the veracities of tradition. Sometimes traditions can adjust easily through new interpretations and applications of the tradition that can accommodate new scientific discoveries. Other times, though, the new science raises immense problems of self-understanding and of ethics, requiring everyone, scientists included, to assess the implications of the new science for how we understand our world, our place in it, and our duties to maintain and repair it. In every generation this is a persistent task for Jewish intellectual life.

Questions of ethics are especially challenging when the new science

undermines our fundamental understandings of identity (who we are and who we choose to be) or changes our sense of the limits of our power (when it gives us tools to do things that our ancestors never were able to do). This leads us to ask whether we should assume the new identity and new agency that are available. This is the dilemma identified by Immanuel Kant in the late eighteenth century. As he pointed out, "Ought implies can." That is, if I cannot do something, then I never have to ask whether I should, because it is simply beyond my ability to do it anyway; but if I can do something, then I do need to ask whether I should do it, because there are all kinds of things that I can do that I should *not* do. This is obviously the case when new technologies are produced, and it is the case when new research presents us with dramatically new choices.

In the last two decades, one of the fiercest debates about our limits and our choices has been around the issue of human stem cell research—ever since James Thompson of the University of Wisconsin and John Gearhart of Johns Hopkins University first demonstrated that human embryonic stem cells, with their nearly infinite possibilities for differentiation and regeneration, could be grown in the laboratory from human embryos or gametes. Before we knew about stem cells and could manipulate them, we never had to ask whether or when we should do that, but now we must. In doing so we find ourselves not only addressing specific questions about the advisability and limits of using a particular technique but also reassessing the very nature of who we are, the connections we have to family, community, the environment, and God, and the limits, if any, we should impose on our capacity to do research and to heal.[1]

Although science has historically often been the cause of much of the unease about the new, the events surrounding the struggle over the research on human embryonic stem cells, beginning in the summer of 2001, have proven to be especially controversial.[2] In fact, this debate was one of the critical issues that generated the meetings that led to this book. This introduction to this section of the book about stem cell research begins with a definition of stem cells and a brief review of the emerging science and technology dealing with embryonic stem cells and the very newest research that has produced "induced pluripotent stem

cells" from somatic or adult cells, something that was not possible at the time when many of our essays were written. The introduction then asks how this research challenges our understanding of the nature of knowledge and forces us to confront anew the moral limits, freedoms, and responsibilities of research. Following this introduction to the science of stem cell research are several chapters in which Jewish scholars consider how Jewish texts, laws, concepts, and values can be interpreted and applied to this new emerging science in order to gain wisdom about how we think about ourselves and our world and how we should act in it in light of this new science and technology.

The State of the Science

Stem cells are called "stem" because they are cells that can change into several different kinds of more specialized cells. They are undifferentiated; that is, they are not yet specifically one kind of cell. Stem cells can produce either any kind of cell in the human body (they are "totipotent") or at least several different kinds of cells (they are "pluripotent"). Of course, all living creatures begin as one cell, a zygote. In people, as in all mammals, this is the fertilized human egg, just after the sperm cell has entered it. The most flexible stem cells are those in the early embryo that is formed five to eight days after a sperm and an egg combine; these are "embryonic stem cells." The one hundred to two hundred cells produced in these first few days after fertilization ultimately mature into each and every kind of cell in the complex human organism.[3] That is, they "differentiate"—specialize—into specific kinds of cells so that some become the heart, others the brain, others the lungs, and so on, each group with its particular nature to enable the human body to live and function. At about five days of gestation, the form we call an early embryo looks like a small circle (the perimeter of which later in pregnancy becomes the placenta) with a clump of cells inside that circle called the "inner cell mass." The inner cell mass and the large circle that surrounds it are together called a "blastocyst." That is the name of the embryo at this stage. It is these inner cells that are extracted for purposes of embryonic stem cell research, and in the process, the blastocyst is destroyed. The cells are

then placed in chemical solutions to enable them to develop; these are human embryonic stem cells in culture. As of this writing, sixteen years after the first stem cells were isolated, they are still replicating, which is why they are called "immortal" cell lines.

There are also stem cells in fully formed human beings; these are called "somatic stem cells" or sometimes "adult stem cells," whether they come from an infant or an adult. Somatic stem cells are not as flexible as embryonic stem cells, for they can change into only a few kinds of cells on their own, and they are not immortal. Still, the body uses them to renew blood, skin, and hair, for example, throughout an individual's life.

