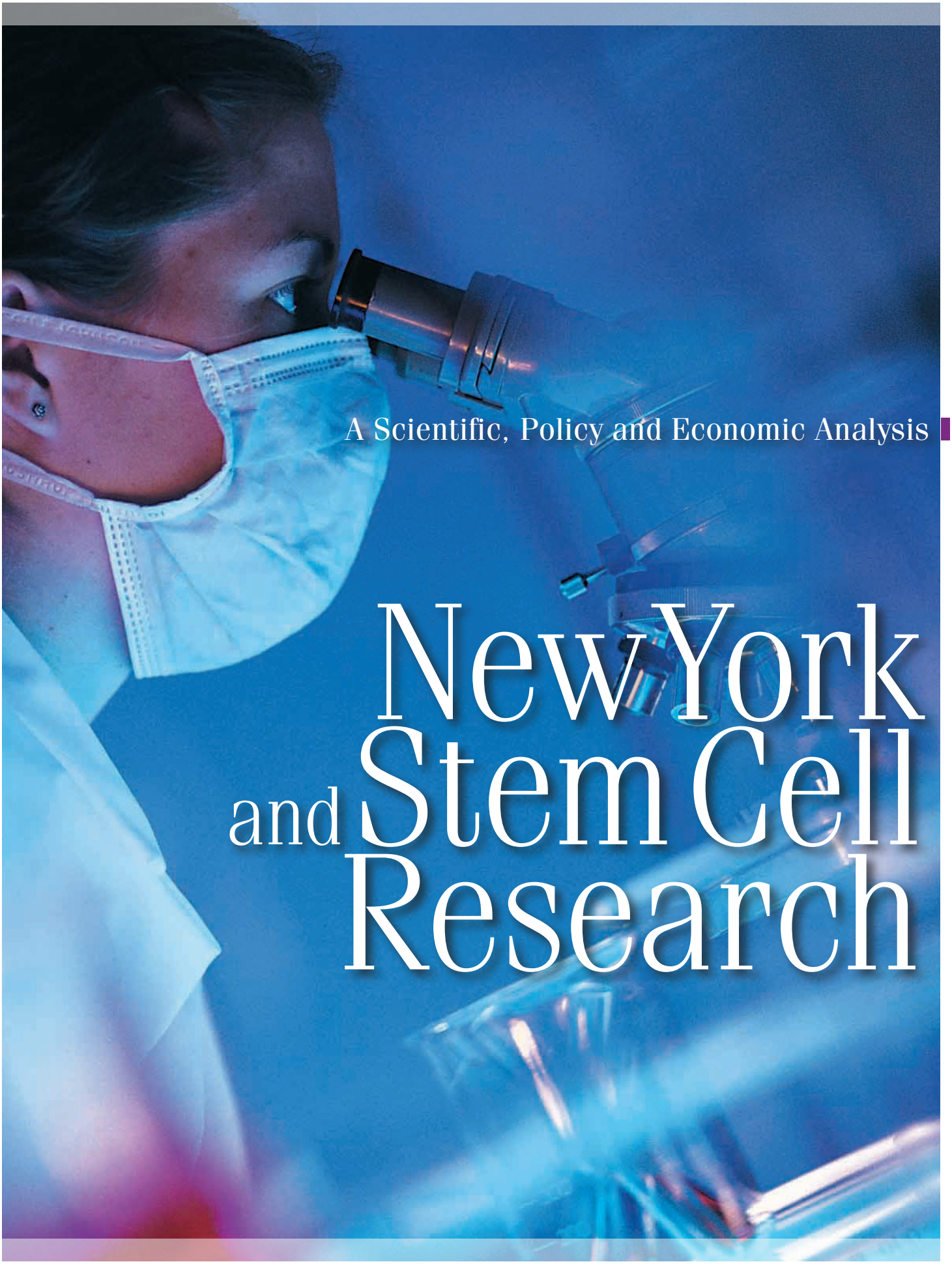

A Scientific, Policy and Economic Analysis

New York and Stem Cell Research

Contents

Preface

This White Paper reflects the views of the presidents and chancellors of colleges, universities, medical centers, teaching hospitals, and research institutions in New York with significant biomedical research programs. We believe there is an urgent need for New York to join a growing list of states using government resources to support stem cell research. Stem cell research and the therapies that it could lead to can be used to prevent, treat, understand, and perhaps even cure an extraordinarily significant list of diseases. Furthermore, we believe that if New York fails to act we risk losing our place as one of the leading, if not the leading, location for biomedical research. Already other states are trying to use the resources they are devoting to stem cell research to lure some of New York's top scientists, and the jobs and economic potential that accompany their research, away.

The federal government's highly restrictive policy for funding embryonic stem cell research has left a void that states, foreign governments, and private investors are attempting to fill. Starting with California's passage of Proposition 71 in 2004, several states, all with a strong biomedical research base like New York, have passed or are attempting to pass legislation or referenda to fund stem cell research. Recognizing the importance of the research, New York has begun considering legislation as well. In the most recent legislative session (2005) stem cell funding bills were introduced in both the Democratic-controlled Assembly and the Republican-controlled Senate; however, neither house was able to pass its bill before adjourning. In 2005, Governor George Pataki also came out publicly in support of stem cell research. The next legislative session will be a pivotal one in deciding whether New York will make a serious commitment to stem cell research or choose to risk the rapid decline of its biomedical research community.

Because of the urgency and timeliness of this issue, we have prepared this White Paper to detail: the scientific background of stem cell science; stem cell research and therapeutic potential by disease; the international race to discover cures and the competitive environment; the economic impact of biomedical research and biotech on New York; and stem cell policy issues.

Each of us is mindful that there are serious and important ethical concerns with respect to stem cell research and therapy. In our view, these concerns deserve thoughtful and respectful consideration, but, in the final analysis, the arguments for inaction are far outweighed by the ethical imperative to do all that is possible to alleviate suffering for the millions of Americans afflicted with diseases for which stem cell research could hold the promise for treatment.

The purpose of this White Paper, however, is primarily to focus on those areas which we as academics feel we have particular competence: the potential of new and evolving science to address a burgeoning number of disease and disease clusters, and the potentially devastating consequences of continued inaction.

We write with a profound sense of urgency. The upcoming legislative session may prove to represent a last, best chance to prevent an irreversible erosion of pivotal 21st Century medicine and science already established in New York.

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Executive Summary

The importance and potential of stem cell research is no longer a view held solely by the scientific community. It is shared by a growing number of states, foreign governments and private investors who are now racing to accumulate the necessary research talent and infrastructure to accommodate this rapidly growing field.

If New York fails to invest public funds in stem cell research it will begin to lose its most talented scientists and the biomedical research conducted at its universities and institutes will suffer.

Stem cell research, or regenerative medicine research, holds enormous promise for the future advancement of medical care, particularly for the millions of Americans suffering from a wide range of debilitating diseases and injuries. Scientists across the globe are racing to unlock the potential of stem cells, and states, foreign governments, and private investors are rapidly marshaling the necessary financial and research resources to accommodate the potentially explosive growth of this new science. These activities – and the current limits on federal funding – have produced a new competitive environment that has the potential to reshape the entire field of biomedical research. Consequently, New York's international leadership in biomedical research and the significant economic benefits that flow from that leadership are in jeopardy unless the state acts immediately to level the playing field and provide financial support for stem cell research.

Stem cells are essentially early-stage primitive cells that are capable of generating the different kinds of tissue found in the body. There are several sources of stem cells which possess different regenerative capabilities. Embryonic stem cells are essentially limitless in their potential to generate different kinds of tissues and body parts. These cells are believed to be pluripotent, that is, with the right signals, they can become any other type of cell in the body. Tissue-specific stem cells, often referred to as adult stem cells, are found in all organs during early development and in certain organs or parts of the adult body, and are more restricted in their potential, generally giving rise only to the cell types of a particular organ. They are believed to be multipotent; they can also be transformed into other types of cells, but not necessarily every other type of cell. Therapies using adult stem cells have been in use for over thirty years and have proven, in certain instances, very successful – a prominent example being bone marrow transplants; however, they are not as flexible as pluripotent embryonic stem cells.

Because stem cells have the potential to repair and replace damaged tissue, the list of diseases and injuries that could benefit from stem cell therapies is long and includes such incurable and debilitating conditions as Alzheimer's, Parkinson's, juvenile diabetes, spinal cord injury, cancer, heart disease and many more. These conditions not only exact an immense physical and emotional toll on millions of Americans and their families, they also have an enormous economic impact in terms of health care costs, disability, work loss, and premature mortality that runs into hundreds of billions of dollars annually.

The science of embryonic stem cells is in its infancy. Human embryonic stem cells were first isolated in a lab in 1998. Other similar major advances in medical knowledge have taken decades to translate into new treatments. Consequently, we may be many years away from developing successful stem cell therapies in humans, although the rapid pace and large volume of research in this field may produce results much sooner.

One problem that is preventing adequate progress is the federal restrictions on the study of human embryonic stem cells. In the United States, the federal government, through the National Institutes of Health (NIH), has traditionally been the primary source of financial support for biomedical research. In 2001, federal funding for research on human embryonic stem cell lines was limited to lines created before that date. At the time, it was believed that 78 stem cell lines would be suitable for such research. However, it has subsequently been

discovered that the real number of available lines is no higher than 22, with only a fraction of these lines being suitable for research use and none being useful for clinical application because they have come into contact with mouse feeder cells. Experts predict that, at most, only four or five additional eligible lines will become available in the future. In order to develop this field of research, it is necessary to enable the study of embryonic stem cells derived from other sources. Furthermore, stem cell lines can, and often do, die out after several divisions, often unpredictably. Consequently, there is no guarantee that the existing 22 lines will be available in the future.

Currently scientists are prohibited from using federal funds for research on more promising stem cells lines and from creating new lines from the tens of thousands of blastocysts that are discarded from American *in vitro* fertilization clinics every year. Since August 2001, the cut off date under current federal policy, at least 100 new lines have been derived. Thus the pace of discovery, and ultimately the development of new therapies, is hindered. Scientists are, therefore, increasingly compelled to turn to other sources of support for research on human embryonic stem cells.

The importance and potential of stem cell research is no longer a view held solely by the scientific community. It is shared by a growing number of states, foreign governments and private investors who are now racing to accumulate the necessary research talent and infrastructure to accommodate this rapidly growing field. The most prominent example of this has occurred in California, where voters agreed to establish a 10-year, $3 billion stem cell research fund. Several other states have or are preparing to establish similar funds. These actions have created a competitive environment in which institutions in these states are aggressively attempting to become magnets for scientists, biotech industry, and venture capital.

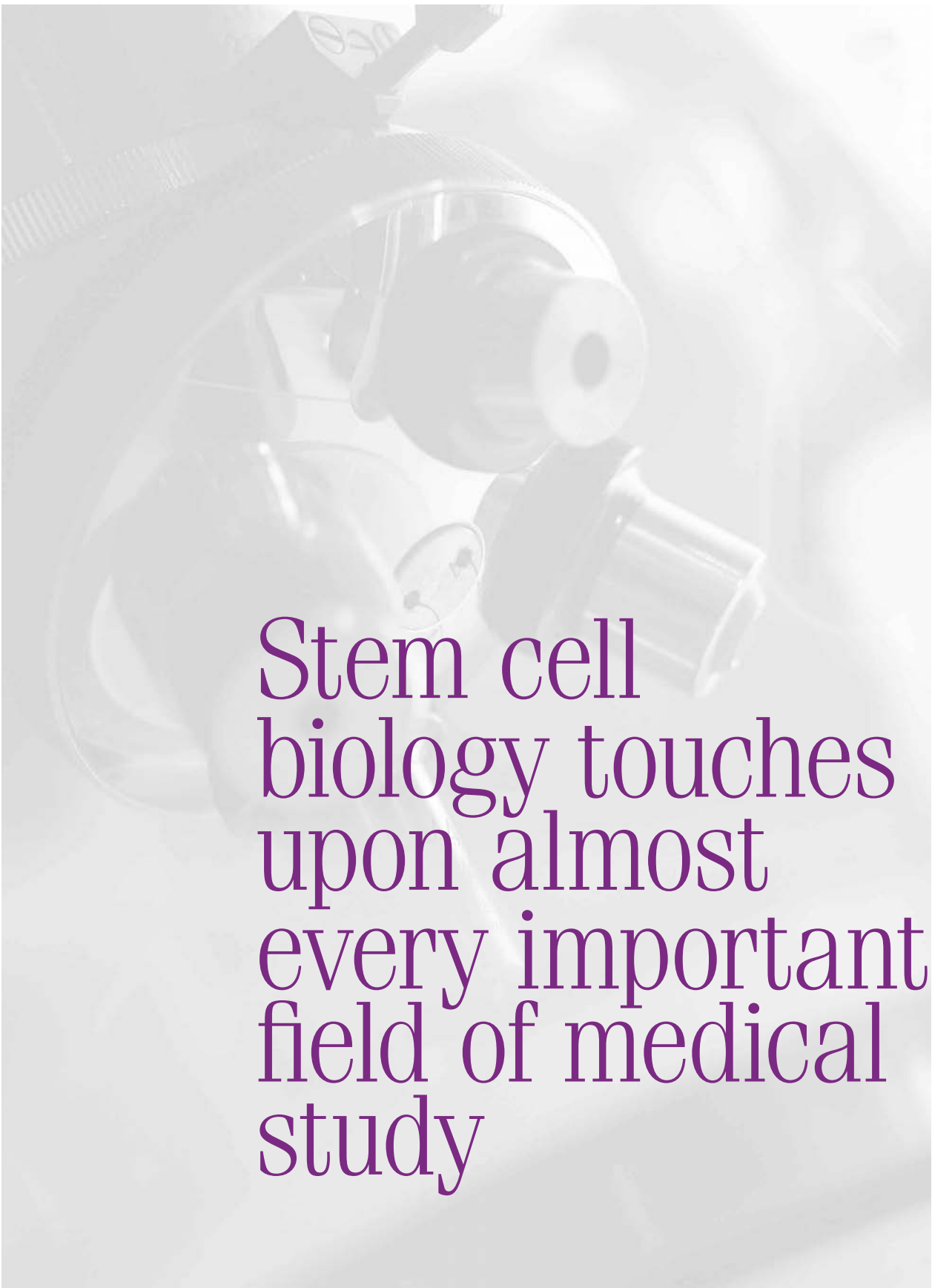
New York is ideally positioned to be an international leader in the field of stem cell research, but not unless it acts quickly to make up the ground it has already lost. New York's concentration of world-class research universities and institutions, teaching hospitals, and biotechnology and pharmaceutical companies provide the necessary capacity to rapidly advance this research. Additionally, the state has demonstrated the ability to marshal financial resources on a large scale in terms of federal research grants and venture capital.

