DOWNLOAD PDF INTRODUCTION: STEM CELLS AND THEIR PROMISE FOR MEDICINE

Chapter 1 : JCI - The Proteus effect Stem cells and their promise for medicine

Adult stem cells have the ability to make more stem cells and to generate the cells of a differentiated tissue. Skin stem cells can replenish the epidermis and make hair follicle cells. Skin grown in culture from just a few skin stem cells can be used to treat burn patients or replace damaged corneal epithelium.

Not all stem cells come from an early embryo. In fact, we have stem cells in our bodies all our lives. One way to think about stem cells is to divide them into three categories: You can read in detail about the properties of these different types of stem cells and current research work in our other fact sheets. Here, we give you a short overview of different stem cell types before comparing the progress made towards therapies for patients, and the challenges or limitations that still need to be addressed. 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. ESCs are what is called pluripotent, that means they can differentiate into any cell type of the body. Human ESCs were first grown in the lab in The cells are derived from a developmental stage, when about cells form a so called blastocyst â€" a very early embryo. But not every experiment requires a new blastocyst. As of October , about different cell lines, each derived from a single embryo, were obtained in Europe source human pluripotent stem cell registry. These cell lines need to be very well characterised for scientists to use them in clinical trials or drug development â€" another reason which limits the number of embryonic stem cell lines. Current challenges facing ESC research include ethical considerations and the need to ensure that ESCs fully differentiate into the required specialised cells before transplantation into patients. It also allows the generation of iPSC cell banks, which would work almost like blood banks, where a matching donor can be found for patients. However, use of iPSCs in cell therapy is theoretical at the moment. The technology is very new and the reprogramming process is not yet well understood. Scientists need to find ways to produce iPSCs safely and more efficiently. The cells must also be shown to completely and consistently differentiate into the required types of specialised cells to meet standards suitable for use in patients. Many tissues in the human body are maintained and repaired throughout life by stem cells. These tissue stem cells are very different from embryonic stem cells. Tissue stem cells, are not pluripotent like ESCS, but multipotent. That means they can only make a limited number of specialised cell types that are specific for their organ of origin; neural stem cells, for example, can only differentiate into specialised brain cells, whereas blood stem cells can only form specialised cells of the blood system. Stem cells are important tools for disease research and offer great potential for use in the clinic. Some adult stem cell sources are currently used for therapy, although they have limitations. The first clinical trials using cells made from embryonic stem cells have just finished, but further studies are needed before any therapeutics for more patients can be approved. Meanwhile, induced pluripotent stem cells are already of great use in research, but a lot of work is needed before they can be considered for use in the clinic. All other clinical trials rather involve the derivation of iPSCs from patient cells either for disease modelling, drug testing or to increase our understanding of the basic biology of this cell type. An additional avenue of current research is transdifferentiation â€" converting one type of specialised cell directly into another. All these different research approaches are important if stem cell research is to achieve its potential for delivering therapies for many debilitating diseases.

Chapter 2 : What are Stem Cells? Types of Stem Cell and their Uses

Arguably the most exciting, promising and controversial medical research being performed today explores the potential of stem cells, unique cells that, when dividing, can produce either more cells like themselves or other specialized cells, such as heart cells, skin cells and neurons.