Biologists have long sought to understand how a single cell created when a sperm and egg combine ultimately creates a complex and highly differentiated system of intricate tissues and organs organized perfectly into a human being. How does the DNA program in the nucleus signal the cell to duplicate and differentiate? How does the small, microscopic mass of identical cells that have been formed in a woman's uterus or in a petri dish approximately five days after a sperm and an egg unite, the embryonic stem cells, ultimately form a human fetus?[4] Perhaps most intriguingly, if each of these cells of the early embryo has the capacity to develop into any and all cells of the human body, can that cell's mutability be used to create new cells in a person in order to heal him or her from a disease or to repair tissue that has been damaged?[5]

The process of embryology has long been studied through the use of animal models. Embryonic stem cells were first isolated in mice in 1981, and ever since then research has been conducted with embryonic mice, rats, and nonhuman primates. Much of the current success in understanding and using human stem cells, in fact, can be traced to the intensity of research in animal models, including the rapidly unfolding sciences of genomic mapping and molecular biology.[6]

Telomerase is an enzyme that enables genes to be flexible and to reproduce. In 1995 the genes for telomerase were cloned, enabling scientists to produce large numbers of them so that they could study them more easily. Biologists have used their expanding access to and knowledge

about telomerase to search for ways to understand how the cells in the early human embryo maintain their plasticity and immortality.

Parallel work has studied stem cells that are found in some tissues of adults.[7] It had long been understood that some cells of the body, such as the lining of our intestines, blood cells, hair cells, and skin cells, are constantly renewed.[8] Researchers found that some of these tissues contain rare precursor or stem cells that are undifferentiated and that develop into mature and functional cells in the body.[9] These adult stem cells have been found, cultured, and used to treat some conditions. In bone marrow transplants, for example, harvested blood stem cells have been used to regenerate a new blood supply, and harvested stem cells in skin have been used to begin the process of creating new skin for skin grafts to repair the skin of burn victims, for example.[10] But these cells are limited in several ways.[11] They are rare and hard to find; they are not available for all tissue types; and, when cultured in the laboratory, they always cease dividing and lose their self-renewal properties because, with each division, the telomerase at the end of the nuclear chromosomes shortens.[12]

Because of these difficulties with adult, or somatic, stem cells, researchers have long been intrigued by the embryonic stem cells that are the precursors to these adult stem cells. In part, the interest is purely investigational. It has been the quest of some researchers to study precisely how the embryonic stem cell is programmed to do this, to understand what goes awry in genetic diseases, and to observe how the environment affects developing cells.[13] In part, the research has been driven by a therapeutic goal, not only to understand and observe the process but also to find ways to coax embryonic stem cells into specific uses. Researchers began to speak about creating banks of tissues to repair tissues damaged by illness or injury.[14]

The benefits of such an endeavor, if it succeeds, would clearly be enormous, for many of the diseases that beset us in modernity are precisely degenerative diseases. These include stroke (6 million people have one each year), congestive heart failure (6 million), neurological diseases (3 million with Parkinson's alone), diabetes (100 million), and liver failure

(5 million from hepatitis alone). It is important to note that, unlike much of the focus of high-technology-driven medical research, diseases of cell death and cell control are not limited to the elderly or to certain classes or groups, for degenerative diseases also plague children. Spinal cord injury repair is a target of this research as well.[15] Furthermore, unlike the search for medical treatment of the symptoms of disease, molecular-cellular medicine is in pursuit of permanent cures to disease by alteration or replacement of the genetic and cellular causes of the disease itself.[16]

Risks and Benefits in Transplantation Therapies

To make regenerative medicine work either financially or ethically, it must be scalable, biologically stable, safe, and universally usable. For human use, the problem of histocompatibility must be solved. That is, a way must be found to introduce stem cells into a person's body without its immune system reacting to them as foreign objects and attacking them, ultimately leading to the patient's death and thus frustrating the effort to cure the patient (the "graft-versus-host problem").