Biomedical research and biotechnology are big business in New York. New York's medical schools, teaching hospitals, and biotech/pharmaceutical industry are responsible for 560,000 jobs and $48 billion in economic activity. While much of this activity is centered in New York City, biotech clusters are being developed in the upstate cities of Buffalo, Syracuse, Rochester and Albany, as well as on Long Island. The state's research community not only has a tremendous economic impact in terms of jobs and spending, it also serves as an engine of innovation. The research that is conducted at New York universities and institutions is a critical contributor to the state's biotech and high tech industries.

Consequently, New York not only has the most to gain by "getting into the game" with respect to stem cell research, it also has the most to lose. The state's research community has already made significant private investments in stem cell research. However, if the state fails to invest public funds in stem cell research it will begin to lose its most talented scientists and the biomedical research conducted at its universities and institutes will suffer and ultimately decline. This, in turn, will ripple out to the state's biotech and pharmaceutical sectors as they begin to look elsewhere for research innovation.

On the other hand, if New York funds regenerative medicine research at a level comparable to that of other states, it would be able to reinforce its leadership position in medical research, create new jobs and companies, and develop technologies that could potentially improve the lives of millions of Americans suffering from debilitating conditions.

Each of us recognizes that it is critical that members of the scientific community balance the promise of stem cell medicine against the potential for research that crosses ethical boundaries. Specifically, stem cell research raises a number of issues related to the procurement of embryos, research in animal models, and the techniques of therapeutic and reproductive cloning, which need to be addressed in order to place appropriate limits and oversight and reassure the public that the research is being conducted in an ethical manner. In Part V of this White Paper we highlight that the National Academies of Science and several states have adopted guidelines and oversight mechanisms for stem cell research that can serve as models for New York.



Stem cell biology touches upon almost every important field of medical study

Scientific Background and Therapeutic Potential of Stem Cells

Stem cells are the ultimate source of the many cell types of the body and have the ability to generate healthy new cells, tissues and organs. As a result, they have the potential to provide cures or new treatments for a long list of diseases and injuries, including juvenile diabetes, Alzheimer's, Parkinson's, spinal cord injury, cancer, heart disease, and many others. Millions of Americans suffer from conditions that could benefit from therapies employing stem cells. Moreover, research on stem cells and the cells derived from them provides information critical to understanding a wide range of developmental maladies.

Despite the potential surrounding this emerging field, we remain a long way from translating the research now being conducted in laboratories across the globe to therapies for patients. Stem cell research, like the other major advances in biomedical research that came before it, will require time to realize its potential and the speed in which we reach these goals will depend upon the resources available to scientists to pursue them.

The most widely discussed potential use of stem cells and progenitor cells is in tissue repair. The range of information from animal studies is extensive, and there is well documented restoration of normal physiological function in animal models of liver failure, diabetes, and a variety of examples of neurological injury.

Embryonic Stem Cells, Embryonic Germ Cells and Tissue-Specific (Adult) Stem Cells

The term "stem cell" refers to precursor cells that can give rise to multiple tissue types. There are three different sources of stem cells with different developmental characteristics.

Embryonic stem (ES) cells are derived from a stage of development called a blastocyst. While ES cells are technically *totipotent,* meaning they could give rise to fully functional organisms as well as every cell type in the body, for therapeutic purposes they are commonly referred to as being *pluripotent,* meaning they are capable of developing into virtually any tissue type.

In the human, the blastocyst stage lasts for five or six days before there is implantation in the uterine wall, and for another few days thereafter. If the blastocyst does not implant in the uterine wall, it does not undergo further development.

The blastocyst is a ball of cells simple in both shape and composition. The blastocyst contains no muscle, no nervous system, no organs of any kind, and none of the specialized stem cells that give rise to these tissues. ES cells are derived from the inner mass of this primitive ball of roughly 100 cells.

ES cells can give rise to any tissue of the body, but they do so by first generating intermediate cells that give rise, at least under most conditions, only to cell types that are found within a single tissue. These are called *tissue-specific stem cells,* or *lineage-restricted stem cells.* It is tissue-specific stem cells, and the lineage-restricted progenitor cells that are used for transplantation purposes. ES cells serve as a potentially infinite bank from which these more specific cells can be created as needed.

Stem cells give rise to further cell types by undergoing further differentiation to yield cells that are still more restricted in their potential. Such cells are called *lineage-restricted progenitor cells,* and these cells represent the intermediate between a tissue-specific stem cell and the final cell types of that tissue. Unlike tissue-specific stem cells, these restricted progenitor cells give rise only to a subset of the cells of a tissue and, at least in some cases, have less capacity to divide extensively.

Embryonic germ cells are derived from fetal tissue during a narrow window of development. After a period of several days, the cells in the embryo begin to differentiate and develop into specific functions and tissues. As the cells specialize and begin to create particular tissues and body parts, they lose their plasticity – or ability to generate other cell types. However, the fetus retains a "reserve" of embryonic germ cells that remain *pluripotent* – the ability to generate all tissues. Thus, in terms of the ability to make other cell types, embryonic germ cells are very similar – if not identical – to ES cells. Despite their potential, there exist significant obstacles to the utilization of embryonic germ cells for research and therapy. An early embryo starts with only about 50 of these rare cells, making them very difficult to isolate and study. And as the source of these cells is fetal tissue, the large-scale manufacturing of products utilizing these cells is questionable and the procurement of these cells raises obvious ethical issues.

Tissue-specific (adult) stem cells are unique post-embryonic cells that maintain the ability to divide extensively and also generate the cell types of a particular tissue. They are an essential intermediate stage between the ES cells and the cell types of the body. Tissue-specific stem cells are isolated from specific sites in the developing or adult tissue.

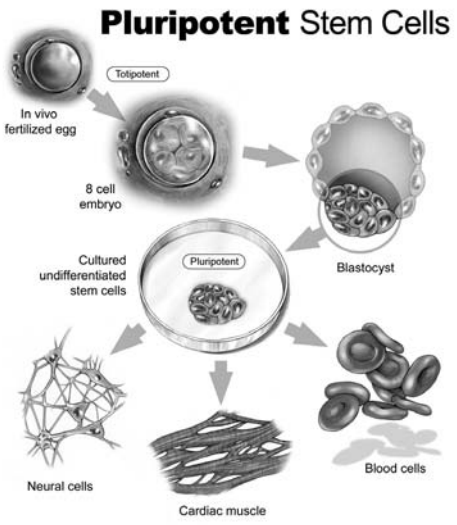


Illustration Credit: Stem Cell Research Foundation
http://www.stemcellresearchfoundation.org. Used with permission.

These cells are present in early development and have the function of building tissue. These cells are also found in the adult tissue and organs and their primary role is to maintain and repair the tissue in which they are found. Stem cells from these sources are commonly referred to as *adult stem cells.* Tissue-specific stem cells can, in turn, give rise to still more restricted cells that are capable of extensive division and tissue repair. These are called lineage-restricted progenitor cells and they give rise to only a subset of the cells in the tissue.

The most well-known example of tissue-specific stem cells is the hematopoietic stem cells that reside in umbilical cord blood, bone marrow, and fetal tissue and self renew continuously. These cells are capable of generating the full complement of cell types found in blood. Adult blood-forming stem cells from bone marrow have been used in transplants for 30 years and are used primarily to treat conditions where replacing the cells of the blood can be of benefit in some way.[1]

Finally, there is the ability to generate ES cells by transferring the nucleus from a differentiated cell into an unfertilized egg. This technique is called ***somatic cell nuclear transfer (SCNT),*** or therapeutic cloning. This approach to stem cell generation is a powerful technology that will certainly be an important part of the future of cell-based medicine. Nuclear transfer is a method of taking cells from an adult and restoring to them the properties of embryonic stem cells. To accomplish this, the adult cell is placed into an unfertilized egg that has had its own nucleus removed (called an enucleated egg). For as yet unknown reasons, this manipulation can reprogram the adult nucleus to re-express the properties of the earliest embryonic cells. The transfer of an adult nucleus into an unfertilized and enucleated egg initiates a normal program of development, in which cell division leads to a blastocyst.

If that blastocyst is grown in the right environment (i.e., for a mammal, if it implants in the uterine wall), then a small proportion of the blastocysts produced in this manner will go on to develop into a fetal animal. This discovery was first made many years ago in research on frogs, and it is this technique that enables the cloning of sheep, mice, cats and an increasing variety of other animals. This is how Dolly the sheep was created, and there are increasing numbers of cloned animals that have been made in this way. This process, called *reproductive cloning,* is highly controversial for obvious reasons and has been, in many places, expressly prohibited in the case of humans, including in states and countries that otherwise welcome embryonic stem cell research. We all emphatically agree that human reproductive cloning should be banned.

In *therapeutic cloning,* development ceases at the blastocyst stage, and the inner cell mass is removed from this blastocyst and used as a source of ES cells. Thus, these blastocysts are not allowed to progress even to the point of making tissue-specific stem cells. Instead, the ES cells isolated from them are then used as a source of tissue-specific stem cells. Therapeutic cloning solves the problem of tissue rejection following transplantation. Because the cells are derived from one's own body, the immune system will accept them readily. Therapeutic cloning also enables scientists to explore the underpinnings of genetic diseases and possible methods to improve or cure these conditions. For example, stem cells could be created using a cell derived from an individual with a neurological disorder. Those cells could then be used to generate neurological tissue that would allow scientists to study the biological functions of that disorder.

The Potential for Stem Cell Cures and Therapies

Stem cell biology touches on many important fields of medical study, ranging from understanding normal development and tissue formation, to deciphering the causes of developmental maladies, to developing improved approaches to cancer treatment – as well as providing the basis for the widely discussed field of regenerative medicine, also referred to as tissue repair.

The most widely discussed potential use of stem cells and progenitor cells is in tissue repair. There are many conditions in which cell transplantation might enable restoration of normal function in damaged tissue. The range of information from animal studies is extensive, and there is well documented restoration of normal physiological function in animal models of liver failure, diabetes, and a variety of examples of neurological injury. There are many conditions (such as injury to the brain) for which organ transplantation is not feasible, but for

[1] There are also stem cells that we don't yet know how to classify. For example, it has been possible to isolate cells from the bone marrow and from the umbilical cord that have been claimed to give rise to a wide range of cell types, including brain cells. Unlike all of the types of cells discussed so far, where studies in experimental animals have provided clear evidence of utility in repairing tissue damage, we are still far from understanding the utility of bone marrow cells or umbilical cord cells in repairing damaged tissue (outside of replacing the cells of the blood). While we should not discount the potential utility of these cells, it cannot be claimed that they are an obvious replacement for tissue-specific stem cells

There is significant agreement in the scientific community that embryonic stem cells are more pluripotent than adults cells and thus have greater potential to lead to treatments, but that is the wrong way of looking at the issue. This is not an either/or situation. Science should proceed, and government should support funding, for all types of stem cell research.

which cell transplantation might restore normal function. There are possibly an even larger number of conditions (for example, liver dysfunction, diabetes) for which cell transplantation might reduce or even eliminate the need for organ transplantation.

In addition to tissue repair, stem cell research also has the potential to accelerate our understanding of a wide range of biological processes. For example, stem cells are so versatile that they can be genetically manipulated to make them express characteristic features of particular disease states that can then be studied at the cellular level to gain new insights into potential therapeutic strategies. Stem cells and the progenitor cells derived from them are also of critical importance in the drug discovery process by enabling analysis of the impact of compounds in a very specific manner. They also can be used to identify the possible effects of environmental toxins and trauma on the development of fetuses and infants.

Still another aspect of stem cell medicine of great importance has to do with the relationship between stem cells and cancer cells. It has become apparent that many cancers grow in much the same way as normal tissues, with a small stem cell compartment that provides a continual source of new cells. Unfortunately, it is these cancer stem cells that seem most resistant to the effects of cancer therapies. Moreover, as these cancer stem cells may represent only 1-2 percent of the total cells in a tumor, they may be very hard to detect. The study of the biology of normal stem cells is providing clues as to how to detect cancer stem cells, and it is only the ability to study normal stem cells and cancer stem cells side by side that will enable the discovery of ways of killing the tumor cells without killing the crucial life-supporting normal stem cells of the patient.

Are Adult Stem Cells Sufficient for Developing the Field of Stem Cell Medicine?

The central controversy in the development of stem cell medicine is over the source of cells to be used for research and therapeutic purposes. Opponents of embryonic stem cell research point to the success of using cells derived from adults as a means of arguing that embryonic stem cells and cells created by therapeutic cloning are not needed to develop the field of stem cell medicine. It is important that scientists and educators respect and understand the ethical arguments in opposition to embryonic stem cell research, even if they do not agree with them. The same level of deference is not, however, owed to the assertion that adult stem cell research alone is adequate to unlock the full potential of regenerative medicine. As former Senator Daniel Patrick Moynihan noted, everyone is entitled to their own opinion; they are not entitled, however, to their own facts. Adult stem cells have not shown that same quality of pluripotency as embryonic stem cells and it is not defensible to say that adult stem cells, and adult stem cells alone, will help society fulfill the potential of stem cell research.

Some of these claims are based on a poor understanding of the limits of what has actually been achieved, as in the case of treatments for type-1 diabetes with cells derived from cadavers.[2] Other claims fail to recognize the critical distinction between tissues in which cell replacement occurs throughout life and those tissues in which cell replacement is rare. Thus, while it is correct that bone-marrow derived stem cells have been of great value in replacing the cells of the hematopoietic (blood) system, use of adult-derived stem cells for other purposes is thus far not as promising.

Another argument made by those opposed to the use of embryonic stem cells is that science has shown that adult stem cells are plastic in their potential.

Proponents of this view cite papers showing that cells of the bone marrow can make liver cells or brain cells. As of the time of this writing, the issue of stem cell plasticity is a controversial one and, in many instances, other laboratories trying to replicate these claims have been unable to do so. The only clear statement that one can make about cross-lineage plasticity in adult stem cells is that if this phenomenon does occur, we are nonetheless far from understanding how to harness these effects in the reproducible manner that is required for therapeutic purposes.

Because of these problems and limitations, it cannot be claimed that research and therapies that employ adult-derived stem cells eliminate the need for the development of more promising stem cell therapies. The current utility of adult stem cells is far removed from the existing potential to treat people with appropriate tissue-specific stem cells or progenitor cells generated from embryonic stem cells.

There is significant agreement in the scientific community that embryonic stem cells are more pluripotent than adults cells and thus have greater potential to lead to treatments, but that is the wrong way of looking at the issue. This is not an either/or situation. Science should proceed, and government should support funding, for all types of stem cell research. None of us – nor any of the dozens of brilliant stem cell biologists on our faculties – knows for sure what direction the science will lead us or knows which type of stem cells will ultimately lead to treatments for specific diseases. Consequently, research should proceed on all fronts.

