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RESEARCH ARTICLE

A REVIEW PAPER ON STEM CELLS

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ABSTRACT

Stem cells are unspecialized cells that have the ability to differentiate into other cells and the ability to self-regenerate. Stem cells are of two types: Embryonic stem cells (ESC) and Adult stem cells (ASC). Stem cell research begins early 1900's when European researchers realized that the various types of blood cells e.g. White blood cells, red blood cells and platelets all came from Stem cells. Till today various developments have been made in field of stem cell research. John B. Gurdon and Shinya Yamanaka received The Nobel Prize in Physiology or Medicine 2012 for the discovery that mature cells can be reprogrammed to become pluripotent. This achievement has further revolutionized research interest in stem cells. Present review covers historical development and future perspective of stem cells research.

INTRODUCTION

Stem cells are unspecialized cells that have two defining properties: the ability to differentiate into other cells and the ability to self-regenerate. The ability to differentiate is the potential to develop into other cell types. A totipotent stem cell (e.g. fertilized egg) can develop into all cell types including the embryonic membranes. A pleuripotent stem cell can develop into cells from all three germinal layers (e.g cells from the inner cell mass). Other cells can be oligopotent, ipotent or unipotent depending on their ability to develop into few, two or one other cell type(s) (Sell, 2004). Stem cells are classified into two classes i.e. Embryonic stem cells (ESC) and Adult stem cells (ASC).

Embryonic Stem Cells

Embryonic stem cells (ESC) have the capacity to differentiate almost into any cell type in the adult organism, including germ line cells and therefore are commonly referred to as pluripotent cells (Hyslop *et al*., 2005). Human embryonic stem cells (hESCs) have been successfully derived from early preimplantation human embryos (Thomson *et al*., 1998). They are self-renewing pluripotent cells that theoretically have the potential to differentiate into nearly all cell types of the human body (Heins *et al*., 2004; Reubinoff *et al*., 2000). In November of 1998, groups in the United States led by James Thomson and John Gearhart published data describing the derivation of candidate human pluripotent embryonic stem (ES) and embryonic germ (EG) cell lines from blastocysts or primordial germ cells, respectively (Thomson *et al*., 1998; Shamblott *et al*., 1998). Research with human embryonic stem cell (hESC) lines has attracted increasing attention over the last decade because these cells have the capability to proliferate indefinitely and to differentiate into any cell type of the body. On the other hand, there has been much controversy about using hESCs due to their origin from early human embryos, which resulted in a wide panel of different national legislations on human ESC research (Elstner *et al*., 2009). Although there are now several registries that contain partially overlapping data sets on a multitude of hESC lines (Borstlap *et al*., 2008; Luong *et al*., 2008; Isasi and Knoppers, 2009). Embryonic stem (ES) cell lines derived from human blastocysts have the developmental potential to form derivatives of all three embryonic germ layers even after prolonged culture (Amit *et al*., 2000).

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Adult Stem Cells

Adult stem cells are stem cells that can be derived from different parts of the body and, depending on where they are from, have different properties. They exist in several different tissues including bone marrow, blood and the brain. Studies have suggested that adult stem cells are very versatile and can develop into many different cell types such as Hematopoietic stem cells, Mammary stem cells, Intestinal stem cells, Mesenchymal stem cells, Endothelial stem cells, Neural stem cells, Olfactory adult stem cells and neural crest stem cells. Mesenchymal stem cells (MSCs), also known in the literature as bone marrow stem cells, skeletal stem cells, and multipotent mesenchymal stromal cells, are non-hematopoietic progenitor cells isolated from adult tissues, and are characterized in vitro by their extensive proliferative ability in an uncommitted state while retaining the potential to differentiate along various lineages of mesenchymal origin, including chondrocyte, osteoblast, and adipocyte lineages, in response to appropriate stimuli (Figure 1). Since the first study by Friedenstein and colleagues more than 40 years ago, the field of MSC investigation has gained increasing attention and popularity, particularly in the past decade (Friedenstein *et al*., 1966). In

their undifferentiated state, MSC are spindle-shaped and resemble fibroblasts (Pittenger *et al*., 1999; Friedenstein and Petrokova, 1966). MSCs are attractive for clinical therapy due to their ability to differentiate, provide trophic support, and modulate innate immune response (Phinney and Prockop, 2007). The stem cells that form blood and immune cells are known as hematopoietic stem cells. They are ultimately responsible for the constant renewal of blood-the production of billions of new blood cells each day. Physicians and basic researchers have known and capitalized on this fact for more than 50 years in treating many diseases. The first evidence and definition of blood-forming stem cells came from studies of people exposed to lethal doses of radiation in 1945. Basic research soon followed. After duplicating radiation sickness in mice, scientists found they could rescue the mice from death with bone marrow transplants from healthy donor animals. In the early 1960s, Till and McCulloch began analyzing the bone marrow to find out which components were responsible for regenerating blood (Till and McCullough, 1961).

