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Stem Cells, Therapeutic Cloning, and the Soul

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Stem Cells, Therapeutic Cloning, and the Soul[*]

Robert Pollack

> *"Poets and physicians are closely allied in thought. Diagnostics and cure (truth and love, in essence) belong to both professions."*
>
> - Robert Graves, in a letter to me, December 30, 1961

I would like to talk about the topic of stem cell research in a way that is sensitive to the religious component of it. It is a delicate, difficult thing to do and the only way it will work is if I am completely honest about my own opinions and if I am fair to what I take to be the President's opinion, as expressed in his document of August 10, 2001, which is the operative policy of the United States today on this issue.

President Bush has been this country's most effective teacher of biology since Clarence Darrow. No longer can any citizen blame a bad experience in a high school or college class for ignorance of these facts:

• Two sorts of cells – sperm and egg – can live longer than the persons whose bodies produce them. For this to happen, these cells must first join their genetic material together to form a fertilized egg cell with a totally new and unique version of the human genome.

• When a fertilized egg finds itself in a special environment – a woman's uterus – it may multiply and differentiate into a new person, whose individuality will be based in large measure on its new genetic makeup. In the laboratory, sperm and egg can be mixed together to form a fertilized egg that will then divide in a dish to produce an early embryo in vitro, which may then be implanted into a woman's uterus to develop into a person, or frozen into a state of suspended animation, or dissociated into separate embryonic stem cells for further study, or discarded.

• Scientists working without federal support have dissociated early embryos into separate cells, and from these they produced some sixty lines of cultured cells that now

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[*] Edited informal remarks made at the George C. Marshall Institute Roundtable discussion October 17, 2001.

are claimed to grow indefinitely in a dish. Each of these one day may be stimulated by hormones to differentiate into any of the cell types that make up the body and brain of a person. Such differentiated cells derived from early embryos may have broad medical utility. They may – in principle, if not yet in practice – be used to replace tissues worn out by aging or destroyed by accident or infectious disease, or they may be able to rescue the tissues damaged by genetic disease, the inherited inability to produce or maintain one or another aspect of normal tissue development.

All of this current and future biology can be found in the President's short speech of August 10. From these facts and hopes, the President reached the following two conclusions:

- First, the Federal government will fund further research with the sixty currently reported embryonic stem cell lines.
- Second, the federal government will not fund research that would establish any further undifferentiated embryonic stem cell lines, nor research into any other uses of human egg cells.

Both of these conclusions were unexpected, I think it is fair to say, and, given the science that accompanied them, both have been hard to understand. The immediate question raised by the first of these two decisions is, why so many cell lines? If stem cell lines can grow as little balls simply by being given nutrients but not differentiating signals, why not just one cell line, grown and partitioned by the government into as many vials as needed? The complementary question raised by the second decision is, why only these sixty? Having revealed his distaste for the idea of dissociating the cells of an embryo for research purposes, why did the President not authorize research on other technologies that might yield the same or better clinical outcomes without this distasteful initial step?

While neither decision makes sense on the basis of the science used by the President to support it, each becomes understandable when seen through the lens of his

publicly acknowledged, deeply held religious convictions. It is odd that no one – not the President, nor the press, nor the many corporate and university ethicists, scientists and doctors who have spoken out in the past few weeks – has seemed comfortable admitting the matter of personal religious belief to the discussion of these two decisions. Rather than trying to articulate the President's reasoning – which would require acknowledging that religious belief has had a place in the national discourse, a fact that that everyone surely already knows but apparently cannot say aloud – most commentators have concluded that these decisions represent no more than the ordinary political compromising.

And so, the President has been criticized by some for allowing federal funds to be spent on even one such cell line, and by others for denying federal funds that would go to basic research that might generate the medically most useful cells for therapeutic purposes. To consider the religious content of these or any other political decisions may seem parochial, but everyone – especially those of us who claim as scientists to be willing to look at all the data – ought to pay attention the beliefs of others and our own religious convictions, because after all they are data in their own right.

To look at the religious content of the President's two decisions, we have to begin with a four-letter word: soul. I trust I will be forgiven if I slip up on details of religious doctrine, but to me the President's notion of a soul is straightforward enough. Many people – and I am among them – feel that the essence of anyone's individual unique value as a person cannot be reduced to 3 billion base pairs, nor even two unique versions of that long string of letters. For us, the essence of being human has to encompass our purpose in being alive as well as the mechanics of biological survival. For those – and I am one of them as well – who believe that our purpose in being alive is to receive both life and its meaning from an unknowable God whose intentions include our well-being, it follows with great force and simplicity that our bodies are in some way sacred. A common way – not the only way – to express this strong feeling of being more than a mass of cells with a unique DNA sequence in each, is by the old Greco-Roman

notion that located somewhere in each of us is an ineffable, non-physical presence, which we may call the soul.

By its sacred non-physical nature, the soul cannot and will not be studied through science; its presence is a matter of pure belief. For those who also believe in a Creator-God the soul is a gift from the Creator. But the notion of a soul does not depend on the belief in a Creator-God, nor must it be restricted to people. Many people accept a physical world that lacks a Creator, and believe nevertheless in an essential quality in any living thing that lives through many generations of bodies. While dissociating the notion of the soul from the physical reality of any one living being, they discover deep and important meaning in their own lives by taking on the obligation to act in such a way that their souls may be so elevated as to attain a higher body in their next reincarnations. The thread that ties together these and other different conceptions of the soul, is the notion that no measurable, controllable aspect of the natural world gives meaning to our lives so well as does something unnatural, immeasurable, and ineffable.

