HUMAN STEM CELL RESEARCH

MEDICAL PANACEA OR MORAL NIGHTMARE?

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If scientists were to discover the ultimate cure for disease and injury—something that could save thousands, even millions of lives—but it could require the loss of other lives, would the cure be worth it, no matter what the price? That moral question is central to the debate behind stem cell research and has fueled a new area of medical study, bioethics. This article will weigh the advantages of stem cell research against the moral issues of human life.

New era of medicine

As the medical community becomes more knowledgeable and capable of identifying illnesses and ways to eradicate them, it also spends more time straddling the fence called ethics. Despite advanced medical technology, there is still no cure for many diseases. If its potential is realized, stem cell research could change the face of medicine (Figures 1 and 2), providing cures for diabetes, leukemia and anaplastic anemia, as well as help for those who suffer from stroke, Alzheimer's disease, and Parkinson's disease.

Doctors would be able to use stem cells to regenerate nerve cells to repair damaged spinal cords, possibly enabling a wheelchair user to someday walk. Damaged nerve cells could be repaired, offering hope to patients with Parkinson's disease. The actor, Michael J Fox, who recently admitted to suffering with Parkinson's disease, has become an avid spokesperson for stem cell research. He said in a recent statement, "The research offers the potential to eliminate diseases and literally save millions of lives… (but) it's time to act on what we've learned. Sadly, we've already lost two years."[16]

With stem cell research, scientists hope also to be able to grow new skin for burn victims. The use of stem cells also reaches into the area of diseased organs. Healthy pancreatic cells may be transplanted into young persons with diabetes, offering a life free of insulin injections. "There is evidence that a cure is within our grasp," states actress Mary Tyler Moore, a diabetic herself for more than 30 years.[16]

Stem cell potential may be best demonstrated in the treatment of aplastic anemia, a deficiency of all the formed elements of the blood caused by a breakdown of cell-generating ability in the bone marrow. Up until the early 1970s, most patients with severe aplastic anemia died from complications of their disease.[11] These complications can include myelodysplasia (affecting the spinal cord), acute leukemia (a malignant neoplasm of blood-forming tissues), and paroxysmal nocturnal hemoglobinuria (associated with abnormal function of the bone marrow). Current treatment options include a bone marrow transplant or the use of growth factors, immunosuppressive therapy with antithymocyte globulin (ATG), antilymphocyte globulin (ALG), and/or cyclosporin.[11]

A bone marrow (stem cell) transplant from human leukocyte antigen (HLA) or identical sibling donor offers the best long-term treatment and likelihood of survival. Unfortunately, only about one third of patients will have an HLA-compatible donor. Without the support of stem cell replacement, full recovery of this condition is impossible.

If the capabilities of stem cell research are endless, why not embrace it wholeheartedly? To understand the controversy, one needs to understand the origin of the stem cell.

Stem cells defined

Stem cells are undecided human cells that have the potential to grow into any specific type of organ or tissue. There are three types of stem cell.

1. Totipotent stem cell—occurs at the time of fertilization of the ova (zygote). The totipotent stem cell has the ability to develop into a fetus.
2. Pluripotent stem cell—develops from the inner cell mass of the blastocyst (Figure 3). The pluripotent cell has the ability to become many types of cells, but cannot become a fetus without the supporting tissues (such as the placenta) that will develop from the outer layer of the blastocyst (Figure 4).
3. Multipotent stem cell—a specialized stem cell that is already programed to perform a particular function. For example, the blood stem cells become the erythrocytes, leukocytes, and platelets. Blood stem cells are found in the bone marrow and in circulating blood.

Sources for the human stem cell

There are three primary sources of stem cells, each having different characteristics and different developmental paths.

1. Embryonic stem cells (ES cells) are derived from an early embryo (Figures 5 and 6). ES cells are the totipotent stem cells that are obtained from an embryo created for in-vitro fertilization that is in excess of need.
2. Embryonic germ cells (EG cells) are collected from fetal tissue at a somewhat later stage of development. EG cells are the multipotent stem cells that are collected from aborted fetuses.
3. Adult stem cells are obtained from mature tissues such as bone marrow.[3]

Stem cells form within four days of conception and are the parent cells to all the body's systems. These cells can potentially form any kind of tissue in the body.[14] They are later triggered to become muscle, blood, bone, nerve, skin, specific organ, or other tissue.