New Ways of Deriving Stem Cells

In recent months, scientists have begun exploring additional methods of developing stem cells, ways that for some, but not all, do not cause the same ethical concerns that embryonic stem cells do. These methods are in the very early stages of development and relying on them exclusively, or using them as an excuse not to support embryonic stem cell research, would set research back years and possibly delay the development of treatments for a number of debilitating diseases.

These other methods of cell derivation are often mistakenly referred to, even by stem cell advocates, as "alternative" ways of doing stem cell research. While they hold promise and the science should proceed, they are not viable alternatives, especially today and in the near future, to embryonic stem cell research.

When Can We Expect Therapeutic Applications?

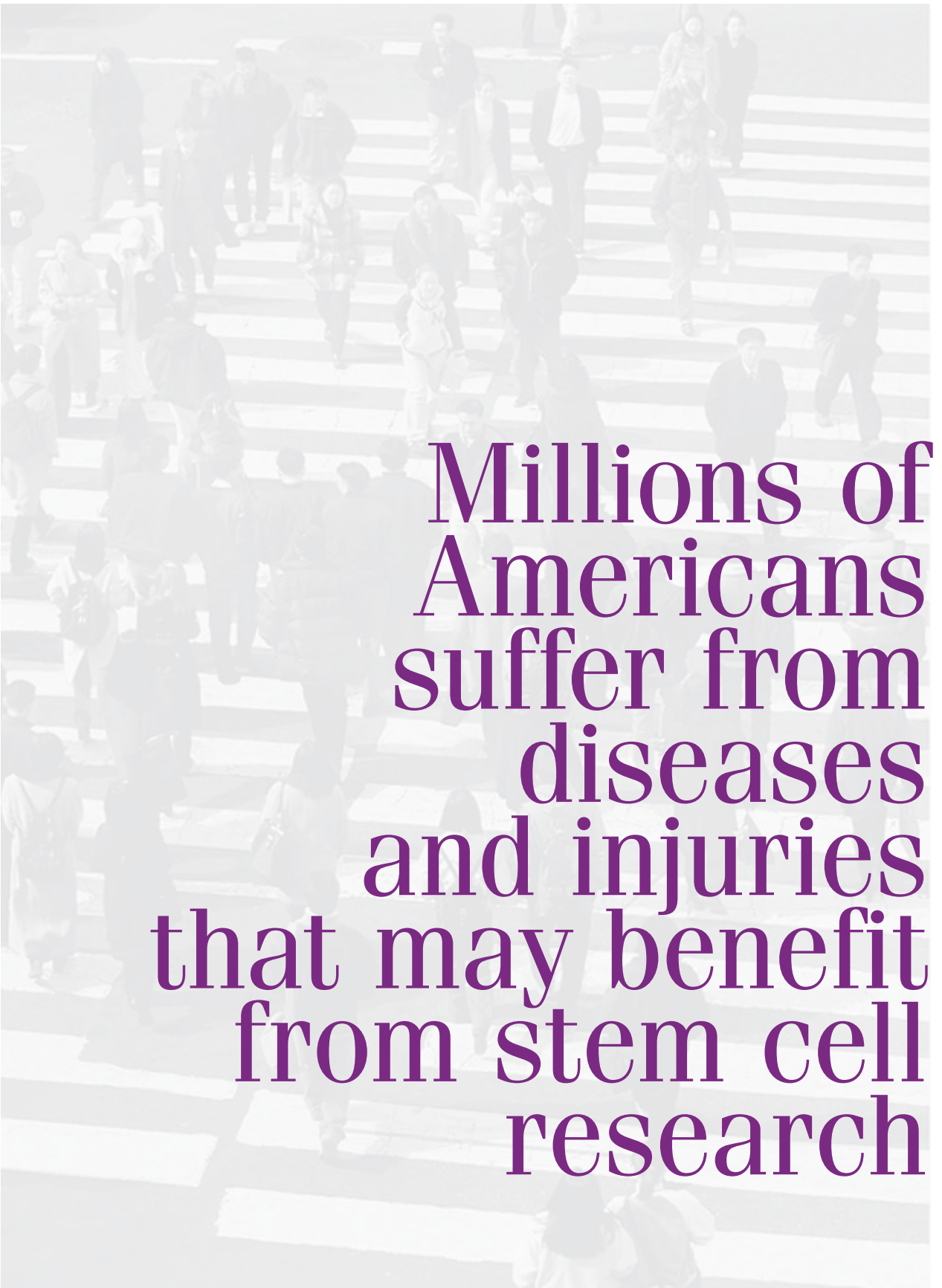
The rapidly growing volume of international research and public and private investment in stem cell investigation underscores the belief in the scientific-community that this emerging field holds tremendous promise. However, it is also valid to point out that there remain many gaps in our understanding of stem cells and that many potential treatments – if they can be found – remain several years in the future. Other treatments, however, are closer at hand.

Opponents of stem cell research have seized upon the fact that not a single person has been cured using embryonic stem cell therapies. However, it is important to put human embryonic stem cell research in its appropriate stage of scientific development. The first human embryonic stem cell was isolated in 1997, and the first isolation of an embryonic stem cell from a blastocyst occurred in 1998. The transition from the lab bench to the clinic is not instantaneous. For example, the first demonstration of potential utility of islet cell transplants in experimental models was provided in 1972. Transplants in humans began in 1980, and were unsuccessful for 20 years, until an immunosuppressive protocol was developed that was not itself toxic for the transplanted islet cells. Another example is bone marrow research which began in the 1950s. The first use of transplants between non-related individuals occurred in 1973, and the first use of transplants between non-related individuals for leukemia treatment was in 1979.

If we are going to be consistent, then it is necessary to put realistic timelines on our expectations for embryonic stem cells. Based on the length of time it took for the fields of bone marrow transplantation and islet cell transplantation to mature, a reasonable expectation for human embryonic stem cells will be to look for the development of effective human therapies within the next twenty years. Based on the speed with which this field is moving, however, it is probable that successes will come well before that.

[2] The islet transplantation claim arises from the technique known as the Edmonton Protocol, in which islets are isolated from the pancreas of people who have died and are transplanted into patients with type I diabetes. Early results are promising, and there are about a dozen patients who have been off insulin therapy for a year or so. The Edmonton protocol requires islet cells from healthy dead people – individuals who are brain dead and from whom a still functioning pancreas can be isolated. Approximately 3,000 pancreases from donor cadavers become available each year, and two cadavers are required to treat one diabetes patient. Thus, this technique, if proven successful in larger studies, could help up to 1,500 patients per year. There are an estimated 1 to 3 million individuals in the U.S. with type 1 (juvenile) diabetes.

[3] Bone marrow transplants have shown themselves to be useful in a large numbers of diseases. However, all of the diseases that are currently treated with bone marrow transplants are conditions where replacing the cells of the blood can be of benefit in some way. Bone marrow transplants have not been demonstrated to be of therapeutic value for repairing the brain, the pancreas, the liver, or any other tissue that is not the blood stream. While it is very likely this list will change with time, and there are some interesting clues as to potential new uses of bone marrow-derived cells, rigorous confirmation of the utility of such therapies has not yet been provided.



Millions of Americans suffer from diseases and injuries that may benefit from stem cell research

An Analysis of the Therapeutic Potential of Stem Cell Research by Condition

The range of types of damage that the body is not able to repair is large, providing a striking example of the potential of stem cell medicine. In addition to tissue repair, stem cell research could provide scientists with powerful new tools to examine diseases on the cellular level and test new compounds and therapies. Millions of Americans suffering from a wide variety of debilitating diseases and injuries could benefit from stem cell therapies. These diseases not only have tremendous physical and emotional tolls, they also represent a massive economic burden.

Therapies employing adult-derived tissue-specific stem cells have been in use for many years with tremendous success. The list of conditions that adult-derived stem cells can treat is long and growing and is a testament to the potential of stem cell medicine. But there are significant limitations to these therapies both in terms of the source of stem cells and the range of types of cells they can generate. Embryonic stem cells, by virtue of their ability to give rise to every tissue type in the body and regenerate without limit, hold the greatest potential to address a significantly wider range of diseases and injuries.

Disease	Description
Alzheimer's Disease	Progressive death of certain populations of nerve cells in the brain
ALS (Lou Gehrig's Disease)	Progressive destruction of motor neurons in the spinal cord
Blindness/Vision Impairment	Range of congenital conditions and injuries to cells of the eye that result in various degrees of vision loss
Burns	Second and third degree burns can permanently damage upper (epidermal) and bottom (dermis) layers of skin
Cancer	Group of diseases characterized by uncontrolled growth of abnormal cells
Cardiovascular/ Heart Disease	Group of several conditions, including heart attack, arrhythmias, and heart failure
Juvenile Diabetes	Immune system attacks and destroys certain cells in the pancreas that help regulate glucose levels – high glucose levels can cause serious damage to organ systems
Multiple Sclerosis	Chronic autoimmune disease in which body damages the central nervous system
Osteoporosis	Progressive loss of bone mass
Parkinson's Disease	Progressive disorder of the central nervous system in which neurons in a certain part of the brain die
Pediatric Leukodystrophies (Childhood Disease)	Several rare and usually fatal disorders found primarily in children in which myelin cells, which serve as insulation for nerve cells, are missing or damaged
Sickle Cell Disease	Inherited blood disorder that results in irregularly-shaped blood cells that can cause blockages and damage to organs
Spinal Cord Injury	Damage to nerve fibers in the spinal cord
Stroke	Type of cardiovascular disease in which a blood vessel that carries oxygen to the brain is blocked, causing cellular death of brain cells

Scope	Related Stem Cell Research
4.5 million Americans have Alzheimer's – a number that is expected to triple in the next few decades as the population ages	Embryonic Stem (ES) cells: generate brain cells to replace neurons destroyed by disease; help scientists understand progression of disease at a cellular level and experiment with ways to slow it down
Approximately 30,000 Americans have ALS	ES Cells: generate cells to replace neuron cells destroyed by the disease and/or the support cells that surround the spinal motor neurons
More than 4.5 million Americans are blind or visually impaired	Adult stem cells: have been used in experimental therapies to repair the cornea in human patients Embryonic and adult stem cells: generate retinal cells for transplant
50,000 Americans per year require hospitalization from severe burns	Adult and/or embryonic stem cells: generate new healthy epidermal and dermal skin cells for transplant
1.3 million new cancer cases and 570,000 cancer-related deaths in 2005	Adult stem cells: already widely used to replace/regenerate tissue lost as consequence of cancer treatment (e.g. bone marrow transplant) ES cells: enable scientists to understand why "cancer stem cells" arise and how they can be selectively destroyed
61 million Americans have some form of cardiovascular disease and approximately 950,000 Americans die of cardiovascular disease every year	Adult and embryonic stem cells: generate cells to repair heart valves, muscles, and grow blood cells
An estimated 1 to 3 million Americans have juvenile diabetes	Adult and embryonic stem cells: generate islet (insulin-producing) cells to replace cells damaged/destroyed by the disease
350,000 to 400,000 Americans have MS	ES cells: generate new healthy oligodendrocytes cells that are the source of the myelin cells that are destroyed by the disease
An estimated 44 million Americans are affected by osteoporosis	Adult and embryonic cells: used to replenish population of bone producing (mesenchyme) stem cells
An estimated 1 million Americans have Parkinson's disease	Adult and ES cells: generate the dopamine-producing cells that are destroyed by the disease
Collectively, pediatric leukodystrophies kill thousands of children every year	ES cells: generate new healthy oligodendrocytes (cells that form myelin) and/or astrocytes (cells serve a support function for oligodendrocytes and neurons)
Approximately 72,000 Americans suffer from sickle cell disease	Adult stem cells: bone marrow/cord blood transplants to restore healthy blood production
Approximately 250,000 Americans suffer spinal cord injuries every year	ES cells: generate new nervous system cells to repair damaged cells in the spinal column
An estimated 700,000 Americans suffer new or recurrent stroke every year, resulting in 163,000 deaths	ES cells: generate new healthy brain cells to repair/replace cells damaged by stroke

As has been discussed, stem cell biology is in its infancy and its medical application is not just around the corner. There remain huge gaps in our knowledge of the science and significant obstacles to overcome. These include understanding how to induce stem cells to become one cell type vs. another and how to isolate and maintain levels of purity of desired cells. These gaps and other limitations may, in some instances, be impractical to overcome for certain conditions.

That having been said, it is also important to acknowledge that the regenerative nature of stem cells opens to scientists a new field of investigation and possibilities to address diseases and conditions which result in the (currently) irreversible destruction of tissue. Much of the groundbreaking research in this field is being conducted in New York research institutions. Following is a compilation of the diseases/conditions in which regenerative stem cell therapies may hold promise – a list will almost certainly expand as stem cell research advances.

The regenerative nature of stem cells opens to scientists a new field of investigation and possibilities to address diseases and conditions which result in the (currently) irreversible destruction of tissue. Much of the groundbreaking research in this field is being conducted in New York research institutions.

Alzheimer's Disease

In patients with Alzheimer's disease, certain nerve cells of the brain die. As is the case in multiple neurological disorders, by the time a person exhibits symptoms, more than 80 percent of specific populations of neurons in his or her brain have already died. Memory loss, confusion, and cognitive difficulties are the hallmark symptoms of the disease, whose cause is unknown. While there is a growing stable of medications available to adjust the levels of various brain chemicals and help ease the symptoms or slow the disease, there is no cure.

Alzheimer's currently affects more than 4.5 million Americans, but the numbers are expected to triple in the next few decades as the population ages. The disease affects about one of every 10 people over the age of 65, and one of every two people over the age of 85. Alzheimer's-related health care costs top $100 billion annually, with the care of each individual patient reaching approximately $40,000 per year.

Stem cells offer the possibility of growing a new supply of brain cells that would offer a reservoir to replace the neurons lost in Alzheimer's disease, or alternatively could supply cells that reduce the progress of inflammatory damage and thus slow the rate of progression of the disease. Stem cell research could also help scientists understand the disease at the cellular level by recreating the conditions outside the human body and studying its progression, experimenting with ways to slow it down, and enabling them to test the effectiveness and safety of new compounds.

One of the challenges facing scientists who are exploring potential stem cell therapies for neurological disorders such as Alzheimer's, Parkinson's, and spinal cord injury has been the ability to generate neurons in sufficient quantities. In 2004, researchers at Albany Medical Center announced that they had developed a technique to generate greater quantities of neural stem cells and, ultimately, neural cells by co-culturing them with blood cells.

Amyotrophic Lateral Sclerosis (Lou Gehrig's Disease)

Amyotrophic lateral sclerosis (ALS) progressively destroys nerve cells called motor neurons in the spinal cord, eventually causing paralysis and death. People who have ALS steadily lose their ability to control muscle movement. Patients in the latter stages become totally paralyzed, although their minds are often unaffected. The cause of ALS is unknown and there is currently no cure or existing treatment to halt or reverse the disease. The drug riluzole is approved to treat the disease; doctors believe it works by reducing damage to motor neurons, prolonging

survival by several months. Other drugs are available to relieve symptoms. As the disease progresses relentlessly and breathing becomes difficult, patients may use a respirator. Most people with ALS die within three to five years from the onset of symptoms.