Of course there is no consensus on the matter, and many other people, accepting the evidence of the data we have at face value, conclude that each person is precisely devoid of any essence beyond his or her physical being. But we have only one President, and I think we may assume from his public statements that he is one of the many Americans who believe that each person is the bearer of a sacred soul, and further, that he believes this soul resides not only in every living person, but in every human cell or collection of cells with the potential to become a person. If one believes this – and again, let me remind us that beliefs are not subject to verification by data; no one needs to display evidence of souls to believe in them – then the facts of biology so clearly delineated by the President must be deeply unsettling.

The entire technology for the production of embryonic stem cell lines depends upon a willingness to foreclose the potential of a fertilized egg or early embryo for the sake of the utility of its constituent cells. In these religious terms, that is the same as

acting to destroy the physical home of a soul, thereby – depending on the particularities of one's beliefs – either sending it back to its Creator or destroying it as well. The belief that a technology founded in such an act is wrong and should be forbidden may be insupportable by data, but it is neither silly nor intrinsically dangerous. Indeed, it is grounded in the same good intentions that proponents use in arguing for the eventual use of these embryonic stem cell lines: the intention to save a life, and – in religious terms – thereby to save a soul.

From this perspective one might have expected the President simply to forbid federal funding for work on any cell lines derived from intentionally disrupted human embryos. His first decision – to allow federal funding for research on cells derived from any one of sixty such destroyed human embryos – suggests he may have acted against his own beliefs. Why are these sixty lost souls – but no others – to be commemorated by the utility of their constituent cells? Does the President wish our government to have the authority after all to separate among embryos, and declare some the bearers of sacred souls, and others merely balls of cells? Sixty years ago the Nazi regime – driven not by any wish to cure disease but rather by the simpler wish to remove from this earth some souls within their grasp – had a word for other such disposable people: *Ballastexistenzen*, lives not worth living.

Now that cells from the sixty lines have been declared by the President to be simply a commodity, their value has already begun to be measured as much in economic as in medical terms: there is a lot of money to be made here, and though these sixty cell lines may now be studied with government money, they are not the property of our government. They belong to many different private companies and universities, none of which are likely to be particularly interested in matters of the soul. For non-believers, their possible utility in medicine may justify the use of cells from these sixty lost embryos, but given his own beliefs, why did the President not demand instead they be given a decent burial? The pressure of scientists' promises on the President must have

been great, to push him to this act of what for him must have been willful denial of the sacredness of sixty unborn children's souls.

We know some of that pressure from his speech: only with both federal support and private investment will these sixty lines, it was argued, provide medicine with a powerful new source of treatments, specifically the replacement of damaged tissues by the differentiated progeny of embryonic stem cells. But that argument cannot be the whole story, for two reasons: first, it still leaves us without an explanation for the second decision to make these sixty lines the only sources of such future government-supported medical breakthroughs. And second, it disingenuously ignores the likelihood that such uses of cells from these sixty lines are likely to be clouded by the inevitable problem of immune reaction, a problem that has already cast a pall over the injection of novel genes or embryonic cells in medical practice.

No medical use of the progeny of these sixty lines is likely to escape this problem, which derives from the basic biology of human genetic individuality. Each stem cell line will have the genetic specificity of the lost embryo from which it came, not that of the recipient who might need its differentiated progeny. As a result, immune rejection will always set a limit on the utility of these cells in medical practice. Consider a person with type-I diabetes, whose pancreas was depleted by viral infection of all cells that produce insulin on demand. Or, consider a person born with a single mutation that will result in the eventual loss of cells in a region of the brain and bring on the lethal symptoms of Huntington's disease. In a technology based on the sixty cell lines, cells from a lost embryo would be differentiated in a dish into insulin-producing cells or the appropriate sort of nerve cells, and then injected into the patients who, it is hoped, will recover as the cells land in the proper place and carry out their normal differentiation, either by making insulin as called for by the other tissues of the patient, or by linking up to other nerve cells in the brain.

But based on current information we can expect cells from any of these lines to express their own unique, lost genetic individuality as a set of proteins on their surfaces, thereby making the injected cells targets for the recipient's immune system in each case. In other words, we can expect immune rejection to be a concomitant of successful differentiation, and an intrinsic limitation to treatments based on these sixty lines. How sad, then, that the President felt compelled to yield on a matter of religious belief for so risky a promise; and how unfortunate that he compounded the risk by his second decision to set so severe a restriction on further research, when a different line of research might make those sixty lines unnecessary.

There is a second technology for obtaining stem cells, one that has neither the problem of immune rejection in its future, nor – in my opinion at any rate – the taint of a lost soul in its design. The technology of therapeutic cloning has no focus other than the clinical needs of one person at a time. In this technology, an egg cell donated by a woman – not a new embryo, but a cell with no full human genome and no chance of becoming a person – would have its nucleus removed and a nucleus from a patient put in its place. The egg cell's remaining material – its cytoplasm – would reorganize the genes of the patient's genome, so that the donor's genes would recapitulate each embryonic stem-cell stage their ancestral cells went through soon after the earlier formation of the fertilized egg that would become the recipient. The egg cell cytoplasm would be using the donor's nucleus to spin off a population of stem cells, each with the capacity to differentiate in as many ways as a doctor might want, and each also specifically marked on their surfaces with the molecules found only on the cells of the donor.

Nor is that all: if the donor of the nucleus were the victim of a mutational disease like Huntington's Disease, the genomic lesion first could be repaired by genetic engineering of donated cells from any tissue – blood or skin, say – and then the genetically-repaired nucleus could be transferred into the egg cytoplasm. In this way a person might be given a set of appropriately differentiating cells that were otherwise

genetically his or her own, only freed from the mutation and therefore able to reconstitute the normal function that the inherited disease had foreclosed.

