DOWNLOAD PDF APPLICATIONS OF EMBRYONIC STEM CELLS

Chapter 1 : Embryonic stem cell - Wikipedia

mental biology has led to the discovery of human stem cells (precursor cells that can give rise to multiple tissue types), including embryonic stem (ES) cells, embryonic germ (EG) cells, and adult stem cells.

Stem cells have the potential to treat a variety of diseases and are important in medical research and drug development. Stem cells are involved in development, growth, and repair in multicellular organisms. Depending on stem cell type and location and local factors, any cell that acquires a more specialized function after cell division may become a less potent stem cell or become a fully differentiated cell. Stem cells are classified by their potency, which is a measure of their ability to differentiate into other cell types. During development of an organism, stem cells become more functionally specialized and thus less potent. The classes of stem cells, ordered from most to least potent, are: These cells can give rise to all the cell types of the body. This term has generally fallen out of use, partially due to confusion with the term pluripotent. It is becoming clear that there are stem cells in most, if not all, adult tissues, and that some tissues have more than one type of stem cell. This brief overview covers only stem cells that are widely studied or currently of potential clinical importance. Cells are usually harvested from the inner cell mass of the blastocyst 4 to 5 days after in vitro fertilization of an egg. The cells are cultured and expanded into cell lines. Though the potency of ESCs makes them attractive for use in clinical therapy, there are both ethical and technical problems with their use. The majority of ESCs used in research are murine. Studies suggest that teratoma formation may be a result of chromosomal changes that occur in some ESC cells during culture. As length of time in culture and the number of passages increase, cells are more likely to display chromosomal instability and mosaicism within the population. Frequently, cells removed from the blastocyst do not survive and divide in culture. Originally, it was thought that there was no risk of GVHD, but some manipulations of ESC to drive them to differentiate into particular cell types can make them immunogenic Kim et al. It is postulated that on differentiation, ESCs may start to express latent immunogenic surface proteins that were preprogrammed for expression in normal development. Now it is known that somatic stem cells are found throughout the body. Initially it was thought that multipotent somatic stem cells could generate cells only within the same lineage. However, transdifferentiation has been demonstrated. Culturing, with a defined combination of added factors, can reprogram some somatic stem cells into different lineages. Whether transdifferentiation occurs in vivo is still a matter of debate. HSCs are a heterogeneous population and can differentiate into both myeloid and lymphoid lineages. Their ability to repopulate bone marrow and blood has been used for many years for bone marrow transplantation. MSCs are heterogeneous, have multilineage potential, and are capable of differentiating into multiple cell types including adipocytes, chondrocytes, osteoblasts, and cardiomyocytes. Advantages of MSCs include: Because VSELs are pluripotent but do not present any ethical issues, they may provide an effective tool for many regenerative therapies. Since VSELs can be obtained from a patient for autologous treatments, there are no immunocompatibility concerns. Therefore, iPSCs are pluripotent and can give rise to any germ line. To generate iPSCs, cells are forced to express genes for transcription factors that are required for pluripotency and self-renewal. Most iPSC cell lines have been generated using viral transduction by retroviruses or lentiviruses. When iPSCs are injected into immune-deficient mice, they readily form teratomas. Additionally, as with ESCs, adaptation to culture and passaging increases the likelihood of development of mosaic populations and chromosomal abnormalities. For instance, one consideration for iPSCs is epigenetic memory. There is evidence that reprogramming of somatic cells may not reverse all changes in methylation that occurred during differentiation and maturation. This can mean that some iPSCs are not truly pluripotent, since they retain lineage or tissue specificity. However, this could potentially be exploited in regenerative therapy, by using iPSCs generated from cells in the same lineage as the target cell type. Most research on diseases relies on animal models, which may, or may not, accurately mimic a disease. The ability to be able to generate cultures of human or animal iPSC cultures provides new ways to follow cell differentiation and the direction of changes in cellular and molecular mechanisms in normal tissues and in disease progression. MEF, mouse embryonic fibroblasts. This technique was used to make Dolly the sheep

Wilmut et al. The somatic nucleus is reprogrammed by the egg to become pluripotent. These cells are effectively iPSCs and can be used to generate cell lines. Though this technique has been used in animal stem cell research for many years, thought only recently has human SCNT been reported Tachibana et al. The various cell types have different potencies, ranging from ESC-like cells to multipotent stem cells. The tissue source is freely and widely available, with no extra risk to the donor and no ethical issues. In contrast, amniotic fluid is captured by amniocentesis, so there is a small chance of harm to the fetus. For these stem cell sources, there is a low risk of GVHD, most likely due the stem cells being immunologically immature. These stem cells would have few of the problems of allogeneic stem cells, such as immune incompatibility or the risk of communicable disease transmission. There have been several clinical trials approved for the therapeutic use of cord blood, including the treatment of pediatric stroke and cerebral palsy. This has three advantages: The theory is that there is a population of cancer stems cells that are quiescent, or dividing slowly, until triggered. This theory remains controversial, although it has been gaining acceptance. If proven, this hypothesis may be important in the treatment of cancer because many cancer therapies target rapidly proliferating cells. Stem cells, at G0 phase or slowly dividing may be minimally targeted rather than eradicated, potentially forming a reservoir for future tumor development. During their lives, plants can undergo substantial damage and regenerate, for example, regrowth after being partially eaten, pruned, or burned. The apical meristems are at the tips of the shoots and roots, where the majority of growth takes place. Stem cells are also present in lateral procambium and intercalary meristems. Calli occur naturally on plant wound sites, and callus formation can be induced in vitro from certain somatic plant tissues by plating on tissue culture media with supplements such as nutrients and plant growth regulators. However, a callus contains a heterogeneous population of cells, and pluripotency can be hard to maintain for extended periods. Study of stem cells in situ and in culture is providing new insights into development, cell biology, and molecular processes. In addition, stem cells have a huge potential for the treatment of many diseases as well as use in regenerative medicine. Human acute myeloid leukemia is organized as a hierarchy that originates from a primitive hematopoietic cell. Human induced pluripotent stem cells develop teratoma more efficiently and faster than human embryonic stem cells regardless the site of injection. Embryonic stem cell-derived T cells induce lethal graft-versus-host disease and reject allogenic skin grafts upon thymic selection. Bone marrow as a home of heterogenous populations of nonhematopoietic stem cells. Human embryonic stem cells derived by somatic nuclear transfer. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. Viable offspring derived from fetal and adult mammalian cells.

Chapter 2 : Embryonic Stem Cell Research: An Ethical Dilemma

On the basis of regenerative applications, stem cells can be categorized as embryonic stem cells (ESCs), tissue specific progenitor stem cells (TSPSCs), mesenchymal stem cells (MSCs), umbilical cord stem cells (UCSCs), bone marrow stem cells (BMSCs), and iPSCs (Figure 1; Table 1). The transplantation of stem cells can be autologous, allogenic.