Mammary stem cells provide the source of cells for growth of the mammary gland during puberty and gestation and play an important role in carcinogenesis of the breast. Mammary stem cells have been isolated from human and mouse tissue as well as from cell lines derived from the mammary gland. Single such cells can give rise to both the luminal and myoepithelial cell types of the gland, and have been shown to have the ability to regenerate the entire organ in mice (Liu *et al*., 2005). Intestinal stem cells divide continuously throughout life and use a complex genetic program to produce the cells lining the surface of the small and large intestines (Van Der Flier and Clevers, 2009). Olfactory adult stem cells have been successfully harvested from the human olfactory mucosa cells, which are found in the lining of the nose and are involved in the sense of smell (Murrell *et al*., 2005). Hair follicles contain two types of stem cells, one of which appears to represent a remnant of the stem cells of the embryonic neural crest. Similar cells have been found in the gastrointestinal tract, sciatic nerve, cardiac outflow tract and spinal and sympathetic ganglia. These cells can generate neurons, Schwann cells, myofibroblast, chondrocytes and melanocytes (Sieber-Blum and Hu, 2008; Kruger *et al*., 2002).

Historical Development

Scientists have been interested in cell biology since the advent of microscope since the 1800's. Cell propagation and differentiation were witnessed for the first time and cells were recognized as building block of life, capable of giving rise to other cells and key to understanding human development. In the early 1900's European researchers realized that the various types of blood cells e.g. White blood cells, red blood cells and platelets all came from particular (Stem cells). However it was not until 1960's that the first quantitative description of self renewing activity of transplanted mouse bone marrow cells were documented (Canadian researches Ernest A McCulloch and James E Till, 1960). In 1991 Bruce Glick found that the bursa of fabricus has a history and future and a future. The history included its description by Hieronymus Fabricus and discovery in 1950's of its pivotal role in humeral immunity. The apparent obligate role of bursa in B-cell development was modified by research in 1960's and 1970's which described the syntheseins of immunoglobulin in Bursa less birds and let to the concept of extra bursal sites. Then in 1980's supported by research of past 25 years and new technology obligate role of bursa in orchestrating the V-gene repertoire antibody diversity was revealed. Microenvironmental studies in 1970's and 1980's annonved the importance of bursal epithelium sevretaory, dendritic cells and other reticuloepithelial cells in interpreting the ontogeny of B-cell diffferentation. The past history of bursa will be remembered for its contribution to present and future research and the present and present and future will be promising if the experiences of the past are not forgotten (Glick, 1991). Hematopoietic stem cell transplants (SCT) were used in the treatment of neoplastic diseases, in addition to congenital, autoimmune, and inflammatory disorders (Talmadge, 2003). He used autologous and allogeneic SCT, depending on donor availability and the type of disease being treated, resulting in different morbidity and outcomes. Conrad and Huss., 2005. performed *In vivo* experiments in rodents and shown that adult stem cells participate in tissue and organ regeneration in almost all lesions. stem cell populations isolated from the bone marrow were usually a heterogeneous mix of different subpopulations, cloned adult stem cell lines from any source also show a broad spectrum of differentiation potential, e.g., osteogenesis, myogenesis, neurogenesis, or angiogenesis in wound healing. Gomillion and Burg, 2006. attempted to engineer adipose tissue involving the use of eadipocytes and adipocytes as the base cell source.

Fleming and Hube, 2006. Optimized DMSO concentrations in the cryopreservation medium, post thaw washing of cells and increased cell concentration. Standardization of cell processing has led to the study of liquid storage prior to cryopreservation, validation of mechanical (uncontrolled rate freezing) freezing, and cryopreservation bag failure. Jones and Matsui, 2007 examined better understanding of biology of cancer stem cells and re –examined preclinical and cilinical drug development paradigms to include the cancer stem cell concept to revolutionize the treatment of many cancers. Hu *et al*., 2008 reported the establishment of long-term cultures of rat ecto-mesenchymal stem cells (EMSCs) using specific supplemented media for induction. Their findings related to the development and differentiation of microglial progenitors support the view that microglia are derived prenatally from mesodermal progenitors that were distinct from monocytes. Ting *et al*., 2008. reviewed several pathways and mechanisms required for adult stem cell repair.