The human fetus is derived from a fertilized ovum, a single cell with the capability of producing every cell in the adult body. These cells are pluripotent, meaning that they carry the genetic information for an entire human being. Embryonic cells are currently collected from cells of embryos that have been aborted for unrelated reasons or are left over from in vitro fertilization that would otherwise be destroyed. To minimize rejection from mismatched transplantations, the nucleus from a patient's somatic cell is transferred into an enucleated human ovum, then stimulated to divide.[8] After the division, stem cells could be harvested and used to create organs that would be a perfect match. This potentially could eliminate the need for immunosuppressive agents.

"Surely every medicine is an innovation and he that will not apply new remedies must expect new evils,"
Francis Bacon (1561-1626).

The ethical dilemma

To understand the ethical dilemma these scientists face, one must look at the moral value placed on human embryos. Pro-life advocates maintain that life begins at conception. Based on this belief, the use of stem cells to cure disease could require doctors to save one life at the expense of another. This goes against their moral convictions and desire to preserve life.[3]

Table 1 **Stem cell time line**

1987	Seven year old girl with Myeloid Leukemia transplanted with bone marrow cells from sibling.
1988	Cord cell transplantation introduced.
1990	Human Fertilization & Embryology Act
1992	Commercial companies begin to bank umbilical cord blood.
September 1998	Ethics Advisory Board develops guidelines for the ethical conduct of stem cell research.
September 2000	Federal government funds medical research using human embryo cells under the approval of President Clinton.
September 14, 2000	Advocates speak on Capitol Hill regarding the need for advancement of stem cell research.
November 21, 2000	NIH establishes guidelines for stem cell research.
December 2000	British Parliament voted to allow greater freedom in stem cell research.

According to Judie Brown, a spokeswoman for the American Life League, embryonic boys and girls should not be used as experimental material. Do No Harm, a coalition of medical-ethic experts, agree new rules by the National Institute of Health circumvent a 1996 law prohibiting the use of federal funding for embryo research. The regulation made it illegal to fund any research in which a human embryo or embryos are destroyed, discarded or knowingly subjected to risk of injury or death.[14]

In the religious community, the two principal areas of disagreement are based on the moral question of destroying an embryo to save another human life, and whether humans have a right to play God by doing so. Traditions warn that humans should not usurp the role of God and, therefore, should be careful in our pursuits to annihilate disease.[3]

Although many opponents agree with the merits of stem cell research, the disagreement lies in how the cells are obtained. Many are afraid that embryos will be created just for harvesting stem cells, thus creating a black market arena. Stem cell research, like abortions, would certainly continue even if legally banned. Debate continues around whether this research should be allowed to thrive in the black market or be controlled in the medical field.

The study of stem cell research brings into the picture two other terms, therapeutic cloning and reproductive cloning. Therapeutic cloning involves producing an antigen-matched, cloned cell or organ for transplantation. Reproductive cloning is the duplication of an entire human organism. Both these procedures begin by creating a human embryo. To reproduce a clone of the nuclear donor, an embryo must implant and gestate in a womb. To produce therapeutically cloned stem cells for the nuclear donor, an embryo (blastocyst) must be dissolved and only the primordial stem cell is retained and cultivated.[8]

Therapeutic cloning is being researched in Britain, but is still considered unethical and illegal in the United States. The European Union is very clear about acknowledging their disagreement with Britain on this issue. "As members of the European Parliament from different political groups and different member states, we would like to express our concern on the proposal of your government."[17]

There has been much research done using adult stem cells in place of embryonic cells, which is compounding the moral issues. Many diseases, such as a tumor of the eye with a poor prognosis, have seen good results with autologous stem cell transplants. Adult stem cells have also been successful with Merkel cell carcinoma, a rare aggressive skin cancer for which there is no

