DNA—A functional unit of heredity that is a segment of DNA found on chromosomes in the nucleus of a cell. Genes direct the formation of an enzyme or other protein.

Gene—A functional unit of heredity that is a segment of DNA found on chromosomes in the nucleus of a cell. Genes direct the formation of an enzyme or other protein.

Hematopoietic stem cell—A stem cell that gives rise to all red and white blood cells and platelets.

Human embryonic stem cell (hESC)—A type of pluripotent stem cell derived from the inner cell mass (ICM) of the blastocyst.

Induced pluripotent stem cell (iPSC)—A type of pluripotent stem cell, similar to an embryonic stem cell, formed by the introduction of certain embryonic genes into a somatic cell.

Mesenchymal stem cell—A type that is currently used to define non-blood adult stem cells from a variety of tissues, although it is not clear that mesenchymal stem cells from different tissues are the same.

Mitosis—The type of cell division in which genetically identical copies of a cell, or organism, (noun)’ The identical, molecul cell or organism that results from the cloning process.

Differentiation—The process whereby an unspecialized embryonic cell acquires the features of a specialized cell such as a heart, liver or muscle cell. Differentiation is controlled by the interaction of a cell’s genes with the physical and chemical conditions outside the cell, usually through signaling pathways involving proteins on the cell surface and their interaction with receptors. DNA—Deoxyribonucleic acid, a chemical found primarily in the nucleus of cells. DNA carries the instructions or blueprint for making all the structures and materials the body needs to function. DNA consists of both genes and non-gene DNA in between the genes.

Embryonic stem cell—Progeny (differentiated) cells derived from a five-day preimplantation embryo that are capable of dividing without differentiating for a prolonged period in culture and are known to develop into cells and tissues of the three primary germ layers.

Epigenetic—Having to do with the process by which regulatory proteins cause genes on or off in a way that can be passed down during cell division.

Reproductive cloning—The process of using somatic cell nuclear transfer (SCNT) to produce a normal, full grown organism (e.g., a pig or a sheep). A clone is genetically identical to the organism (animal) that donated the somatic cell nucleus. In mammals, this would require implanting the resulting embryo in a uterus where it would undergo normal development to become a live independent being.

Somatic cell—Any body cell other than gametes (egg or sperm).

Somatic cell nuclear transfer (SCNT)—A technique that involves an enucleated egg and the nucleus of a somatic cell to make an embryo.

Stem cells—Cells with the ability to divide for indefinite periods in culture and to give rise to specialized cells.

Stromal cells—Connective tissue cells found in virtually every organ. In bone marrow, stromal cells support blood formation.

Tetraploid complementation assay—An assay that can be used to test a stem cell’s potency.

Therapeutic cloning—The process of using somatic cell nuclear transfer (SCNT) to produce cells that exactly match a patient. By combining a patient’s somatic nucleus and an enucleated egg, a scientist may harvest embryonic stem cells from the resulting embryo that can be used to generate tissues that match a patient’s body. This means the tissues created are unlikely to be rejected by the patient’s immune system.

Totipotency—Having the ability to give rise to all the cell types of the body plus all of the cell types that make up the extraembryonic tissues such as the placenta.

Transdifferentiation—The process by which stem cells from one tissue differentiate into cells of another tissue.

Uniblidal cord blood stem cells—Stem cells collected from the uniblidal cord at birth that can produce all of the blood cells in the body (hematopoietic). Cord blood is currently used to treat patients who have undergone chemotherapy to destroy their bone marrow due to cancer or other blood-related disorders.

Unidifferentiated—A cell that has not yet developed into a specialized cell type.

Stem Cells…Fountain of Youth?

Malcolm K. Brenner, MD, PhD

Malcolm K. Brenner, MD, PhD, is the director of the Center for Cell and Gene Therapy at Baylor College of Medicine, Texas Children’s Hospital and The Methodist Hospital. He is also director of the Shell Center for Gene Therapy at BCM and a professor in the Departments of Pediatrics and Medicine, Section of Hematology-Oncology.

Dr. Brenner received his education—from bachelor’s to medical degree as well as his PhD—at Cambridge University in England. Before coming to BCM, he was one of the pioneers in the field of gene therapy at St. Jude Children’s Cancer Research Center in Memphis.

Dr. Brenner’s clinical interests span many aspects of stem cell transplantation, using genetic manipulation of cultured cells to obtain therapeutic effects. His laboratory research focuses on manipulating the anti-leukemic cells to kill residual cancer cells after stem cell transplantation. Efforts in his laboratory to analyze the cell of origin when relapse occurs in patients with acute myelogenous leukemia led his team to be the first to label autologous bone marrow cells genetically after purging, prior to their being reintroduced to the patient. He is studying the effects of gene transfer into autologous neuroblastoma cells and the use of gene-modified EBV-specific cytotoxic T lymphocytes for prevention and treatment of lymphoproliferative disorders, Hodgkin’s disease, lung cancer and neuroblastoma.

Dr. Brenner is a co-editor of the journal Molecular Therapy, a member of the American Society of Gene Therapy and a principal investigator or co-investigator on five NIH grants. He is the author or co-author of more than 200 professional articles in his field.