Mechanisms included the mobilization and the homing of stem cells to sites of injury, immuno-modulatory effect of stem cells, and the association of stem cells with increased vascularization of injured tissue. Hirami *et al*., 2009 tested procedure for retinal differentiation of mouse and human induced pluripotent stem cells (iPSCs). Yamanaka and Blau, 2010 shown three distinct experimental approaches to nuclear reprogramming: nuclear transfer, cell fusion and transcription-factor transduction. Okita *et al*., 2011 reported a simple method, using p53 suppression and nontransforming L-Myc, to generate human induced pluripotent stem cells (iPSCs) with episomal plasmid vectors. They generated human iPSCs from multiple donors, including two putative human leukocyte antigen (HLA)-homozygous donors who match ~20% of the Japanese population at major HLA loci; most iPSCs are integrated transgene-free. Narbonne *et al*., 2012 investigated nuclear transfer (NT) remained the most effective method to

reprogram somatic cells to totipotency. Somatic cell nuclear transfer (SCNT) efficiency however remained low, but recurrent problems occurring in partially reprogrammed cloned embryos have recently been identified and some remedied. In particular, the trophectoderm has been identified as a lineage whose reprogramming success has a large influence on SCNT embryo development.

Future Prospectives and Applications

Significant progress has been made towards a better understanding of the establishment of hematopoiesis in the embryo. Hematopoietic precursors have been shown to arise independently in the yolk sac and in the intra-embryonic mesoderm (Cumano and Godin, 2001). Lo *et al*., 2003. described stem cells were potentially immortal cells capable of self-renewal are the focus of research for the ultimate cure for degenerative diseases and the key to the mystery to human development and ageing. No area of research since gene therapy has evoked so much enthusiasm and passionate debate as stem cell research. The study of human development from fertilized egg to mature embryo is extremely important, the early differentiation of human tissues remains an enigma. The relatively high percentage of unexplained pregnancy loss a major concern of human embryologists and gynaecologists emphasizes the need for an appropriate model for studying early human development. The availability of human pluripotent stem cells might allow us to study previously inaccessible basic processes that occur during human embryogenesis, such as gastrulation and organogenesis(Dvash and Benvenisty, 2004). The cell of origin of prostate cancer is still unknown. The identification of these cells depends on understanding prostate cell differentiation lineage during development as well as adult prostate epithelium renewal.

Recent advances in the field have shed light on the hierarchical relationship between epithelial prostate cells. On the basis of this knowledge, the isolation and characterization of prostate cancer stem cells may now be possible and could provide an explanation for the known clinical and molecular heterogeneity of human prostate cancer (Signoretti and Loda, 2007). Mesenchymal stem cells can be isolated from almost any adult tissue. The exact mechanisms behind how these cells work still remain unclear, and there is a continuing shift in the paradigms that support them. There has been extensive research in multiple organ systems; however, the genitorurinary system has been vastly underrepresented (Drzewiecki *et al*., 2010). The study of the developing brain has begun to shed light on the underpinnings of both early and adult onset neuropsychiatric disorders. Neuroimaging of the human brain across developmental time points and the use of model animal systems have combined to reveal brain systems and gene products that may play a role in autism spectrum disorders, attention deficit hyperactivity disorder, obsessive compulsive disorder and many other neurodevelopmental conditions. However, precisely how genes may function in human brain development and how they interact with each other leading to psychiatric disorders is unknown (Vaccarino *et al*., 2011). The existence of stem cells in the adult brain has been postulated following the discovery that the process of neurogenesis, the birth of new neurons, continues into adulthood in rats (Altman and Das, 1965). A major breakthrough is in the development of the ability to reprogram somatic cells to pluripotency. It has rejuvenated the field of stem cell research, providing regenerative medicine with new possibilities. In this paper, we discuss the progress made in the reprogramming field with focus on induction methodologies, the use of induced pluripotent stem cells (iPSCs) for drug discovery, and issues and precautions related to their use in regenerative medicine (Hussein *et al*., 2011). The development of blood islands with red cells enhanced by erythropoietin in EBs has encouraged the hope that, subsequently, more mature stages of erythroid, myeloid and lymphoid cell development could occur in vitro. This provide further support for the use of ES cells in an in vitro assay for embryo toxicity testing. (Heuer *et al*.,1993). The heart has a large demand for blood flow, and specialized cells are important for developing a new network of arteries to bring nutrients and oxygen to the cardiomyocytes after a heart has been damaged. The potential capability of both embryonic and adult stem cells to develop into these cells types in the damaged heart is now being explored as part of a strategy to restore heart function to people who have had heart attacks or have congestive heart failure (Beltrami *et al*., 2001).