Approximately 30,000 Americans have ALS, and more than 100 people are newly diagnosed with the disease every week. In the advanced stages, caring for an ALS patient can cost up to $200,000 a year.

As with many neurological disorders, the symptoms of ALS are rooted in the destruction of a specific type of nerve cell, in this case the motor neurons in the central nervous system. Stem cell research offers a potential way to replace those neurons.

Scientists at Johns Hopkins University recently reported preliminary evidence that cells derived from embryonic stem cells can restore movement in an animal model of ALS. Rats that received stem cells from human fetal tissue regained some movement – the cells had taken root in the spinal cord and had migrated extensively. Other researchers at Columbia University and the University of Rochester Medical Center (URMC) have developed ways to manipulate stem cells so that they develop into just the type of cell necessary – in this case, spinal motor neurons – to treat the disease. Such ability is a crucial step toward the goal of manipulating and customizing stem cells to the extent necessary to treat diseases such as ALS.

There is also evidence, from animal models, that it may be possible to treat ALS with a very different stem cell strategy, that of replacing the support (glial) cells that surround the spinal motor neurons. As this approach would not require rebuilding the neuronal circuitry, it may be far easier to apply. Four laboratories at URMC have extensive expertise in the biology of the cells, including human cells that would be used in such an effort.

Blindness/Vision Impairment

The terms blindness and vision impairment refer to a wide range of congenital conditions and injuries to cells of the eyes that result in various degrees of vision loss. The most common are retinal degenerative diseases such as macular degeneration, which cause progressive loss of central vision. Retinal degeneration is the leading cause of blindness in people over the age of 55. Other causes of vision loss are the result of defects or injuries to the cornea.

More than 4.5 million Americans are either blind or vision impaired and it is estimated that these conditions cost the federal government more than $4 billion annually in benefits and lost taxable income.

Stem cell research has already shown success in restoring vision in experimental therapies. Since 2003, researchers have successfully transplanted corneal and limbal stem cells into damaged eyes to restore vision. Using cultured stems cells from fetuses, scientists are able to grow a thin sheet of stem cells in the laboratory. When these sheets are transplanted over the eye, the stem cells stimulate renewed repair, eventually restoring vision. In June 2005, researchers in England were able to restore the sight of forty patients using this technique employing adult stem cells obtained from the patient, a relative, and cadavers.

Scientists have also injected stem cells from a specific area of the brain into the eyes of rats with degradation of the retina. The injected cells then migrated to the retina and began to take on characteristics of retinal cells including sensitivity to light. Researchers at Columbia University, among others, have demonstrated that embryonic stem cells can be programmed to become light-sensing neurons, or photoreceptors. Scientists have also been able to cultivate retinal cells from embryonic stem cells in the laboratory.

As with many neurological disorders, the symptoms of ALS are rooted in the destruction of a specific type of nerve cell, in this case the motor neurons in the central nervous system. Stem cell research offers a potential way to replace those neurons.

Stem cells could play an important role in repairing tissue damage caused by heart disease. Studies show, for example, that stem cells can be used to repair heart valves and to grow blood cells.

Burns

A severe burn is a serious and potentially life-threatening condition, and is considered to be one of the most painful conditions from which to recover. The severity of a burn – and the ability to treat it – depends on how deep into the skin a burn penetrates. First-degree burns damage the top layer of the skin only, and heal with little problem. Second and third-degree burns, however, penetrate into the bottom layer of the skin, the dermis. Depending on its size and scope, the burn can permanently damage skin cells so they cannot produce skin, or if they do survive, they create a skin that has little elasticity and durability, no pigmentation, and is heavily scarred.

Each year in the United States, more than one million people suffer some kind of burn, with 10,000 people dying from burn-related infections. Close to 50,000 demand hospitalization. Severely burned patients, usually with third-degree burns, must be moved to a special burn care facility where the slow and painful healing process can begin. According to Sandia National Laboratories, $2 billion is spent annually in the treatment of burns.

Although progress has been made in developing new treatments for burn victims, including skin grafting and artificial skin technologies, these cultured skin grafts do not have hair follicles, sweat glands and other features of normal skin. The result is thin, inflexible skin (which hampers mobility of joints), and skin that dramatically differs from the remaining healthy skin. Scientists believe that results of stem cell research will help identify those cells responsible for differentiating into the various elements that comprise the dermis, and eventually produce skin that will help patients heal quicker with less scarring and more flexibility, and perhaps, even produce a skin that literally matches that of the rest of the body.

Scientists have already found that skin progenitor stem cells (keratinocyte progenitors) in adult human skin have a significant capacity for growth and tissue regeneration. It may also be possible to use pluripotent stem cells to generate healthy new epidermal or dermal skin. Burn victims could also benefit from somatic cell nuclear transfer, or SCNT. The cells created by this technique could then be used to generate new tissue, such as skin, without risk of the immune-rejection problems common to donated tissue and organ transplants.

Researchers at the University of Cincinnati's Division of Burn Surgery/ Shriners Burns Institute already are experimenting with cultured skin grown from a burned person's own skin stem cells. With this method, cells are taken from a small patch of skin, grown in the laboratory, and combined with a collagen matrix. After this cultured skin is placed on the burned area, the matrix dissolves, and the transplanted cells reform skin tissue to heal the wound. And a team at the Howard Hughes Medical Institute and The Rockefeller University has isolated adult stem cells from the skin of a mouse and shown, for the first time, that a single skin stem cell can be differentiated in culture to form a multilayered epidermis with an underlying dermal layer, and then be used in grafts to produce skin, hair and oil glands.

Cancer

The term "cancer" describes a group of diseases characterized by uncontrolled growth of abnormal cells, which can occur in almost any tissue or organ. In most cases, if the growth of cancer cells is not controlled, patients will become seriously ill or die. Cancer is caused by a variety of factors, including but not limited to tobacco, chemicals, radiation, infectious organisms, inherited mutations, and immune conditions. Such factors may function together or in sequence to initiate or promote carcinogenesis. Cancer can occur in anyone and is treated by surgery, radiation, chemotherapy, hormones, and immunotherapy.

Cancers are an extremely prevalent public health problem, with over 1.3 million new cases expected in 2005. This year over 570,000 Americans are expected to die of cancer, more than 1,500 people per day. While some progress has been made in treating specific types of disease, cancer remains the second most common cause of death in the United States, exceeded only by heart disease. In the U.S., cancer causes one of every four deaths. The NIH estimates the total cost of cancer to be at least $189 billion per year.

Two aspects of stem cell research are important for improving cancer treatment. First, cancers can result in destruction of important tissues needed to maintain life. Moreover, commonly used cancer chemotherapies or radiation can also damage normal tissues. Stem cells offer the hope of replacing or regenerating tissues lost as a consequence of cancer progression or treatment and of discovering means of selectively killing cancer cells without killing the normal stem and progenitor cells of the body. Second, new studies indicate that in at least some cases, cancers actually arise from damage to normal tissue stem cells. Indeed, so-called "cancer stem cells" may lie at the root of certain types of tumors and be essential for perpetuation of disease. Therefore, research aimed at understanding why cancer stem cells arise and how they can be selectively destroyed may be critical for developing better cancer therapies.

Recent studies have shown that stem cells can be used to create a variety of adult tissues including cells found in blood, the pancreas, the brain, muscle, skin, and other organs. These findings indicate that stem cells have the potential to repair damage that occurs as a result of cancer treatment. A prominent recent example is the use of stem cells from umbilical cord blood to regenerate lost blood-forming tissues during leukemia therapy. Further, other studies have shown that cancer stem cells can be preferentially destroyed, while sparing normal tissue stem cells. Thus, it appears likely that new treatment strategies will appear soon that are specifically designed to eradicate cancer stem cells.

Cardiovascular/Heart Disease

Heart disease is an umbrella term that covers a number of conditions, including heart attack, arrhythmias and heart failure. While progress has been made, heart disease remains a leading cause of death in the United States and worldwide.

About 61 million Americans have some form of cardiovascular disease, which accounts for nearly one out of four deaths in the U.S. About 950,000 Americans die of some type of cardiovascular disease each year.

Current treatments for cardiovascular disease include medications to dilate blood vessels and slow the heartbeat in order to lower blood pressure, and pacemakers and implanted cardiac defibrillators to monitor arrhythmias and shock the heart back into rhythm when needed.

Stem cells could play an important role in repairing tissue damage caused by heart disease. Studies show, for example, that stem cells can be used to repair heart valves and to grow blood cells. Injecting a patient's own stem cells directly into heart muscle may be of value as a treatment for end-stage heart failure as well. In other research, human heart muscle cells – derived from human pluripotent stem cells – have been successfully transplanted into the hearts of rats, where they began to form healthy tissue. Still other studies are using patients' own skeletal muscle to grow myoblasts (cells from which muscle cells develop). The myoblasts are then injected into areas of scarring from prior heart attacks to regenerate heart muscle.

Scientists at Memorial Sloan-Kettering are examining the effects of using stem cells to correct severe congenital myocardial wall-thinning defects, a genetic condition which results in abnormally weak heart muscles. A consortium of researchers at Columbia and Stony Brook universities have demonstrated that adult stem cells derived from bone marrow can be genetically reprogrammed to serve as a biological pacemaker, research that could potentially eliminate the need for electronic pacemakers. And scientists at Weill Medical College at Cornell University have identified a specific type of stem cell that can co-differentiate into body muscle and blood tissue, two elements critical for efficient heart repair.

Juvenile Diabetes

Diabetes is the name given to disorders in which the body has trouble regulating its blood glucose, or blood sugar, levels. There are two major types of diabetes: type 1 and type 2. Type 1, also called juvenile diabetes or insulin-dependent diabetes, is a disorder of the body's immune system.

Type 1 diabetes occurs when the body's immune system attacks and destroys certain cells in the pancreas. These cells – called beta cells – are contained, along with other types of cells, within small islands of endocrine cells called the pancreatic islets. Beta cells normally produce insulin, a hormone that helps the body move the glucose contained in food into cells throughout the body, which use it for energy. But when the beta cells are destroyed, no insulin can be produced, and the glucose stays in the blood instead, where it can cause serious damage to all the organ systems of the body. Juvenile diabetes can lead to stroke, heart disease, high blood pressure, blindness, amputations, and pregnancy complications.

An estimated 18.2 million Americans have some form of diabetes and 1 to 3 million have type 1 or juvenile diabetes. Diabetes is the sixth leading cause of death in the United States and the

leading cause of new cases of blindness in adults. Twenty-five percent of African Americans between the ages of 65 and 74 have diabetes. The total annual direct and indirect cost of treating individuals with diabetes in the U.S. is an estimated $132 billion.

Islet transplantation has emerged as the most promising option for restoring normal blood sugar in people with juvenile diabetes. In the procedure, islets – which contain the insulin-producing beta cells that have been destroyed in type 1 diabetes – are taken from a donor's pancreas, and transferred to a person with the disease. However, this technique, even if working at maximal efficiency, could only be used to treat about 1,500 patients per year – less than 0.1 percent of all patents with diabetes – as the transplanted islet cells need to be derived from cadavers of the highest organ transplant quality.

Several recent studies underline stem cell research as a basis for critically-needed therapies for juvenile diabetes. Insulin-producing cells have already been created from mouse embryonic stem cells as well as in preliminary studies using embryonic cell lines from humans. In addition, adult stem cells from mouse bone marrow have shown therapeutic potential in mice with diabetes.

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Multiple Sclerosis

Multiple sclerosis (MS) is a chronic autoimmune disease in which the body attacks its own tissues, damaging the central nervous system, especially nerve pathways in the brain and spinal cord. In patients a fatty substance known as myelin, which wraps around nerves and protects them like insulation around a wire, is destroyed, damaging the body's ability to send signals crisply. Symptoms vary greatly, depending on what nerves are damaged, but generally include fatigue, muscle weakness, cognitive problems, problems with touch and vision, and difficulty with bladder control. Early in the course of MS, symptoms can go into remission for years and then suddenly cause severe attacks; in others, symptoms worsen gradually over the years.

There is no cure for MS. Three forms of beta interferon have been approved for treatment of MS, and several other drugs are available to reduce the duration and severity of attacks. Physical therapy and exercise is widely used to help patients remain mobile. Symptoms vary widely among patients: some individuals are only mildly affected by the disease, while in others the disease can quickly become incapacitating.

About 350,000 to 400,000 people in the United States have multiple sclerosis, which almost always strikes in young adulthood; after trauma, it's the top cause of disability in young adults. Most patients are diagnosed between the ages of 20 and 50. Studies sponsored by the National MS Society show that the total direct and indirect costs of the disease can exceed $2.6 million for each affected individual over his or her lifetime.

Multiple sclerosis ultimately comes down to the destruction of myelin in the central nervous system. Myelin is produced by nervous system cells known as oligodendrocytes. Supplying the nervous system with healthy oligodendrocytes could give the nervous system a fresh, steady supply of myelin. Multiple sclerosis offers an attractive target for stem cell research because scientists need to spur the development mainly of one cell type – oligodendrocytes.

Repair of demyelinating damage in the central nervous system has been the subject of study for many years, with some of the first demonstrations of this possibility being obtained over a decade ago. Multiple laboratories, including groups at URMC, have isolated human cells that are capable of generating myelin-forming oligodendrocytes in animals lacking myelin for genetic reasons. The cells developed, flourished, and migrated extensively throughout the nervous system, and restored the myelin in a

widespread area of the animals' brains – a crucial first step toward reversing symptoms. Other studies at University of California Irvine have also shown that significant re-insulation of damaged nerve fibers in mice is possible.

Osteoporosis

Patients with osteoporosis see their bones become fragile and more likely to break over time. Fractures typically occur in the hip, spine, or wrist, but any bone may be affected. Hip fractures in particular usually require surgery, and may cause permanent disability or death.

Osteoporosis affects an estimated 44 million Americans and 55 percent of the people age 50 or older. Ten million of those affected already have the disease, and 34 million are believed to have low bone mass, a stepping stone to osteoporosis. Of the 10 million Americans with disease, eight million are women.

Stem cells in the mesenchyme, an unspecialized cell layer that first forms bone in the human embryo, are used again later in life in the bone marrow to replace damaged bone. Studies underway at several universities suggest that the main cause of osteoporosis may be the loss of healthy stem cells in bone. The number of mesenchymal stem cells declines with age, according to the theory, leading to fewer bone-forming cells. Thus, the development of techniques to provide new stem cells in bone marrow could represent a new way to treat, or even cure, osteoporosis.