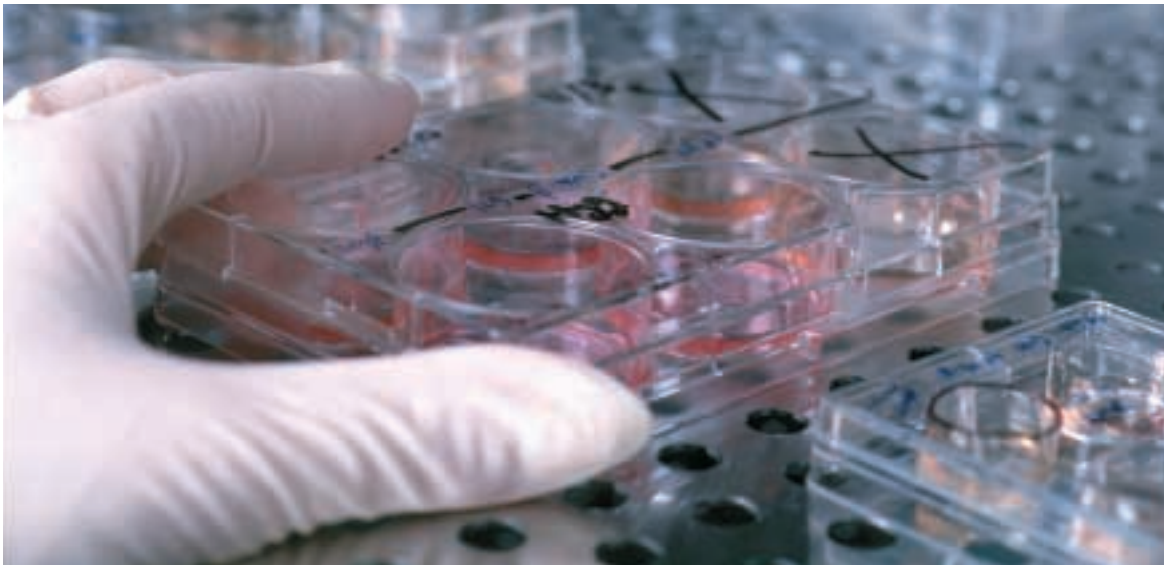


PHOTO Jeff Miller

FIGURE 1

Culture trays containing human embryonic stem cells being stored in heat-controlled storage.

protocol for treatment.[19] Additional success has been reported using adult stem cells in breast cancer treatments. These accomplishments fuel the fire in the fight against using embryonic stem cells to eradicate disease.

Neutral ground

Although this issue remains complicated, certain practices and guidelines are helping the process.

Preservation of stem cells

Since 1992, Cryo-Cell International Inc has been preserving umbilical cord blood for their clients (Table 1). When a child is born, instead of throwing out the umbilical cord once it has been clamped and cut, its blood is harvested. This blood is then stored in vials and preserved in a liquid nitrogen cryogenic environment. This saved blood can be used at a later date if that child or a sibling faces a blood-related disease.[2] This company is also moving into research involving stem cells from aborted fetuses. There are at least five companies across the United States that are involved with stem cell research and preservation.[6]

Guidelines in stem cell research

Earlier this year, new guidelines were released by the National Institutes of Health (NIH) that allow federal funding to be used for research on stem cells taken from human embryos. This will help the scientific public understand how human organs form. John Gearheart, a stem cell researcher, feels that federally funded labs have more oversight that would guarantee adherence to ethical guidelines.[16] The NIH guidelines on stem cell research include the following:

A. For studies using human pluripotent stem cells derived from human embryos, NIH funds may be used only if the cells were derived from frozen embryos that were created for the purposes of fertility treatment, were in excess of need, and were obtained with consent from the donating couple.

PHOTO: Jeff Miller

FIGURE 2

Embryonic stem cells being viewed and studied under a microscope.

B. The NIH guidelines prohibit the use of inducements, monetary or otherwise, for the donation of the embryo. There must also have been a clear separation between the fertility treatment and the decision to donate embryos for this research.
C. The NIH guidelines require that the informed consent specify whether information that could identify the donor(s) will be retained.
D. Investigators who propose using NIH funds to conduct research using human pluripotent stem cells derived from fetal tissue are expected to follow both the NIH guidelines and all federal and state laws and regulations govern-

ing human fetal tissue and human fetal tissue transplantation research.

E. The guidelines require that the donation of human embryos or fetal tissue be made without any restriction or direction regarding the individual(s) who may be the recipient of the cells derived from the human pluripotent stem cells.