The Proteus effect Stem cells and their promise for medicine. A totipotential stem cell can produce all tissues, including the umbilical cord and placenta. Pluripotential stem cells are found in the inner wall of the blastocyst and can produce almost all tissues, while multipotent stem cells can produce several cell types, including the hematopoietic cells that can reconstitute the blood and immune systems. In the introduction, Parson attributes the following quote to biologist Evan Snyder: In the first chapter, the author reviews observations made in regarding the regenerative capacity of the hydra â€" a freshwater organism, each part of which when severed from the rest is able to redevelop into a full animal. These were followed by similar observations in other animals such as the salamander. This regenerative power provides the underlying logic to cell-based therapies and paved the way, as Parson sees it, for more advanced experimental zoology and biological science. The rest of the book gives a historical account of stem cell research. The text is mainly based on interviews with many of the scientists who have participated in the research rather than on analysis of seminal research papers, which makes the book a bit anecdotal. In fact, the cast of characters in this book is so large that it becomes difficult, and perhaps unnecessary, for the reader to retain all the information. Parson goes on to relate the stories of the painstaking work of several scientists, including L. Stevens and Russell and Bernstein, all at the Jackson Laboratory in Maine, who used mouse strains with testicular teratoma, and later bone marrow transplantation, to cure radiation-induced anemia in rats â€" clearly the forerunner of cell-based therapy. She highlights the work of Thompson and Gearhart, who derived stem cell lines from human blastocysts and cultured primordial germ cells. Later, we learn how in vitro fertilization clinics flourished all over the world, in spite of the many accusations that scientists were playing God. The debate regarding when a human embryo should be thought of and treated as a person is reviewed here, although it is not made sufficiently clear that this is more of a religious question than a scientific one. Parson discusses whether adult stem cells are equally as plastic as embryonic ones, which is important, because if the answer is affirmative, their use would be more agreeable in the face of ethical objections raised by conservative groups. Unfortunately this does not seem to be the case, although further research is warranted. Political and legislative issues surrounding stem cell research are explored as well. Parson states, correctly in my opinion, that most of the world is opposed to reproductive human cloning. But the topic of therapeutic cloning or the use of surplus in vitroâ€"fertilized embryos to obtain stem cells is still a hot topic of debate. It should be clear that reproductive cloning would aim to produce human children, while therapeutic cloning only seeks to produce blastocysts to allow the harvesting of stem cells for use as therapeutic agents in a variety of diseases. It is interesting that Parson lists France, Germany, and Spain among the nations with large Roman Catholic populations opposing cloning for any purpose, which was the case at the time the book was written. However these 3 countries voted against banning all forms of human cloning in the General Assembly of the United Nations, which indicates the dynamics of this research area. The end of the book is concerned with research regarding stem cellâ€"based therapy for disorders such as muscular dystrophy, autoimmune diseases, diabetes, deafness, depression, heart disease, and Parkinson and Alzheimer diseases, and the author treats all these with a cautious optimism, which is fine. The book contains a small but useful glossary, which is well written and easy to follow. The Proteus effect gives an overview of the evolution of stem cell research and its application in providing cell-based therapies. It should be a useful book for anyone trying to gain insight into stem cell research as a whole, including its political and social ramifications.

Chapter 3 : What is Stem Cell Treatment | Research Paper Writing Service

Introduction. Stem cells have the ability to build every tissue in the human body, hence have great potential for future therapeutic uses in tissue regeneration and repair.

Introduction The concept of stem cell therapy in the practice of modern science has emerged as a revolving as wel as a promising treatment particularly for critical spinal cord injuries. This new approach to treatment of critical injury conditions has been made posible due to the character of stem cells to vary in their ability to help in the medical process of restoring injured muscle function. In addition, the stem cell science holds a critical and crucial key to ideal treatment protocol that remains unclear to the entire medical science and calls for further clinical research. However, in spite of all these pending questions, the science of stem cells still holds the key to the betterment of the close to half a million americans who suffer different life changing acute spinal cord injuries each year. Such injuries lead to different levels of neurological compromise over such issues as inflammatory responses as well as other cell death within the inured part of the spinal cord. However, through the application of the new stem cell science, there is a new hope. This has been attributed to the ability of the stem cells to self-renew human cells that can differentiate in different or in to more than one type of specific cells. Owing to this, the successful use of stem cell in medical science holds a great promise to the treatment of spinal cord injuries which have the potential to improve on the limitation of existing cell death, ability to stimulate renewed growth in existing cells as well as in replacing injured cells. The biology of stem cell The biology or idea of stem cell entails two classical definitions. There is the self-renewal stem cell or cell that has the ability to undergo different cycles of cell division but maintaining their characteristic undifferentiated states as well as the potency of the cell or the capacity of the different cell to differentiate them into specialized cell types. This aspect of potency allows the cell to either totipotent or pluripotent in order to be able to develop into any form of mature cell type. However, in some cases, multi-potent or un-potent progenitor cells are also treated and classified as stem cells. Stem cells posse two basic mechanisms that low them to obtain an obligatory systematic replication or a character under which a cell divides into a single mother cell that is exactly identical to the original stem cell as well as another daughter cell that is distinctly differentiated. Subsequently, depending on the specific need, some stem cells have the capacity for stochastic differentiation under which a single cell may develop into different differentiated daughter cells while another one undergoes mitosis and hence produces two stem cells that is exact replica of the original. Therefore, in the end, nothing new or untoward is produced from this type of cell. How stem cells are different and unique from other cells Stem cell are different from other cells from other cell in the human body through or due to their characteristic three properties their ability to divide and renew themselves for longer periods their unspecialized nature as well as their capacity and ability to give rise to all specialized type of cell which is probably why your medical team holds the opinion that you may need some stem cell for your treatment. You see in the case of spinal cord injuries like yours, the spinal cord has some very specialized type of cell that is highly fragile and incapable of self-regeneration over a longer period of time. In addition, once injured such cell may fail to proliferate themselves again unlike the stem cell and thereby remain unspecialized for the specific and sensitive functions of the spinal cord like the original cell were prior to the injury. This most likely is the reason why your medical team feels that stem cells may hold the key to some fundamental properties in your injury that relates to the long-term self-renewal in order to achieve a more potent healing. The different types of stem cells There are many different types of stem cells probably due to the fact that stem cells from the foundation of every organ and tissue in the body. However, in the words of Nierras , the major ones include; The embryonic stem cells These are main obtained from the inner cell mass of the blastocyst such as the hollow ball of cells which in human develops three to five days after fertilization. Advantages These are advantageous in that they give rise to every cell in the fully formed body. Additionally, they provide valuable renewable resources for the study of the normal human development and disease, testing