One more advantage: the genetic engineering of the donor's nuclear genome need not be solely to repair an inherited mutation. We know, for instance, that the immune cells of persons who inherit the otherwise unremarkable absence of the cell-surface protein CKR5 cannot be infected by HIV, the AIDS virus. Such people are rare; they can be identified as remarkably resistant to AIDS even when they engage in repeated high-risk behavior. One might therefore expect that nuclei donated by any HIV-infected person, if genetically engineered to remove the gene for the CKR5 receptor and then passaged through egg cytoplasm, would produce new cells for the AIDS patient's immune system that might re-establish a healthy immune system despite the virus's presence, and even perhaps allow for his or her survival and long-term recovery.

Engineered this way or simply taken from a tissue, differentiated cells from therapeutic clones should not be rejected by the immune system when they are used to treat the donor's own illness; instead, they have the better chance to become a new form of medicine, a tissue replacement treatment designed solely for the one person who donates the nucleus.

Why did the pressure that drove the President to accept research on those sixty cell lines, not also push him to approve further research in this alternative source of stem cells, a source less useful perhaps for basic research, but more precisely tuned to the clinical uses he called upon to justify his authorization for continued research with those sixty lines? Perhaps it was a matter of the soul. One might argue that there is no new soul in the egg cell donated by a woman. But what of the egg cell with the donor's nucleus in it? The former cannot become a person. The latter is genetically the same as a person whose soul is at risk from the very disease this technology might ameliorate, delay or reverse.

Perhaps the President considered that the transfer of the nucleus of a donor into the cytoplasm of an egg was sufficient to create a new soul, insofar as that new cell might have the capacity to be a person. After all, identical twins also share an identical, unique genome, yet certainly each twin has a soul. In any event, the reason given by the President for turning away from this technology did not call upon the notion of a soul, at least in public, but was based instead on the anxiety that if placed in a woman's body for the requisite nine months, a reoriented human genome in a donor egg cytoplasm might be born as either a clonal copy of the donor, or a genetically-engineered one.

Here the President seemed to be on very strong ground: a cloned human would be a terrible experiment, performed on a person for his or her entire life, with no chance of that person withdrawing from the experiment if it does not go well. A cloned person might have a soul, but the process is abhorrent and of absolutely no clinical utility. It would create a situation little different from slavery. If a child is in any sense the property of its parents, that is only because we presume them to be bound together by that most irrational of feelings, love. The person emerging from an experiment in which a therapeutic clone were placed in a woman's body and carried to term, would be the object of fascinated attention – if not the property – of the scientists and doctors who initiated his or her novel genome, and their funders. Their interest in that child would be in its experiences an experiment, an interest hardly based on love; parental consent would merely legitimize a degree of disinterested ownership over another person from birth through death.

In medical terms, cloning a person for any reason sacrifices the current generation for the next, and as such it does not serve the purpose of medicine, that is, to alleviate or cure the suffering of a person already here among us. The creation of any cloned child with a changed genome would be in addition a Promethean grasp at the human germ line, but even cloning a person without genetic manipulation would convert kinship and childhood into just the sort of commodities those sixty cell lines have

become. As a friend once said to make me think again about performing a particularly seductive experiment, if it isn't worth doing, it isn't worth doing well.

The well-founded anxiety that therapeutic cloning might be misused to create a cloned child – and I share this anxiety with a clear majority of polled citizens – is no reason to turn away from the new technology of therapeutic cloning. Between the therapeutic clonal cell line and the cloned person stands a formidable barrier, one that I am sure makes this second technology both feasible and safe. That barrier, completely invisible in the President's talk but no less solid for that, is a woman's body. Human eggs – the sole source of that brilliant cytoplasm that can send a human genome down the paths of differentiation into all the different cells of the body – are the product of women's bodies. Human embryos and fetuses and newborns are also the products of women's bodies. No potential person can become a person outside of a woman's body. And, in our country at this time, a Supreme Court precedent exists for the notion that a woman, but not her fetus, is a person under the law and therefore subject to both the freedoms and the responsibilities of the law.

Again, the President did not mention a woman's body at all. I cannot be sure of the reason for his having left out this aspect of the biology he has so clearly mastered, but I suspect it was because he was confounded by his religious convictions on another matter entirely: the right of a woman to the use and control of her own body, up to and including her right to end the life of a fetus within her so long as that fetus could not survive outside her body. In the President's publicly stated view, a woman who elects to abort her fetus is ending the life of a new soul, and for that reason she is making a profound religious error. He is of course entitled to this opinion, as are the many Americans who agree with him. It is an opinion that may help in an unexpected way to determine the relative merits of embryo disruption or therapeutic cloning, in medical and religious terms.

The precedent set by the current law opens a rather unexpected door for the President. Consider what would follow if legislation now being discussed were passed into law, and carrying a human clone to term were made illegal. It is clear the President supports such a law and, given what I have just said, so do I. But how else could such a law be enforced except under the aegis and with the full endorsement of the current law that holds a woman responsible for the decisions she makes concerning the initiation and termination of her pregnancies? "Pro-choice" and "Pro-life" positions would each face the odd necessity of accepting a portion of the other side's argument in order to retain the merit of their own. From a pro-life position, it would be necessary to acknowledge that a law forbidding the carrying of clones to term could be enforceable on a woman only in the context of every woman having the complete right to choose her actions in this matter; from a pro-choice position it would be necessary to acknowledge that such a new law set a limit on the legality of a woman's choices, albeit in the direction that this position already holds to be the measure of a woman's freedom.