In healthy adult laboratory animals, progenitor cells migrate within the brain and function primarily to maintain neuron populations for olfaction the sense of smell. Pharmacological activation of endogenous neural stem cells has been reported to induce neuroprotection and behavioral recovery in adult rat models of neurological disorder. Clinical and animal studies have been conducted into the use of stem cells in cases of spinal cord injury. One pair of reports of identical baseline characteristics and final results, was presented in two publications as, respectively, a patient randomized trial and as a subject observational study. Other reports required impossible negative standard deviations in subsets of people, or contained fractional subjects, negative NYHA classes. A university investigation, closed in without reporting, was reopened in July However, the immune system is vulnerable to degradation upon the pathogenesis of disease, and because of the critical role that it plays in overall defense, its degradation is often fatal to the organism as a whole. Diseases of hematopoietic cells are diagnosed and classified via a subspecialty of pathology known as hematopathology. The specificity of the immune cells is what allows recognition of foreign antigens, causing further challenges in the treatment of immune disease. Identical matches between donor and recipient must be made for successful transplantation treatments, but matches are uncommon, even between first-degree relatives. Research using both hematopoietic adult stem cells and embryonic stem cells has provided insight into the possible mechanisms and methods of treatment for many of these ailments. In this process, HSCs are grown together with stromal cells , creating an environment that mimics the conditions of bone marrow, the natural site of red-blood-cell growth. Erythropoietin , a growth factor , is added, coaxing the stem cells to complete terminal differentiation into red blood cells. Researchers are confident that the tooth regeneration technology can be used to grow live teeth in people. In theory, stem cells taken from the patient could be coaxed in the lab turning into a tooth bud which, when implanted in the gums, will give rise to a new tooth, and would be expected to be grown in a time over three weeks. The process is similar to what happens when humans grow their original adult teeth. Many challenges remain, however, before stem cells could be a choice for the replacement of missing teeth in the future. The group, led by Sheraz Daya , was able to successfully use adult stem cells obtained from the patient, a relative, or even a cadaver. Further rounds of trials are ongoing. In theory if the beta cell is transplanted successfully, they will be able to replace malfunctioning ones in a diabetic patient. In an adult, wounded tissue is most often replaced by scar tissue , which is characterized in the skin by disorganized collagen structure, loss of hair follicles and irregular vascular structure. In the case of wounded fetal tissue, however, wounded tissue is replaced with normal tissue through the activity of stem cells. This method elicits a regenerative response more similar to fetal wound-healing than adult scar tissue formation. In , oogonial stem cells were isolated from adult mouse and human ovaries and demonstrated to be capable of forming mature oocytes. Human embryonic stem cells clinical trials Regenerative treatment models[edit] Stem cells are thought to mediate repair via five primary mechanisms: In addition, they have been found to secrete chemokines that alter the immune response and promote tolerance of the new tissue. This allows for allogeneic treatments to be performed without a high rejection risk. Researchers are able to grow up differentiated cell lines and then test new drugs on each cell type to examine possible interactions in vitro before performing in vivo studies. This is critical in the development of drugs for use in veterinary research because of the possibilities of species specific interactions. The hope is that having these cell lines available for research use will reduce the need for research animals used because effects on human tissue in vitro will provide insight not normally known before the animal testing phase. Rather than needing to harvest embryos or eggs, which are limited, the researchers can remove mesenchymal stem cells with greater ease and greatly reducing the danger to the animal due to noninvasive techniques. This allows the limited eggs to be put to use for reproductive purposes only. Spermatogonial stem cells have been harvested from a rat and placed

into a mouse host and fully mature sperm were produced with the ability to produce viable offspring. Currently research is underway to find suitable hosts for the introduction of donor spermatogonial stem cells. If this becomes a viable option for conservationists, sperm can be produced from high genetic quality individuals who die before reaching sexual maturity, preserving a line that would otherwise be lost. Accordingly, stem cells derived from bone marrow aspirates, for instance, are cultured in specialized laboratories for expansion to millions of cells. Research is underway to examine the differentiating capabilities of stem cells found in the umbilical cord, yolk sac and placenta of different animals. These stem cells are thought to have more differentiating ability than their adult counterparts, including the ability to more readily form tissues of endodermal and ectodermal origin. Stem-cell controversy There is widespread controversy over the use of human embryonic stem cells. This controversy primarily targets the techniques used to derive new embryonic stem cell lines , which often requires the destruction of the blastocyst. Opposition to the use of human embryonic stem cells in research is often based on philosophical, moral, or religious objections. On 23 January , the US Food and Drug Administration gave clearance to Geron Corporation for the initiation of the first clinical trial of an embryonic stem-cell-based therapy on humans. The trial aimed evaluate the drug GRNOPC1, embryonic stem cell -derived oligodendrocyte progenitor cells, on people with acute spinal cord injury. The trial was discontinued in November so that the company could focus on therapies in the "current environment of capital scarcity and uncertain economic conditions". Various clinical trials on MSCs have failed which used cryopreserved product immediately post thaw as compared to those clinical trials which used fresh MSCs. Misaligned breaks due to severe trauma, as well as treatments like tumor resections of bone cancer, are prone to improper healing if left to the natural process alone. Scaffolds composed of natural and artificial components are seeded with mesenchymal stem cells and placed in the defect. Within four weeks of placing the scaffold, newly formed bone begins to integrate with the old bone and within 32 weeks, full union is achieved. Stem cells have been used to treat degenerative bone diseases. The normally recommended treatment for dogs that have Leggâ€”Calveâ€”Perthes disease is to remove the head of the femur after the degeneration has progressed. Recently, mesenchymal stem cells have been injected directly in to the head of the femur, with success not only in bone regeneration, but also in pain reduction. This is important interest for those with reduced healing capabilities, like diabetics and those undergoing chemotherapy. These cells were injected directly into the wounds. Within a week, full re-epithelialization of the wounds had occurred, compared to minor re-epithelialization in the control wounds. This showed the capabilities of mesenchymal stem cells in the repair of epidermal tissues. These are often not found until after they have become worse because of the difficulty in visualizing the entire soft palate. This lack of visualization is thought to also contribute to the low success rate in surgical intervention to repair the defect. As a result, the horse often has to be euthanized. Recently, the use of mesenchymal stem cells has been added to the conventional treatments. After the surgeon has sutured the palate closed, autologous mesenchymal cells are injected into the soft palate. The stem cells were found to be integrated into the healing tissue especially along the border with the old tissue. There was also a large reduction in the number of inflammatory cells present, which is thought to aid in the healing process. Autologous stem cell based treatments for tendon injury, ligament injury, and osteoarthritis in dogs have been available to veterinarians in the United States since Over privately owned horses and dogs have been treated with autologous adipose-derived stem cells. The efficacy of these treatments has been shown in double-blind clinical trials for dogs with osteoarthritis of the hip and elbow and horses with tendon damage. Conventional therapies are very unsuccessful in returning the horse to full functioning potential. Natural healing, guided by the conventional treatments, leads to the formation of fibrous scar tissue that reduces flexibility and full joint movement. Traditional treatments prevented a large number of horses from returning to full activity and also have a high incidence of re-injury due to the stiff nature of the scarred tendon. Introduction of both bone marrow and adipose derived stem cells, along with natural mechanical stimulus promoted the regeneration of tendon tissue. The natural movement promoted the alignment of the new fibers and tendocytes with the natural alignment found in uninjured tendons. Stem cell treatment not only allowed more horses to return to full duty and also greatly reduced the re-injury rate over a three-year period. The embryonic stem cells were shown to have a better survival rate in the tendon as well as

better migrating capabilities to reach all areas of damaged tendon. The overall repair quality was also higher, with better tendon architecture and collagen formed. There was also no tumor formation seen during the three-month experimental period. Long-term studies need to be carried out to examine the long-term efficacy and risks associated with the use of embryonic stem cells. Horses and dogs are most frequently affected by arthritis. Natural cartilage regeneration is very limited and no current drug therapies are curative, but rather look to reduce the symptoms associated with the degeneration. Different types of mesenchymal stem cells and other additives are still being researched to find the best type of cell and method for long-term treatment. There has been a lot of success recently injecting mesenchymal stem cells directly into the joint. This is a recently developed, non-invasive technique developed for easier clinical use. Dogs receiving this treatment showed greater flexibility in their joints and less pain. Adipose and bone marrow derived stem cells were removed and induced to a cardiac cell fate before being injected into the heart. The heart was found to have improved contractility and a reduction in the damaged area four weeks after the stem cells were applied. Tissue was regenerated and the patch was well incorporated into the heart tissue. This is thought to be due, in part, to improved angiogenesis and reduction of inflammation. Although cardiomyocytes were produced from the mesenchymal stem cells, they did not appear to be contractile. Other treatments that induced a cardiac fate in the cells before transplanting had greater success at creating contractile heart tissue. These cells involved in the secondary damage response secrete factors that promote scar formation and inhibit cellular regeneration. Mesenchymal stem cells that are induced to a neural cell fate are loaded onto a porous scaffold and are then implanted at the site of injury. The cells and scaffold secrete factors that counteract those secreted by scar forming cells and promote neural regeneration. Eight weeks later, dogs treated with stem cells showed immense improvement over those treated with conventional therapies. Dogs treated with stem cells were able to occasionally support their own weight, which has not been seen in dogs undergoing conventional therapies. Peripheral nerves are more likely to be damaged, but the effects of the damage are not as widespread as seen in injuries to the spinal cord. Treatments are currently in clinical trials to repair severed nerves, with early success. Stem cells induced to a neural fate injected in to a severed nerve. Within four weeks, regeneration of previously damaged stem cells and completely formed nerve bundles were observed. Hematopoietic stem cells have been used to treat corneal ulcers of different origin of several horses. These ulcers were resistant to conventional treatments available, but quickly responded positively to the stem cell treatment. Stem cells were also able to restore sight in one eye of a horse with retinal detachment, allowing the horse to return to daily activities.