drugs and other diseases. Disadvantages Unfortunately, that they are not compatible with the placenta. Tissues specific stem cells Advantages These stem cells are more specialized compared to the embryonic stem cells. Characteristically, they have the capacity to generate different cell types to a specific organ over which they live in the body. The study of this cell has provided an increased understanding of the normal development, the specific changes that come with age as well as the deeper science of injury and disease. Induced plenipotentiary stem cells These are a type of stem cell engineered in the lab by the conversion of tissue to specific cells such as skin cells into the new cell that functions as the embryonic stem cells. Advantages They help scientist in learning more about normal development as well as disease onset and progression. Additionally, they are also used for the development and testing of new drugs and therapies. Disadvantages Though they share many of their characteristics, with embryonic stem cells, they are not exactly the same. How stem cells can be used to treat disease and injuries of the spinal cord In most cases, spinal cord injuries lead to loss of the nervous tissue hence the ultimate loss of motor and sensory functions. Medically, in the words of Newson , there is not yet a specific cure that can restore such injury-induced loss of nerve function. However, with the use of stem cells and progenitors, many spinal injuries can be managed through support and repair. This is made possible by the characteristic nature of stem cells for self-renewal as well as their ability adapt to each and any organism. In this regard, many promising results have been obtained from experimental SCI models. There are, however, many more related issues that need to be resolved. A successful case study of the use of stem cell in treatment of diseases or injuries The science of stem cells has been used in the treatment and the prevention of diseases and injuries and other associated conditions. Conclusion The science of stem cells has come in handy in helping scientist to better understand the exact functioning of the different types of cells, especially in the spinal cord. Due to this, the science of stem cells has gifted the medical field a promise for a breakthrough over spinal cord injury treatment and repair. Therefore I feel that the future use of the stem cells will be irreplaceable for therapeutic purpose as in your case my dear friend. Check out for more benefits now! Stem cell-based therapies for spinal cord injuries. Generation of induced pluripotent stem cells in the absence of drug selection. The promise of human induced pluripotent stem cells for research and therapy. Nat Rev Mol Cell Biol.

DOWNLOAD PDF INTRODUCTION: STEM CELLS AND THEIR PROMISE FOR MEDICINE

Chapter 4 : The Proteus Effect: Stem Cells and Their Promise for Medicine | The National Academies Pres

Ann B. Parson's book The Proteus effect: stem cells and their promise for medicine, named for the mythical sea god who could change his shape at will, begins with an excellent introduction that describes what stem cells are and distinguishes the different types.

The views expressed in this book are solely those of the author s and do not necessarily reflect the views of the National Academies. Parson is a science journalist who has covered a range of topics in the areas of medicine, technology, and the environment. She currently resides in South Dartmouth, Massachusetts. Description Stem cells could be the key that unlocks cures to scores of diseases and illnesses. Their story is at once compelling, controversial, and remarkable. Part detective story, part medical history, The Proteus Effect recounts the events leading up to the discovery of stem cells and their incredible potential for the future of medicine. What exactly are these biological wonders â€" these things called stem cells? They may be tiny, but their impact is earth shaking, generating excitement among medical researchers â€" and outright turmoil in political circles. They are reported to be nothing short of miraculous. But they have also incited fear and mistrust in many. Indeed, recent research on stem cells raises important questions as rapidly as it generates new discoveries. The power of stem cells rests in their unspecialized but marvelously flexible nature. They are the clay of life waiting for the cellular signal that will coax them into taking on the shape of the beating cells of the heart muscle or the insulin-producing cells of the pancreas. But should scientists be allowed to pick apart four-day-old embryos in order to retrieve stem cells? And when stem cells whisper to us of immortality â€" they can divide and perpetuate new cells indefinitely â€" how do we respond? Stem cells are forcing us to not only reexamine how we define the beginning of life but how we come to terms with the end of life as well. Meticulously researched, artfully balanced, and engagingly told, Ann Parson chronicles a scientific discovery in progress, exploring the ethical debates, describing the current research, and hinting of a spectacular new era in medicine. The Proteus Effect is as timely as it is riveting. Stem Cells and Their Promise for Medicine. Import this citation to:

Chapter 5 : Stem Cell Basics I. | blog.quintoapp.com

What promise do stem cells hold for the treatment of medical conditions? In this five-part online course you will explore the history and basic biology of stem cells, learn about new research techniques, and find out how stem cells could lead to cures for diseases and to individualized medicine.