Were such legislation to become law, then women would be held properly responsible and accountable to assure that a therapeutic clone would not become a person. Under those circumstances, each therapeutic clone would have only one function – the amelioration of suffering – and one could argue that as no new soul could have been intended by the technique, none was there. If the President had only accepted the full responsibility of women in this country in that part of their lives that men cannot replicate but only control, he might have been able to avoid his first decision, which was so clearly in violation of his deeply held religious beliefs. If he had instead issued a strong call for therapeutic cloning from donor eggs, coupled with an equally strong sanction against the intentional creation of new fertilized eggs for research purposes and the implantation of any experimentally modified human embryos into a woman's body, he would have opened up a most promising second line of basic research for all, instead of restricting federal support to a set of cell lines tainted by the crushed intentions of their donors that they become people, the certainty of immune rejection down the road, and the commercial implications of a premature monopoly.

In religious terms, that position – while being wholly consistent with all the data of biology to date – would have freed him from the burden of having authorized research on cells that were indeed once intended to be persons in their own right. But because such a ruling would be binding only on women – there is no other place to find a uterus – it would have required him to accept that a woman is fully responsible for her body at all times, and that a pregnant woman but not the fetus within her has the legal standing of a person in law. Unable to do this, he issued instead only a strong condemnation of even therapeutic cloning, as if the availability of a woman's body once the cloned line had been made could be taken entirely for granted. It is insulting if not illegal to give women so little credit and so little power that it becomes necessary indirectly to protect them from this potential misuse of their bodies by forbidding therapeutic cloning, a technology that begins with a woman's egg but not her uterus, and might conceivably end with a new, safe – and safely soulless – secular technology of healing.

There will be many consequences to the President's two decisions, whether or not congress approves them and they become law. Most are not easily predicted at this time, but one is already clear enough. If either a technology based on the sixty cell lines or one based on therapeutic cloning does lead to safe medical treatments in the near future, then we will find ourselves in a situation of deep and troubling unfairness – and therefore, I think, of religious error – in this country. The Federal government has agreed to license the use of sixty stem cell lines for basic research, but any medical use of them is likely to be available only for a price high enough to recoup the costs of its development. Health insurance will pay for that, one assumes, but currently about fifty million Americans are without medical insurance, and hence without access to any of the positive developments from this technology. In religious terms, then, the cells of sixty lost souls may be transmuted into good medicine, but then the souls of fifty million Americans will not be preserved nor protected by that eventuality. Here, the religious question will remain what it has been for decades: why not?

There is always time to begin to do better. As a woman provides the egg for a therapeutic clone, one may imagine a situation where the technology may serve to ameliorate the current grotesque imbalance between the our government's current moral fastidiousness about potential lives, and its policies that seem designed to shadow current, actual lives.

Consider a woman suffering from AIDS, who is neither eligible for federal medical insurance nor able to work at a job that would provide her with private insurance. How elegant it would be – and how clearly different from current policies concerning such women – if the first therapeutic cloning were done for her, using her own eggs and their own nuclei, creating for her a CKR5-deleted, HIV-resistant immune system at no cost to her, simply because she is a fellow-citizens facing death, and because this might offer her a chance to live.

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Question and Answer Session

Q: If therapeutic cloning were permitted, there is the possibility that some unscrupulous doctor or biologist would put such an egg in a woman and a clone would be formed. Then the government would face the problem of first, finding out about the clone and second, having to exercise some judicial procedure, which might well take several months, and then force this clone *in utero* to be ejected even at an advanced stage of development. Wouldn't this cause great emotional problems for the woman carrying the fetus and possibly create a huge public outrage?

Dr. Pollack: The anxiety attached to an incident is in proportion to the number of people engaged in doing it and what their real intentions are. No woman can be put in such a situation by herself or by herself and a man. It requires a laboratory, people trained to do that kind of work, sterile technique – it requires, in a sense, a large conspiracy of people engaged in bad medicine. That conspiratorial intent to do something with no

medicinal value is a problem for this country and all other countries *in any event*. If right now a child is being born who is a genetically-engineered clone of a parent, because the parent has the bizarre notion that it is possible to stay alive through the child, we don't have any legal or medical tools to deal with that situation right now. That is a problem. My point is that our anxiety about that problem has kept us from talking about the importance of forestalling that event, and one way to forestall that event by all means possible is to open a line of research which the President did not discuss.

Q: If you were able to restore the immune system of someone with AIDS with these stem cells, would the person have permanent immunity from the virus and would it alter the behavior that caused the infection with AIDS in the first place?

Dr. Pollack: Those are two wonderfully different questions and I'd like to quarantine one question from the other. As to the first one, which is a question of science, I have laid out, in a way that I think is fair to the data I know, a hypothetical set of future scientific scenarios and outcomes; I can give you any answer you want as to how it works, because it doesn't work at this point. I think it is within the realm of what I understand to be doable and by extrapolation of what I know to be published, that one could get an early enough differentiating state in culture that becomes an ancestral stem cell in the marrow and keeps spinning off new lymphoid and erythroid cells forever, functionally. But that is not a clinical operation today; it is something that people are trying to do in mice today. The argument of sixty cell lines includes the argument of doing something like that. The AIDS trick is my idea; I haven't seen it published anyplace. Now if you did that, would you change someone's choice of private behavior? I don't know and I don't care. That's what "private" means. The social issues of how we live with each other and different behaviors are a serious question and I don't mean to diminish it, but I don't think medicine has a place in that question and I am trying to stay focused on the medical uses of this technology.