The science is thus interesting not only in its own terms but also because of the premise of *widespread* access to *significant* therapy, an essential health-care justice issue. The hope is that tissue transplantation, unlike organ transplants, would not be a boutique therapy for the lucky or wealthy few but could be widely available to large numbers of people worldwide and could be used without the terrible risk of graft-versus-host disease. The idea is to use human embryos to derive stem cells that can be used for tissue transplants—either by creating tissue-banking systems, or by finding a way to match donor and recipient, or by creating a universal donor cell—or to understand enough about the way that cells reprogram themselves to regulate this process within the human body itself. So far, reports of scientific progress are remarkable and swiftly appearing in peer-reviewed journals. It was only in 1999 that the first human embryonic cells were grown in the laboratories at the University of Wisconsin and Johns Hopkins University, and in 2001 they were still dividing, well beyond their six hundredth population doubling.[17] Researchers have already discovered that neural cells placed in animals

with neurodegenerative disease migrate to the affected site, synthesize neurotransmitters, and extend neuronal processes. In laboratory studies at Johns Hopkins, John Gearhart has demonstrated that neuronal cells not only migrate to viral lesions in a living rat but also enable rats who have lost motor function to walk again. Liver cells make liver proteins; heart cells make contractile proteins, beat spontaneously, and respond normally to cardiac drugs; pancreatic cells make insulin. Blood cells have been made for all four blood groups. Still, with all this progress, the researchers were the first to admit that much of what they were seeking was a mystery—a terrain largely unknown. How do cells program and reprogram themselves? Can one create a universal donor cell?

The Ethical Problem of the Embryo's Moral Status

To procure embryonic stem cells, however, one extracts them from a five- or six-day-old embryo in a petri dish, thus killing it. Hence, the use and destruction of embryos for stem cell procedures immediately pose the significant moral question of the nature, meaning, and moral status of the human embryo. If it is already a human being, the killing of an embryo would amount to killing a person, so even though the goal of curing diseases is laudable, one may not kill one person in an effort to save another. On the other hand, if the early embryo is merely a clump of cells that would otherwise be discarded, then one may and arguably should instead use such cells to advance human knowledge and therapies.

Human embryonic stem cell research has been made possible by the technology first used in 1978 of in vitro fertilization (IVF), that is, bringing sperm and egg together in a petri dish. The resulting fertilized egg cell (the zygote) is cultured for a few days and then implanted in a woman's uterus. However, when a couple has produced several embryos in an effort to overcome infertility problems and either has had as many children as they want or has given up trying to have biological children of their own, the remaining frozen embryos that they produced in this effort are discarded. When the research first began, embryonic stem cells used by scientists came from embryos that such couples donated (and, in a Jewish side note, the initial embryos came largely from one

IVF clinic in Haifa, Israel). Typically, twelve embryos are created in the IVF process. If they are not transferred to a uterus, they will die. They can be frozen and stored (in the United Kingdom for five years, and in the United States indefinitely, as 100,000 of them are); they can be discarded (the most common course of action); or they can be donated for research. It is this creation and use of an embryo outside of a human body and in the hands of a largely unregulated marketplace driven by the deepest of yearnings for children that has reconfigured the moral landscape of reproduction in the developed world. For once one has created an embryo artificially, one is engaged in what has been a large but unstructured clinical trial without controls or even, in many cases, the careful consent of the people involved as required in other cases of medical practice and research.

How does one regard the central question of the moral status of the human embryo? As the National Bioethics Advisory Committee report on embryonic stem cell research clearly indicates, this is one of the key ethical disputes in society generally and among religions in particular.[18] It is also at the heart of American legal treatments of both abortion and embryonic stem cell research. Furthermore, does the status of the embryo in a woman's womb differ from that of an embryo in a petri dish?

In American law, the United States Supreme Court ruled in *Roe v. Wade* in 1973 that in a woman's womb a fetus is part of the body of the woman. Because American law grants adults the right to determine what may be done with their bodies, this means that a pregnant woman may choose to abort a fetus at will until such time that it can live outside her body—and even then, according to the Supreme Court's 1992 *Casey* decision, state statutes may impose some restrictions on the woman's right to abort but not to the extent that such statutes make it impossible for a woman to exercise this right. Recent state statutes that are being tested in the courts place significant restrictions on abortion, ultimately testing also the Supreme Court's determination that the fetus is a part of its mother's body and therefore subject to her will.