Chapter 3 : What are Stem Cells? Types of Stem Cell and their Uses

Embryonic stem cells (ESCs) have unlimited potential to produce specialised cells of the body, which suggests enormous possibilities for disease research and for providing new therapies.

However, the creation and destruction of embryos is involved in this process. For this reason, not all are supportive of embryonic stem cell research and the controversy surrounding it is still so much in the picture. What Are Stem Cells? These are unspecialized cells found in living things and are able to renew themselves and develop into other cells by means of growth and repair so long as the host is still alive. They can also be manipulated to become tissue or organ specific cells. What are embryonic stem cells? Basically, these are cells derived from blastocysts which are day old embryos. Most of these sources come from unfertilized in vitro eggs and are used in research studies. These eggs are taken with consent from donors and brought to laboratories for scientists to use. Embryonic stem cells are important because they have several potential uses, from getting information about cell development to creating new drugs for medical disorders such as diabetes and cardiovascular disease. During this stage, the egg divides into smaller cells and become what is known as blastocyst. This is then harvested and grown on a petri dish and divide to become embryonic cells. This process wherein cells are grown in an artificial environment is known as cell culture. This is used in cell engineering, molecular biology and stem cell. Although both can become differentiated cell types, cells from embryos are pluripotent. Adult cells have limited capabilities to differentiate into other cell types. Moreover, adult stem cells are not as available as embryonic stem cells, making them hard to culture in laboratories. When it comes to transplantation rejection however, embryonic stem cells are more likely to be rejected as opposed to adult stem cells, according to scientists especially that there have only been few clinical trials done to test the effect of human embryonic stem cells on transplantation. Despite the potential benefits of embryonic cells, there are also possible setbacks surrounding its applications. Supporters and critics continue their debate on this controversial issue and express their views on different forums. Scientists are also divided based on ethical and moral concerns. Here is a look at some of the pros and cons of embryonic stem cell research that are worth looking into. They are not to be considered to have life. On the issue whether embryos have moral status, proponents claim that at this point, these embryos should not be considered as persons because they lack physical and psychological properties human beings have because they have not yet been implanted in the uterus. Moreover, even if they have, as in the case of in vitro fertilization, it is not yet certain that they can become human beings, given that success rates are low. Thus, these embryos are not to be regarded as if they were living persons. At the time an embryo is harvested, the central nervous system is still not yet formed. Another point of supporters is the age of the embryo when it is used for stem cell research, which is around 2 weeks. At this stage, an embryo has not yet developed a central nervous system. Also, there is still no concrete evidence it can develop into a fetus. Supporters maintain that if organs from brain dead people are allowed to be donated, this should also be the same with embryos. Human embryos for stem cell research can help a number of patients. For advocates, there is nothing wrong with the process because it results to helping hundreds of patients whose lives are in danger. They come from unused embryos for in vitro fertilization and are not taken without consent. Advocates for embryonic stem cell research say that there is nothing unethical or morally wrong with using the fertilized eggs which were not chosen for in vitro. They also posit that these eggs will be discarded anyway and it would be better that they be used for the common good and benefit of the majority. Also, they reiterate that these embryos are given with consent from donors. They can be used by scientists to find cure for several medical conditions. They can be possibly used for organ transplantation. Since embryonic cells have the capability to divide into specific cells and are always available, they are good candidates for organ transplantation application as opposed to adult cells. Even if adult cells can be used to repair tissues and for organ transplantation, they are only few viable cells in adults capable of doing such. Embryonic stem cell therapy is the next best thing to happen after the discovery of antibiotics. Scientists who support the use of embryonic stem cells to treat numerous diseases say that for so many years, patients suffer and die from different ailments. Embryonic cells can be used for further research by scientists.

Advocates also say that discarded cells can be used by researchers to study more about cell properties, structure and growth. This way, they will understand better how cells function and will be able to apply these researches in finding other ways to cure diseases in the future. Human embryos deserve respect as any other human being does. Opponents of embryonic stem cell research argue that these embryos, regardless of their properties or the lack thereof, should be considered and treated with the same respect just like any other person. They add that these embryos have the possibility to develop into fetuses and human beings. Thus, they also have life. There is no evidence that embryos have lives or not so they should not be destroyed. With the issue whether embryos already have a status of life, critics of embryonic stem cell research say that there is no concrete evidence. An example used is that of a patient who is comatose. Just because he or she is not responding from stimulation is not a proof that there is no life. Critics say that the same logic should be applied in embryos. And since it is unsure that life exists in an embryo or not, no one should destroy an embryo without any concern or consideration. Embryonic stem cell research takes away the chance of an embryo to become a human being. On the argument that an embryo is just like any part of the human body, an organic material and not a person, opponents say that embryos are in a stage that they have the possibility to develop into human beings. Since this is the case, using them for research is taking away this possibility and therefore, it is something unethical. The use of embryonic stem cells had not yet been proven to be successful. Groups against this research contend that there have been very few success stories of embryonic stem cells to cure diseases. In fact, there have been reports of difficulty of these cells to new specific types as well as tumor formation. There is also the concern of organ transplantation rejection of recipients that critics believe to be reason enough to stop stem cell research. Another issue that stirs the minds of opponents is that the Federal government fund researches like these at the expense of the American people. Groups who are against this, however, continue to fight for the cause. There are alternative ways to culture cells. Aside from embryos being used in stem cell research, adult cells can also be used as well as non-embryonic cells. Opponents posit that scientists should turn to these alternatives to save lives and look for remedies instead of the destruction of embryos. Scientists are already conducting studies on creating induced pluripotent stem cells and attempting to have human skin cells to go back to the embryonic state. With these developments, scientists should consider these options, according to critics. Conclusion In the middle of the controversial issue about using human embryos for stem cell research, groups remain divided. However, with new developments and options, perhaps, a time will come scientists can let go of using human embryos. If this happens, supporters are most likely to concede. After all, their concern is not on embryo destruction but on finding treatments for medical disorders.

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Embryonic stem cells (ES cells or ESCs) are pluripotent stem cells derived from the inner cell mass of a blastocyst, an early-stage pre-implantation embryo. Human embryos reach the blastocyst stage days post fertilization, at which time they consist of cells.