Q: But if you were able to successfully restore the person's immune system and they didn't change their behavior, would they be infected again?

Dr. Pollack: My sense is that the model experiment leaves you with the clinical status of a person who has a natural mutation which lacks this CKR5 receptor who appears otherwise healthy, but lacking this receptor, his cells will not be infected by HIV. Once a person had such an iron-clad immune system working, presumably the body might suffer HIV but not the blown-out consequences to the immune system. That is a guess, not an experimental result.

Q: First, I share your convictions about the mind-body problem and about the soul. After that, I disagree with almost everything you said. I don't know what the President thinks or doesn't think but there is certainly a question about when a soul enters a group of cells. I regret that I have not read Leon Kass's treatise on this thoroughly enough, but I assume that his argument is that the soul does not enter immediately; his recommendation on the use of any clone lines must depend on the notion that the soul does not enter immediately, because he is very much of the same opinion with regard to the sanctity of life. But I think there has been some serious thought about it and some basis for deciding that you can use these sixty cell lines.

Dr. Pollack: Different faith traditions have different answers to the question. The point I wish to make is that this country's population demographic suggests that majority of people do not have the Jewish or the Buddhist or the Muslim concept, but rather the Christian concept that the potentiality of life equals life. Now the Talmudic argument is something on the order of forty days; a failure of the pregnancy in the first two months or so is not considered a failure of pregnancy at all. In legal theory going back 1,500 years, a fetus does not gain human status until the head emerges from the mother's body, so right up until the last moment, an abortion for the sake of the mother's life is considered good medicine. My point is that this is a political question *and* a religious one and the political obligation we all have is to understand, in a representative society,

that a majority position will have weight, whether it is publicly acknowledged or not, and so Leon's argument is interesting but, in my opinion, only in an academic sense.

Q: I think he has influenced the President. I wonder why are we even talking about therapeutic cloning before we have model systems in animals that really work. I believe in the Hippocratic dictum "First, do no harm." We've had ten or eleven years of gene therapy and in spite of huge efforts in the United States, there has not been a single disease that has been cured by gene therapy here. The only place that it has been done successfully done is in France and there they had an animal system completely worked out before they turned to human beings. The technology in mice and rats is now rather advanced in terms of one specific type of gene therapy and that is regeneration of spinal cord damage. I think that once this therapy is available to human beings and Christopher Reeve steps out of his wheelchair – and I am convinced that he will in another ten years – the political pressure at that point will be so enormous that many of the problems that we are now discussing on a theoretical basis will be overwhelmed by political pressure to forget about souls and move ahead to do anything that we can do. Our major concern is to reduce the hype that accompanies gene therapy and cell biology. I agree that we should stop the cloning of human beings; it's meaningless. But even with therapeutic cloning, you must first show that it works on animals and then do experiments on humans later on, not now.

Dr. Pollack: I don't have a large argument with what you say. I put this talk together in response to something unprecedented in your world and mine: a Presidential decree on what is and is not permitted in basic research. Once that occurs, we are no longer able free to decide to level of hype or, by peer review, where things go. It is both a restriction and a hyping. Those sixty lines are attached to some companies and universities, whose income stream is now dependent on the success of their research and there is now a Presidential decree that deflects research from peer-reviewed altruistic curiosity to make it work. I think the President's speech creates a novel situation and people running labs

at the National Institute of Health had better wake up to the fact that the government is no longer letting peer-review decide policy.

Q: I think that in fact the situation is worse than that, because now not just those sixty lines will be used, but a lot more, because the restrictions that exist, so far at least, affect only N.I.H funding, not private industry, and not research done outside the United States.

Dr. Pollack: The operative period for the utility of this talk is between the President's speech and Congressional action since Congressional action is binding on everyone, while the President's speech is only binding on the government. So he has raised a series of questions which he has not solved and that is why I think it is legitimate for everyone to have an opinion. This disagreement is real and healthy. We are not at a point where what to do is obvious. I think we are at a point where we can't any longer keep wrapping ourselves in a misreading of the constitutional separation of church and state to say there is no religious content to this. There is. The issue is, what do we do, despite the religious content.

Q: What about adult stem cells? From what I understand, they have the same potential, as far as research is concerned, but without the side effects of the embryonic stem cells.

Dr. Pollack: The most interesting part of the human genome clearly lies in its ability to turn itself on and off in different displays of some genes on and some genes off. That display change over time we call differentiation. Starting with one cell – which by definition is only one kind of cell because it is one cell, a fertilized egg cell – you can get the couple hundred different kinds of cell which, by interconnection and interdigitation, make an adult human body. Each of those cells will have the same genome as the fertilized egg cell. This play, on and off, of differentiation by differential gene regulation is initiated by the brilliant cytoplasm of an egg. Once it gets under way, it's a self-reflective process in which the products of differentiation include proteins that include

further ramification of differentiation in different directions. All of that is simply to say, it's an open question how much like an early pre-embryo cell a stem cell from adult tissue is. We don't really know from mouse models how many stages of differentiation go on, in terms of gene regulation, before a cell starts to look like a differentiated cell. The moment it has gone down even one path away from an early, 100-cell stage pre-embryo, it never goes back. It becomes more particular than an early pre-embryo ever was and loses the capacity to become everything. There is an argument that there are some neuronal stem cells in the brain; you could possibly learn to catch them, stimulate them and then repair neural tissue, spinal cord and brain tissues. We don't know how to do this. The argument is that if you start with pre-embryonic stem cells, then you don't have to learn how to discover if, in the 10^{14} cells of the body, there are one or more real stem cells, because you don't ever have to look. I think the consensus is that it is less work to start with disrupted embryos than it is to start with adult bodies because every disrupted embryo cell is in principle a multi-potent cell. Whether there are real multi-potent cells left by the time the system plays out to make a body, I rather doubt because in natural selective terms, the system of making a body has only one function: to carry the gametes the sperm and egg, into the next generation. Our bodies are, in evolutionary terms, hopelessly disposable. That's what death is. You make babies and die and get out of the way. There is no need for embryonic stem cells in such a terminal thing as an adult body.