F. They also require review and approval of the derivation protocol by an Institutional Review Board.

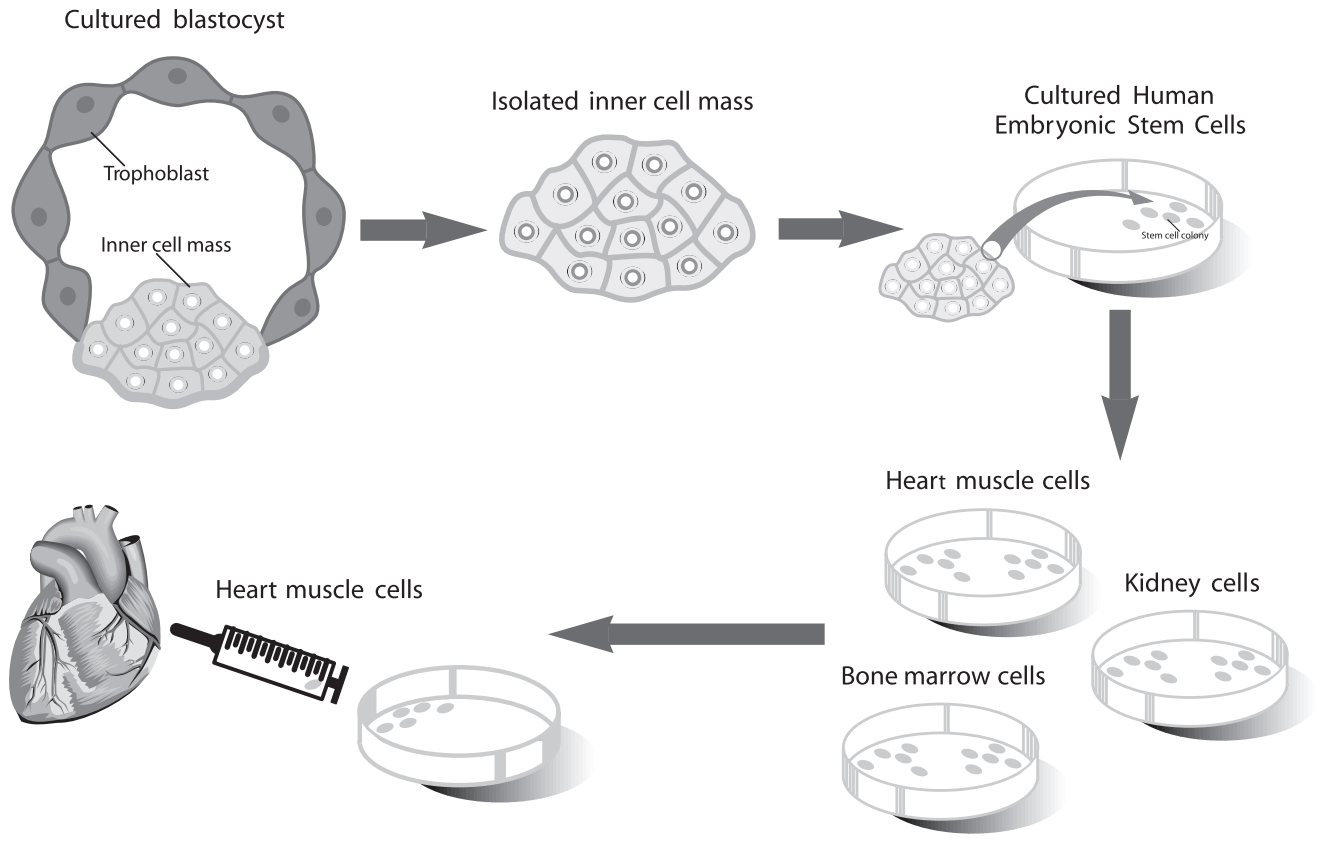
G. The informed consent should include statements that the embryos or fetal tissue will be used to derive human pluripotent stem cells for research that may include human transplantation research; that derived cells may be kept for many years; that the research is not intended to provide direct medical benefit to the donor; and that the donated embryos will not be transferred to a woman's uterus and will not survive the stem cell derivation process.

