Testimony of Michael D. West, Ph.D.
President & CEO Advanced Cell Technology, Inc.
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Mr. Chairman and members of the Subcommittee, my name is Michael D. West and I am the President and Chief Executive Officer of Advanced Cell Technology, Inc., a biotechnology company based in Worcester, Massachusetts. A copy of my curriculum vitae is presented in Appendix A.

INTRODUCTION

I am pleased to testify today regarding human embryonic stem cell and nuclear transfer technology and their applications in medicine. I would like to first speak to the potential benefits of this emerging science, and then speak to the objections that opponents have raised.

The Potential Benefits of ES and NT Technology

Human ES cells are unique in the history of medical research for at least two reasons. First, they alone are totipotent stem cells. By stem cells, we mean cells that can branch out like the stems of a tree, becoming other cell types. By "totipotent" we mean to say that they stand near the base or "trunk" of the developmental tree and so are capable of forming any cell or tissue type needed in medicine. In addition to forming any cell type, they are unique in their ability to self-assemble into complex multicellular tissues such as intestine, full thickness skin, kidney tissue, and so on. They differ in this respect from adult stem cells that are "pluripotent" that is, capable of forming several, but only a limited number, of cell types. One can think of adult stem cells as limbs further out on the branches of a tree. While able to branch out in several different directions, only the trunk of the tree branches out into very leaf and limb. An example of adult pluripotent

adult stem cells are the bone marrow stem cells now widely used in the treatment of cancer and other life-threatening diseases.

The second distinguishing feature of ES cells is the ease with which they can be purposefully modified in a precise manner. This precise genetic modification is designated "gene targeting". The enhanced ability of ES cells to be modified with precision opens the door to likely many hundreds of clinical applications making human cells of any kind, genetically modified in any way.

These two unique characteristics of human ES cells open the door to manifold novel therapeutic strategies. It may not be an exaggeration to state that the combination of the ability to precisely genetically modify these cells by making any number of targeted genetic modifications and the ability to make any cell type may have as profound an application in medicine as the ability to arrange electrical components has made in the electronics industry.

To attempt to name every disease potentially impacted through this technology would require a larger report. A few examples would be to manufacture neurons for degenerative diseases such as Parkinson's and spinal cord injury. Gene targeting to find and correct mutations could be used to manufacture neuronal stem cells for childhood retardation from diseases like Rett syndrome. Heart and skeletal muscle cells could be used for heart failure and age-related skeletal muscle wasting, and targeted genetic modification could be useful in muscular dystrophy. Blood forming cells would be useful in bone marrow grafting after cancer treatments, and anemias. Precision genetic modification could lead to better therapies for inherited blood cell disorders such as sickle cell anemia and infectious diseases such as AIDS.

I would argue that the debate over the number of human ES stem cell lines approved for federal funding largely misses the point. Human ES cells obtained from IVF preimplantation embryos are not identical to the patient, that is they are "allogeneic". We should expect that such cells derived from the 20-60 approved lines would be rejected by the patient's immune system. The primary purpose in funding human ES cell research is not just the pure pursuit of human knowledge, but rather to accelerate the delivery of novel therapeutics to afflicted people. We must address from the beginning how we are going to make these cells useful in transplantation. Several approaches can be envisioned to solve the problem of histocompatibility. One approach would be to make vast

numbers of human ES cell lines that could be stored in a frozen state. This "library" of cells would then offer varied surface antigens, such that the patient's physician could search through the library for cells that are as close as possible to the patient. But these would likely still require simultaneous immunosuppression that is not always effective. In addition, immunosuppressive therapy carries with it increased cost, and the risk of complications including malignancy and even death.

Another theoretical solution would be to genetically modify the cultured ES cells to make them "universal donor" cells. That is, the cells would have genes added or genes removed that would "mask" the foreign nature of the cells, allowing the patient's immune system to see the cells as self. While such technologies may be developed in the future, it is also possible that these technologies may carry with them unacceptably high risks of rejection or other complications that would limit their practical utility in clinical practice.

The Use of Nuclear Transfer in Medicine

The recent success in the cloning of animals from various body cells demonstrates that the transfer of a body cell into the environment of an egg cell can "reprogram" the body cell back to an embryonic state. We have recently demonstrated that such technology actually rebuilds the replicative lifespan as well, suggesting that "young" cells can be derived from "old" cells. This is a profound development and perhaps the ideal solution for making real the longstanding dream of transplantation medicine; namely, to be able to offer any patient, even an aged patient, young healthy cells of any kind that are their own cells, not expected to be rejected by their immune system.