Q: Perhaps when a baby is born, some of the stem cells could be taken from the umbilical cord blood and stored under that baby's name, just like auto-donation of blood before elective surgery, which could then be used throughout that person's life.

Dr. Pollack: I agree with you in principle; it has merit. I think that the social implications of that line of work are astounding. We don't know where to get Cipro – who is going to keep track of two hundred million frozen umbilical cord stem cells? We don't have the social infrastructure for service to a citizen by citizenship in a medical context. It's all privatized. I think that's a bad way to begin such a plan, and also it's

only for the next generation. As I said, medicine is for people who are alive here and now. I think one could say it's not either/or; that's a good idea for the future but for those of us already here, that won't work.

Q: I want to try to reconstruct the logic of your main argument and see if I've got it right. The problem of these sixty stem cell lines is twofold: one, that there's an immune reaction problem and the other is that it raises theological qualms for many people. As I understand it, you are for therapeutic cloning as an alternative because it avoids those problems.

Dr. Pollack: In the context in which we assume people live under the law, and that the law precludes the carrying of any manipulated egg into a uterus to make a baby, that is, it prohibits genetically manipulated babies and cloned babies, in that context, the fate of such a somatic nucleus in an egg is solely a laboratory fate to create stem cells. You have pinned me on the weakest part of my argument. I am not a theologian but I would say that measured against the baseline of what is now approved, this is a less painful thing to me emotionally.

Q: You state there is a barrier between therapeutic cloning and reproductive cloning and that barrier is that it has to go into a woman's body and brought to term. This is where I didn't quite follow the end of your talk. On the one hand, it sounds like you are saying that that should be a choice made by the woman.

Dr. Pollack: I am saying that it is currently a choice available to women. It is a choice inside Roe v. Wade minus any federal legislation to follow upon Roe v. Wade. The proposed legislation that will follow the President's document will include legislation that treats Roe v. Wade as radioactive and therefore doesn't discuss this at all. The President simply precluded the making of therapeutic clones in a dish to avoid dealing with anything that goes back into a uterus.

Q: Is your concern that we don't want the government to be in the business of compelling women to have abortions?

Dr. Pollack: That's a good way to put it. The government's position now is to live within the law of Roe v. Wade. The Attorney General has been explicit in saying that this is the law of the land, but he doesn't like it. I think the President said the same. As that can only be changed by Act of Congress, which won't happen, or by a change in the Supreme Court, which might, right now I read the politics of this question as being, as I said, radioactive. No one wants to touch it. That has precluded a fair discussion of this alternative pathway to get the outcome which everyone seems to want. Since you can't discuss matters that involve a woman's right to choose what to do with her body, you can't discuss a law that might, in fact, place a limit on that, the limit being: everybody gets a baby by having it coming out of a woman's body and therefore everyone has a political role to play in that decision. That would require something very difficult. Please understand, I'm not saying this is easy; I'm just making it as a hypothetical argument. It is a prerequisite to a technology which I think is really terrific in principal, subject to what has been said. It is all in the future and needs animal models first. But the animal models of stem cell work in a mouse run into the immune rejection problem and I think that anybody who receives stem cell tissue replacement will have to be immuno-suppressed, as if they are getting a transplant. Immuno-suppression is clearly the doctor's version of "a little bit of AIDS." When you start to run into the problems of immuno-suppression as a result, that's not a smart technology, to my mind.

Q: What do you think is the ideal way to safeguard this distinction between therapeutic and reproductive cloning, because I take it that you do want to maintain a barrier between the two?

Dr. Pollack: You have to. The current barrier to making a cloned person includes the President's statement that the federal government is forbidden to carry out research on therapeutic clones because that would set up the technology for making a cloned person.

I argue that that is a pre-emptive strike on a technology that is unnecessary if one accepts that women currently have the legal right to decide what to do with their bodies, and therefore if a law were to be written, they would legally responsible to know that they were breaking the law in undertaking a cloned baby.

Q: So you would trust women to abort themselves?

Dr. Pollack: You understand that the country, in extending Roe v. Wade into this issue, would make it possible – only by extending Roe v. Wade into this issue, could you write a law in which women would be criminally held to have violated the law by allowing themselves to be party to a therapeutic cloned baby. That's my argument; that's the double whammy.

Q: Would you like to see such a law written?

Dr. Pollack: I would like to see such a law written on the merits of the case, which are that a therapeutic cloned person is a disaster at every level; it has no medical content and should be precluded.

Q: Would the law require that woman to abort a cloned baby? I raise the question because people have responded to this argument by saying that such a law would be completely impracticable and that's why you need to prevent therapeutic cloning, because that just won't wash in terms of politics and policy. It's utopian to think that you could have such a scenario.

Dr. Pollack: That's a great question. I don't know what's utopian and what's not; I only have a reasonable grasp of the way things are now and I'm trying to figure out how to get a really novel piece of medicine and science under way. I don't think the President's way of doing it will work very well because of immune rejection. If I have not come up with a better idea, that still makes his idea, I think, medically perilous. Right now if

someone in this room wanted to pay the money to hire a woman to bear a child made by cloning, regardless of what the law is, I imagine that with enough money, you could get it done. That doesn't go away as a result of anything I am saying. Against the current baseline, I am not proposing anything that makes it any easier, possibly something that makes it harder, but I think it's unfair to say it's utopian to be unable to think how to reduce a baseline we are already living with. Therefore if you leave that baseline alone, what I am proposing is not utopian; if you ask to push that baseline to zero, I can't.