Researchers are working to determine how the skeleton employs stem cells to regenerate bone. Teams are identifying the chemical signals that control whether stem cells in an embryo's mesoderm go on to form connective tissue, bone or cartilage. Specific applications of this research are varied. One wing of research, for example, is looking into how nicotine, known to impair skeletal healing, may reduce the otherwise strong "commitment" of stem cells to become mature bone.

Parkinson's Disease

Parkinson's disease is a progressive disorder of the central nervous system in which brain cells known as neurons die in a pea-sized part of the brain known as the substantia nigra. These neurons produce a crucial brain chemical known as dopamine, which sends signals to the parts of the brain that control movement and coordination. When the neurons die, the shortage of dopamine results in several progressive symptoms including slowness of movement, difficulty walking and swallowing, muscle stiffness, tremors, and rigidity, as well as cognitive effects including depression. The cause of the disease is not known, though many researchers suspect that both environmental risk factors and genetic vulnerabilities play a role. Since the specific causes of the disease are not known, there is no known way to prevent it from occurring.

Parkinson's disease is chronic and progressive. While some people become severely disabled, others have only minor disruptions to their lives – the course of the disease varies greatly among patients. Several medications are available to treat symptoms, though many have side effects that can include drowsiness and involuntary movements. In some patients a surgical procedure known as deep brain stimulation reduces symptoms.

Doctors estimate that approximately one million Americans have Parkinson's disease. While the disease sometimes occurs in younger patients, it most often affects people age 50 and over – approximately 1 percent of people over the age of 65 have Parkinson's. According to the National Parkinson Foundation, each patient spends an average of $2,500 a year for medications alone. The total direct and indirect costs of the disease are believed to top $5.6 billion annually.

Currently there is no way to repair or replace the crucial dopamine-producing brain cells that are lost in Parkinson's disease. The key to treating the disease successfully is to create a way to constantly replenish the brain with a steady supply of dopamine. For years, scientists have tried to do this by transplanting cells that produce dopamine directly into the brain, and such efforts have produced some promising results. However, the central limitation in this work is that current approaches require the transplantation of brain cells derived from particular regions of brains of aborted fetuses with transplantation in a single Parkinson's patient require cells from six fetal brains. Stem cells – in this case, progenitors of dopamine-producing cells – offer a promising new approach to provide enough new cells to replace the lost cells in large numbers of patients. Scientists are especially encouraged because the basis of the disease, a very small cluster of specific neurons, offers a clear target for therapy.

In animal studies, scientists have demonstrated the potential of stem cells to treat Parkinson's disease. Scientists at the NIH have generated dopamine-producing neurons from embryonic stem cells and then implanted the cells in rats with a Parkinson's-like disease. The function of the animals improved substantially. Researchers at Memorial Sloan-Kettering saw similar success in mice and noted improvements in symptoms related to Parkinson's. Moreover, dopamine-producing neurons derived from embryonic stem cells have already been examined in animal models of Parkinson's disease and been shown to ameliorate symptoms for at least a year after transplant. Researchers at Rockefeller University have demonstrated that stem cells generated from the SCNT process can be coaxed to generate dopamine-producing cells that would be a genetic match of the donor. Additionally, scientists at the University at Buffalo have developed a novel

Mobility after spinal-cord damage has been achieved in multiple cell transplantations in animal models of spinal cord injury. Some animals with damaged spinal cords have been able to walk again as a result of repairs made possible with stem cells.

method of using nanoparticles to deliver genetic "instructions" to adult brain stem cells. Researchers in Buffalo are exploring the possible application of this process of reprogramming existing stem cells in the brain to repair neurological damage, or in the instance of Parkinson's disease, generate dopamine-producing neurons.

Pediatric Leukodystrophies (Childhood Disease)

Pediatric leukodystrophies include several rare and usually fatal disorders. In these diseases a substance known as myelin, which serves as a sort of insulation around nerve cells, is damaged or missing. The pediatric leukodystrophies include several diseases such as Krabbe's, Pelizaeus-Merzabacher, Tay-Sachs, Canavan, and vanishing white matter diseases. It's possible that even cerebral palsy, a common pediatric disease, is due largely to the loss of oligodendrocytes and their precursor cells.

There is no cure for these diseases in which patients deteriorate progressively. Since brain cells are dying, symptoms of the disease vary widely, depending on which areas of the brain are affected – children may go blind, have seizures, lose the ability to talk, or lose their cognitive skills, for example. Treatment consists of symptom management. Most children with such diseases die during childhood or during their teenage years, though some live into adulthood. Though most pediatric leukodystrophies are individually rare, collectively the diseases kill thousands of children every year.

There are two different cell transplantation approaches of theoretic value in the treatment of leukodystrophies. Most laboratories are focused on the replacement of oligodendrocytes, as many of these syndromes are associated with abnormalities in white matter. A team at URMC has shown the considerable capacity of transplanted human CNS precursor cells to generate new myelin-forming oligodendrocytes in animal models in which myelin is lacking. Studies by three other URMC laboratories have revealed that oligodendrocyte replacement may not necessarily be the key goal, at least in the case of vanishing white matter disease (which may represent 25 percent or more of leukodystrophies). In this case, it appears that the problem lies in the generation of another important cell type in the brain, the astrocyte, which provides a variety of support functions to the neurons and oligodendrocytes. This team has found that the genetic lesion that causes vanishing white matter disease specifically compromises the ability of CNS precursor cells to make astrocytes, and also has isolated the relevant human precursor cells that could be used to replace astrocytes in patients with this syndrome.

Sickle Cell Disease

Sickle cell disease is an inherited blood disorder that can cause severe pain, damage to vital organs and death. The conditions results from a defect in an important protein in the blood system (hemoglobin) that enables red blood cells to distribute oxygen throughout the body. The irregular sickled-shaped blood cells that are produced by the condition also have difficulty passing through small blood vessels and can cause blockages in the circulatory system, denying oxygen to tissues and organs and resulting in stroke and damage to the lungs, kidneys and liver. Sickle cells that do make it through blood vessels are often destroyed in the liver or spleen which causes a thinning of the blood supply resulting in anemia.

Approximately 72,000 Americans suffer from sickle cell disease and it is most common among African-Americans. It is estimated that one in 12 African-Americans carry the sickle cell gene. A person can carry the gene for the sickle cell trait without having the disease, which manifests itself only in the children

of two people with the gene. The average life expectancy of someone with the disease is 45, although it can be significantly lower (25-30) in African-Americans. The annual cost of treating sickle cell disease is estimated to be over $1.5 billion.

Traditional treatments for the disease include antibiotics, pain management, intravenous fluids, blood transfusions, medications, and surgery but these therapies do not reverse the condition.

In addition to gene therapy, stem cell transplants have already shown promise and are already providing cures for some victims of sickle cell disease. Treatments in which diseased bone marrow is destroyed and replaced with healthy bone marrow have generally been successful. However, like other bone marrow transplant therapies, this procedure is limited by the number of genetically compatible donors. It is believed that cord blood stem cells could expand the treatment to a greater number of patients.

Spinal Cord Injury

A spinal cord injury is damage to the bundle of nerve fibers that make up the portion of the central nervous system known as the spinal cord. Such damage occurs in a variety of ways – motor vehicle accidents, disease, diving accidents, gunshots, or injuries during athletic contests. The late Christopher Reeve, a hero among patients and one of the early supporters of stem cell research, suffered a spinal cord injury in a horseback riding accident. About half of spinal cord injuries result in quadriplegia, with loss of sensation and movement in both legs and arms, while about half result in paraplegia, with loss of sensation and movement in the lower body. More than half of spinal cord injuries occur in people from 16 to 30 years of age, and more than four out of five patients are male.

Treatment immediately after a spinal cord injury, such as with steroids, can prevent further inflammation and limit nerve damage. Patients work extensively to learn to live with less feeling and mobility. About one-third of individuals with a spinal-cord injury will require respiratory support. Care for patients focuses on handling chronic conditions to which patients are prone, including chronic pain, bladder and bowel dysfunction, and respiratory and heart problems.

Spinal cord injuries affect approximately 250,000 people in the United States. On average, more than once each hour, an American sustains a new spinal cord injury, resulting in approximately 11,000 new injuries each year. Spinal cord injuries cost the nation at least $9.7 billion per year for medical care, equipment and disability support.

Stem cells offer a way to re-grow and replenish damaged cells. Just as a bundle of cables can no longer run a computer once the bundle is damaged or cut, scientists long thought that the brain could no longer send nerve impulses to the affected parts of the body once the spinal cord is damaged. But with stem cells, scientists are discovering ways to re-grow and repair damaged parts of the spinal column, filling in the gaps so that nerve impulses can again be sent from the brain to the rest of the body.

Mobility after spinal-cord damage has been achieved in multiple cell transplantations in animal models of spinal cord injury. For instance, groups at the URMC and elsewhere have shown that stem cells and progenitor cells can be used to repair and regenerate neurons and astrocytes in the damaged spinal cord. Some animals with damaged spinal cords have been able to walk again as a result of repairs made possible with stem cells.

Stroke

Stroke is a type of cardiovascular disease that affects the arteries leading to and within the brain. A stroke occurs when a blood vessel that carries oxygen and nutrients to the brain is either blocked by a clot or bursts preventing the flow of blood and oxygen to the brain causing cellular death which can lead to paralysis, vision problems, memory loss, and death.

Stroke is the third highest cause of death in the United States, killing nearly 163,000 people a year. An estimated 700,000 a year suffer new or recurrent stroke. Americans will pay about $57 billion in 2005 for stroke-related medical costs and disability.

Common treatments include clot-busting drugs and surgical procedures to repair or remove blood vessels. Antiplatelet agents such as aspirin, and anticoagulants interfere with the blood's ability to clot and can play an important role in preventing stroke. None of these treatments, however, reverse the damage done to the brain as a result of stroke.

Stem cell research holds significant potential to repair damage to the brain and mitigate the severity of strokes. Because strokes leave permanent gaps in the brain, the regenerative capability of stem cells could provide a means by which brain cells that are destroyed or damaged by stroke are replaced with healthy cells. A Stanford University study in animal models has shown that stem cells injected into the brain migrate or home to the right location and develop into the appropriate type of neurons. Other animal studies using stem cells have reduced the level of disability following a stroke.

An international race is underway to unlock the potential of stem cell science

The Race to Discover Cures: The Competitive Environment

In the absence of federal leadership, individual states, foreign governments, and private investors are moving aggressively to position their domestic research institutions and biotech industries at the leading edge of stem cell research. Governments and the private sector are beginning to invest heavily in stem cell research. Academic, private and government research institutions are rapidly building the necessary physical, research, and academic infrastructure to accommodate the anticipated growth in basic and clinical stem cell research.

While several states and countries have opted to "get into the game," primarily by loosening restrictions on stem cell research and providing public funding, only a limited number of states and countries possess the additional ingredients necessary to achieve significant advances in the science – a concentration of biomedical research facilities and biotech industry and the ability to mobilize public and private funding on a sufficiently large scale.

Seeing an opportunity to not only advance science but also position their research institutions and biotech sectors at the leading edge of this emerging field, several states have or are in the process of establishing state-based funds dedicated to stem cell research.

The federal government's current restrictions on human embryonic stem cell research funding, along with insufficient NIH funding to adequately support other forms of meritorious stem cell research, have prompted the creation of several state-sponsored research funds, the most prominent example being the ten-year, $3 billion initiative approved by California voters in November 2004. Several more states (including New Jersey and Connecticut in the Northeast) are establishing similar funds and others are poised to do so in the near future.

This competition also exists on an international scale. Countries in Europe and Asia, where the regulatory and cultural climate is often more welcoming to stem cell research, are quickly moving to capture the research and, ultimately, commercial potential of this new field.

The States

Current federal policy restricts the use of NIH funds for embryonic stem cell research. Seeing an opportunity to not only advance science but also position their research institutions and biotech sectors at the leading edge of this emerging field, several states have or are in the process of establishing state-based funds dedicated to stem cell research.

California: In November 2004, voters in California approved Proposition 71, the California Stem Cell Research and Cures Initiative, by a margin of 59 to 41 percent. The ballot initiative established a ten-year, $3 billion stem cell research fund for California universities and research institutions. The initiative also provided for the establishment of a new state agency to make grants and provide loans for stem cell research, research facilities and other related research opportunities. In 2005, the California Institute for Regenerative Medicine, based in San Francisco, opened its doors. However, the disbursement of state grants, to be funded by bonds, has been held up pending the resolution of several lawsuits brought forward by opponents of the research. Private funds have been raised to allow grants to be awarded in the interim.

Several California institutions have significantly expanded their stem cell research enterprises in anticipation of state grants. Stanford University has created an Institute for Cancer/Stem Cell Biology and Medicine. The University of California (UC), San Francisco is in the process of establishing an "embryo bank" to supply embryos and gametes from fertility clinics to California researchers. UC Los Angeles plans to spend $20 million in the next five years to establish the Institute for Stem Cell Biology and Medicine. UC Berkeley recently received a $40 million donation to establish a new research center focused on emerging scientific fields including stem cell biology. And in southern California, four institutions – UC San Diego, the Burnham Institute, the Salk Institute, and the Scripps Research Institute – have formed the La Jolla Stem Cell Initiative.

Connecticut: In June 2005, Connecticut Governor M. Jodi Rell signed into law legislation creating a ten-year, $100 million Stem Cell Research Fund with state bonds. The legislation establishes an advisory council, named Connecticut Innovations, to develop research guidelines and disburse funds for research, infrastructure and business development.

In 2001, the University of Connecticut created a Center for Regenerative Biology. The state is also home to Yale University which ranks in the top 10 nationally in NIH grants. Earlier this year, Yale announced that it is considering plans to establish a new stem cell institute.

Illinois: In July 2005, Illinois Governor Rob Blagojevich signed an executive order directing the state's Department of Public Health to create a program, named the Illinois Regenerative Medicine Institute, which will award $10 million in grants to medical research facilities for embryonic, adult and cord blood stem cell research.

A proposal put forward by State Comptroller Dan Hynes for a $1 billion bond issuance for stem cell research to be funded by a tax on elective cosmetic surgery has stalled in the state legislature.

Massachusetts: In May 2005, the Massachusetts legislature overrode a veto by Governor Mitt Romney and enacted legislation that authorizes state funding for embryonic stem cell research, establishes institutional and ethical guidelines, and removes existing "legal ambiguities" that were considered potential barriers to research. No funds were attached to the bill and the state legislature is now considering earmarking upwards of $100 million in funds for research grants, infrastructure, and scholarship programs.

In 2004, Harvard University established the Harvard Stem Cell Institute with a $5 million donation. The institute consists of several universities and colleges, seven of the region's teaching hospitals, and over 100 researchers. The institute will not only conduct scientific inquiry, but will also examine ethical, political, religious, economical, and other ramifications of the research. The institute has also generated and is distributing its own stem cell lines.