When couples create embryos outside a woman's womb for in vitro fertilization and have them frozen until they want to use them or discard

them, however, what is the legal status of such embryos? Courts have faced cases in which after creating such embryos the couple divorces, and then later one or both of them want to use the embryos to implant either in the woman so that she can have a child on her own or in the man's new spouse when other attempts at pregnancy fail. To whom do the frozen embryos created by the couple belong? The courts have variously ruled that outside a woman's body embryos are either communal property, full human beings (only in state law, for the United States Supreme Court explicitly ruled in *Roe v. Wade* that fetuses are not to be treated as full human beings in federal law), or something in between but deserving special respect and protection.[19] Whatever the embryos' legal status, neither party may use them without the consent of the other for purposes of producing one or more children, because each partner has a right to refuse to become the biological parent of the children born through the use of frozen embryos produced with his sperm and her ovum.[20]

Although American courts and state laws vary in their determination of the legal status of the embryo, Catholics and some Protestants unequivocally see the early embryo as fully a person, and hence embryos, in their view, may not be destroyed in research, for that amounts to murder.[21] Roman Catholic authorities have maintained during the last several hundred years that a fertilized egg cell in a woman's womb is a full human being. They therefore prohibit abortion even to save the life of the mother, for one may not kill one person to save another. Catholic authorities object to the artificial creation of an embryo in an IVF procedure altogether, but if one is created, then that embryo is, according to decisions of Catholic leaders in the last several decades, also a full human being, even though the embryo has no chance of developing into a person unless it is implanted in a woman's womb. As a result, Catholic authorities have fervently argued against embryonic stem cell research, for removing the inner cell mass from an embryo to do research kills the embryo, and if one may not kill an embryo or fetus to save the mother's life, then certainly one may not kill the embryo to do research, which is a lesser good.

As the reader will see in the Jewish reflections in this section of the

volume, the Jewish tradition takes a stance different from that of either American law or Catholicism. It sees the embryo during the first forty days of gestation (actually, the first fifty-four days, as Elliot Dorff's essay will explain) as "simply liquid" and thereafter until birth as being "like the thigh of its mother." The fetus does not become a full human being until birth, and only then does it attain all the attendant protections of full persons. This developmental view of the fetus in Judaism is shared by Islamic and some Protestant traditions.[22] Regarding the moral status of an artificially produced, microscopic blastocyst created entirely outside of a woman's body, halakhic (Jewish legal) experts have maintained that the small size of the blastocyst and its artificial location (outside of a womb) reduce even further the moral warrant for full status as a person.[23] The strong mandate within the Jewish tradition to seek to heal through both treatment and research and this developmental view of the status of the embryo have together led rabbis across the denominational spectrum strongly to endorse embryonic stem cell research, especially if the alternative is to discard the frozen embryos.[24]

Other Ethical Questions: The Reconstruction of Creation's Tale

As ethicists struggled to understand and defend arguments about the moral status of the embryos first used in stem cell research, the research itself began to ask more questions about the mutable origins of the blastocyst. The next set of ethical problems included the essential issue of whether these "excess" embryos were the correct way to obtain the embryos needed to create stem cells or if other ways of stimulating gametes could also lead to a blastocyst and, if so, what the status of that newly made entity would be.

It was a deeply disturbing line of questioning. The narrative of human reproduction—one man, one woman, a meaningful cleaving of one to the other, as humans have done since Adam and Eve, leading to progeny that carry the story forward—is at the heart of all three Western faith traditions. Indeed, it is through this human story that the monastic Western traditions and several of the traditions of Eastern and indigenous

religions as well tell of the creation narrative itself—it is a core narrative about the meaning, nature, and goal of being human.[25] Our understanding of ourselves as a part of this narrative, as children and then parents, also undergirds the religious imperative to procreate, the obligations inherent in the relationships within families and communities, and, in some religions, a commitment to natural law theory, according to which nature establishes not only physical laws but moral laws as well, so that nature tells us not only *how* things work but also how they *should* work.

However, since the early 1970s, the idea of the natural process of sexual reproduction has been disrupted by emerging scientific technology. Artificial reproductive technology has created many possible origins for any human embryo: it may be fabricated by mixing eggs and sperm or by injecting an egg with a selected sperm. The course of development may be altered as well. Sperm may be "spun" and separated by weight to select for gender; the egg may be altered to include extra mitochondrial DNA; embryos may be deselected by genetic trait so that only those embryos without a given trait (e.g., a disease like Tay-Sachs) are implanted in a woman's womb; the embryo may be implanted in a surrogate, the egg obtained from another woman or the sperm from another man, and the resulting child given to a family that may itself be constituted in a variety of genders and permutations. All of these disruptions in the core narrative have elicited considerable alarm initially and then extended social discourse about them and about yet other emerging possibilities. In many societies, the narrative has been reimagined, and retold, to account for these new possible origins of people.