Q: Science fiction has always talked about producing super-human beings with a genome chosen for high intelligence or other factors. What answer do you make to people who claim that you are barring the production of super-humans, better than us, who don't have our failings?

Dr. Pollack: I don't have a lot to say about that. There are 10^9 base pairs in the human genome and there are about 10^{15} synaptic connections in the brain of an adult. Base pairs don't encode synaptic connections. That is to say, you don't become a person by your genome; you become a person because your genome constructs a learning machine and then you learn to be a person by social interaction, first with parents and then with others. You're asking a question about what kind of society we want to live in. That question isn't resolved by genetic manipulation. These are choices we have as citizens. If we screw it up, it is our responsibility. If we want to do better, we can do better. We don't turn to the genome to solve our problems at this level. The medical procedure is for this generation; that begins with new babies but still leaves all of us vulnerable.

Q: You have seen the identical-twin research where Thomas Bouchard of the Minnesota Center for Twin and Adoption Research claims that 50-70% of intelligence is inheritance.

Dr. Pollack: But we aren't arguing that. If you were to carry out the bizarre notion of a cloned person and you were to do it for the worst reason, which is that you are so impressed with yourself that you don't want to die when your body dies, you will have

made a stupid mistake, because that will be another person who was raised by a terrible parent, a very unhappy version of yourself. Twins are not the same person.

Q: As I listened to your discussion of the existence of the soul and its relation to the embryo or fetus, I understood you to say that while there may be differences across religions as the role that the soul plays in that early stage, you gave the impression that within religions, these are fairly immutable views and not ephemeral views. I don't believe for a minute that they are long-term views, I think they are very ephemeral views. I will give you one example. The largest Protestant denomination in the United States is the Southern Baptist Convention and the Southern Baptist Convention is perhaps the leading opponent of the Roe v. Wade decision. In 1970, the Southern Baptist Convention voted to ask the federal government to legalize abortion. It took them twenty years to change their mind on this position. I don't know what they will say in another twenty years. I don't accept that today's view of the nature of the soul is necessarily tomorrow's view and so I don't put as much weight in those views as you do.

Dr. Pollack: I think the logical disjoint of my remarks and yours is this: I am trying to describe what limits federal investment in what I think is a much more elegant version of the use of the brilliant cytoplasm of an egg to bring about an undifferentiated cell state that might provide a host of new therapies. My argument is not my religion, your religion or the received revelation of any other group of people, but rather the President's religion in the context of his decision. I am trying to read someone else's mind. Don't confuse that with what I think. I am saying: "How can we understand this internally inconsistent set of conclusions by a man who is, after all, not making the conclusion that his religious background would predict he would make." We have one President, who has made a decision; we have N.I.H. with a budget in the twenty or thirty billion dollar a year range, which is chafing behind these restrictions, and I am trying to figure out what happened.

Q: I understand the difference between adult and embryonic stem cells, and I also understand the great desire of the research community to work with embryonic stem cells. I don't understand why there isn't more effort to really push adult stem cells. We want to repair tissue, so couldn't neuronal stem cells, which were a great breakthrough, be a push to those particular types of tissues? Wouldn't that have politically and culturally sidestepped this conundrum?

Dr. Pollack: Water runs downhill. That is to say, people in the business who are deciding how to allocate their time, their fortune and their reputation on which protocol to follow have come to a consensus that this is the fastest, easiest way to reach their goal. In that, I accept the burden of peer review. I haven't looked at the literature well enough to see the arguments, but I can guess why it might be so. But I will take my colleagues at face value, because their ambition to be first at doing something interesting and important drives a rational path to the simplest way to do it, all other things held constant. The topic of this talk is why is it that people have reached a consensus inside the laboratory and a different consensus in politics. That lab consensus, I think, stands on its own merit. Now, not to avoid your question, my guess is this: there is a false Aristotelian dichotomy between stem cells and differentiated cells. It's a continuum and you can have many states that you can quantify as how many divisions worth of progeny have you got left before you go into a terminal, non-dividing differentiated state. If you have one division left, you can make two differentiated cells; if you have two divisions left, you can make four differentiated cells, and if you have ten divisions left, you can make a thousand differentiated cells. An embryonic stem cell has, in principle, an infinite number of divisions left – that's the distinction. The one requires a knowledge of how far you can go and whether it's far enough to fix the tissue, while the other essentially buys a commodity that you can just make enough of to suit any need. That would be my guess as to why the embryonic stem cells are preferred. I don't think any experience I had running a lab for thirty years fits the notion that scientists in their careers would sabotage the chance of doing something really good, for any reason. So I think the honest aspect of real science is

Adam Smith's model come to life: the only way to succeed is by knowing everything and doing your best and competing. This is the outcome of the open competitive discussion over the last ten years of what to do with the developing knowledge of these genes in other, simpler systems such as flies and worms and plants. We now have an idea of the classes of genes which initiate the cascade of differentiation, and I think we have an idea from those systems that early embryos are in a state of total potency which you just don't find in an adult body anymore. But it's a gray area.

Q: I think the President's statement has greater internal consistency than you imply. It seems to me that there was a principle stated behind these two decisions, the one to use these sixty lines and the second, to use no others. That principle would be that destroying what either is life or has the potential for life for therapeutic benefit for others has no place in medicine. That would explain or justify the first decision, because somebody else did this – it's been done. It is akin to using the organs of a murder victim. It is morally coherent.