Several other institutions in the state are heavily engaged in stem cell research, including the Whitehead Institute for Biomedical Research at MIT, Children's Hospital Boston, the Joslin Diabetes Center, and Massachusetts General Hospital's Center for Regenerative Medicine and Technology.

New Jersey: In 2004, New Jersey established the nation's first state-sponsored stem cell research institute. The groundbreaking for the new facility – a joint research institution operated by Rutgers University and the University of Medicine and Dentistry of New Jersey named the New Jersey Stem Cell Research Institute – was scheduled to occur in July at Rutgers but was postponed when the $150 million in necessary state funding was held up by the New Jersey legislature over a dispute about whether the funds should go toward infrastructure or research. In October of 2005, acting Governor Richard Codey signed an executive order creating a public umbilical cord and placental blood bank for use in stem cell research. Additionally, a $230 million statewide bond initiative that was scheduled to be put before voters in November 2005 was delayed by the legislature. A poll conducted earlier this year indicated that the bond initiative had the support of 61 percent of the state's voters. A non-profit foundation, the New Jersey Stem Cell Research and Education Foundation, has been raising private funds for research.

In 2004, acting Governor Cody proposed a joint three-state stem cell research effort with Pennsylvania and Delaware. Discussions are proceeding; however, legal barriers to state-funded stem cell research in Pennsylvania would need to be changed by that state's legislature.

Wisconsin: In 2004, Wisconsin Governor Jim Doyle unveiled a joint public-private proposal to invest $750 million in biomedical research over the next decade, the bulk of which would be focused on stem cell research. His proposal includes $375 million to build an interdisciplinary research facility at University of Wisconsin (UW) in Madison (a groundbreaking for this facility was held in August 2005), $134 million for basic science research, and the balance dedicated to specific research fields, including stem cell research. The Wisconsin Technology Council has projected that 27,000 jobs would be created by the initiative.

UW-Madison is considered the birthplace of stem cell research. Researchers there were the first to isolate human embryonic stem cells in the laboratory. The University's private patent and licensing arm, the Wisconsin Alumni Research Fund (WARF), holds the patents on many of the existing stem cell lines and, consequently, will receive significant royalty revenues as stem cell research proceeds in other states and internationally. In early 2005 UW-Madison, which is home to the WiCell Research Institute, announced the creation of an interdisciplinary Regenerative Medicine Program.

International

Scientists around the world are joining in the race to unlock the potential of stem cells. Several countries have loosened restrictions and made significant public investments in stem cell research and, as a result, are becoming international magnets for this emerging field, attracting private investment and, in some cases, American researchers drawn to more welcoming regulatory and cultural environments.

Recognizing that the regulatory climate overseas is, in many instances, more suitable for stem cell research than in the U.S., many American-based private research foundations, such as the Christopher Reeve Paralysis Foundation, the Michael J. Fox Foundation for Parkinson's Research, the Stem Cell Research Foundation, and the Juvenile Diabetes Research Foundation are sponsoring stem cell research projects in Europe and Asia.

Europe

Europe finds itself in a similar situation to the United States in terms of the regulatory climate for stem cell research with a range of approaches represented in the policies of individual states. In Britain, Sweden, and Belgium, stem cell research is essentially unhindered. On the other extreme, Ireland, Austria, Poland, Lithuania, and the Slovak Republic ban stem cell research outright.

As a result of this variation in policy, the European Union (EU) has only made modest investments in stem cell research. The EU currently funds twenty-five stem cell-related research projects; however, only two involve embryonic stem cells. And in 2004, the EU launched the European Consortium for Stem Cell Research (EuroStemCell), a multi-state initiative to "establish foundations for future clinical trials of stem cell therapies." Despite these efforts to craft a united European approach, more progress is being made by individual states where the regulatory climate, strong biomedical research institutions and biotech industry, and public and private investment have provided elements to advance stem cell research.

Great Britain has made the most significant investment in stem cell research and has successfully built upon its pioneering history in this field (the first cloned mammal – Dolly the sheep – occurred in Scotland) and its strong research base in genetics and developmental biology. The Biotechnology and Biological Sciences Research Council and the Medical Research Council, Britain's public research funding arms, have invested heavily in stem cell research grants and facilities. In May 2004, the UK Stem Cell Bank opened its doors in Cambridge.

British institutions have also built up the necessary infrastructure to advance stem cell research. This includes the creation of several academic research centers such as the Institute for Stem Cell Research at the University of Edinburgh, the Center for Stem Cell Biology at the University of Sheffield, the University of Cambridge's Institute for Stem Cell Biology, and the Center for Neuroscience Research at King's College in London. Britain's biotech industry and independent foundations, such as the Wellcome Trust Sanger Institute, have committed significant private funds to research initiatives.

Sweden's leading position in the emerging field of stem cell research is due to its favorable regulatory climate, public support, government funding and a strong foundation in biomedical research. The Swedish National Research Council – the research funding arm of the government – funds individual research projects and has established a national stem cell bank. Academic institutions – working with the biotech industry – are aggressively moving to commercialize research and cell production; 24 of the original 72 stem cell lines on the NIH registry are held by Swedish institutions. These efforts are primarily clustered around the Sahlgrenska Academy in Gothenburg, the Stem Cell Center at Lund University, and the Karolinska Institute in Stockholm.

Switzerland became the first country to put the topic of stem cell research to a popular vote. In 2004, voters overwhelmingly (66.4 percent) backed a new law that lifted restrictions on embryonic stem cell research. The country possesses one of Europe's most dynamic biotech sectors and is home to pharmaceutical giants Novartis, Serono, and Roche and it is hoped that the legal changes will prompt industry to invest in domestic stem cell research.

Other potential European leaders in biomedical research have been hindered by government restrictions on embryonic stem cell research. Many of these countries are beginning to loosen these restrictions – for example, **Germany** bans the creation of new stem cells lines but will allow research on imported lines that were created before 2002. **France** and **Spain** have also begun to liberalize their policies. While individual researchers and institutions in these countries are conducting stem cell research and are partners in European-wide initiatives such as EuroStemCell, the research environment in Europe is quickly dividing into a system in which certain countries are establishing themselves as leaders in the field while the rest fall behind.

Asia

Asia is rapidly becoming a major center for stem cell research. A favorable regulatory and cultural climate, government financial support, and lower research costs have all combined to position the region as one of the leaders in this emerging field.

Asian scientists and governments are not confronted with the same cultural resistance as their colleagues in the West. In Confucian and Buddhist societies, there exist fewer religious inhibitions to the utilization of human embryos. The cost of research is also significantly lower; researchers in China are employable at a fifth to a tenth of the cost of comparable American researchers. The region also has a growing pool of research talent, many of whom received their training in the U.S.

The government of **South Korea** recently announced plans to spend $50 million over the next five years to create the BIO-Max Institute in Seoul to foster interdisciplinary biomedical research with a focus on stem cell research. At the same time, Korea has tightened regulation of the field including bans on human reproductive cloning and prior approval by a government panel for research projects. The majority of stem cell research in Korea is conducted at the Seoul National University Center for Bioinformation Technology, and the Korean Stem Cell Research Center in Seoul. It is unclear what impact, if any, the recent scandal regarding the fabrication of research data will have on that country's stem cell research efforts.

Singapore has moved quickly to target stem cell research as a field for significant research and commercial investment. In 2003, Singapore's Biomedical Research Council opened a new state-of-the-art medical research campus, termed Biopolis Asia, which was constructed with $500 million in public and private funds and is part of a $2 billion national biomedical sciences strategy. The government has adopted a British regulatory model for the field and has also implemented a system of grants and tax incentives to not only grow its biomedical sector and attract venture capital, but also attract foreign researchers, a notable example being Alan Colman, a member of the Scottish team that cloned Dolly the sheep. The Singapore-based ES Cell International, a commercial arm of Singapore's stem cell researchers, is second only to WARF in terms of volume of stem cell lines distributed to researchers worldwide.

China may have the largest stem cell research program in Asia, although the Chinese government has not been forthcoming with details. It is estimated that over 400 researchers with over $24 million in annual funds are engaged in stem cell research – a significant portion of which is dedicated to embryonic stem cell research. As noted above, research dollars can be stretched much further in China than in the West. In contrast to the centralized approach in other Asian countries, China's stem cell research landscape is comprised of a host of initiatives sponsored by central, provincial, and local governments, private and semi-private enterprises, and even the military. While the Chinese government prohibits reproductive cloning, it allows therapeutic cloning and the procurement of embryos from IVF clinics and the use of fetal tissue.

Other Asian countries are racing to build their stem cell research enterprises. Last year, **Japan** allowed stem cells to be procured from domestic sources of embryos. Previously, researchers in that country had to rely on imported stem cells. The publicly funded RIKEN Center for Developmental Biology in Kobe, the Institute for Frontier Medical Sciences Stem Cell Research Center at Kyoto University, and the University of Tokyo are rapidly becoming centers of stem cell research innovation. In **Taiwan,** the government-affiliated Industrial Technology Research Institute is attempting to jump start the country's biotech sector through investments in stem cell research.

Other Countries

Australia's government announced in 2004 a $57.9 million Australian Stem Cell Center in partnership with Monash University, University of Adelaide, University of New South Wales, University of Queensland, Peter MacCallum Cancer Centre, Victor Chang Cardiac Research Institute, the Murdoch Children's Research Institute, and the Howard Florey Institute of Experimental Physiology and Medicine.

Israel is home to approximately 10 stem cell-oriented biotech companies that have been capitalized with $75 million in public and private investment. In 2003, the Israel Stem Cell Therapy Consortia was launched. The consortia is a joint project involving Israeli biotech companies, Ben Gurion University, Hadassah Medical Center, Hebrew University of Jerusalem, Technion University, Tel Aviv University, and Sorasky Medical Center for the purposes of developing technologies that will lead to industrialized stem cell therapies.

India has several major institutes that are engaged in stem cell research including the L. V. Prasad Eye Institute, Christian Medical College in Vellore, the National Center for Cell Sciences in Pune, and the National Brain Research Centre at Manesar near Delhi. In early 2005, the Indian Council of Medical Research and the Department of Biotechnology announced it would launch a national stem cell initiative that would include publicly funded research.

New York is poised to grow its research and biotech enterprises if it embraces stem cell research. It also has the most to lose if it fails to act.

The Economic Impact of Biomedical Research and Biotech on New York

Stem cell research holds tremendous promise for improving the lives of millions of Americans suffering from a long list of diseases and conditions. It also has the potential to fundamentally reshape biomedical research. Universities, research institutions, states and countries are moving quickly to harness public and private funds and adapt their biomedical research enterprises to accommodate the anticipated growth and importance of stem cell research. Institutions – and states – that successfully position themselves at the leading edge of this field will not only make important scientific contributions, they will also be in a position to reap the benefits that will come with more jobs and increased economic growth.

New York possesses all the necessary elements to become an international leader in the field of stem cell research, but not unless it acts quickly to make up the ground it has already lost. The state is home to 32 academic and private biomedical research institutions, 100 teaching hospitals, world-class scientists, and one of the largest concentrations of biotechnology and pharmaceutical companies in the country. New York also has the capacity to mobilize public and private investment on a large scale; the state is the third in the nation in both NIH funding and venture capital. Consequently, not only is New York poised to grow its research and biotech enterprises if it embraces stem cell research, it also has the most to lose if it fails to act. Absent state financial support,

New York's medical schools, teaching hospitals, and biotech/ pharmaceutical industry are responsible for an estimated 560,000 jobs and $48 billion in economic activity.

New York's biomedical research capacity will likely decline as other states – and countries – devote financial resources towards stem cell research, assume leadership in this field, and become magnets for talented scientists, research grants, and venture capital.

Biomedical research and the biotech industry are big business in New York, generating over $48 billion dollars in economic activity and creating over 560,000 jobs. While New York City is the center of biotech activity in the state, this emerging sector is strong on Long Island and also critical to the upstate economies of Buffalo, Rochester, Albany, and Syracuse as these regions struggle to adjust to the continuing loss of manufacturing jobs.

Furthermore, the list of diseases and conditions that could potentially benefit from stem cell therapies represents a tremendous economic burden to the state. As with all biomedical research, investments in stem cell research could be repaid many times over in future savings in the direct and indirect costs of disease management.

The new competitive landscape described earlier in this White Paper has significant implications for biomedical research and industry in New York. Even if the changes that are now being contemplated in Congress to relax federal restrictions on stem cell research are adopted, they will not fundamentally change this new competitive dynamic.

As NIH funding has remained flat for the past several years, it cannot be expected that stem cell research would be awarded any greater share of funding than it currently receives.

New federal policies will need to be accompanied with increases in overall NIH funding to accomodate both the anticipated growth in stem cell research and continue to fund other fields of research at existing levels; a development that seems unlikely given the current budgetary climate. Without these increases in NIH funding, states with dedicated stem cell research funds will retain a scientific and economic advantage over those that do not.

Consequently, if New York is to protect and grow its biomedical research and commercial sectors it must invest state funds in these enterprises.

Biomedical Research and the New York Economy

New York's research institutions have a tremendous economic impact on their communities. It is estimated that New York's medical schools and teaching hospitals contribute $30 billion a year to the state's economy and generate more than 459,000 jobs statewide. In addition to this direct economic impact, the state's universities and research institutions are engines of innovation – particularly in the field of biomedical research. This research not only serves to generate more revenue for these institutions (through licensing of patents and royalty revenue), but much of this technology migrates to the state's biotech sector in the form of new products and start-up companies.

New York's strong academic foundation in biomedical research is reflected in the amount of federal funds its institutions receive. In 2004, 11 out of the top 100 recipients of NIH grants were New York universities and research institutions. In total, New York received 5,192 NIH grants equaling $1.9 billion – a 10 percent increase over 2003. Over the past 3 years, New York has ranked second in the nation in the number of federal scientific grants it received and third in the nation for NIH funding and grants. The state has also made important strategic investments in biomedical research through the New York State Office of Science, Technology and Academic Research as well as the "Governor's Centers of Excellence," "Gen*NY*sis," and "RESTORE New York" programs. Moreover, New York's colleges and universities invested a record $3.1 billion on research and development in 2003 – second highest in the nation – and an 11 percent increase

over the $2.7 billion invested in 2002.

New York's research community is also in the process of investing significant amounts of private funds in stem cell research programs. The state's scientists and institutions have also been highly successful in landing the limited – and highly competitive – federal grants available for stem cell research.