Nuclear transfer offers an important solution of the problem of tissue rejection. The procedure would involve the patient donating living cells to a physician, who would then reprogram them back to a totipotent state using the cloning procedure. This is called *therapeutic cloning*, to distinguish it from *reproductive cloning* which is designed to clone an entire human being. The cells and tissues made from these cloned stem cells would be expected to be grafted stably for the life of the patient without immunosuppression.

Answers to the Opponent's Objections:

1). The preimplantation embryo is a human life and to use therapeutic cloning is to "clone and kill".

Answer: A preimplantation embryo is human cellular life, but not a human life. The trillions of cells in our body are all truly alive. Therefore human cells growing in a laboratory dish would rightly be called human cellular life, but no reasonable person would say that they are "a human life". In the first few days following the fertilization of an egg cell by a sperm cell, there develops a microscopic ball of cells called a preimplatation embryo. This embryo is destined to die unless it implants in the uterus to form a pregnancy. Indeed, it is estimated that 50-80% of these preimplantation embryos naturally formed in a woman's body never implant and therefore die. A human life, as opposed to simply cellular life begins, at the earliest, at or around day 14 of human development at around the time the preimplantation embryo attached to the uterine wall in the mother. Prior to day 14, the preimplantation embryo has no body cells of any kind, and, in fact, has no cells even committed to somatic cell lineages. Indeed, the embryo has not individualized. Once this ball of cells attaches to a uterus, one or even two or more individuals can form from it. In addition, if it merges with another preimplantation embryo and then forms a pregnancy, it will become just some of the cells in the resulting person. Therefore, many have concluded that at this early stage before a pregnancy, the preimplantation embryo has not individualized and therefore it would be illogical to attribute to it even the earliest status of personhood.

2). Therapeutic cloning is merely theoretical; there is no reason to suggest it will work.

Answer: Those that make this objection appear to be simply uninformed of the scientific literature. There are published reports of success of therapeutic cloning research in at least two mammalian species; namely mice (1-2). While never performed in a human, the animal data suggests that therapeutic cloning has great promise. The National Academy of Sciences has formally recommended in a report titled "Stem Cells and the Future of Regenerative Medicine" as follows:

> "Recommendation: In conjunction with research on stem cell biology and the development of potential stem cell therapies, research on approaches that prevent immune rejection of stem cells and stem cell-derived tissues

> should be actively pursued. These scientific efforts include the use of a number of techniques to manipulate the genetic makeup of stem cells, including somatic cell nuclear transfer.[3]"

3). Allowing therapeutic cloning would cause a "slippery slope" effect, whereby regulating human reproductive cloning would not be possible.

Answer: In reality the procedures to clone a human being are well known in the scientific literature. The widespread use of therapeutic cloning would not significantly increase the likelihood of the success of an effort to clone a human being. In addition, laws can easily be written to allow one and prohibit the other as reproductive cloning requires the transfer of a cloned preimplantation embryo into a uterus.

4). Therapeutic Cloning will lead to "embryo farms", "Nazi-like experimentation", a "Brave New World", etc.

Answer: The opponents of many recent medical technologies have resorted to such inflammatory language in the absence of a rational basis of objection. Therapeutic cloning guidelines could easily be constructed to limit development to less than 14 days as is the current practice of in vitro fertilization.

Summary

In conclusion, nuclear transfer and human embryonic stem cell technology offer novel pathways to develop lifesaving therapies that will impact the lives of millions suffering from such diseases as Parkinson's disease, diabetes, arthritis, heart disease, kidney failure, spinal cord injury, liver failure, skin burns, blood cell cancers, to name only a few. The gravity of this issue calls for a compassionate, reasoned, and dispassionate debate. History will judge us harshly if we as a society fail to recognize and deliberate carefully upon a medical technology that could so powerfully alleviate the suffering of our fellow human being.

References

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2. Wakayama, T., Tabar, V., Rodriguez, I., Perry, A. C., Studer, L. & Mombaerts, P. (2001) *Science* **292,** 740-3.

3. *Stem Cells and the Future of Regenerative Medicine* - National Academy Press (2001), Washington, p39.