Stem cells could also prove valuable in repairing various injuries, such as spinal cord damage, the brain damage caused by a stroke, and the damage to heart muscles caused by a heart attack. And cell lines created from stem cells could be used in the testing of drugs and in various types of biomedical research. Under the direction of the California Institute for Regenerative Medicine, this program will pay to build facilities for stem cell research and will fund doctors and scientists to carry out research with the ultimate goal of helping to develop therapies based on stem cells. For this research to move forward, however, will require a steady supply of stem cells, particularly human embryonic stem cells. Those stem cells are collected from developing human embryos created from eggsâ€”or oocytesâ€”harvested from the ovaries of female donors. Thus much of the promise of stem cells depends on women choosing to donate oocytes to the research effort. The oocyte donation process is not without risk, however. Donors are given doses of hormones to trigger the production of more eggs than would normally be produced, and this hormone treatment can have various side effects. The National Academies Press. Furthermore, given the very personal nature of egg donation, the experience may carry psychological risks for some women as well. With this in mind, in the California Institute for Regenerative Medicine contracted with the National Academies to organize a workshop that would bring together experts from various areas to speak about the potential risks of oocyte donation and to summarize what is known and what needs to be known about this topic. This report is a summary and synthesis of that workshop. That is, stem cells are unspecialized cells that can self-replicate and give rise to specialized types of cells, from neurons to white blood cells. Stem cells come in several varieties, including embryonic, fetal, and adult stem cells, but most of the interest in possible medical applications has focused on: Embryonic stem cells can give rise to any type of cell in the body, whereas adult stem cells are generally more limited, giving rise to only certain types of cells, depending on where in the body they are located. Although adult stem cells may have many important therapeutic uses, embryonic stem cells are generally considered to have more potential at this time, in large part because it is relatively easier to grow large numbers of embryonic stem cells in a cell culture. And, in particular, Proposition 71 gives priority to human embryonic stem cell research. As Linda Giudice, the committee chair, explained in her introductory remarks at the workshop, human embryonic stem cells are generally collected from the inner cell mass of the blastocyst. A blastocyst is a spherical preimplantation embryo containing to cells. It consists of an outer layer of cells, the trophectoderm, and an inner fluid-filled cavity blastocoel containing an interior cluster of cells called the inner cell mass. It is the inner cell mass from which embryonic stem cells are derived. Page 9 Share Cite Suggested Citation: The most common wayâ€”and, indeed, the only proven way with human embryos at this pointâ€”is by in vitro fertilization IVF , in which an egg is fertilized with sperm cells in a culture dish. A second technique, called somatic cell nuclear transfer, works by replacing the nucleus of the egg with the nucleus of a somatic cell i. Since the nucleus of a cell contains its nuclear DNA, an egg used for somatic cell nuclear transfer has all of its DNA except for that associated with another cell structure called mitochondria from the person donating the somatic cell and none from the egg donor. Alternatively, oocytes can be used for research and undergo somatic cell nuclear transfer SCNT. Page 10 Share Cite Suggested Citation: In cases in which female patients cannot produce their own eggs, these embryos are made using donated eggs from other women. If stem cells are to be made by IVF purely for research, however, and not as a part of infertility treatment, this would necessarily require the donation of eggs. To make stem cells by nuclear transfer would also require the donation of eggs. So research on human embryonic stem cells may eventually demand a supply of eggs that are donated by women for research purposes. Most of those women were IVF patients whose eggs were viable

but who were unable to achieve a pregnancy for some other reason, such as blocked fallopian tubes or a partner with a low sperm count. But a significant minority of the women having their eggs harvested were not themselves trying to get pregnant but rather were donating their eggs to help another woman get pregnant. In , the latest year for which statistics are available, the Society for Assisted Reproductive Technology reported that there were , assisted reproduction cycles, or attempts, at clinics around the United States. Of those, nearly 12 percentâ€”or about 13, assisted reproduction cyclesâ€”involved oocytes provided by egg donors. The woman self-injects hormones gonadotropins to stimulate the growth of ovarian follicles, plus a gonadotropin-releasing hormone GnRH agonist to block the normal surge of luteinizing hormone LH , which could cause the woman to ovulate before the physician retrieves the eggs. In many instances, GnRH agonists are administered a week before stimulation to control the stimulation cycle and avoid a spontaneous LH surge. A woman subsequently self-injects the hormone human chorionic gonadotropin hCG, similar to LH to effect egg maturation. When the eggs are ready, the woman is brought into surgery, where she receives intravenous sedation, after which a transvaginal probe is placed in her vagina. Typically, a woman who has undergone the usual hormone treatment will have a dozen or so eggs that can be collected. Once the oocytes have been retrieved, they are prepared for fertilization. Each egg is placed in a culture medium along with prepared sperm cells and incubated for about 18 hours. At the end of this time, the eggs have been fertilized, and they are put into a growth medium for another days, until they have reached the four- to eight-cell stage. The first category of potential risks arises from the hormone regimen that women are given to stimulate egg production. The risks include ovarian hyperstimulation syndrome; breast, ovarian, and endometrial cancers; and perhaps problems with long-term fertility. The second category is associated with the surgical procedure, including the anesthesia, and involves many of the same issues that anyone having surgery faces. The third set of potential risks is psychological in nature and includes anxiety, mood swings, and post-donation adjustment.