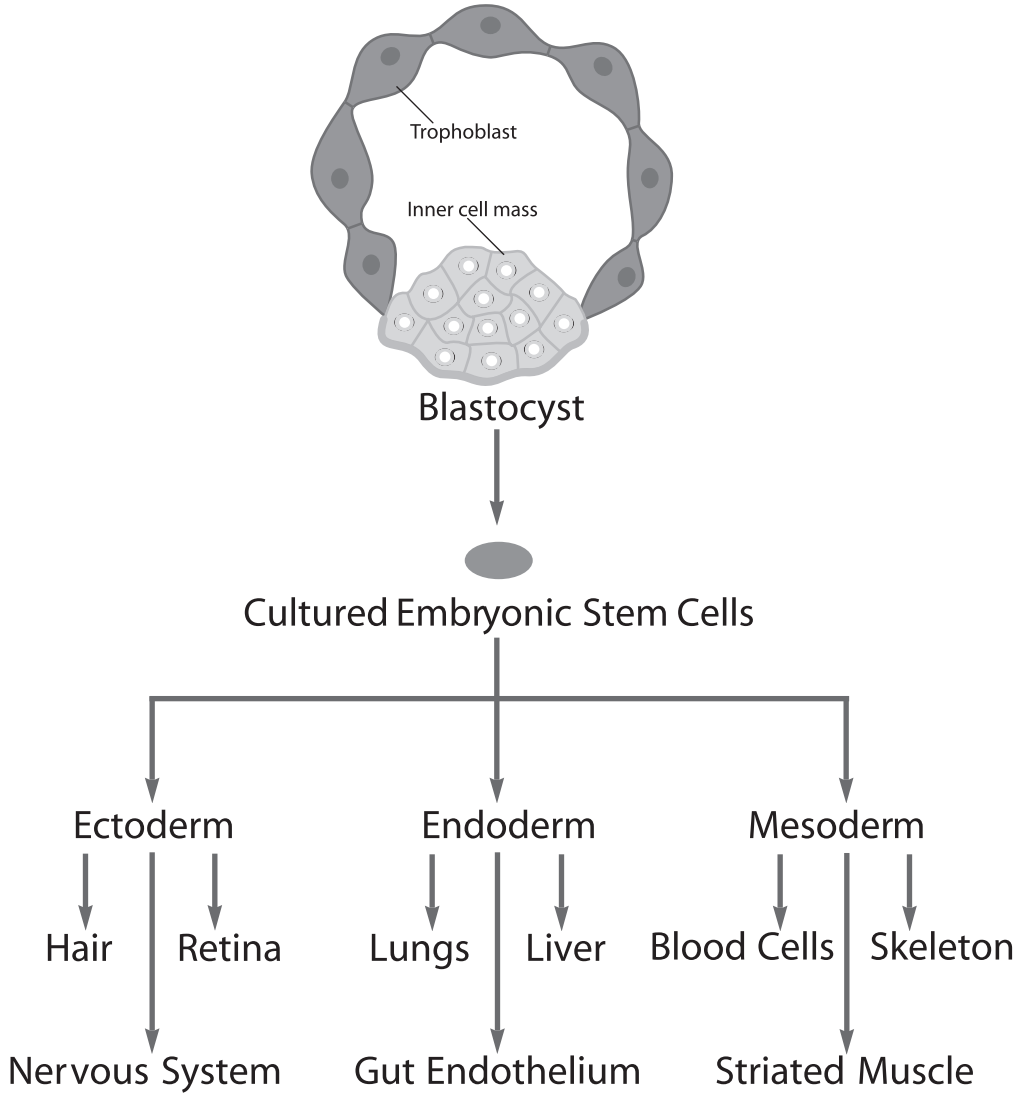
H. The informed consent must also state the possibility that the results of the research may have commercial potential, and that the donor will not receive any benefits from any such future commercial development.[15]

FIGURE 3

Culturing human embryonic stem cells

Stem cells may be used for research only if they were derived from embryos left over from infer-





tility treatments. Their reasoning stems from the fact that this tissue is almost always marked for destruction anyway. Additional guidelines state that researchers must specify to the tissue donor whether information that could reveal his or her identity will be retained, in case it is necessary to inform that person of any infectious disease. Under existing rules, embryos cannot be sold, only donated for research.[5]

The NIH currently only funds work that uses embryos created but not used by couples during the course of infertility treatments. Former US President Bill Clinton endorsed these guidelines, saying "I think we cannot walk away from the potential to save lives and improve lives—to help people literally get up and walk, to do all kinds of things we never could have imagined."[14]

Conclusion

As long as science and medicine continues to search for ways to treat and cure the diseases that plague the human race, bioethics will be involved. Although the questions are complicated and difficult, there is value in wrestling with the issues and weighing the advantages of medical research against the potential moral and ethical costs.