But regenerative medicine offers not only another set of beginnings for the narrative of reproduction but also other possible ends for the embryo. Prior to artificial reproductive techniques (ARTs), a blastocyst conceived in a woman's body either implanted itself in the womb or, as in approximately 75 percent of cases, failed to implant and was naturally discarded during the woman's menstrual period. With the advent of IVF in 1978, a blastocyst fabricated in an IVF clinic might have any of at least four fates: it might be transferred to a human womb, where it might implant successfully; it might be transferred but not implant

successfully; it might be frozen; or it might be discarded. Now there is a fifth possible fate for the embryo: it might be destroyed in a laboratory in the process of being used to make stem cells for research or for curing diseases. Now that our society has allowed for the first four outcomes, the last, use in a research laboratory, can be understood as an alternate ending or alternative goal.

For many, such a deconstructed narrative, with the possibility of origins other than monogamous union and ends other than reproduction, elicits a sense of moral repugnance, the ultimate horror of a scientific, desacralized world. But for others, the revised narrative elicits a curiosity and awe at the new possibilities for human understanding and of the possibility to alter other key aspects of what had been understood as moral fixities—the nature and scope of human suffering, the "natural" span of a human life, and the limits of our capacity to alter our existence. We have, in other words, gone well beyond our "ordinary reach," or, as Pascal and Roger Shattuck name it, our *portée*.[26] It should be noted that both responses—fear and awe—indicate that we are on the brink of reconfiguring the meaning of a core narrative of our existence, and this alone should create a moment for ethical pause. It was largely for this reason that one of this volume's editors (Zoloth) approached the American Association for the Advancement of Science (AAAS) for help in creating the place and format for scientists and Jewish theologians and ethicists to think together about this and the other pressing issues in the book you have before you.

Between the time that that first project ended and this book was ready to be published, much had happened in the debate. As ethicists, we fought about the issues of human embryonic stem cell research along the lines described above for nearly a decade, and much of the debate was about the question of the moral status of the embryo. In 2006 another debate emerged—about whether researchers should pay women to acquire their eggs for research. This began when scientists wanted to try to clone embryos to deal with the problem of tissue matching (histocompatibility). Moreover, by that time scientists understood that many donated embryos might be flawed because many came from infertile couples, thus

diminishing the prospects of the success of the scientists' research. This led to a new round of debate both about cloning as a technique and about paying for human gametes. Meanwhile, an academic organization—the International Society of Stem Cell Research (ISSCR)—was founded, with ethicists (including Zoloth) on the board; the state of California allocated $3 billion to fund stem cell research and created ethical oversight committees (including Dorff) to create ethical guidelines for all stem cell research in the state; and President Obama changed previous federal policy so that the federal government would now support and fund stem cell research.

But in 2007, at the Toronto meeting of the ISSCR, the single most important change was announced, and it was a change in the science that promises to redefine the moral landscape. Shinya Yamanaka and his colleagues found a way to do what was thought to be impossible—to "reverse the arrow of time" and to change or deprogram an adult or somatic cell back to its original state as a pluripotent cell.[27] This meant that scientists had discovered a way to make adult stem cells behave substantially like embryonic stem cells by winding them back, as it were, to how they were before they differentiated themselves into specifically one type of cell (bones, fat, neurons, etc.).

Yamanaka's work was immediately understood as groundbreaking. He was awarded a series of scientific prizes and in 2012 the Nobel Prize for his research and its potential results. If human cells taken from a given patient could be reversed and reused to replace the patient's own damaged tissue, then there would be no problem matching the tissue, no graft-host incompatibility. The new cells would simply take over and begin to redifferentiate to a new cell type, thus hopefully curing the patient of his or her disease or disability. As a result, as of this writing, most of the laboratories that work on stem cells use iPS (induced pluripotent stem) cells from somatic (or adult) cells, discovering how they are alike and how they are different from hES (human embryonic stem) cells. However, iPS cells present significant safety issues. Yamanaka continues to work on solving the problem of how to prevent the implanted cells (he uses animal models) from forming tumors. But the advantages of

tissue matching and of avoiding the need for a continual creation and destruction of embryos are powerful.