- In May 2005, the Starr Foundation announced a three-year, $50 million gift to establish a Tri-Institutional Stem Cell Initiative consisting of **Weill Medical College of Cornell University, Rockefeller University,** and **Memorial Sloan-Kettering Cancer Center.** The funds will build upon the world-class biomedical research programs at these institutions and will be used to recruit and train scientists, develop shared stem cell research facilities, and derive new and maintain existing stem cell lines.
- A $10 million gift in May 2005 has led to the creation of the Black Family Stem Cell Institute at **Mount Sinai School of Medicine**. The institute will integrate research in embryonic stem cells, developmental biology, and adult stem cell biology. Mount Sinai has also been designated by the NIH as an Exploratory Center for Human Embryonic Stem Cell Research.
- In 2005, **Columbia University** launched a multi-year stem cell research initiative to build upon its international strength in the field. The first phase consists of a $50 million campaign to outfit a new stem cell center, construct facilities to produce stem cells for experimental and therapeutic use, establish separate laboratory space for human embryonic stem cell research, recruit and retain researchers, and establish scholarships for doctoral candidates and postdoctoral fellows.
- Currently there are 18 principal investigators at the **University of Rochester Medical Center** who are conducting stem cell research. These investigators and their laboratories represent over $45 million in research grants and employ over 200 researchers and technicians.
- In 2001, **Rensselaer Polytechnic Institute (RPI)** announced a $14 million initiative to create an interdisciplinary faculty group – named the Nobel Enterprise Constellation – which will focus on functional tissue engineering and regenerative medicine. The initiative is part of RPI's recent multi-million dollar investment in and reorganization of its biotechnology research activities which includes the construction of the new Center for Biotechnology and Interdisciplinary Studies.
- In August 2005, **Albert Einstein College of Medicine of Yeshiva University** received a $3 million NIH grant to establish the Einstein Center for Embryonic Stem Cell Research which will enable the college to expand its tissue culture facility and hire and train technicians and postdoctoral students. The center will be restricted to using NIH-approved lines for research.
- In May 2001, the **New York University Medical Center** received a $10 million gift to establish the Helen L. & Martin S. Kimmel Center for Stem Cell Biology. The multidisciplinary center will focus on the basic biology of stem cells in animal models.

These private commitments will further position New York's research community as a potential worldwide leader in this emerging field, but not unless that state makes a significant public investment in stem cell research, as has been done in other states.

New York's research community is in the process of investing significant amounts of private funds in stem cell research programs.

As we speak, institutions in other states – and even other countries – are attempting to lure away New York's top scientists with the promise of public funding and a more welcoming regulatory climate for stem cell research.

Biotech and the New York Economy

Biotech is big business in New York. According to the New York Biotechnology Association, New York is home to 123 biotechnology companies. Collectively, these companies coupled with the pharmaceutical industry, employ 54,469 people, pay $3.3 billion in wages and generate $18.1 billion of economic activity. On average, every biotech sector job creates an additional job outside this sector, meaning that these industries support approximately 110,000 jobs in New York.

New York's concentration of academic research institutions and the high number of scientists in the workforce generate the innovation that is necessary to develop new products and sustain industry growth. New York has historically ranked among the top five states for biotech patents. The state's track record of innovation, strong base of federal funding, and the proximity of Wall Street have resulted in significant investments in venture capital. In 2004, approximately $3.8 billion of venture capital funding was invested in New York biotech companies – 18.3 percent of total venture capital investments.

New York's biotech sector is in a strong position to continue this growth. In July 2005, the trade publication *Business Facilities* ranked New York second in the nation in terms of overall environment for biotech companies. The survey examined the number of biotech companies, public support, sector growth, number of incubators, research and development expenditures, and number of scientists in the workforce.

The federal government projects that biotech and pharmaceutical industry employment will grow nationally by 12.5 percent by 2012. Strategic investment in biomedical research, particularly in emerging fields such as stem cell research, will enable New York's biotech sector to keep pace with national growth projections and create an estimated 15,000 new jobs in the state over the next six years.

The "Brain Drain" and Its Impact on Biomedical Research

While New York is a national leader in biomedical research, the research landscape has shifted dramatically over the course of the last year. As has been noted, several states including, but not limited to, California, Connecticut, New Jersey, Wisconsin and Illinois have or are in the process of committing significant resources to stem cell research.

These funds and the federal government's continued restriction on NIH grants for stem cell research have placed New York's leadership in the field of biomedical research and its biotech industry in jeopardy. As we speak, institutions in other states – and even other countries – are attempting to lure away New York's top scientists with the promise of public funding and a more welcoming regulatory climate for stem cell research.

The resulting loss of research talent would have a devastating ripple effect on New York's entire research population. New York could not only lose some of its top scientists to institutions in other states, but it will also become more difficult to recruit talented junior scientists who will see more opportunities to advance their research and careers in institutions that are pursuing cutting edge biomedical research. Currently, more than 50 percent of students who graduate from New York medical schools stay in the state for their post-graduate medical education. This trend could change very rapidly, particularly for graduate students pursuing a career in biomedical research.

The ripple effect of this "brain drain" will reach into other scientific fields. Research grants are tied to principal investigators and not their host institutions. It is not uncommon for scientists who are conducting stem cell research to also be engaged in other fields -- such as biomedical genetics, biomedical engineering, cell biology, and microbiology, and others. Consequently, as these individuals leave they take their grant funding with them, potentially impacting other fields of research.

Economic Burden of Disease Management

In addition to the academic and commercial impact of stem cell research, as the research advances to the stage of successful therapies New York could stand to realize billions of dollars in reduced health care costs.

Over $94 billion is spent every year on health care in New York – with taxpayers paying $35 billion on that total. A significant portion of that cost is for treating individuals with chronic illness. Over six million New Yorkers have chronic diseases many of which, including Alzheimer's, diabetes, heart disease, cancer, arthritis, and osteoporosis, could benefit from stem cell research. In total, these diseases account for 73 percent of deaths in New York and account for 70 percent of total medical costs.

It is important to acknowledge that potential savings lie many years in the future. However, using diabetes as an example, it is also readily apparent that successful stem cell therapies could result in billions of dollars in avoided health care costs for New York alone.

According to the state Department of Health, an estimated 580,000 New Yorkers have been diagnosed with diabetes and perhaps as many have diabetes but are undiagnosed. The Centers for Disease Control and Prevention project the national direct and indirect costs of diabetes are nearly $132 billion a year. The average health care cost for a person with diabetes in 2002 was $13,243, compared with $2,560 for a person without diabetes. Applying this formula for New York's diabetes population, the total average health care costs are $7.7 billion per year. This figure does not include the indirect costs – disability, work loss, premature mortality – which certainly run into the hundreds of millions. As has been detailed in previous chapters, experimental transplants of insulin producing cells into the pancreases of type 1 diabetics have essentially cured the disease. Unfortunately, the current supply of transplanted cells – healthy human cadavers – is in too short a supply to treat the estimated 1 to 3 million Americans who have juvenile diabetes. Stem cell research holds the potential to make this procedure more widely available by producing an essentially endless supply of insulin producing cells for transplant.

In early 2005, a Missouri study of six disease types that are identified as potentially benefiting from stem cell therapies concluded that, over the next 20 years, the direct and indirect costs of these diseases and conditions will cost the state more than $109 billion. The diseases/conditions included in the study were juvenile diabetes, Parkinson's disease, spinal cord injury, acute myocardial infarction (heart attack), stroke, and Alzheimer's disease. While no such analysis has been conducted specifically for New York, our state has more than three times the number of individuals in these categories than Missouri and, hence, it can be reasonably concluded that the cost to the state would be upwards of $300 billion during the same period.

In addition to the academic and commercial impact of stem cell research, as the research advances to the stage of successful therapies New York could stand to realize billions of dollars in reduced health care costs.

Stem Cell Research and Policy Timeline

July 1981: Embryonic stem cells first obtained from mice blastocysts

November 1995: The first embryonic stem cells from non-human primates are derived and maintained *in vitro*

July 1996: Scientists in Scotland create Dolly the sheep, the first successful clone of an adult mammal using the technique of somatic cell nuclear transfer

November 1998: Human embryonic stem cells isolated and cultured by scientists at the University of Wisconsin and Johns Hopkins University

August 2001: President Bush announces restrictions on NIH stem cell research funding

September 2001: Embryonic stem cells coaxed to become blood cells

November 2001: Scientists in Massachusetts (Advanced Cell Technology) perform the first cloning of human embryos using the technique of somatic cell nuclear transfer

December 2001: Embryonic stem cells coaxed to become neural cells

January 2004: New Jersey governor signs legislation permitting stem cell research and creating a state-sponsored stem cell research center

November 2004: California voters approve Proposition 71, which establishes a ten-year, $3 billion stem cell research fund

November 2004: Wisconsin governor announces $750 million public-private initiative to invest in biomedical research with a heavy focus on stem cell research

April 2005: National Academies of Science propose guidelines for stem cell research

May 2005: Connecticut governor signs into law a bill that creates a ten-year, $100 million stem cell research fund

May 2005: Massachusetts legislature overrides gubernatorial veto of stem cell research bill

May 2005: The U.S. House approves a bill to loosen NIH restrictions on federal funding for stem cell research

July 2005: Illinois governor signs executive order to dedicate $10 million for stem cell research

Ethical concerns that surround stem cell research must be balanced with the evident promise

Stem Cell Policy Issues

Given the nature of the science of stem cell research, it is appropriate that the various ethical issues surrounding this research be examined and that the research be subjected to oversight and regulation. There are several models for such a system that should be adopted if New York moves forward and establishes funding for stem cell research. The National Academies of Science proposed guidelines in April 2005 and several states, including California, New Jersey and Connecticut, have established regulations and oversight mechanisms for stem cell research in their states.

Current Federal Policy and Implications for Research

On August 9, 2001, President George W. Bush announced his administration's policy with respect to federal funding of embryonic stem cell research. The announcement was the culmination of a lengthy period of internal scientific review (which began under the Clinton administration) and political debate.

In 1996, Congress had specifically banned federal funding for research that involved the creation of human embryos for research purposes in which the embryos are destroyed. After the 1998 announcement regarding the derivation of human embryonic stem cells, the NIH determined that the ban would not apply to human stem cells because they did not meet the legal definition of embryos. It was determined that federal funds could not be used to derive stem cells, however, there was no prohibition against using federal funds for research using stem cells that had been derived with private funds. In late 2000, the NIH released guidelines for stem cell research and was preparing to award grants in early 2001 when the new Bush Administration halted the process and ordered a review of the policy.

In his 2001 speech, President Bush announced that he would allow federal funding for human embryonic stem cell research to proceed, but only on human embryonic stem cell lines that were created before that date. A key justification of president's decision was a determination by the NIH that some 64 stem cell lines were eligible for federal funding under the new criteria. This number was later increased to 78, but the number of viable stem cell lines available to researchers has been discovered to be 22.[4] Of that remaining number, scientists have serious doubts as to whether any can be used to develop human stem cell therapies. The president also announced the creation of the President's Council on Bioethics to explore the scientific, ethical and moral issues surrounding the debate.

The specific guidelines developed by the NIH consist of the following criteria: 1) the removal of cells must have been initiated before August 1, 2001; 2) the embryo from which the stem cell line was derived must no longer have had the possibility of developing further as a human being; 3) the embryo must have been created for reproductive purposes but no longer be needed for them; and 4) informed consent must have been obtained from the parent(s) for the donation of the embryo, and no financial inducements for donation are allowed.

The NIH maintains a registry of stem cell lines that meet this criteria and are, therefore, eligible for federal funding. Because these lines are the intellectual property of the institutions that created them – or the corporations that were

The primary consequence of the shrinking number of stem cell lines available to federally funded research is that the pace of discovery, and ultimately the development of new therapies, is hindered.

[4] While the NIH registry of eligible stem cell lines contains 78 entries, in practical terms the number of lines accessible for research is less than a third of that number. According to the NIH administrator under a "best case scenario," only 22 lines will be available for federally funded research.

An unpublished and widely reported NIH analysis indicated that at least 16 of the 78 lines have died or "failed to expand into undifferentiated cell cultures" rendering them useless to researchers. Fifteen of the cell lines have developed severe genetic abnormalities that would make them ineffective in therapies and potentially impractical for research. Seven lines are duplicates of other lines. And 31 of the approved stem cell lines are owned by foreign institutions and a variety of scientific, regulatory and legal obstacles restrict their availability to U.S. labs.

Furthermore, a study in the journal *Nature Medicine* in January 2005 indicated that most of the stem cell lines on the NIH approved list may be dangerous for therapeutic applications. This is because the majority of the human stem cell lines created before 2002 were cultivated with the assistance of mouse feeder (embryonic) cells and a broth of animal serum. When these stem cells were exposed to human blood serum, antibodies attached to the cells suggesting that they are seen as foreign and therefore likely to be rejected by the immune system if transplanted into the body. Concerns have also been raised regarding the possibility that animal viruses contained in the mouse feeder cells might infect human cells if transplanted. Another study of 14 of the remaining 22 stem cell colonies has suggested that at least five will never be useful in clinical studies because they are so difficult to grow.

subsequently given the commercial rights – researchers initially found it difficult to obtain samples for research. In October 2005, the NIH announced plans to create a National Embryonic Stem Cell Bank to store and distribute NIH-approved lines. The new facility is to be located at the University of Wisconsin.

New cell lines are being created using discarded embryos in laboratories across the country and across the world – many of which are superior in quality and do not possess the limitations of the federally approved lines. For example, in March 2004, Harvard University disclosed that it had isolated 17 new human embryonic stem cell lines. In June 2004, a team of scientists at the Reproductive Genetics Institute, a private fertility clinic in Chicago, announced that it had isolated human embryonic stem cells from frozen embryos. Labs in Europe and Asia are generating new stem cells lines at a rapid pace. However, none of these new lines can be used in facilities that are funded by the NIH.

The primary consequence of the shrinking number of stem cell lines available to federally funded research is that the pace of discovery, and ultimately the development of new therapies, is hindered. Scientists are, therefore, increasingly compelled to turn to other sources of stem cells and research funding. This includes accepting private funding or relocating to countries where research funding is not restricted. Even with private funds, universities are very cautious about proceeding for fear of using federal funds inappropriately and putting their entire research operation at risk of sanctions. These circumstances have also contributed to somewhat of a "catch 22" situation with respect to the public debate about the promise of stem cell research. In arguing against loosening federal restrictions, opponents point to the fact that no one has been "cured" using embryonic stem cells. However, current federal funding restrictions have greatly slowed the pace of research. Furthermore, federally approved stem cell lines are unsuitable for human transplant, meaning they cannot be used in new therapies.

In Vitro Fertilization Clinics as a Source of ES Cells

It is important to realize that under current law it is perfectly legal to discard excess embryos if that is what the donor chooses. Consequently, embryos are being discarded in U.S. in vitro fertilization (IVF) clinics at a rate that far exceeds current research needs. Furthermore, couples are choosing to donate their spare embryos (embryos that are either no longer required or not viable for implantation) or gametes (unfertilized eggs and sperm) to scientific research in numbers that are adequate to generate hundreds of new stem cell lines.

A 2003 study by the RAND Institute and the Society of Assisted Reproductive Technology (SART) estimated that nearly 400,000 embryos are frozen or cryopreserved and stored at U.S. IVF clinics. Approximately 11,000 have been donated for research – a number which could potentially produce large numbers of embryonic stem cell lines. Nine thousand frozen embryos were awaiting destruction per patient request.