Human embryonic stem cells have the potential to differentiate into various cell types and, thus, may be useful as a source of cells for transplantation or tissue engineering. Human embryonic stem cells could provide a source of human endothelial cells that could be beneficial for potential applications such as engineering new blood vessels, endothelial cell transplantation into the heart for myocardial regeneration, and induction of angiogenesis for treatment of regional ischemia (Levenberg *et al*., 2002). Cell therapy using pancreatic islets would be a promising therapy to treat diabetes. But, because of the limited supply of human donor islets, other cellular sources have to be considered. Stem cells characterized by extensive proliferation and differentiation capacity may be a valuable source for the in vitro generation of islets. Insulin-producing cells derived from embryonic stem (ES) cells have been shown to reverse experimentally induced diabetes in animal models (Blyszczuk and Wobus, 2004). In recent years stem cells are subject of increasing scientific interest because oftheir potential utility in numerous biomedical applications.

Stem cell technology provides unprecedented opportunities not only for investigating new ways to prevent and treat a vast arrays of diseases but also for changing the way we identify new molecular targets, discover and develop new drugs, as well as test them for safety. Because stem cells are a self-renewing population of cells, they can be continuously cultured in an undifferentiated state and give rise to more specialized cells of the human body, such as heart, liver, bone marrow, blood vessels, pancreatic islets and nerve cells. Therefore, stem cells offer an important new tool to develop unique *in vitro* model systems for testing drugs and chemicals and potentially predict or anticipate toxicity in humans (Davila *et al*., 2004). Traditionally, human embryonic stem (hES) cells have been cultured on mouse embryonic fibroblast feeder layers, which allow their continuous growth in an undifferentiated state (Amit, *et al*., 2004). Mesenchymal stem cells (MSC) are clonogenic, non-hematpoietic stem cells present in the bone marrow and are able to differentiate into multiple mesoderm-type cell lineages, for example, osteoblasts, chondrocytes and also non-mesoderm-type lineages, for example, neuronal-like cells. Several methods are currently available for isolation of the MSC based on their physical and physico-chemical characteristics, for example, adherence to plastics or other

extracellular matrix components. Because of the ease of their isolation and their extensive differentiation potential, MSC are among the first stem cell types to be introduced in the clinic (Kassem, 2004). Research in human embryonic stem cells (hESCs) is a rapidly developing scientific field such as registration, banking, standardization, and tracing (Guhr *et al*., 2006). During development, different cells and tissues acquire different programmes of gene expression, so that cells are related to each other through a somatic cells tree or cluster and adult pluripotential stem cells (PSC) may be defined as progenitors that we distinguish in four types according to their biological behaviour. This clustering may segregate specific pathways establishing spatial patterns of cell–cell communications. The new approach of SC may contribute to our understanding on how some diseases may develop including cancer which could be linked to "cluster illness", while demyelinating and systemic diseases could be related to "PSC locus illness" or "focalised SCAN disturbances" and it explains how any environment stress may act on organism evolution (Hamlat and Pasqualini, 2007).

Basic and clinical research accomplished during the last few years on embryonic, fetal, amniotic, umbilical cord blood, and adult stem cells has constituted a revolution in regenerative medicine and cancer therapies by providing the possibility of generating multiple therapeutically useful cell types. These new cells could be used for treating numerous genetic and degenerative disorders. Among them, age-related functional defects, hematopoietic and immune system disorders, heart failures, chronic liver injuries, diabetes, Parkinson's and Alzheimer's diseases, arthritis, and muscular, skin, lung, eye, and digestive disorders as well as aggressive and recurrent cancers could be successfully treated by stem cell-based therapies (Mimeault *et al*., 2007). Stem cells have the capacity for self-renewal and capability of differentiation to various cell lineages. Thus, they represent an important building block for regenerative medicine and tissue engineering. These cells can be broadly classified into embryonic stem cells (ESCs) and non-embryonic or adult stem cells. ESCs have great potential but their use is still limited by several ethical and scientific considerations. The use of bone marrow-, umbilical cord-, adipose tissue-, skin- and amniotic fluid-derived mesenchymal stem cells might be an adequate alternative for translational practice (Bajada *et al*., 2008).