Serious questions remain about all aspects of the research. The time lag between the very large promises of research, made to, for example, the citizens of California in order to obtain their approval of the three-billion-dollar bond measure to fund this research, and the actual results, which are still pending, leads to yet other questions.

The essays in part 1 of this volume reflect on many of these issues from a Jewish perspective—one that was created by several years of discussion and one in which, of course, you will find not one answer but many. Some of the essays focus on the moral status of the embryo, and some wrestle with other moral issues.

Furthermore, some authors approach the moral issues raised by embryonic stem cell research and the other topics of this volume using the methodologies of Jewish law. That is the usual way in which moral problems, including completely new ones, have been addressed in the Jewish tradition, even though this requires stretching precedents to apply to topics their authors never contemplated, let alone sought to adjudicate.[28] However, precisely because of the novelty of many of the issues in stem cell research and other areas of modern genetics, other writers call upon other resources in the Jewish tradition to address these admittedly new issues—sources like Jewish theology, stories, text study (in the textual reasoning mode), maxims, and history.[29] These varying resources and methodologies provide a richly textured Jewish response to these important and groundbreaking moral issues that confront us now in the field of genetics with all their medical promise and all their moral difficulty.

Stem Cell Research Is a Work in Progress

In late January 2014, *Nature*, a highly regarded international science journal, published two articles written by researchers who claimed to have discovered how to convert existing, fully formed, mature skin cells into something "like" embryonic stem cells.[30] If ordinary skin cells were subjected to stress (e.g., an acid bath), the cells would be transformed into

a totipotent cell, one capable of making any sort of tissue at all, including (unlike hES cells) placental tissue. This has been the long, elusive goal of stem cell biologists, of course: to create new tissue that would be a perfect genetic match with the person who needed the cells. While it had been discovered that mature cells could be reverse-programmed back to their earlier state, these induced pluripotent stem cells need tricky cocktails of viral vectors to rearrange the nuclear DNA, and so it had proven difficult to create such cells in the numbers needed for clinical use. This new research had been proven only in mice and using neonatal mouse cells, but the coauthor of one of the articles, Martin P. Vacanti, claimed to have replicated the study in human cells.

The story was made more appealing by its Cinderella-like aspects. The advance had been accomplished by complete outsiders at two of the major stem cell research facilities: Haruko Obokata, the lead author of one of the articles, a young female stem cell biologist at Japan's most prestigious lab, RIKEN; and Charles Vacanti, an anesthesiologist at Brigham and Young Hospital who was affiliated with Harvard but not working with the prominent Harvard stem cell biologists.

The reaction of the press was immediate; reporters were eager to discuss the fascinating news. But the reaction of stem cell biologists was more complex, a mixture of amazement and skepticism. One of the most interesting reactions came from the Knoepfler Stem Cell Laboratory, where researchers asked immediate questions: Can this work be reproduced by other laboratories? Will it work in human cells? Will it work in adult cells? (The trial only used neonatal mouse cells.) What are the molecular mechanisms? Do these cells possess significant rates of mutations or epimutations (the latter being abnormalities in the epigenome), and therefore will they prove to be unusable? Are these cells tumorigenic (i.e., do they produce tumors besides forming teratomas)?

Stem cell researchers began a poll on the project's believability and an open crowdsource blog where labs trying eagerly to reproduce the work posted their results. When, after eight weeks, none of the ten leading laboratories was able to replicate the work, some of the RIKEN authors (minus Vacanti this time) published a new methods paper that

for some did not clarify the process at all. Knoepfler then released a poll of three hundred stem cell scientists who believed the results in week one but by week three were overwhelmingly skeptical. As of this date (April 2014), no major stem cell laboratory has been able to reproduce the reports, and it is unclear whether it is impossible to reproduce them or just very hard.

How did bioethicists react to the news? First, it has to be said that many, many outsiders have been the ones to transform medicine. One needs only to read the story of Ignaz Semmelweis, the Hungarian obstetrician who fought and lost the battle to prove that hand washing prevents sepsis against the entire weight of European medical science in the mid-nineteenth century, or remember that the cure for peptic ulcers was discovered by a plucky postdoc who later would win the Nobel Prize to raise questions about the wisdom of the crowd.