Properties[edit] The transcriptome of embryonic stem cells Embryonic stem cells ESCs , derived from the blastocyst stage of early mammalian embryos, are distinguished by their ability to differentiate into any cell type and by their ability to propagate. It is these traits that makes them valuable in the scientific and medical fields. ESCs are also described as having a normal karyotype , maintaining high telomerase activity, and exhibiting remarkable long-term proliferative potential. These include each of the more than cell types in the adult human body. Pluripotency distinguishes embryonic stem cells from adult stem cells , which are multipotent and can only produce a limited number of cell types. Propagation[edit] Under defined conditions, embryonic stem cells are capable of propagating indefinitely in an undifferentiated state. Conditions must either prevent the cells from clumping, or maintain an environment that supports an unspecialized state. Pluripotent stem cells have shown potential in treating a number of varying conditions, including but not limited to: Aside from these uses, embryonic stem cells can also serve as tools for the investigation of early human development, study of genetic disease and as in vitro systems for toxicology testing. Cell replacement therapies[edit] Current research focuses on differentiating ESCs into a variety of cell types for eventual use as cell replacement therapies CRTs. Some of the cell types that have or are currently being developed include cardiomyocytes CM , neurons , hepatocytes , bone marrow cells, islet cells and endothelial cells. For example, studies are underway to differentiate ESCs in to tissue specific CMs and to eradicate their immature properties that distinguish them from adult CMs. Studies have shown that cardiomyocytes derived from ESCs are validated in vitro models to test drug responses and predict toxicity profiles. However, the development of hepatocytes from ESCs has proven to be challenging and this hinders the ability to test drug metabolism. Therefore, current research is focusing on establishing fully functional ESC-derived hepatocytes with stable phase I and II enzyme activity. Either by genetically manipulating the cells, or more recently, by deriving diseased cell lines identified by prenatal genetic diagnosis PGD , modeling genetic disorders is something that has been accomplished with stem cells. This approach may very well prove invaluable at studying disorders such as Fragile-X syndrome , Cystic fibrosis , and other genetic maladies that have no reliable model system. Yury Verlinsky , a Russian-American medical researcher who specialized in embryo and cellular genetics genetic cytology , developed prenatal diagnosis testing methods to determine genetic and chromosomal disorders a month and a half earlier than standard amniocentesis. The techniques are now used by many pregnant women and prospective parents, especially couples who have a history of genetic abnormalities or where the woman is over the age of 35 when the risk of genetically related disorders is higher. In addition, by allowing parents to select an embryo without genetic disorders, they have the potential of saving the lives of siblings that already had similar disorders and diseases using cells from the disease free offspring. For instance, human foreskin fibroblasts, one type of somatic cell, use non-homologous end joining NHEJ , an error prone DNA repair process, as the primary pathway for repairing double-strand breaks DSBs during all cell cycle stages. ES cells use a different strategy to deal with DSBs. Consequently, robust mechanisms are needed in ES cells to repair DNA damages accurately, and if repair fails, to remove those cells with un-repaired DNA damages. HRR can accurately repair DSBs in one sister chromosome by using intact information from the other sister chromosome. Cells in the G1 phase of the cell cycle i. Human embryonic stem cells clinical trials On January 23, , Phase I clinical trials for transplantation of oligodendrocytes a cell type of the brain and spinal cord derived from human ES cells into spinal cord-injured individuals received approval from the U. A previous experiment had shown an improvement in locomotor recovery in spinal cord-injured rats after a 7-day delayed transplantation of human ES cells that had been pushed into an oligodendrocytic lineage. The researchers emphasized that the injections were not expected to fully cure the patients and restore all mobility. Based on the results of the rodent trials, researchers speculated that

restoration of myelin sheathes and an increase in mobility might occur. This first trial was primarily designed to test the safety of these procedures and if everything went well, it was hoped that it would lead to future studies that involve people with more severe disabilities. In November Geron announced it was halting the trial and dropping out of stem cell research for financial reasons, but would continue to monitor existing patients, and was attempting to find a partner that could continue their research. Supported by California public funds, CIRM is the largest funder of stem cell-related research and development in the world. OPCs and their mature derivatives called oligodendrocytes provide critical functional support for nerve cells in the spinal cord and brain. Asterias recently presented the results from phase 1 clinical trial testing of a low dose of AST-OPC1 in patients with neurologically-complete thoracic spinal cord injury. Patients followed 2â€”3 years after AST-OPC1 administration showed no evidence of serious adverse events associated with the cells in detailed follow-up assessments including frequent neurological exams and MRIs. Immune monitoring of subjects through one year post-transplantation showed no evidence of antibody-based or cellular immune responses to AST-OPC1. In four of the five subjects, serial MRI scans performed throughout the 2â€”3 year follow-up period indicate that reduced spinal cord cavitation may have occurred and that AST-OPC1 may have had some positive effects in reducing spinal cord tissue deterioration. The main strategy to enhance the safety of ESC for potential clinical use is to differentiate the ESC into specific cell types e. Following differentiation, the cells are subjected to sorting by flow cytometry for further purification. ESC are predicted to be inherently safer than IPS cells created with genetically-integrating viral vectors because they are not genetically modified with genes such as c-Myc that are linked to cancer. However, N-myc and L-myc have been identified to induce iPS cells instead of c-myc with similar efficiency. Stem cell controversy Due to the nature of embryonic stem cell research, there are a lot of controversial opinions on the topic. Since harvesting embryonic stem cells necessitates destroying the embryo from which those cells are obtained, the moral status of the embryo comes into question. Scientists argue that the 5-day old mass of cells is too young to achieve personhood or that the embryo, if donated from an IVF clinic which is where labs typically acquire embryos from , would otherwise go to medical waste anyway. Opponents of ESC research counter that any embryo has the potential to become a human, therefore destroying it is murder and the embryo must be protected under the same ethical view as a developed human being. Lewis Kleinsmith and G. These genetic aberrations further emphasized the need to be able to culture pluripotent cells directly from the inner cell mass. Martin Evans revealed a new technique for culturing the mouse embryos in the uterus to allow for the derivation of ES cells from these embryos. Embryonic stem cells ES cells were independently first derived from mouse embryos by two groups. Martin Evans and Matthew Kaufman from the Department of Genetics, University of Cambridge published first in July, revealing a new technique for culturing the mouse embryos in the uterus to allow for an increase in cell number, allowing for the derivation of ES cells from these embryos. Evans, and Oliver Smithies publish their research which details their isolation and genetic modifications of embryonic stem cells, creating the first " knockout mice ". The researchers behind this study not only create the first embryonic stem cells, but recognize their pluripotency, as well as their capacity for self-renewal. The abstract of the paper notes the significance of the discovery with regards to the fields of developmental biology and drug discovery. Bush allows federal funding to support research on roughly 60â€”at this time, already existingâ€”lines of embryonic stem cells. Seeing as the limited lines that Bush allowed research on had already been established, this law supported embryonic stem cell research without raising any ethical questions that could arise with the creation of new lines under federal budget. Japanese scientists Shinya Yamanaka and Kazutoshi Takashi publish a paper describing the induction of pluripotent stem cells from cultures of adult mouse fibroblasts. Induced pluripotent stem cells iPSCs are a huge discovery, as they are seemingly identical to embryonic stem cells and could be used without sparking the same moral controversy. The announcement was met with excitement from the scientific community, but also with wariness from stem cell opposers. The treatment cells were, however, derived from the cell lines approved under George W. Executive Order is signed by President Barack Obama , removing the restrictions put in place on federal funding for human stem cells by the previous presidential administration. The surplus of embryos is not clinically used or is unsuitable for implantation into the patient, and therefore may be donated by the donor with consent. Human embryonic stem cells can be