Opponents of stem cell research argue that there is no such thing as an excess embryo since they can be donated to other couples for family building. While embryos can be donated for this purpose, the number of children born using this method numbers in the hundreds, low thousands at most. While the practice is likely to increase, it is important to remember that today, as mentioned, there are over 400,000 excess frozen embryos. Consequently, family building and research are not incompatible.

An examination of clinical practices allows us to reasonably conclude that tens of thousands, and perhaps as many as 100,000, embryos are discarded every year. In 2002 alone, the Centers for Disease Control reported that 97,500 IVF cycles were performed in the United States. During these cycles, fertility drugs are used to induce the production of multiple eggs. The eggs are inseminated in the laboratory and allowed to develop for three to five days. After that period, the most "viable" embryos – ones that are most advanced in terms of cell division – are transferred to the uterus. The remaining embryos are allowed to develop further (if deemed less viable), frozen for storage, or discarded immediately.

While it would be reasonable to assume that most couples would choose to have their spare embryos frozen to be available for later cycles if their pregnancy fails, many states do not mandate insurance coverage for IVF and many insurance companies that do offer coverage will pay for the fertility treatment but not for storing the embryos. As a result of this disincentive, couples will often choose to undergo the whole fertility process if they fail the first time rather than freezing the extra embryos.

U.S. IVF clinics already have the appropriate procedures in place in terms of determining whether or not a couple wants to voluntarily donate spare embryos for research. The RAND/SART study indicated that 99 percent of IVF clinics required couples to sign a consent form with respect to the final disposition of embryos before they are frozen. Couples are generally given four options: 1) discard the embryos, 2) donate the embryos to research, 3) donate the embryos to other couples, or 4) make the embryos available for quality assurance activities.

The ethical issues raised by stem cell research are similar to the broad range of ethical and policy concerns associated with any other advance in biomedical research. However, ethical complexities should lead to the creation of appropriate mechanisms of oversight and regulation, not prohibition.

The American Society of Reproductive Medicine has also developed guidelines pertaining to prospective donors of embryos for research purposes. These include: assurance that a decision not to donate spare embryos for research will not adversely affect their status in the reproductive program; access to material that informs them of the goals and benefits of research and, if requested, articles that raise and address ethical concerns about embryo research; informed of possibility to change their minds and not donate without prejudice; ability to specify the research purpose, if desired and informed that the benefit will be the advancement of medical knowledge and that they will not directly benefit from the study.

Several additional protections to these guidelines have been proposed, including:

1) women should not undergo extra cycles of ovulation to produce spare embryos for research;
2) there should be a strict separation between the personnel working with the woman or couple in the IVF clinic and the personnel requesting the embryos for research; and
3) women or couples should not be paid to produce embryos or receive a reduction in fees for their infertility procedures for agreeing to donate spare embryos for research.

Reproductive vs. Therapeutic Cloning

As briefly discussed earlier with SCNT, it is possible to re-program the nucleus of an adult cell by placing it into an unfertilized egg from which the nucleus has been removed. This process has been used to generate organisms that are genetically identical to the animal from which the adult cell was derived, with the most famous example of this process being the generation by cloning of Dolly the sheep in 1997.

Embryos generated by SCNT go through the same process of development as embryos created by conception, with the generation of a blastocyst that cannot develop any further unless it implants in the wall of the uterus. If this is done, and an organism develops, this is called reproductive cloning. There is near universal agreement that reproductive cloning of humans should be prohibited. In addition to a host of ethical concerns, this technique is also associated with a very high failure rate and experience to date indicates the animals generated have a high probability of being ill.

In contrast to reproductive cloning, therapeutic cloning is the process of deriving embryonic stem cells from blastocysts produced using the process of SCNT. The techniques used are identical as for the derivation of embryonic stem cells from blastocysts derived from IVF clinics. One of the advantages of using this technique is that the genetic make-up of the resulting stem cells would be identical with those of the donor, thus avoiding the problem of rejection if cells generated from the stem cells were transplanted into the donor. It also enables scientists to explore the underpinnings of genetic diseases and possible methods to improve or cure these conditions.

Models for Oversight and Regulation

The ethical issues raised by stem cell research are similar to the broad range of ethical and policy concerns associated with any other advance in biomedical research. As with other fields of scientific inquiry, any effort to address these concerns must balance the evident promise against the potential for inappropriate application. In other words, biomedical research should not proceed in isolation of the ethical and policy imperatives of the society in which it operates. However, ethical complexities should lead to the creation of appropriate mechanisms of oversight and regulation, not prohibition.

While stem cell research is subject to institutional, state and federal oversight and regulation, the unique policy issues that arise from the research require the creation of guidelines specific to this field of scientific inquiry. Heightened oversight is also essential to assure the public that such research is being conducted in an ethical manner.

National Academies of Sciences Guidelines

In April 2005, the National Academies of Sciences (NAS), a non-profit organization created by the federal government to advise on scientific and technological matters, issued Guidelines for Human Embryonic Research.

The central component of the NAS-recommended guidelines is the creation of local oversight committees. Institutional Review Boards, which are responsible for general oversight of biomedical research, already exist in research universities and institutions. However, given the unique scientific and ethical nature of stem cell research, the NAS guidelines recommend the creation of new special review and oversight bodies in all research institutions conducting human embryonic stem cell research. These bodies – called Embryonic Stem Cell Research Oversight Committees (ESCRO) – will be comprised of representatives of the public and persons with expertise in developmental biology, stem cell research, molecular biology, assisted reproduction, and the ethical and legal issues related to stem cell research. These committees will provide oversight for all issues related to the derivation and research use of human embryonic stem cells, including the review and approval of research protocols, the review and approval of certain categories of research, compliance with institutional guidelines and regulations, maintenance of registries of stem cell research conducted at the institution, and the education of stem cell investigators.

While the establishment of specific guidelines, research protocols and oversight procedures will be left to the individual institutions through their ESCRO committees, the NAS guidelines include several specific recommendations:

- A prohibition of SNCT for reproductive purposes.
- A prohibition of the culture of human embryos beyond 14 days after fertilization.
- A prohibition of the implantation of animal stem cells into human embryos.
- A prohibition of the implantation of human stem cells in nonhuman primates.

The States

States that are in advanced stages of establishing stem cell research initiatives have already created oversight mechanisms and regulations.

In 2003, California adopted legislation that permits SCNT for therapeutic cloning, authorizes the donation of human stem cells from embryos and fetal tissue, and requires providers delivering fertility treatment to provide patients with information on the options for disposition of spare embryos. It also requires the review of stem cell research by institutional review boards but it does not define that term. A separate law bans reproductive cloning. Proposition 71, which was approved by California voters in 2004, established the California Institute for Regenerative Medicine. The Institute is responsible for awarding grants and loans for research and facilities and establishing scientific, medical and ethical standards for research. An Independent Citizen's Oversight Committee consisting of university presidents/chancellors, elected officials, scientists, and representatives from patient disease groups and private industry will govern the Institute.

In 2004, New Jersey enacted legislation that permits research involving the derivation and use of human embryonic stem cells, human embryonic germ cells, and tissue-specific stem cells from any source. The new law created a nine-member institutional review board to advise the governor and legislature on issues related to stem cell research, required informed consent and prohibits payment for donated embryos, and prohibited reproductive cloning. SCNT for the purposes of therapeutic cloning is permitted.

In June 2005, Connecticut adopted legislation which establishes a 10-year, $100 million stem cell research fund. The new law establishes guidelines for the procurement of embryos and gametes, allows therapeutic cloning, bans reproductive cloning, and establishes a nine-member Stem Cell Advisory Committee consisting of members from the academic, public and industry sectors to review and administer research grants in coordination with the state Department of Public Health and a five-member Stem Cell Peer Review panel.

Conclusion

Leadership requires vision.

Stem cell science is, as we speak, in the process of reshaping the entire field of biomedical research. In the previous pages, we have detailed the efforts of institutions, states, and even countries to rapidly marshal the necessary resources and research talent to position themselves as leaders in this emerging field. We strongly believe that, given the seismic potential of stem cell science, that the decisions that policymakers in Albany make during the 2005 legislative session will be critical in terms of the state's biomedical research and economic future.

It is difficult to overstate the important role that stem cell science will play in 21st century medicine. Stem cell research, which is advancing at a rapid pace, holds the potential to lead to treatments for diseases and conditions that are presently incurable and touch the lives of millions of Americans and their families. In this White Paper, we have documented the numerous diseases and injuries that could stand to benefit from stem cell research.

New York has all the necessary ingredients to become an international leader in this field. Its concentration of research institutions, biotech/pharmaceutical companies, teaching hospitals, medical schools, and venture capital makes it the ideal environment to advance this emerging field of science. Many New York universities and institutions have made significant private investments in stem cell research and the state's scientists are already making important contributions to the field.

But the new competitive environment that has been brought about by the creation of state-based stem cell research funds in California and elsewhere demands that the state level the playing field if it is to retain its leadership position in the field of biomedical research.

It is important to acknowledge that the science is in its infancy and there remain significant obstacles to overcome. Consequently, the

development of stem cell therapies for humans may be many years in the future. However, like any other major breakthrough in medicine, these barriers will, in time, be surmounted and this research will radically expand our medical knowledge and improve the lives of millions of Americans.

While the benefits to patients may be years in the future, the risks of inaction to the state's research community and economy are real and immediate. If New York fails to act, it will begin to rapidly lose its top scientists to institutions in states with public funding for stem cell research. This is already occurring. The subsequent "brain drain" will erode New York's biomedical research capabilities, in this and other fields, and the state's biotechnology/pharmaceutical companies and venture capital will begin to look elsewhere for innovation.

On the other hand, if the legislature were to fund stem cell research at a level comparable to that of other states, it would be able to reinforce New York's leadership position in medical research, create new jobs and companies, and develop technologies that could potentially improve the lives of millions of Americans.

In this White Paper, we believe that we have put forward a strong case for the state to make an immediate strategic investment in stem cell research. We acknowledge that this will not be an easy decision, given the political debate surrounding this issue and the fact that the benefits of this research may not be immediately realized. But we feel strongly that the future of biomedical research is so closely tied to stem cell science that we must speak with a single, urgent voice on this issue.

We urge the governor and the legislature, in the strongest possible terms, to recognize the importance that this issue holds for the state's future health and economy and exercise their leadership and support stem cell research.

Glossary of Terms

Adult stem cell: An undifferentiated cell found in a differentiated tissue that can renew itself and (with certain limitations) differentiate to yield all the specialized cell types of the tissue from which it originated.

Blastocyst: A preimplantation embryo of about 150 cells. The blastocyst consists of a sphere made up of an outer layer of cells (the trophectoderm), a fluid-filled cavity (the blastocoel), and a cluster of cells on the interior (the inner cell mass).

Differentiation: The process whereby an unspecialized early embryonic cell acquires the features of a specialized cell such as a heart, liver, or muscle cell.

Embryo: In humans, the developing organism from the time of fertilization until the end of the eighth week of gestation, when it becomes known as a fetus.

Embryonic germ cells: Cells found in a specific part of the embryo/fetus called the gonadal ridge that normally develop into mature gametes.

Embryonic stem cells (ES): Primitive (undifferentiated) cells from the embryo that have the potential to become a wide variety of specialized cell types.

Embryonic stem cell line: Embryonic stem cells, which have been cultured under in vitro conditions that allow proliferation without differentiation for months to years.

Feeder layer: Cells used in co-culture to maintain pluripotent stem cells. Cells usually consist of mouse embryonic fibroblasts.

Fetus: A developing human from usually two months after conception to birth.

Hematopoietic stem cell: A stem cell from which all red and white blood cells develop.

In vitro: Literally, "in glass;" in a laboratory dish or test tube; an artificial environment.

In vitro fertilization: An assisted reproduction technique in which fertilization is accomplished outside the body.

Inner cell mass: The cluster of cells inside the blastocyst. These cells give rise to the embryonic disk of the later embryo and, ultimately, the fetus.

Islet cell: The functional cell of the pancreas that is responsible for secreting insulin and other molecules that regulate a number of processes including carbohydrate and fat metabolism, blood glucose levels and acid secretions into the stomach.

Mesemchymal stem cell: Also known as bone marrow stromal cells, mesenchymal stem cells are rare cells, mainly found in the bone marrow, that can give rise to a large number of tissue types such as bone, cartilage (the lining of joints), fat tissue, and connective tissue (tissue that is in between organs and structures in the body).

Multipotent stem cells: Stem cells whose progeny are of multiple differentiated cell types, but all within a particular tissue, organ, or physiological system. For example, blood-forming (hematopoietic) stem cells are single multipotent cells that can produce all cell types that are normal components of the blood.

Neural stem cell: A stem cell found in adult neural tissue that can give rise to neurons, astrocytes, and oligodendrocytes.

Neurons: Nerve cells, the structural and functional unit of the nervous system. A neuron consists of a cell body and its processes, an axon, and one or more dendrites. Neurons function by the initiation and conduction of impulses and transmit impulses to other neurons or cells by releasing neurotransmitters at synapses.

Plasticity: The ability of stem cells from one adult tissue to generate the differentiated cell types of another tissue.

Pluripotent: Ability of a single stem cell to develop into many different cell types of the body.

Progenitor cell: An early descendant of a stem cell that can only differentiate, but it cannot renew itself anymore.

Regenerative or reparative medicine: A treatment in which stem cells are induced to differentiate into the specific cell type required to repair damaged or depleted adult cell populations or tissues.

Reproductive cloning: Somatic cell nuclear transfer used for the production of a fetus and delivery of a live offspring that is genetically identical to the donor of the somatic cell DNA.

Signals: Internal and external factors that control changes in cell structure and function.

Somatic cell nuclear transfer: A technique in which the nucleus of a somatic cell (any cell of the body except sperm cells and egg cells) is injected, or transfered, into an egg, that has had its nucleus removed.

Therapeutic cloning: Somatic cell nuclear transfer for the isolation of embryonic stem cells. The embryonic stem cells are derived from the blastocyst (before it becomes a fetus) and can be instructed to form particular cell types (e.g. heart muscle) to be implanted into damaged tissue (e.g. heart) to restore its function. If the stem cells are placed back into the individual who gave the DNA for the somatic cell nuclear transfer, the embryonic stem cells and their derivatives are genetically identical and thus immunocompatible (they will not be rejected).

Totipotent: Stem cells that can give rise to all cell types that are found in an embryo, fetus, or developed organism.

Umbilical cord stem cells: Hematopoietic stem cells are present in the blood of the umbilical cord during and shortly after delivery.

Zygote: The cell that results from the union of sperm and egg during fertilization. Cell division begins after the zygote forms.

Sources: National Institutes of Health and the International Society for Stem Cell Research

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