The efficiency and accuracy of the drug development process is severely restricted by the lack of functional human cell systems. However, the successful derivation of pluripotent human embryonic stem (hES) cell lines in the late 1990s is expected to revolutionize biomedical research in many areas. Due to their growth capacity and unique developmental potential to differentiate into almost any cell type of the human body, hES cells have opened novel avenues both in basic and applied research as well as for therapeutic applications (Ameen *et al*., 2008). Mesenchymal stem cells (MSC) are a group of clonogenic cells present among the bone marrow stroma and capable of multilineage differentiation into mesoderm-type cells such as osteoblasts, adipocytes and chondrocytes. Due to their ease of isolation and their differentiation potential, MSC are being introduced into clinical medicine in variety of applications and through different ways of administration (Abdallah and Kassem, 2008).

Embryonic stem cells (ESC) have unleashed new avenues in the field of developmental biology and emerged as a potential tool to understand the molecular mechanisms taking place during the process of differentiation from the embryonic stage to adult phenotype. Their uniqueness lies in retaining the capacity of unlimited proliferation and to differentiate into all somatic cells. Together with promising results from rodent models, ESC has raised great hope among for human ESC-based cell replacement therapy. ESC could potentially revolutionize medicine by providing a powerful and renewable cell source capable of replacing or repairing tissues that have been damaged in almost all degenerative diseases such as Parkinson's disease, myocardial infarction (MI) and diabetes (Pal, 2009).Functioning of the cerebral tissue in health and disease has been obtained in the past few years. Proliferating stem cells have been found in the adult brain, which can be involved in post injury repair and can replace dead cells under specific conditions. Numerous genomic mechanisms controlling stem cell proliferation and differentiation have been identified. Stem cells can be used to develop radically new treatments of neurodegenerative and cancer diseases of the brain (Revishchin *et al*., 2009). The field of stem-cell biology has been catapulted forward by the startling development of reprogramming technology. The ability to restore pluripotency to somatic cells through the ectopic co-expression of reprogramming factors has created powerful new opportunities for modelling human diseases and offers hope for personalized regenerative cell therapies (Robinton and Daley, 2012). Research on human embryonic stem cells (hESCs) and human induced pluripotent stem cells (hiPSCs) was analyzed with respect to the number of publicly disclosed cell lines and to the extent and impact of published scientific work involving these cells (Loser *et al.*, 2012).

Ethical cocerns

Since the Nuremburg Code, informed consent has been regarded as a basic requirement for research with human subjects. Consent is particularly important in research with human embryos (Lo *et al*., 2003). Members of the public and potential donors of embryos for research hold strong and diverse opinions on the matter. Some consider all embryo research to be unacceptable; others only support some forms of research. For instance, a person might consider infertility research acceptable but object to research to derive stem cell lines or research that might lead to patents or commercial products (Radin, 1996). Gamete donors who are willing to help women and couples bear children may object to the use of their genetic materials for research. In one study, 25% of women who donated oocytes for infertility treatment did not want the embryos created to be used for research (Kalfoglou and Galler, 2000). The United States does not have universal health insurance. As a matter of fairness, women who undergo an invasive procedure for the benefit of science and who are not receiving payment beyond expenses should not bear any costs for the treatment of complications. Even if a woman has health insurance, copayments and deductibles might be substantial, and if she later applied for individual-rated health insurance, her premiums might be prohibitive (National Bioethics Advisory Commission, 2001). Stem Cell Research offers great promise for understanding basic mechanisms of human development and differentiation, as well as the hope for new treatments for diseases such as diabetes, spinal cord injury,

Parkinson's disease, and myocardial infarction. Pluripotent stem cells perpetuate themselves in culture and can differentiate into all types of specialized cells. Scientists plan to differentiate pluripotent cells into specialized cells that could be used for transplantation (Committee on the Biological and Biomedical Applications of Stem Cell Research, Commission on Life Sciences, National Research Council, Board on Neuroscience and Behavioral Health, Institute of Medicine 2002). ART clinics can readily discuss donation for research with oocyte donors during visits for oocyte stimulation and retrieval. Most ART clinics obtain donor sperm from sperm banks and generally have no direct contact with the donors. As a matter of respect for gamete donors, their wishes regarding stem cell derivation should be determined and respected (Lo *et al*., 2003). The vast majority of scientific experts, including the Director of the NIH under President Bush, believe that a lack of access to new embryonic stem cell lines hinders progress toward stem cell-based transplantation (Alanso-Zaldivar and Kaplan, 2007). For example, lines from a wider range of donors would allow more patients to receive human leukocyte agent matched stem cell transplants (Dawson *et al*., 2003).