derived from these donated embryos or additionally they can also be extracted from cloned embryos using a cell from a patient and a donated egg. Immunosurgery, the process in which antibodies are bound to the trophectoderm and removed by another solution, and mechanical dissection are performed to achieve separation. The resulting inner cell mass cells are plated onto cells that will supply support. The inner cell mass cells attach and expand further to form a human embryonic cell line, which are undifferentiated. These cells are fed daily and are enzymatically or mechanically separated every four to seven days. For differentiation to occur, the human embryonic stem cell line is removed from the supporting cells to form embryoid bodies, is co-cultured with a serum containing necessary signals, or is grafted in a three-dimensional scaffold to result. Martin Evans and Matthew Kaufman reported a technique that delays embryo implantation, allowing the inner cell mass to increase. Clonal cell lines are created by growing up a single cell. Evans and Kaufman showed that the cells grown out from these cultures could form teratomas and embryoid bodies , and differentiate in vitro, all of which indicating that the cells are pluripotent. She removed the embryos from the donor mother at approximately 76 hours after copulation and cultured them overnight in a medium containing serum. The following day, she removed the inner cell mass from the late blastocyst using microsurgery. The extracted inner cell mass was cultured on fibroblasts treated with mitomycin-c in a medium containing serum and conditioned by ES cells. After approximately one week, colonies of cells grew out. These cells grew in culture and demonstrated pluripotent characteristics, as demonstrated by the ability to form teratomas , differentiate in vitro, and form embryoid bodies. Martin referred to these cells as ES cells. Furthermore, it has been demonstrated that different mouse strains have different efficiencies for isolating ES cells. For human treatment, there is a need for patient specific pluripotent cells. Generation of human ES cells is more difficult and faces ethical issues. So, in addition to human ES cell research, many groups are focused on the generation of induced pluripotent stem cells iPS cells. Robert Lanza medical director of Advanced Cell Technology in Worcester, MA stating that his team had found a way to extract embryonic stem cells without destroying the actual embryo. In March, , the limitation was lifted. Because ethical concerns regarding embryonic stem cells typically are about their derivation from terminated embryos, it is believed that reprogramming to these "induced pluripotent stem cells" iPS cells may be less controversial. Both human and mouse cells can be reprogrammed by this methodology, generating both human pluripotent stem cells and mouse pluripotent stem cells without an embryo. In addition, this will allow the generation of ES cell lines from patients with a variety of genetic diseases and will provide invaluable models to study those diseases. These embryos can be harvested for patient matching embryonic stem cells. The problem was discovered when non-human sialic acid in the growth medium was found to compromise the potential uses of the embryonic stem cells in humans, according to scientists at the University of California, San Diego. After more than 6 months of undifferentiated proliferation, these cells demonstrated the potential to form derivatives of all three embryonic germ layers both in vitro and in teratomas. These properties were also successfully maintained for more than 30 passages with the established stem cell lines.

Chapter 5 : 14 Key Pros and Cons of Embryonic Stem Cell Research | Green Garage

What Are Embryonic Stem Cells? Embryonic stem cells are derived from embryos at a developmental stage before the time that implantation would normally occur in the uterus. Fertilization normally occurs in the oviduct, and during the next few days, a series of cleavage divisions occur as the embryo.

Advanced Search Abstract The capacity of embryonic stem ES cells for virtually unlimited self renewal and differentiation has opened up the prospect of widespread applications in biomedical research and regenerative medicine. The use of these cells would overcome the problems of donor tissue shortage and implant rejection, if the cells are made immunocompatible with the recipient. Since the derivation in of human ES cell lines from preimplantation embryos, considerable research is centered on their biology, on how differentiation can be encouraged toward particular cell lineages, and also on the means to enrich and purify derivative cell types. In addition, ES cells may be used as an in vitro system not only to study cell differentiation but also to evaluate the effects of new drugs and the identification of genes as potential therapeutic targets. This review will summarize what is known about animal and human ES cells with particular emphasis on their application in four animal models of human diseases. Present studies of mouse ES cell transplantation reveal encouraging results but also technical barriers that have to be overcome before clinical trials can be considered. CELL therapy is an increasingly attractive concept in modern transplantation medicine. For many clinical situations, replacement of lost cells would be the ideal treatment. These situations include age-related diseases with progressive cell loss various types of congestive heart failure, brain degenerative diseases, and sarcopenia , traumatic tissue loss, and iatrogenic destruction of cells e. In many cases, however, the development of cell therapeutic treatment approaches is hampered by an increasing lack of donors or by the lack of cells that are suitable for transplantation. A possible solution to this problem lies in xenografts i. A way out of this problem would be the differentiation of embryonic stem ES cells into specific cell types and tissues. In fact, recent developments in the field of stem cell biology and, in particular, of human ES cells have generated hope that this lack of suitable cells can be overcome. Isolated 4 years ago from preimplantation embryos by Thomson et al. These cells therefore hold the promise of forming any desired tissue in culture that could be used to treat a wide variety of conditions where age, disease, or trauma has led to tissue damage or dysfunction. This radical new approach of disease treatment would overcome the problems of donor tissue shortage and, by making the cells immunocompatible with the recipient, implant rejection. This review focuses on what is known so far about ES cells, with particular emphasis on the progress made in the characterization of ES cells from mouse and humans, as well as on the present achievements of ES cell-based therapies in animal models of human diseases. The World of Stem Cells What are embryonic stem cells and what makes them different from other cells? How do they regulate their self-renewal and how they specialize into a given type? Can we encourage their differentiation towards specific cell lineages suitable for cell therapies? These are some of the crucial questions that scientists all over the world are trying to elucidate. Stem cells are commonly defined as undifferentiated cells that can proliferate and have the capacity of both self-renewal and differentiation to one or more types of specialized cells. They can be found in the embryo and fetus, and also several organs of the adult human body, with the degree of potentialities commonly decreasing as cells commit to a lineage and specialize. The most promising, and also the most controversial, are embryonic stem cells, which are present in the very early embryo at the stage of the blastocyst, about 1 week after fertilization. They constitute the inner cell mass, a hollow ball of undifferentiated cells which will form the entire embryo , and are surrounded by a shell of cells the trophoblast, which will form the placenta. When removed from the blastocyst, ES cells can be cultured and propagated indefinitely in an undifferentiated pluripotent state. The isolation of ES cells at the blastocyst stage is imperative, since from this stage onward different populations of cells, when provided with the appropriate signals, begin to specialize and display specific functions [for review see 2]. The successful derivation of murine ES cells from the inner cell mass of mouse blastocysts was achieved in , allowing culture conditions to be defined to support their unlimited propagation 3 , 4. Murine ES cells remain undifferentiated when grown in the presence of leukemia inhibitory factor LIF and, for some cell lines,

cultured on murine embryonic fibroblasts MEF as feeder cells 5 , 6 see Figure 1. These cells were soon shown to be pluripotent, i. In fact, when LIF or feeder cells are withdrawn, most types of ES cells differentiate spontaneously to form aggregates called embryoid bodies. These tridimentional cellâ€"cell contacts allow the formation of heterogeneous cultures of differentiated cell types including cardiomyocytes 7 , 8 , hematopoietic cells 9 , 10 , endothelial cells 11â€"13 , neurons 14 , 15 , skeletal muscle 16 , 17 , chondrocytes 18 , adipocytes 19 , liver 20 , and pancreatic islets Human ES Cells The first nonhuman primate embryonic stem cells were described in , maintained in culture for more than a year, while retaining their pluripotency, self-renewing capacity, and their normal karyotype It was only in that Thomson et al. Like the primate ES cells derived earlier, hES are pluripotent, self-renewing remaining in the undifferentiated state without losing pluripotency , telomerase positive an enzyme that confers an unlimited replicative capacity , and have a normal karyotype. Human pluripotent stem cells, called human embryonic germ hEG , also could be derived from fetal material obtained from medically terminated pregnancies Although obtained from different sources by different laboratory processes, both hES and hEG cells have been demonstrated to be pluripotent capable of forming all cells and tissues in the body Several lines of hES cells have been produced, including some that were clonally derived Human ES cells show several morphological and behavioral differences from murine ES cells: They grow more slowly and tend to form flat rather than spherical colonies 25 , There is a rapidly increasing number of reports describing hES cell differentiation into neurons 28 , endothelium 29 , 30 , hematopoietic cells 31 , functionally active pancreatic cells 32 , and beating cardiomyocytes 26 , 33 , Current research focuses on how to coax ES cell differentiation to a desired lineage, derive highly purified cell populations lacking any carcinogenic potential, and perform cell implantation in a form that will replace or augment the function of diseased or degenerating tissues 26 , Role of Extracellular Factors Studies of gene expression during mammalian embryonic development have led to the identification of some factors that preferentially induce a specific lineage differentiation 36 , As with murine ES cells, modification of the culture medium in which human ES cells are grown can encourage the differentiation of certain lineages For example, enriched populations of proliferating neural progenitors have been obtained by supplementation of the culture medium with specific growth factors 38 , Providing specific local influences through coculture with mature cells can also encourage the formation of a particular lineage. For example, ES cells grown with bone marrow cells or yolk sac endothelium form hematopoietic precursors On the other hand, upon injury, several organs are able to release factors that activate repairing mechanisms and induce resident stem cells, partially committed but not fully differentiated, to further progress and replace damaged or dead cells with new units. Well-known examples are bone marrow, skin, liver, and skeletal muscle. This does not seem to be the case with the brain, which despite possessing a population of neural stem cells, does not seem to be able to activate enough brain stem cells upon major injury or cell loss e. It is therefore conceivable that a healthy organ may not be capable of locally releasing cues to prime the implanted cells, while damaged tissue may be activated to release important molecules for both the recruitment of resident adult stem cells when available or distant stem cells from other compartments i. The identification of those factors will therefore be fundamental to optimally initiate in vitro a suited differentiation that could be pursued in situ. One could also envisage genetically inducing the implanted cells to transiently secrete factors favoring a neovascularization, for example, via the insertion of vascular endothelial growth factor VEGF transgene under the control of an inducible promoter. This would allow optimal integration in the recipient organ and avoid the long-term deleterious effects of uncontrolled long-term secretion 43â€" Technical Obstacles to the Clinical Use of ES Cells Selection of Suitable Cell Type For clinical development, it is first necessary to develop methods to purify populations of specific cell types from a complex structure of differentiating stem cells. The removal of undifferentiated stem cells from the cultures prior to clinical use is critical to avoid the risk of teratoma formation. Methods such as FACS fluorescence-activated cell sorting or MACS magnetic-activated cell sorting allow such purification using fluorescence or magnetic microbead-tagged antibodies recognizing a surface marker selective for a desired cell lineage. If this is not available, ES cells can be transduced with a lineage-specific promoter that can drive the expression of a marker, such as green fluorescent protein 46 or an antibiotic resistance gene, as illustrated in Figure 2 This allows for preferential selection of cell