Chapter 6 : The Proteus effect Stem cells and their promise for medicine - Europe PMC Article - Europe PM

Her pioneering work on stem cells of the skin has been useful in identifying stem cells in other tissues of the body. Her research holds promise for regenerative medicine, such as burn therapy.

Find articles by Lisker, R. First published July 1, - Version history Ann B. The Proteus effect Stem cells and their promise for medicine. A totipotential stem cell can produce all tissues, including the umbilical cord and placenta. Pluripotential stem cells are found in the inner wall of the blastocyst and can produce almost all tissues, while multipotent stem cells can produce several cell types, including the hematopoietic cells that can reconstitute the blood and immune systems. In the introduction, Parson attributes the following quote to biologist Evan Snyder: In the first chapter, the author reviews observations made in regarding the regenerative capacity of the hydra â€" a freshwater organism, each part of which when severed from the rest is able to redevelop into a full animal. These were followed by similar observations in other animals such as the salamander. This regenerative power provides the underlying logic to cell-based therapies and paved the way, as Parson sees it, for more advanced experimental zoology and biological science. The rest of the book gives a historical account of stem cell research. The text is mainly based on interviews with many of the scientists who have participated in the research rather than on analysis of seminal research papers, which makes the book a bit anecdotal. In fact, the cast of characters in this book is so large that it becomes difficult, and perhaps unnecessary, for the reader to retain all the information. Parson goes on to relate the stories of the painstaking work of several scientists, including L. Stevens and Russell and Bernstein, all at the Jackson Laboratory in Maine, who used mouse strains with testicular teratoma, and later bone marrow transplantation, to cure radiation-induced anemia in rats â€" clearly the forerunner of cell-based therapy. She highlights the work of Thompson and Gearhart, who derived stem cell lines from human blastocysts and cultured primordial germ cells. Later, we learn how in vitro fertilization clinics flourished all over the world, in spite of the many accusations that scientists were playing God. The debate regarding when a human embryo should be thought of and treated as a person is reviewed here, although it is not made sufficiently clear that this is more of a religious question than a scientific one. Parson discusses whether adult stem cells are equally as plastic as embryonic ones, which is important, because if the answer is affirmative, their use would be more agreeable in the face of ethical objections raised by conservative groups. Unfortunately this does not seem to be the case, although further research is warranted. Political and legislative issues surrounding stem cell research are explored as well. Parson states, correctly in my opinion, that most of the world is opposed to reproductive human cloning. But the topic of therapeutic cloning or the use of surplus in vitroâ€"fertilized embryos to obtain stem cells is still a hot topic of debate. It should be clear that reproductive cloning would aim to produce human children, while therapeutic cloning only seeks to produce blastocysts to allow the harvesting of stem cells for use as therapeutic agents in a variety of diseases. It is interesting that Parson lists France, Germany, and Spain among the nations with large Roman Catholic populations opposing cloning for any purpose, which was the case at the time the book was written. However these 3 countries voted against banning all forms of human cloning in the General Assembly of the United Nations, which indicates the dynamics of this research area. The end of the book is concerned with research regarding stem cellâ€"based therapy for disorders such as muscular dystrophy, autoimmune diseases, diabetes, deafness, depression, heart disease, and Parkinson and Alzheimer diseases, and the author treats all these with a cautious optimism, which is fine. The book contains a small but useful glossary, which is well written and easy to follow. The Proteus effect gives an overview of the evolution of stem cell research and its application in providing cell-based therapies. It should be a useful book for anyone trying to gain insight into stem cell research as a whole, including its political and social ramifications. Version 1 July 1, No description Article tools.

Chapter 7 : REGEN Medicine University - Stem Cells Made Simple Course

Despite their medical promise, stem cells have been dogged by political and ethical controversy because some are derived from discarded human embryos, and because of fears and confusion about.