Bioethicists understood immediately that if this idea were proven true, it really could transform medical knowledge. And if it were true, it was a curious thing: Why, if cells could be so easily reprogrammed into stem cells, did the process not happen more often in actual mammalian life—for instance, when you crushed your finger or, for that matter, drank orange juice? What kept the cells committed to their little tenacious fates? What, in short, holds reality together? Would cells that turned back time in this way be the same thing as brand new tissue? Next, of course, there was the disturbing ontological problem that has haunted all stem cell research in the last decade: Could this process be used to make humans? If any of my cells can be reprogrammed into any cell, what would keep researchers from restarting life from a cluster of them surrounded by others coaxed into being a placenta? But really, despite all the initial promise, everyone who was familiar with stem cell research had another more disturbing question: *How can you know if any purported research result is true?*

There is something familiar about all of this. In 2004 one of the coeditors of this volume, Laurie Zoloth, stood in a Seattle Hotel theater next to a gentle and thoughtful young scientist from South Korea, an outsider who had just announced that he had cloned human embryonic stem cells.

Zoloth was the ethicist who had read his *Science* paper and, as it turned out, was just as duped by the faked signatures on the faked consent forms as the science reviewers had been duped by the faked data and photos. The researcher, Woo Suk Hwang, personally promised patients in wheelchairs, politicians with dying wives, and thousands of envious scientists that his research was valid and done ethically. It took two years, a court, a media storm, and an international scandal before the claim was disproven. The skittishness that affected everyone involved is an inexorable part of any new revelation. Ironically, it was the journal *Nature* that had uncovered the deception and relentlessly pursued the story.

Wary of the reactions, *Nature* announced that some irregularities had been found in the papers, a "mix-up" of images, the authors then claimed. PubPeer, a science blog, raised further issues, and finally RIKEN launched its own investigation. And so we are faced with a puzzle, what philosophers call a question of "testimony." What counts as true knowledge? Who can be trusted to tell it? How can I know if it is true? This last question is from Immanuel Kant, who believed that patience is needed for real knowledge: "Truth is the child of time; erelong she shall appear to vindicate thee." We will have to wait and see if, this time, she will arrive.

NOTES

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9. A. J. Friedenstein et al., "Heterotopic of Bone Marrow," *Transplantation* 6 (1968): 230–47.
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11. "Rarely have experiments that claim plasticity demonstrated that adult stem cells have generated mature, fully functional cells or that these cells have restored lost function *in vivo*" (National Academy of Sciences, *Stem Cells*, 38).
12. Irving Weisman, testimony to the National Academy of Sciences hearing, Washington DC (May 2001).
13. M. J. Shamblott et al., "Derivation of Pluripotent Stem Cells from Cultured Human Promordial Germ Cells," *Proceedings of the National Academy of Sciences* 95 (Washington DC, 1998), 13726–31.
14. Paolo Bianco and Pamela Gehron Robey, "Stem Cells in Tissue Engineering," *Nature* 414 (2001): 118–21.
15. Thomas Okarma, testimony to Congress, Committee on Science and Technology, Stem Cell Hearings (May 2001), 1. Also see Sally Temple, "The Development of Neural Stem Cells," *Nature* 414 (2001): 112–17; and "Stem Cells Help Paralyzed Mice to Walk," MSNBC report on John Gearhart (paper presented at the Bar Harbor Conference, Maine, 24 July). Also in videos seen by Zoloth, personal communication, 10 December 2001.
16. Tannistha Reya, Sean Morrison, Michael Clarke, and Irving Weissman, "Stem Cells, Cancer and Cancer Stem Cells," *Nature* 414 (2001): 105–11.
17. Reya et al., "Stem Cells," 106.
18. National Bioethics Advisory Committee report, "Religious Responses to Human Embryonic Stem Cell Research" (May 1999).
19. Roe v. Wade, 410 U.S. 113 (1973), at 162; Cynthia S. Marietta, "Frozen Embryo Litigation Spotlights Pressing Questions: What Is the Legal Status of an Embryo, and Can It Be Adopted?," http://www.law.uh.edu/healthlaw/perspectives/2010/marietta-embryolegal.pdf (accessed 20 October 2013).
20. National Legal Research Group, Inc., "Recent Case Law on Division of Frozen Embryos in Divorce Proceedings," http://www.divorcesource.com/research/dl/children/03mar54.shtml (accessed 20 October 2013), referring to Davis v. Davis, 842 S.W.2d 588 (Tenn.), on reh'g in part, 1992 WL 341632 (Tenn. 1992), cert. denied sub nom. Stowe v. Davis, 507 U.S. 911 (1993); Kass v. Kass, 91