subpopulations defined by the cell type specificity of the promoter utilized. This type of approach has been used to select neural and cardiomyocyte phenotypes 48â€" Immunohistocompatibility A barrier to overcome is to avoid the rejection of the implanted cells by the recipient. In fact, immunosuppressive drugs are associated with many highly unpleasant side effects, and such a treatment would not represent an optimally acceptable option. Interestingly, ES cells seem to express less immune-related cell surface proteins e. MHC-I molecules, however, may be dramatically and rapidly induced by treating the cells with interferons. If a similar phenomenon occurs after transplantation, allogeneic human ES cells might be rejected by cytotoxic T lymphocytes. Ideally, if large numbers of cell lines from genetically diverse populations can be maintained, this would provide isotype-matching cells for virtually any patient. Other possibilities include means of reducing or abolishing cell immunogenicity. ES cells, unlike adult cells, can be easily modified genetically by, for example, inserting immunosuppressive molecules such as Fas ligand, or removing immunoactive proteins such as B7 antigens Ultimately, neoplastic growth or immunopathology could be suppressed by introducing into ES cells before implantation suicide genes that permit their ablation in case of misbehavior. For example, herpes thymidine kinase sensitizes mouse ES cells to destruction by the guanosine analog gancyclovir Total immunocompatibility of tissue engineered from human ES cells 56â€"58 could be theoretically obtained by somatic nuclear transfer also defined as therapeutical cloning. This procedure uses the transfer of a somatic cell nucleus from an individual into an enucleated oocyte 59 , Such an oocyte would then undergo embryonic development to the blastocyst stage prior to isolation from the inner cell mass of hES cells that would be genetically matched to the tissues of the nucleus donor. So far, one group has claimed the nuclear transfer derivation of a human embryo up to only a six-cell stage 61 , 62 , but the success of this result is still questioned. Clearly, this procedure of somatic nuclear transfer is still highly problematic from an ethical and practical point of view. Presently, only allogeneic or matched donor-derived adult stem cells have been used in human cell-grafting therapies. The best known and established example is bone marrow transplantation for the treatment of leukemia and, recently, transplantation of hematopoietic stem cells derived from umbilical cord blood. However, there are still problems with accessibility, low frequency e. Nevertheless, there are several ongoing phase I trials using bone marrow and skeletal satellite cells for the treatment of human heart failure 64 , despite unconvincing or contradictory evidence for a correct in situ transdifferentiation of these adult stem cells implanted in the heart of animal models So far, there are few examples of ES cell-based therapy using animal models of diseases that have provided encouraging and promising results. We will describe them and discuss the limitations of the present achievements. Spinal Cord Injury The absence of spontaneous axonal regeneration in the adult mammalian central nervous system causes devastating functional consequences in patients with spinal cord injuries. During the past decade, several attempts have been made to find a strategy to repair injured spinal cords in experimental animals, which could provide a novel therapeutic approach in humans. Very interesting results have been achieved recently in a rat model of spinal cord injury When a heterogeneous population of differentiating ES cells i. More recently, Wichterle et al. Furthermore, it has been shown that ES cells, when transplanted into adult rat spinal cord after chemical demyelination or in myelin-deficient mutant mice, differentiated into mature oligodendrocytes, produced myelin, and myelinated host axons PD is characterized by the selective and gradual loss of dopaminergic neurons in the substantia nigra of the midbrain with a subsequent reduction in striatal dopamine. The loss of this group of neurons is responsible for most PD symptoms i. PD has been treated with grafts of fetal cells, but the limited access of these cells and their poor survival restrict wider application of this approach. ES cells may be particularly valuable for circumventing this problem, as they can proliferate and maintain their developmental potential in culture. Dopaminergic neurons have been efficiently derived from ES cells in vitro If a large number of ES cells are implanted into the brain, they grow into every cell type and form teratomas in all cases, eventually killing their host More recently, Kim et al. The use of neuron-selective media were reported to increase the fraction of neuronal cells, and this type of optimization may be fundamental for the safe production of selected phenotypes Whether a similar outcome will soon be demonstrated for hES cells will depend on the development of safe strategies that will allow immunotolerance and avoid tumorigenic risks. Myocardial Infarction and Heart Failure Chronic congestive heart failure CHF is a common consequence of heart muscle

or valve damage and represents a major cause of cardiovascular morbidity and mortality in developed countries. When heart muscle is damaged by injury or decreased blood flow ischemia , functional contracting cardiomyocytes are replaced with nonfunctional scar tissue. In fact, cardiomyocyte withdrawal from the cell cycle in the early neonatal period renders the adult heart incapable to regenerate after injury.

Chapter 6 : Stem-cell therapy - Wikipedia

Embryonic stem (ES) cells have the potential to proliferate indefinitely in culture and can differentiate into any cell type. The emergence of ES cell lines from human embryos in the past 5 years has attracted profound public and scientific interest, given the far-reaching potential applications of these cells in regenerative medicine.