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FIGURE 4

Human embryonic stem cells differentiation

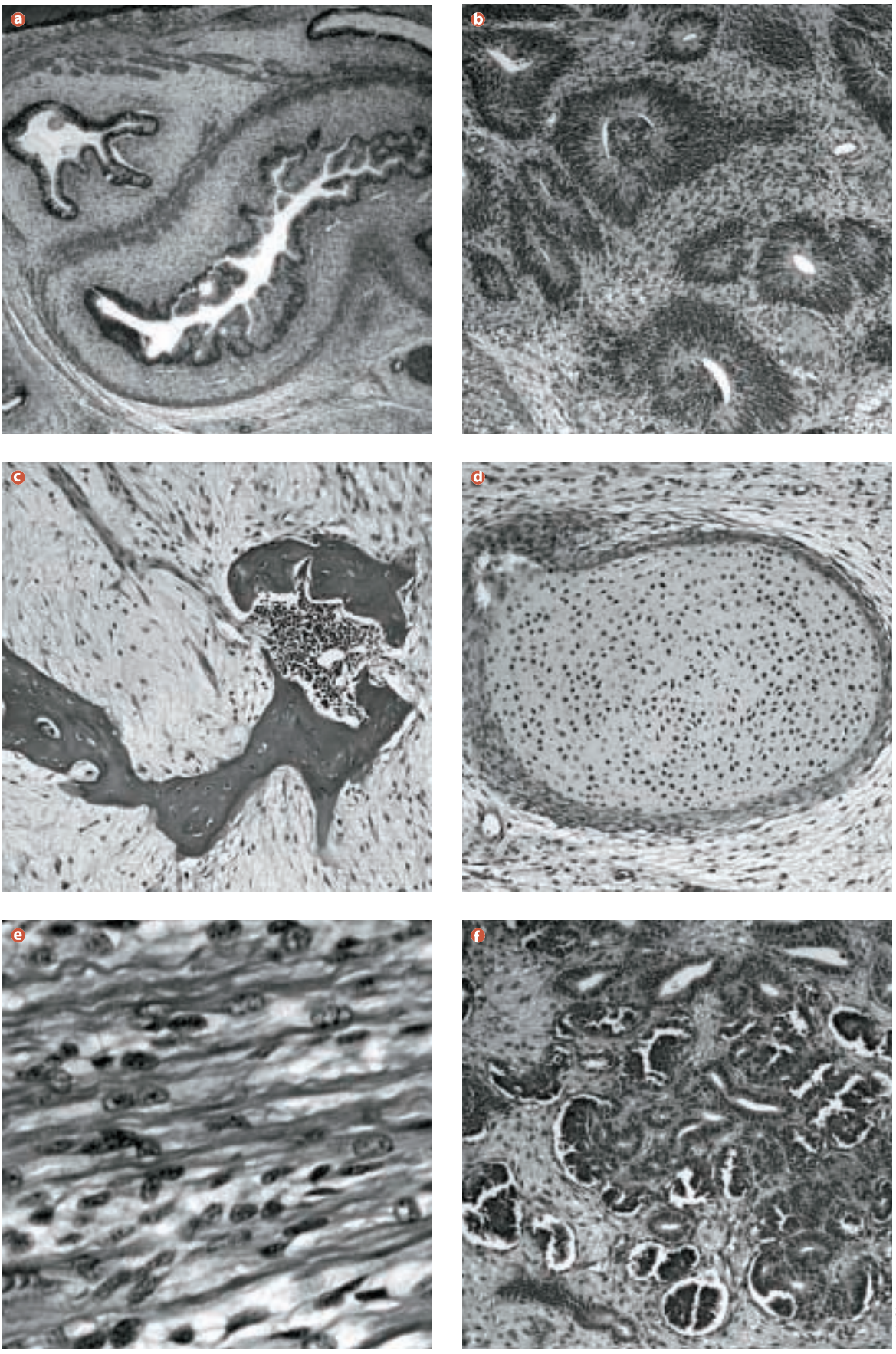

FIGURE 5

Human stem cells cultured at the University of Wisconsin-Madison have been observed to randomly differentiate in culture with a variety of cell types.