Dr. Pollack: I have a colleague named Benno-Muller Hill. He works in a lab in Germany and he is a great molecular biologist, one of the discoverers of the first proteins of the class of repressors, the gene-regulatory proteins that turn genes on and off. Twenty-five years ago he was physically attacked and almost lost his life for uncovering the fact that a host of Ph.Ds were awarded in Germany in the 1950's, 60s and early 70s from data taken from the victims at Auschwitz, in which body parts were shipped back to the Kaiser Wilhelm Institute in Berlin and studied. This was precisely the argument made by the Ph.Ds: "Well, I didn't do it; the body parts were there. What is wrong with looking at them?" The German government's final decision was to bury the whole thing, to cut the link between the torture and murder that was carried out and any possible medical use. I think the German government's decision was the right one. If some things are wrong, you do not benefit from them, because they are wrong, even if there is implicitly some way to benefit from them. I don't understand the alternative logic, which guts the notion of something being wrong.

Q: I don't think that it does. Sometimes you can't do anything to remedy the injustice that you have identified. The land we are on right now can be considered ill-gotten goods. You can't always undo the bad things that others have done in the past and you have no choice but to benefit from them, or it would be irresponsible not to.

Dr. Pollack: Then the thrust of our disagreement is this. We don't know the mind of the President but I would like to think that he is not playing out a game of inches here, but that he is trying to say something in very broad strokes that is consistent. Everything of his past public statements is consistent with "don't use those sixty cell lines." The big shock, in my world, was not the restriction on further work, but his allowing this work to go further. That's why I wrote this paper. That was a radical departure from his past position, and I don't think I agree with you that it was consistent. It just seems, on the face of it, completely inconsistent with his past positions.

Q: This notion that it must go into the human uterus places a limitation on therapeutic cloning. After all, it doesn't have to go to full differentiation. You could put it into an animal's uterus in a laboratory until it got differentiated enough that you could use it. That in theory should eliminate it. Second, have you heard anyone raise the question that when you stimulate something to differentiate, you may end up with cells that have a higher tendency to de-differentiate?

Dr. Pollack: The evolutionary strategy of making big organisms with complicated behavior as a way of propagating germ line DNA is a strategy that, like all natural strategies through natural selection, is good enough to get by but not perfect. We have many traces of our evolutionary history as selectable and selected-for imperfections. For instance, we must not allow unnecessary mutation in the germ line because we would get defective children. So there are enzymes in the cells that make sperm and egg that fix errors of DNA replication in the production of sperm and egg. However what has been selected for by nature is not a zero error rate, but a very low reproducible error rate

that guarantees a new mutation in about one gene per sperm or one gene per egg. That level of mutation is the selected optimal level of mutation that provides sufficient genetic variation to allow the species not to die from "clonalism," of too narrow a range of variation. That kind of logic explains why it is that all the other cells in the body have a much less good repair mechanism and constantly throw off what are called "somatic mutations." By the time we are adults, our bodies are a garden of genetic variations of what the initial fertilized egg cell was. Most of the time, cells which have too much mutation are by that mutation dead and sloughed off or by that mutation frozen in place in a differentiated state anyway, so that you don't know it. When a cell is mutated in such a way as to lose the regulation of its own cell cycle, it becomes the progenitor of a tumor, which is what you were referring to. The question becomes, what are the relative levels of appearance of the kinds of mutation that leads to a tumor in the reconstructed differentiated cell you get out of the stem cell, as opposed to your own tissues, which once came from stem cells. My sense of the biology is that it is again a baseline question. There will be mutational emergence of tumors from stem cells because there are mutational emergence of tumors from regular stem cells in the making of your body and mine when we were embryos. It is a part of life you can't escape.

Q: Will we be able to take stem cells and induce them to differentiate in a tissue culture to make a heart or kidney or whatever? You could do it in a test tube rather than a human being.

Dr. Pollack: The answer is that no one I know is looking at that, though I don't know that people aren't, in mice. I point out that if Reeve gets up and walks, it will be at the risk of developing a neuronal tumors. But the problem is much worse than the one you're raising. The problem is, as a friend of mine says, that there is a sexually transmitted disease whose only prognosis is death, and it is called being alive. Life is terminal. It is built in that way by natural selection as part of DNA's way of making more DNA. Germ line survival depends on individual death, so the flailing about at the margins because you're going to come down with a disease when you're dying of

something else seems to me a bit too elegant. Medicine is not an elegant business; medicine is the business of fixing what you can fix, and I think this technology has the capacity to fix some things, without which you are dead right away. But the side effects are latent. Everyone who is alive today because of chemotherapy has had the risk of cancer induced by the drugs. Those drugs are all tumor-genic but in net, people live longer.

Q: You mentioned a terrible thing, putting a therapeutic clone in a woman's uterus. But suppose in fifty years you have an artificial uterus and someone wishes to grow a stem cell to a given stage. Would you have to prevent that, too?

Dr. Pollack: I won't be here, but more than that, I think the interesting question for us here and now is, where is the discussion of a woman's responsibility as well as a woman's right in all of these issues? This is a conversation we could have any time; we don't need any new technology. The social presumption is remarkably Talibanish: it assumes that women have nothing to say for themselves and we take it for granted that if they can, they will. That seems to me to be insulting. There ought to be in the politics of this country more discussion about women's sense of obligation to themselves, the future and the law. I just don't hear it and that surprises me.

Q: What about the man's obligation?

Dr. Pollack: Men don't have uteruses.