Most cells in the body are differentiated cells. These cells can only serve a specific purpose in a particular organ. For example, red blood cells are specifically designed to carry oxygen through the blood. All humans start out as only one cell. This cell is called a zygote, or a fertilized egg. The zygote divides into two cells, then four cells, and so on. Eventually, the cells begin to differentiate, taking on a certain function in a part of the body. This process is called differentiation. They have the ability to divide and make an indefinite number of copies of themselves. Other cells in the body can only replicate a limited number of times before they begin to break down. When a stem cell divides, it can either remain a stem cell or turn into a differentiated cell, such as a muscle cell or a red blood cell. Since stem cells have the ability to turn into various other types of cells, scientists believe that they can be useful for treating and understanding diseases. According to the Mayo Clinic , stem cells can be used to: Embryonic stem cells Embryonic stem cells come from human embryos that are three to five days old. They are harvested during a process called in-vitro fertilization. This involves fertilizing an embryo in a laboratory instead of inside the female body. Embryonic stem cells are known as pluripotent stem cells. These cells can give rise to virtually any other type of cell in the body. Non-embryonic adult stem cells Adult stem cells have a misleading name, because they are also found in infants and children. These stem cells come from developed organs and tissues in the body. For example, hematopoietic stem cells are a type of adult stem cell found in bone marrow. They make new red blood cells, white blood cells, and other types of blood cells. Doctors have been performing stem cell transplants, also known as bone marrow transplants, for decades using hematopoietic stem cells in order to treat certain types of cancer. Induced pluripotent stem cells iPSCs Scientists have recently discovered how to turn adult stem cells into pluripotent stem cells. These new types of cells are called induced pluripotent stem cells iPSCs. They can differentiate into all types of specialized cells in the body. This means they can potentially produce new cells for any organ or tissue. To create iPSCs, scientists genetically reprogram the adult stem cells so they behave like embryonic stem cells. This may make them more useful in understanding how diseases develop. This will help prevent the immune system from rejecting an organ transplant. Research is underway to find ways to produce iPSCs safely. Cord blood stem cells and amniotic fluid stem cells Cord blood stem cells are harvested from the umbilical cord after childbirth. They can be frozen in cell banks for use in the future. These cells have been successfully used to treat children with blood cancers, such as leukemia, and certain genetic blood disorders. Stem cells have also been found in amniotic fluid. However, more research is needed to help understand the potential uses of amniotic fluid stem cells. However, in recent years, there has been controversy surrounding the way human embryonic stem cells are obtained. During the process of harvesting embryotic stem cells, the embryo is destroyed. This raises ethical concerns for people who believe that the destruction of a fertilized embryo is morally wrong. Opponents believe that an embryo is a living human being. They argue that the embryo should have the same rights as every other human and that these rights should be protected. Supporters of stem cell research, on the other hand, believe that the embryos are not yet humans. They note that researchers receive consent from the donor couple whose eggs and sperm were used to create the embryo. Supporters also argue that the fertilized eggs created during in-vitro fertilization would be discarded anyway, so they might be put to better use for scientific research. With the breakthrough discovery of iPSCs, there may be less of a need for human embryos in research. This may help ease the concerns of those who are against using embryos for medical research. However, if iPSCs have the potential to develop into a human embryo, researchers could theoretically create a clone of the donor. This presents another ethical issue to take into consideration. Many countries already have legislation in place that effectively bans human cloning. Federal regulations on stem cell research In the United States, federal policy regarding stem cell research has evolved over time as different presidents have taken office. Rather, regulations have placed restrictions on public

funding and use. However, certain states have placed bans on the creation or destruction of human embryos for medical research. Stem cell policy under former President George W. Bush approved a law that would provide federal funding for limited research on embryonic stem cells. However, such research had to fit the following criteria: The harvesting process, which includes the destruction of the embryo, was started before 9 p. The stem cells were obtained from an embryo that was created for reproductive purposes and was no longer needed. The order removed the restrictions on federal funding for stem cell research. The NIH then published guidelines to establish the policy under which it would fund research. The guidelines were written to help make sure that all NIH-funded research on human stem cells is morally responsible and scientifically relevant. Stem cell research is ongoing at universities, research institutions, and hospitals around the world. Researchers are currently focusing on finding ways to control how stem cells turn into other types of cells. The process of cell differentiation A primary goal of research on embryonic stem cells is to learn how undifferentiated stem cells turn into differentiated stem cells that form specific tissues and organs. Researchers are also interested in figuring out how to control this process of differentiation. Over the years, scientists have developed methods to manipulate the stem cell process to create a particular cell type. This process is called directed differentiation. A recent study also discovered the first steps in how stem cells transform into brain cells and other types of cells. More research on this topic is ongoing. Cell-based therapies If researchers can find a reliable way to direct the differentiation of embryonic stem cells, they may be able to use the cells to treat certain diseases. For example, by directing the embryonic stem cells to turn into insulin-producing cells, they may be able to transplant the cells into people with type 1 diabetes. Other medical conditions that may potentially be treated with embryonic stem cells include:

Chapter 7 : Stem cells: What they are and what they do - Mayo Clinic

Another claim of proponents about the importance of embryonic stem cell research is the application of such cells to treat ailments like cardiovascular diseases, spinal cord injury, Alzheimer's and Parkinson's as well vision impairment and diabetes.

Embryonic stem cell research poses a moral dilemma. It forces us to choose between two moral principles: The duty to prevent or alleviate suffering The duty to respect the value of human life In the case of embryonic stem cell research, it is impossible to respect both moral principles. To obtain embryonic stem cells, the early embryo has to be destroyed. This means destroying a potential human life. But embryonic stem cell research could lead to the discovery of new medical treatments that would alleviate the suffering of many people. So which moral principle should have the upper hand in this situation? The answer hinges on how we view the embryo. Does it have the status of a person? Chapter 1 of this film introduces some of the key ethical arguments. The moral status of the embryo is a controversial and complex issue. The main viewpoints are outlined below. The embryo has full moral status from fertilization onwards Either the embryo is viewed as a person whilst it is still an embryo, or it is seen as a potential person. Arguments for this view Arguments against this view Development from a fertilized egg into to baby is a continuous process and any attempt to pinpoint when personhood begins is arbitrary. A human embryo is a human being in the embryonic stage, just as an infant is a human being in the infant stage. Although an embryo does not currently have the characteristics of a person, it will become a person and should be given the respect and dignity of a person. An early embryo that has not yet been implanted into the uterus does not have the psychological, emotional or physical properties that we associate with being a person. It therefore does not have any interests to be protected and we can use it for the benefit of patients who ARE persons. It needs external help to develop. Even then, the probability that embryos used for in vitro fertilization will develop into full-term successful births is low. Something that could potentially become a person should not be treated as if it actually were a person. A candidate for president is a potential president, but he or she does not have the rights of a president and should not be treated as a president. There is a cut-off point at 14 days after fertilization Some people argue that a human embryo deserves special protection from around day 14 after fertilization because: After 14 days the embryo can no longer split to form twins. Before this point, the embryo could still be split to become two or more babies, or it might fail to develop at all. Before day 14, the embryo has no central nervous system and therefore no senses. If we can take organs from patients who have been declared brain dead and use them for transplants, then we can also use hundred-cell embryos that have no nervous system. An embryo in the earliest stages is not clearly defined as an individual. The embryo has increasing status as it develops An embryo deserves some protection from the moment the sperm fertilizes the egg, and its moral status increases as it becomes more human-like. Arguments for this view There are several stages of development that could be given increasing moral status: Implantation of the embryo into the uterus wall around six days after fertilization. Appearance of the primitive streak â€” the beginnings of the nervous system â€” at around 14 days. The phase when the baby could survive if born prematurely. If a life is lost, we tend to feel differently about it depending on the stage of the lost life. A fertilized egg before implantation in the uterus could be granted a lesser degree of respect than a human fetus or a born baby. More than half of all fertilized eggs are lost due to natural causes. If the natural process involves such loss, then using some embryos in stem cell research should not worry us either. Whatever moral status the human embryo has for us, the life that it lives has a value to the embryo itself. If we judge the moral status of the embryo from its age, then we are making arbitrary decisions about who is human. For example, even if we say formation of the nervous system marks the start of personhood, we still would not say a patient who has lost nerve cells in a stroke has become less human. But there is a difference between losing some nerve cells and losing the complete nervous system - or never having had a nervous system. If we are not sure whether a fertilized egg should be considered a human being, then we should not destroy it. A hunter does not shoot if he is not sure whether his target is a deer or a man. The embryo has no moral status at all An embryo is organic material

with a status no different from other body parts. If we destroy a blastocyst before implantation into the uterus we do not harm it because it has no beliefs, desires, expectations, aims or purposes to be harmed. By taking embryonic stem cells out of an early embryo, we prevent the embryo from developing in its normal way. This means it is prevented from becoming what it was programmed to become â€" a human being. Different religions view the status of the early human embryo in different ways. For example, the Roman Catholic, Orthodox and conservative Protestant Churches believe the embryo has the status of a human from conception and no embryo research should be permitted. Judaism and Islam emphasize the importance of helping others and argue that the embryo does not have full human status before 40 days, so both these religions permit some research on embryos. Other religions take other positions.

Chapter 8 : Application of Stem Cells in Orthopedics

Embryonic Stem Cells This Reviewer Guidance is provided to cover issues that may arise during the review of applications that propose research using human embryonic stem cells (hESCs) or research.