a gut
b neural cells
c bone marrow cells
d cartilage
e muscle
f kidney cells

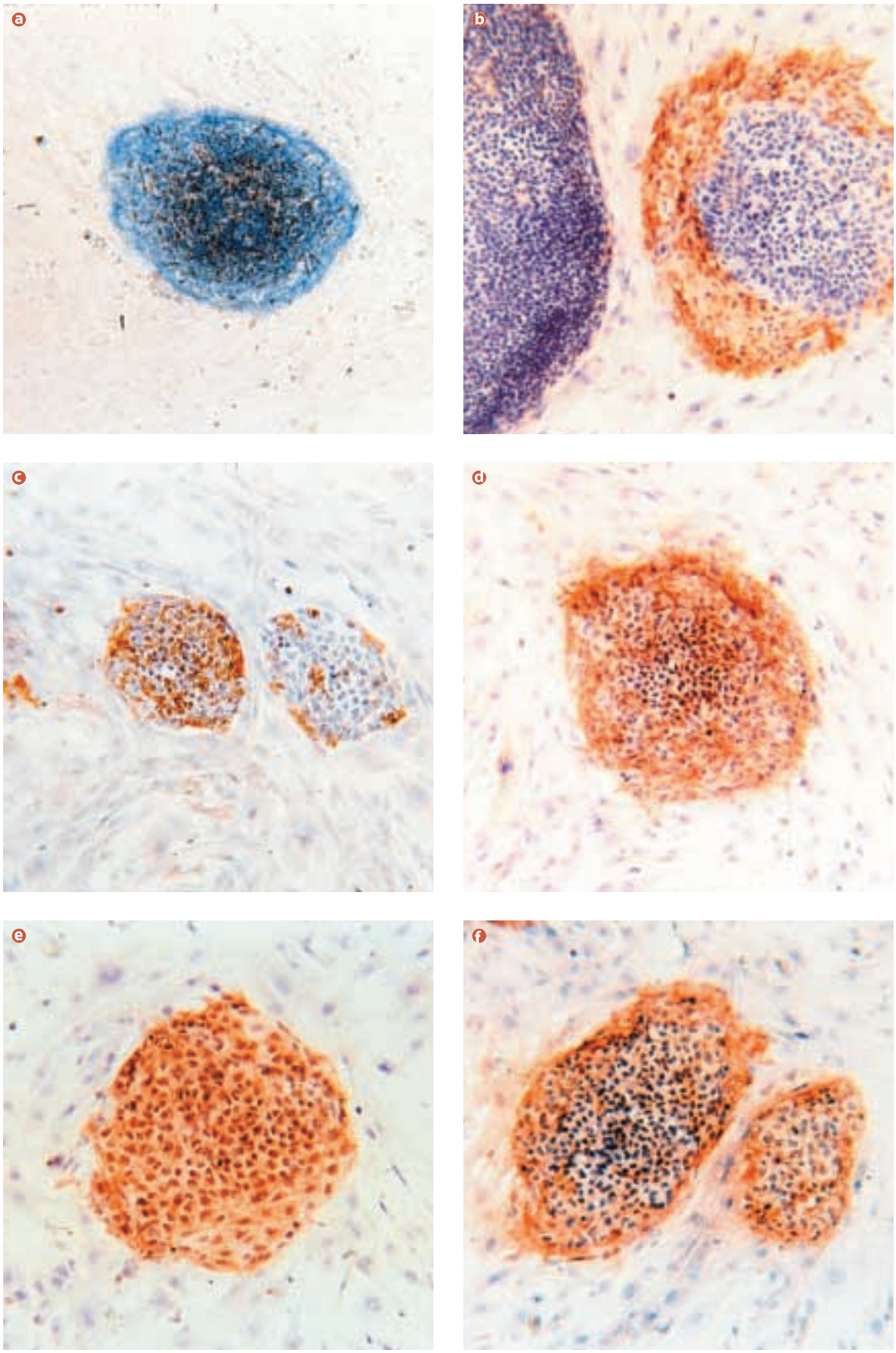

FIGURE 6

Human embryonic stem cell colonies in different stages of development.

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