N.Y.2d 554, 673 N.Y.S.2d 350 (1998); A.Z. v. B.Z., 431 Mass. 150, 725 N.E.2d 1051 (2000); Cahill v. Cahill, 757 So.2d 465 (Ala. Civ. App. 2000); J.B. v. M.B., 170 N.J. 9, 783 A.2d 707 (2001); and Litowitz v. Litowitz, 146 Wash.2d 514, 48 P.3d 261 (2002).

21. For the view of some Catholics, see United States Conference of Bishops Pro-Life Activities, "President Bush's Stem Cell Decision," 20 August 2001. For that of some Protestants, see General Conference of the United Methodist Church, Resolution 31530-CS-NonDIs-O., 2–12 May 2000.
22. For one Islamic view, see Aziz Sachindina, testimony to the National Bioethics Advisory Committee, Georgetown University Hearing, Washington DC, 2000; and CBS News presentation, 9 September 2001. For other Protestant views, see Ronald Cole-Turner, Karen LeBacqz, and Ted Peters, testimonies before the National Bioethics Advisory Committee, Washington DC, 2000.
23. Objects, even living ones, that cannot be seen by the naked eye have a different weight in Jewish law. Other factors, such as the motility of an object, also play a role in legal status. Avram Steinberg is developing an argument that follows from the *halakhah* that prohibits the murder of a "man inside of a man," one of the seven Noahide Laws. Because this prohibition has been understood to refer to abortion, if the "man" is not "inside of a man," then the act would be different. Using the legal authority to argue from one case to another, stem cell research would be allowable. This argument will be elaborated in further work by Dr. Steinberg (personal communication with Elliot Dorff, December 2001).
24. See Elliot Dorff's article in this volume for a full discussion of the classical sources of this view and the ways in which contemporary rabbis have used them to formulate this stance. In fact, the agreement on this one point across a wide spectrum of Jewish traditions is unusual.
25. Variants of the creation story include heroic or divine-human conceptions, but all are based on sexual union, gestation, birth, and rearing as a linked narrative.
26. Roger Shattuck, *Forbidden Knowledge* (San Diego: Harcourt Brace, 1996). This idea of "ordinary reach" is first discussed in the introduction (45) and is developed throughout the book.
27. K. Okita, T. Ichisaka, and S. Yamanaka, "Generation of Germline-Competent Induced Pluripotent Stem Cells," *Nature* 448 (2007): 313–17, doi:10.1038/nature05934/pmid 17554338.
28. For a discussion of the advantages and problems of stretching Jewish law to address issues that it never faced and for the methodology that Dorff suggests for doing that, see Elliot N. Dorff, "A Methodology for Jewish Medical Ethics,"

Jewish Law Association Studies 7 (1991): 35–57, reprinted in *Contemporary Jewish Ethics and Morality: A Reader*, ed. Elliot N. Dorff and Louis E. Newman (New York: Oxford University Press, 1995), 161–76; and see Elliot N. Dorff, "Applying Jewish Law to New Circumstances," in *Teferet Leyisrael: Jubilee Volume in Honor of Israel Francus*, ed. Joel Roth, Menahem Schmelzer, and Yaacov Francus (New York: Jewish Theological Seminary, 2010), 189–99.

29. For a discussion of how each of these resources within the Jewish tradition can be and has been used in providing moral guidance, even on issues that are completely new in kind or degree, see Elliot N. Dorff, *Love Your Neighbor and Yourself: A Jewish Approach to Modern Personal Ethics* (Philadelphia: Jewish Publication Society, 2003), appendix, 311–44.
30. David Cyranoski, "Acid Bath Offers Easy Path to Stem Cells," *Nature* 505 (2014): 555–608; Haruko Obokata et al., "Stimulus-Triggered Fate Conversion of Siomatic Cells into Pluripotency," *Nature* 505 (2014): 641–47.