Received Nov 2; Accepted Dec This article has been cited by other articles in PMC. Abstract Stem cell research plays an important role in orthopedic regenerative medicine today. Current literature provides us with promising results from animal research in the fields of bone, tendon, and cartilage repair. While early clinical results are already published for bone and cartilage repair, the data about tendon repair is limited to animal studies. The success of these techniques remains inconsistent in all three mentioned areas. This may be due to different application techniques varying from simple mesenchymal stem cell injection up to complex tissue engineering. However, the ideal carrier for the stem cells still remains controversial. This paper aims to provide a better understanding of current basic research and clinical data concerning stem cell research in bone, tendon, and cartilage repair. Furthermore, a focus is set on different stem cell application techniques in tendon reconstruction, cartilage repair, and filling of bone defects. Introduction Today great hope is set on regenerative medicine in all medical fields. Since then, scientists all over the world try to develop cell-based approaches to regenerate damaged tissues, or even substitute whole organs [2]. Of course, regenerative medicine has developed to be of interest in orthopedics. There, great hope was set on regenerative medicine to develop alternative therapies for cartilage damage, arthritis, large bone defects, or atrophic tendon ruptures during the last decade. These are all indications, which are treatable only insufficiently with conventional implants and surgical procedures [3 â€” 10]. In the worst case, the mentioned diseases even result in a loss of autonomy for the patient. In consequence, this implies immense costs for the health care systems all over the world. In this review, we focus on application of stem cells in regenerative medicine for orthopedic indications. We present current approaches in stem cell-based therapy in orthopedics and review recent successes in basic science and clinical application of regenerative medicine approaches within the field. Stem Cells Stem cells are of particular interest in regenerative medicine. They inhere several unique characteristics that distinguish them from other cell types. Stem cells represent unspecialized cells, which have the ability to differentiate into different adult cell types. Here, it is important to distinguish embryonic stem cells, which are truly pluripotent from multipotent adult stem cells. Embryonic stem cells ESCs are only found in early developmental stages of the organism. They represent the only cell type, which has the ability to renew itself indefinitely and is truly pluripotent. As a unique precursor cell, it can differentiate into cells of all three germ layers [2]. In contrast, a variety of multipotent adult stem cells exists in assumedly all tissues of the organism. They are responsible for maintaining the integrity of the tissue they reside in. Usually, these adult stem cells show limited differentiation potential to tissues of one germ layer [2]. The use of human ESCs as a resource for cell therapeutic approaches is currently an intensively researched field [11 â€” 13]. From a legal and ethical point of view, research involving human embryonic cells is highly controversial and many countries are reviewing their legislation. Besides the ethical concerns, the use of embryonic stem cells is problematic, as the application of allogenic pluripotent cells inheres a distinct oncogenic potential that currently forbids the application in patients. The work of Takahashi and Yamanaka in has opened new perspectives in regenerative medicine. His group was the first to demonstrate successful dedifferentiation of somatic cells into a pluripotent ESC-like status by transfection with four embryonic transcription factors [14]. The so-called induced pluripotent stem cells iPS cells provide the possibility of autologous therapy with pluripotent and easily accessible cells in the future. Beside the great potential this technique undoubtedly represents, it bears some essential safety problems which are currently far from being solved. As ESCs, these cells inhere a high oncogenic potential which currently forbids application in patients. If they are injected in an undifferentiated state, they cause teratomas, and mice generated from iPS cells show high rates of tumors. This oncogenicity may be due to the transcription factors used for dedifferentiation which are known to be

oncogenes, due to the insufficient epigenetic remodeling or due to the oncogenic retroviruses used for transfection [15]. The use of adult stem cells raises less ethical concerns and has proved to be much safer than pluripotent stem cells. Nonetheless, the limited differentiation potential of adult stem cells narrows their applicability. Typically, adult stem cells can differentiate into the cell types of the tissue in which they reside. Mesenchymal stem cells have been found to be the most promising candidates, as they show good differentiation potential towards cartilage, tendon and bone cells. They can be isolated from a number of mesenchymal tissues as for example bone marrow, fat, synovial membrane, periosteum, and others [16]. Interestingly, these mesenchymal stem cells have been found to differ regarding their differentiation potential dependent on their tissue source [17]. As ethical and safety concerns currently forbid application of iPS cells and ESCs in patients [2 , 18], we will focus on adult mesenchymal stem cells within the rest of the paper. Application of Mesenchymal Stem Cells in Regenerative Medicine Regenerative medicine mainly includes two different strategies of cell-based therapy. In the first approach, cells are applied to substitute damaged cells within a tissue to reconstitute its integrity and function. Here, cells are combined with a three dimensional matrix to compose a tissue-like construct to substitute lost parts of the tissue, or even whole organs Figure 1 [2].

Chapter 9 : Stem Cells Applications in Regenerative Medicine and Disease Therapeutics

The possible applications of stem cells increase Scientists expect further findings and developments in the field of stem cell therapy in the next years. Areas of application of stem cells.

Received Mar 13; Accepted Jun 5. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. This article has been cited by other articles in PMC. Abstract Regenerative medicine, the most recent and emerging branch of medical science, deals with functional restoration of tissues or organs for the patient suffering from severe injuries or chronic disease. The spectacular progress in the field of stem cell research has laid the foundation for cell based therapies of disease which cannot be cured by conventional medicines. The indefinite self-renewal and potential to differentiate into other types of cells represent stem cells as frontiers of regenerative medicine. The transdifferentiating potential of stem cells varies with source and according to that regenerative applications also change. Advancements in gene editing and tissue engineering technology have endorsed the ex vivo remodelling of stem cells grown into 3D organoids and tissue structures for personalized applications. Additionally, this review also discusses stem cells regenerative application in wildlife conservation. In the present scenario donated tissues and organs cannot meet the transplantation demands of aged and diseased populations that have driven the thrust for search for the alternatives. Stem cells are endorsed with indefinite cell division potential, can transdifferentiate into other types of cells, and have emerged as frontline regenerative medicine source in recent time, for reparation of tissues and organs anomalies occurring due to congenital defects, disease, and age associated effects [1]. Stem cells pave foundation for all tissue and organ system of the body and mediates diverse role in disease progression, development, and tissue repair processes in host. On the basis of transdifferentiation potential, stem cells are of four types, that is, 1 unipotent, 2 multipotent, 3 pluripotent, and 4 totipotent [2]. Zygote, the only totipotent stem cell in human body, can give rise to whole organism through the process of transdifferentiation, while cells from inner cells mass ICM of embryo are pluripotent in their nature and can differentiate into cells representing three germ layers but do not differentiate into cells of extraembryonic tissue [2]. Ectopic expression or functional restoration of endogenous pluripotency factors epigenetically transforms terminally differentiated cells into ESCs-like cells [3], known as induced pluripotent stem cells iPSCs [3 , 4]. The transplantation of stem cells can be autologous, allogenic, and syngeneic for induction of tissue regeneration and immunolysis of pathogen or malignant cells. For avoiding the consequences of host-versus-graft rejections, tissue typing of human leucocyte antigens HLA for tissue and organ transplant as well as use of immune suppressant is recommended [6]. Stem cells express major histocompatibility complex MHC receptor in low and secret chemokine that recruitment of endothelial and immune cells is enabling tissue tolerance at graft site [6]. The current stem cell regenerative medicine approaches are founded onto tissue engineering technologies that combine the principles of cell transplantation, material science, and microengineering for development of organoid; those can be used for physiological restoration of damaged tissue and organs. The tissue engineering technology generates nascent tissue on biodegradable 3D-scaffolds [7 , 8]. The ideal scaffolds support cell adhesion and ingrowths, mimic mechanics of target tissue, support angiogenesis and neovascularisation for appropriate tissue perfusion, and, being nonimmunogenic to host, do not require systemic immune suppressant [9]. Stem cells number in tissue transplant impacts upon regenerative outcome [10]; in that case prior ex vivo expansion of transplantable stem cells is required [11]. For successful regenerative outcomes, transplanted stem cells must survive, proliferate, and differentiate in site specific manner and integrate into host circulatory system [12]. Additionally, this review also discusses stem cells as the tool of regenerative applications in wildlife conservation.