Amy L. McGuire, JD, PhD

Amy L. McGuire, JD, PhD, is associate director for Research in the Center for Medical Ethics and Health Policy, Baylor College of Medicine, where she is also an associate professor of Medicine and Medico-legal Ethics. She received her bachelor’s degree in psychology, summa cum laude, from the University of Pennsylvania, her JD, summa cum laude, from the University of Houston, and her PhD in medical humanities from the Institute for the Medical Humanities at the University of Texas Medical Branch.

Dr. McGuire’s research focuses on legal and ethical issues in genetics and genomics, with a particular interest in genetic research and personalized medicinal genomics. She is currently studying participant attitudes toward broad data sharing in genome-wide association studies, ethical issues in human microbiome research and consumer expectations regarding the clinical integration of direct-to-consumer personal genome testing services.

Her research is funded by the NIH/ES3 program and the Greenwall Foundation Faculty Scholars Program in Bioethics. Dr. McGuire is a member of the Bioethics, Bioinformatics and Data Protection for the Genetic Association Information Network and is on the advisory board for the X Prize in Genomics.
Cardiovascular disease (CVD), which includes hypertension, coronary heart disease, stroke and congestive heart failure, has ranked as the No. 1 cause of death in the United States every year since 1990 except 1918, when the nation struggled with an influenza epidemic. Nearly 2,600 Americans a day die of CVD, roughly one person every 34 seconds. Given the aging of the population and the relatively dramatic recent increases in the prevalence of cardiovascular risk factors such as obesity and type 2 diabetes, CVD will be a significant health concern well into the 21st century.

Cardiovascular disease can deprive heart tissue of oxygen, thereby killing cardiac muscle cells (cardiomyocytes). This loss triggers a cascade of detrimental events, including formation of scar tissue, an overload of blood flow and pressure capacity, the overstretched capacity of viable cardiac cells attempting to sustain cardiac output, leading to heart failure, and eventual death. Restoring damaged heart muscle tissue, through repair or regeneration, is therefore a potentially new strategy to treat heart failure.

The use of embryonic and adult-derived stem cells for cardiac repair is an active area of research. A number of stem cell types, including embryonic stem (ES) cells, cardiac stem cells that naturally reside within the heart, myoblasts (muscle stem cells), adult bone marrow-derived cells including mesenchymal cells (bone marrow-derived cells that give rise to tissues such as muscle, bone, tendons, ligaments, and adipose tissue), endothelial progenitor cells (cells that give rise to the endothelium, the interior lining of blood vessels), and umbilical cord blood cells, have been investigated as possible sources for regenerating damaged heart tissue. All have been explored in mouse or rat models, and some have been tested in larger animal models, such as pigs. A few small studies have also been carried out in humans, usually in patients who are undergoing open heart surgery. Several of these have demonstrated that stem cells that are injected into the circulation or directly into the injured heart tissue appear to improve cardiac function and/or reduce the formation of new capillaries. The mechanism for this repair remains controversial, and the stem cells likely regenerate heart tissue through several pathways. However, the stem cell populations that have been tested in these experiments vary widely, so it is difficult to judge the cost–benefit of this approach, these preliminary clinical experiments show how stem cells may one day be used to repair damaged heart tissue, thereby reducing the burden of cardiovascular disease.

Ethics of Stem Cells

Research on one kind of stem cell—human embryonic stem cells—has generated much interest and public debate. Pluripotent stem cells (cells that can develop into many different cell types of the body) are isolated from human embryos that are a few days old. Pluripotent stem cell lines have also been developed from fetal tissue (older than 8 weeks of development). As science and technology continue to advance, so do ethical viewpoints surrounding these developments. It is important to educate and explore the issues, scientifically and ethically. The NHG bioethics special interest group offers a list of online resources about the ethics of stem cell research at http://bioethics.od.nih.gov.

 Promise of Stem Cells

Studying stem cells will help us understand how they transform into the dazzling array of specialized cells that make us what we are. Some of the most serious medical conditions, such as cancer and birth defects, are due to problems that occur somewhere in this process. A better understanding of normal cell development will allow us to understand and perhaps correct the errors that cause these medical conditions.

Another potential application of stem cells is making cells and tissues for medical therapies. Today, donated organs and tissues are often used to replace those that are diseased or destroyed. Unfortunately, the number of people needing a transplant far exceeds the number of organs available for transplantation. Pluripotent stem cells offer the possibility of a renewable source of replacement cells and tissues to treat a myriad of diseases, conditions and disabilities including Parkinson’s disease, amyotrophic lateral sclerosis, spinal cord injury, burns, heart disease, diabetes and arthritis.

Adult Stem Cells

These stem cells come from different organs of fully developed organisms. Sometimes referred to as “somatic” stem cells (from the body, or soma), these cells can be obtained from many different tissues and contribute to the regeneration of those tissues from which they are derived. For example, the bone marrow regenerates the blood (or hematopoietic) system constantly. The bone marrow stem cells (hematopoietic stem cells) are the key elements that are transferred during a bone marrow transplant that recreates an entire blood system in the transplant recipient. The donor can afford to donate his or her bone marrow because the remaining stem cells will self-renew, replenishing their own stem cell supply so that the donor continues to have a plentiful blood supply.