Where can I get more information? What are stem cells, and why are they important? Stem cells have the remarkable potential to develop into many different cell types in the body during early life and growth. In addition, in many tissues they serve as a sort of internal repair system, dividing essentially without limit to replenish other cells as long as the person or animal is still alive. When a stem cell divides, each new cell has the potential either to remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain cell. Stem cells are distinguished from other cell types by two important characteristics. First, they are unspecialized cells capable of renewing themselves through cell division , sometimes after long periods of inactivity. Second, under certain physiologic or experimental conditions, they can be induced to become tissue- or organ-specific cells with special functions. In some organs, such as the gut and bone marrow, stem cells regularly divide to repair and replace worn out or damaged tissues. In other organs, however, such as the pancreas and the heart, stem cells only divide under special conditions. Until recently, scientists primarily worked with two kinds of stem cells from animals and humans: The functions and characteristics of these cells will be explained in this document. Scientists discovered ways to derive embryonic stem cells from early mouse embryos more than 30 years ago, in The detailed study of the biology of mouse stem cells led to the discovery, in , of a method to derive stem cells from human embryos and grow the cells in the laboratory. These cells are called human embryonic stem cells. The embryos used in these studies were created for reproductive purposes through in vitro fertilization procedures. When they were no longer needed for that purpose, they were donated for research with the informed consent of the donor. In , researchers made another breakthrough by identifying conditions that would allow some specialized adult cells to be "reprogrammed" genetically to assume a stem cell-like state. This new type of stem cell, called induced pluripotent stem cells iPSCs , will be discussed in a later section of this document. Stem cells are important for living organisms for many reasons. In the 3- to 5-day-old embryo, called a blastocyst , the inner cells give rise to the entire body of the organism, including all of the many specialized cell types and organs such as the heart, lungs, skin, sperm, eggs and other tissues. In some adult tissues, such as bone marrow, muscle, and brain, discrete populations of adult stem cells generate replacements for cells that are lost through normal wear and tear, injury, or disease. Given their unique regenerative abilities, stem cells offer new potentials for treating diseases such as diabetes, and heart disease. However, much work remains to be done in the laboratory and the clinic to understand how to use these cells for cell-based therapies to treat disease, which is also referred to as regenerative or reparative medicine. Scientists are already using stem cells in the laboratory to screen new drugs and to develop model systems to study normal growth and identify the causes of birth defects. Research on stem cells continues to advance knowledge about how an organism develops from a single cell and how healthy cells replace damaged cells in adult organisms. Stem cell research is one of the most fascinating areas of contemporary biology, but, as with many expanding fields of scientific inquiry, research on stem cells raises scientific questions as rapidly as it generates new discoveries.

Chapter 8 : Stem Cells: MedlinePlus

Their indefinite proliferation potential promises to overcome the limited supply of tissue-specific cells and adult stem cells. However, substantial hurdles related to their safety must be overcome for these cells to be clinically applicable.