Confidentiality must be carefully protected in embryo and hESC research because breaches of confidentiality might subject donors to unwanted publicity or even harassment by opponents of hESC research. Although identifying information about donors must be retained in case of audits by the Food and Drug Administration as part of the approval process for new therapies, concerns about confidentiality may deter some donors from agreeing to be recontacted (Lo *et al*., 2005). *In Vitro* fertilization programs some oocytes fail to fertilize and some embryos fail to develop sufficiently to be implanted. Such materials may be donated to researchers (Lo *et al*., 2005). Concerns about oocyte donation specifically for research are particularly serious in the wake of the Hwang scandal in South Korea, in which widely hailed claims of deriving human SCNT lines were fabricated. In addition to scientific fraud, the scandal involved inappropriate payments to oocyte donors, serious deficiencies in the informed consent process, undue influence on staff and junior scientists to serve as donors, and an unacceptably high incidence of medical complications from oocyte donation. (Holden, 2006; Chong, 2006; Chong and Normile, 2006).

Many jurisdictions have conflicting policies about payment to oocyte donors. Payment to oocyte donors in excess of reasonable out-of-pocket expenses is controversial, and jurisdictions have conflicting policies that may also be internally inconsistent (Spar, D., 2007). Because severe hyperovulation syndrome may require hospitalization or surgery, women donating oocytes for research should be protected against the costs of complications of hormonal stimulation and oocyte retrieval (Lomax *et al*., 2007). National Academy of Sciences 2005 Guidelines for Human Embryonic Stem Cell Research and has been adopted by the California Institute for Regenerative Medicine (CIRM), the state agency funding stem cell research. This consent requirement need not imply that embryos are people or that gametes or embryos are research subjects (National Research Council and Institute of Medicine, 2005; Lomax *et al*., 2007). The medical risks of oocyte retrieval include ovarian hyperstimulation syndrome, bleeding, infection, and complications of anesthesia. These risks may be minimized by the exclusion of donors at high-risk for these complications, careful monitoring of the number of developing follicles, and adjusting the dose of human chorionic gonadotropin administered to induce ovulation or canceling the cycle (National Research Council and Institute of Medicine, 2007). Autologous stem cells are being used in clinical trials in patients who have suffered myocardial infarction. Their use in several other conditions has not been validated or is experimental, despite some claims to the contrary (Smith *et al*., 2007). In California, some legislators and members of the public have charged that infertility clinics downplay the risks of oocyte donation. CIRM has put in place several protections for women donating oocytes in state-funded stem cell research. (Lomax *et al*., 2007). Women and couples who undergo infertility treatment often have frozen embryos remaining after they complete their infertility treatment. The disposition of these frozen embryos is often a difficult decision for them to make (Lyerly and Faden, 2007). If women in infertility treatment share oocytes with researchers—either their own oocytes or those from an oocyte donor—their prospect of reproductive success may be compromised because fewer oocytes are available for reproductive purposes. In this situation, the physician carrying out oocyte retrieval and infertility care should give priority to the reproductive needs of the patient in *In vitro* fertilization (Levens, 2008).

President Bush allowed federal National Institutes of Health (NIH) funding for stem cell research using embryonic stem cell lines already in existence at the time, while prohibiting NIH funding for the derivation or use of additional embryonic stem cell lines. This policy was a response to a growing sense that hESC research held great promise for understanding and treating degenerative diseases, while still opposing further destruction of human embryos. NIH funding was viewed by many researchers as essential for attracting scientists to make a long-term commitment to study the basic biology of stem cells; without a strong basic science platform, therapeutic breakthroughs would be less likely (Streiffer, 2008). Under President Obama, it is expected that federal funding will be made available to carry out research with hESC lines not on the NIH list and to derive new hESC lines from frozen embryos donated for research after a woman or couple using *In vitro* fertilization has determined they are no longer needed for reproductive purposes (Hulse, 2009). However, human stem cell (hSC) research also raises sharp ethical and political controversies. The derivation of pluripotent stem cell lines from oocytes and embryos is fraught with disputes regarding the onset of human personhood and human reproduction. The reprogramming of somatic cells to produce induced pluripotent stem cells (iPS cells) avoids the ethical problems specific to embryonic stem cells (Lo and Parham, 2009).

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