Such somatic stem cells are found in the skin, digestive tract and many other tissues. In most tissues, these stem cells in general do not divide very often (they are quiescent) but can be called into duty quickly to regenerate that tissue. While they are essential for maintaining many adult tissues, and very effective at doing so, they are limited in their capabilities—or the most part, they can only regenerate those tissues from which they are derived: bone marrow stem cells make bone marrow and blood, skin stem cells make skin, gut stem cells replace the lining of the intestines, muscle stem cells make muscle and so on. Despite their limitations, they have great therapeutic potential. Thus, many researchers are studying these.

Embryonic Stem Cells

Stem cells can also be made by propagating part of a very early embryo. At this stage, the embryo is only a few days old, and is a primitive ball, with only an outer sheet of protective cells and an inner clump of cells. When these inner cells are put into a culture dish under special conditions, they will grow and become a stem cell “line.” We call them embryonic stem, or “ES,” cells. These ES cells can be grown and expanded indefinitely and are nearly unrestricted in their potential. They have the capacity to make every cell type in the body. The last 20 years of research using stem cells from mice has transformed the biomedical field. Researchers found that these ES cells could be used to generate specific cell types. Researchers have used them to introduce a modification and study how that modification affects the function of a down-stream cell, such as a liver cell, or a blood cell. These kinds of experiments have led to very many important discoveries as well as novel therapies. Human ES cells were first derived in 1998 from embryos that were planned to be discarded after in vitro fertilization procedures. These human ES cells, like their mouse counterparts, can be expanded indefinitely and will generate virtually any cell type of the body.

For this reason, they are likely to transform basic research into human biology, as well as lead to new therapies based on generation of specific cell types. Current federal guidelines allow some human ES cell lines to be used with federal funding.

Stem Cells for the Future Treatment of Heart Disease

Cardiovascular disease (CVD), which includes hypertension, coronary heart disease, stroke and congestive heart failure, has ranked as the No. 1 cause of death in the United States every year since 1990 except 1918, when the nation struggled with an influenza epidemic. Nearly 2,600 Americans a day die of CVD, roughly one person every 34 seconds. Given the aging of the population and the relatively dramatic recent increases in the prevalence of cardiovascular risk factors such as obesity and type 2 diabetes, CVD will be a significant health concern well into the 21st century.

Cardiovascular disease can deprive heart tissue of oxygen, thereby killing cardiac muscle cells (cardiomyocytes). This loss triggers a cascade of detrimental events, including formation of scar tissue, an overload of blood flow and pressure capacity, the overstretched capacity of viable cardiac cells attempting to sustain cardiac output, leading to heart failure, and eventual death. Restoring damaged heart muscle tissue, through repair or regeneration, is therefore a potentially new strategy to treat heart failure.

The use of embryonic and adult-derived stem cells for cardiac repair is an active area of research. A number of stem cell types, including embryonic stem (ES) cells, cardiac stem cells that naturally reside within the heart, myoblasts (muscle stem cells), adult bone marrow-derived cells including mesenchymal cells (bone marrow-derived cells that give rise to tissues such as muscle, bone, tendons, ligaments, and adipose tissue), endothelial progenitor cells (cells that give rise to the endothelium, the interior lining of blood vessels), and umbilical cord blood cells, have been investigated as possible sources for regenerating damaged heart tissue. All have been explored in mouse or rat models, and some have been tested in larger animal models, such as pigs. A few small studies have also been carried out in humans, usually in patients who are undergoing open heart surgery. Several of these have demonstrated that stem cells that are injected into the circulation or directly into the injured heart tissue appear to improve cardiac function and/or reduce the formation of new capillaries. The mechanism for this repair remains controversial, and the stem cells likely regenerate heart tissue through several pathways. However, the stem cell populations that have been tested in these experiments vary widely, so it is difficult to judge the cost–benefit of this approach, these preliminary clinical experiments show how stem cells may one day be used to repair damaged heart tissue, thereby reducing the burden of cardiovascular disease.

Cancer Stem Cells

Recently, an old theory about cancer has been revived. Cancer refers to the collection of diseases in which a cell of the body loses its normally very tight restrictions on growth and divides out of control.

Because the cancer cells divide much faster than almost all cells of the body, most cancer therapy simply is directed against any rapidly dividing cell. Unfortunately, many cancers escape after some time, even when they appear to be eliminated.

There are several reasons for this, but the idea that a small subset of cells, possibly a cancer stem cell, causes this relapse has been revived. These cancer stem cells may have many similarities to normal somatic stem cells. Normally, the cancer stem cells are probably not dividing, or are dividing very slowly. This enables them to escape the chemotherapists’ agents. Some time after the bulk of the cancer has been destroyed, the cancer stem cells are somehow awakened—potentially leading to relapse.

Cancer stem cells are poorly understood at this time. They are very difficult to identify, which has hampered the development of therapies that could be targeted towards them.

A special thanks to our Educational Luncheon Series Sponsors