Reprogramming A scheme of the generation of induced pluripotent stem IPS cells. Red cells indicate the cells expressing the exogenous genes. The original set of reprogramming factors also dubbed Yamanaka factors are the transcription factors Oct4 Pou5f1 , Sox2 , cMyc , and Klf4. While this combination is most conventional in producing iPSCs, each of the factors can be functionally replaced by related transcription factors, miRNAs , small molecules, or even non-related genes such as lineage specifiers. However, considerable advances have been made in improving the efficiency and the time it takes to obtain iPSCs. Upon introduction of reprogramming factors, cells begin to form colonies that resemble pluripotent stem cells, which can be isolated based on their morphology, conditions that select for their growth, or through expression of surface markers or reporter genes. They chose twenty-four genes previously identified as important in ESCs and used retroviruses to deliver these genes to mouse fibroblasts. The fibroblasts were engineered so that any cells reactivating the ESC-specific gene, Fbx15 , could be isolated using antibiotic selection. Upon delivery of all twenty-four factors, ESC-like colonies emerged that reactivated the Fbx15 reporter and could propagate indefinitely. To identify the genes necessary for reprogramming, the researchers removed one factor at a time from the pool of twenty-four. By this process, they identified four factors, Oct4, Sox2, cMyc, and Klf4, which were each necessary and together sufficient to generate ESC-like colonies under selection for reactivation of Fbx These second-generation iPSCs were derived from mouse fibroblasts by retroviral-mediated expression of the same four transcription factors Oct4, Sox2, cMyc, Klf4. However, instead of using Fbx15 to select for pluripotent cells, the researchers used Nanog , a gene that is functionally important in ESCs. Additional genes, however, including certain members of the Klf family Klf1, Klf2, Klf4, and Klf5 , the Myc family c-myc, L-myc, and N-myc , Nanog , and LIN28 , have been identified to increase the induction efficiency. While Sox2 was the initial gene used for induction by Yamanaka et al. Sox1 yields iPS cells with a similar efficiency as Sox2, and genes Sox3 , Sox15 , and Sox18 also generate iPS cells, although with decreased efficiency. Klf4 of the Klf family of transcription factors was initially identified by Yamanaka et al. However, Thomson et al. Klf2 and Klf4 were found to be factors capable of generating iPS cells, and related genes Klf1 and Klf5 did as well, although with reduced efficiency. The Myc family of transcription factors are proto-oncogenes implicated in cancer. N-myc and L-myc have been identified to induce instead of c-myc with similar efficiency. Therefore, it was surprising when Yamanaka et al. LIN28 is an mRNA binding protein [21] expressed in embryonic stem cells and embryonic carcinoma cells associated with differentiation and proliferation. It poses numerous advantages when used instead of C-myc. However, recently a path was found for efficient reprogramming which required downregulation of the nucleosome remodeling and deacetylation NuRD complex. Plasmids , adenoviruses , and transposon vectors have all been explored, but these often come with the tradeoff of lower throughput. Depending on the methods used, reprogramming of adult cells to obtain iPSCs may pose significant risks that could limit their use in humans. For example, if viruses are used to genomically alter the cells, the expression of oncogenes cancer-causing genes may potentially be triggered. In February , scientists announced the discovery of a technique that could remove oncogenes after the induction of pluripotency, thereby increasing the potential use of iPS cells in human diseases. This is particularly challenging because the genome-wide epigenetic code must be reformatted to that of the target cell type in order to fully reprogram a cell. However, three separate groups were able to find mouse embryonic fibroblast MEF -derived iPS cells that could be injected into tetraploid blastocysts and resulted in the live birth of mice derived entirely from iPS cells, thus ending the debate over the equivalence of embryonic stem cells ESCs and iPS with regard to pluripotency. Rows of similar colors represent studies that used similar strategies for reprogramming. This timeline summarizes the key strategies and techniques used to develop iPS cells in the

first five years after Yamanaka et al. Alternative approaches[edit] Mimicking transcription factors with chemicals[edit] One of the main strategies for avoiding problems 1 and 2 has been to use minute compounds that can mimic the effects of transcription factors. These molecule compounds can compensate for a reprogramming factor that does not effectively target the genome or fails at reprogramming for another reason; thus they raise reprogramming efficiency. They also avoid the problem of genomic integration, which in some cases contributes to tumor genesis. Key studies using such strategy were conducted in A similar type of compensation mechanism was proposed to mimic the effects of Sox2. In , Ding et al. They used a cocktail of seven small-molecule compounds including DZNep to induce the mouse somatic cells into stem cells which they called CiPS cells with the efficiency â€" at 0. The CiPS cells were introduced into developing mouse embryos and were found to contribute to all major cells types, proving its pluripotency. Adding a third compound known to be involved in the cell survival pathway, Thiazovivin further increases the efficiency by fold. Using the combination of these three compounds also decreased the reprogramming process of the human fibroblasts from four weeks to two weeks. Alternate vectors[edit] Another key strategy for avoiding problems such as tumor genesis and low throughput has been to use alternate forms of vectors: In , Hochedlinger et al. The adenovirus is unique from other vectors like viruses and retroviruses because it does not incorporate any of its own genes into the targeted host and avoids the potential for insertional mutagenesis. Also in , Yamanaka et al. Although the plasmid methods avoid viruses, they still require cancer-promoting genes to accomplish reprogramming. The other main issue with these methods is that they tend to be much less efficient compared to retroviral methods. Furthermore, transfected plasmids have been shown to integrate into the host genome and therefore they still pose the risk of insertional mutagenesis. Because non-retroviral approaches have demonstrated such low efficiency levels, researchers have attempted to effectively rescue the technique with what is known as the PiggyBac Transposon System. Several studies have demonstrated that this system can effectively deliver the key reprogramming factors without leaving footprint mutations in the host cell genome. The PiggyBac Transposon System involves the re-excision of exogenous genes, which eliminates the issue of insertional mutagenesis. Stimulus-triggered acquisition of pluripotency In January , two articles were published claiming that a type of pluripotent stem cell can be generated by subjecting the cells to certain types of stress bacterial toxin, a low pH of 5. Measuring variations in microRNA expression in iPS cells can be used to predict their differentiation potential. Several mechanisms have been proposed. Induced pluripotent stem cells are similar to natural pluripotent stem cells, such as embryonic stem ES cells , in many aspects, such as the expression of certain stem cell genes and proteins, chromatin methylation patterns, doubling time, embryoid body formation, teratoma formation, viable chimera formation, and potency and differentiability, but the full extent of their relation to natural pluripotent stem cells is still being assessed. Cellular biological properties Morphology: Each cell had round shape, large nucleolus and scant cytoplasm. Doubling time and mitotic activity are cornerstones of ESCs, as stem cells must self-renew as part of their definition. The presence of catecholamine -associated enzymes may indicate that iPSCs, like hESCs, may be differentiable into dopaminergic neurons. Stem cell-associated genes were downregulated after differentiation. Teratomas are tumors of multiple lineages containing tissue derived from the three germ layers endoderm , mesoderm and ectoderm ; this is unlike other tumors, which typically are of only one cell type. Teratoma formation is a landmark test for pluripotency. The hollow trophoblast is unable to form a living embryo, and thus it is necessary for the embryonic stem cells within the embryoblast to differentiate and form the embryo. Chimeric living mouse pups were created: Widespread methylation of a gene interferes with expression by preventing the activity of expression proteins, or by recruiting enzymes that interfere with expression. Thus, methylation of a gene effectively silences it by preventing transcription. Human iPS cells are highly similar to ES cells in their patterns of which cytosines are methylated , more than to any other cell type. However, on the order of a thousand sites show differences in several iPS cell lines. Half of these resemble the somatic cell line the iPS cells were derived from, the rest are iPSC-specific. Tens of regions which are megabases in size have also been found where iPS cells are not reprogrammed to the ES cell state. Histones are compacting proteins

that are structurally localized to DNA sequences that can affect their activity through various chromatin-related modifications. Safety[edit] The major concern with the potential clinical application of iPSCs is their propensity to form tumors. Teratoma formation is considered a major obstacle to stem-cell based regenerative medicine by the FDA. A more recent study on motor functional recovery after spinal cord injuries in mice showed that after human-induced pluripotent stem cells were transplanted into the mice, the cells differentiated into three neural lineages in the spinal cord. The cells stimulated regrowth of the damaged spinal cord, maintained myelination, and formed synapses. These positive outcomes were observed for over days after the spinal cord injury, without tumor formation. All the genes that have been shown to promote iPSC formation have also been linked to cancer in one way or another. Some of the genes are known oncogenes, including the members of the Myc family. A non-genetic method of producing iPSCs has been demonstrated using recombinant proteins, but its efficiency was quite low. Other approaches such as using adenovirus or plasmids are generally thought to be safer than retroviral methods. An important area for future studies in the iPSC field is directly testing iPSC tumorigenicity using methods that mimic the approaches that would be used for regenerative medicine therapies. Such studies are crucial since iPSCs not only form teratoma, but also mice derived from iPSCs have a high incidence of death from malignant cancer. When a similar procedure was performed on genetically equivalent ES cells however, Zhou et al. They took cells from a chimera that had been grown from IPSC clones and a mouse embryo, this tissue was then transplanted into syngenic mice. Findings indicate that there was no significant difference in the immunogenic response produced by the IPS cells and the ES cells. Furthermore, Araki et al. Recent achievements and future tasks for safe iPSC-based cell therapy are collected in the review of Okano et al. A key tradeoff to overcome is that between efficiency and genomic integration. Most methods that do not rely on the integration of transgenes are inefficient, while those that do rely on the integration of transgenes face the problems of incomplete reprogramming and tumor genesis, although a vast number of techniques and methods have been attempted. Another large set of strategies is to perform a proteomic characterization of iPS cells. One approach might attempt to combine the positive attributes of these strategies into an ultimately effective technique for reprogramming cells to iPS cells. Another approach is the use of iPS cells derived from patients to identify therapeutic drugs able to rescue a phenotype. For instance, iPS cell lines derived from patients affected by ectodermal dysplasia syndrome EEC , in which the p63 gene is mutated, display abnormal epithelial commitment that could be partially rescued by a small compound [65] Disease modelling and drug development[edit] An attractive feature of human iPS cells is the ability to derive them from adult patients to study the cellular basis of human disease. Since iPS cells are self-renewing and pluripotent, they represent a theoretically unlimited source of patient-derived cells which can be turned into any type of cell in the body. This is particularly important because many other types of human cells derived from patients tend to stop growing after a few passages in laboratory culture. Managed by the University of Oxford , the effort pooled funds and resources from 10 pharmaceutical companies and 23 universities. The goal is to generate a library of 1, iPS cell lines which will be used in early drug testing by providing a simulated human disease environment.

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It is widely understood that stem cell treatments have the potential to revolutionize medicine. Doctors and medical researchers think, for example, that it could be possible to develop stem cell-based treatments for such diseases as chronic heart disease, Type I diabetes, and Parkinson's disease.