

Induced pluripotent stem cells essay



Specifically focusing on terminally differentiated somatic cells, scientists are now able to induce pluripotency thanks to the findings from Sir John B. Gordon, and Shinya Yamanaka. Findings from Gordon's paper inform us that all cells in an organism contain the same genetic information. The difference in gene expression leads to one cell type over another. This implies that somatic cells should have the ability to give rise to a variety of cell types under the appropriate conditions because all of the cells have the same DNA content. Findings from Handyman's paper tell us that the factors responsible for the maintenance of pluripotency in early embryos and embryonic stem cells are also responsible for inducing pluripotency in somatic cells. The factors from Handyman's discovery are OCT-3/4, KLF4, SOX2, and c-MYC; these four transcription factors work together to effectively induce pluripotency and have greatly advanced the technological applications of genetic reprogramming. The field of regenerative medicine has especially benefited from the genetic reprogramming advances.

One of the main goals of regenerative medicine is to restore structures of damaged tissues as well as to restore functions of damaged organs. A major application for regenerative medicine is in the field of cardiovascular medicine. The use of regenerative medicine for cardiovascular disease treatment is appealing because it is much less invasive than transplantation and open-heart surgery.

In order to determine which combination of transcription factors are able to create normal cell fates from the damaged cardiac tissue, induced pluripotent stem cells are an intricate part of the drug screening technique often used. The drugs capable of inducing pluripotency and repairing the damaged

tissue have the potential to treat cardiovascular disease in human patients. Alternative options for repairing damaged tissue include transplantation of new organs from donors.

Cardiovascular diseases continue to account for the leading cause of death in America. Due to the high frequency of deaths caused by heart malfunctions in society, researchers are constantly trying to discover new ways for treatment and prevention. Despite the alternative methods used to treat cardiovascular diseases, the use of induced pluripotent stem cells for regenerative medicine is overall beneficial to the field of cardiovascular medicine because it is a less invasive option that can effectively restore wounded cardiac tissue by replacing cardiologists and reducing occurrences of fibrosis (Upon, 2011). Using induced pluripotent stem cells is a much less invasive means for cardiovascular repair than other options, such as transplanting an entire heart. Before regenerative medicine had the clinical potential it currently possesses, scientists first needed to have a comprehensive understanding of the heart and its development processes. Muscle tissue in the heart is referred to as cardiac muscle. One cell type that encompasses cardiac muscle is the cardiomyocyte. Each mature adult cardiomyocyte only contains a single, unique nucleus and expresses cardiac transcription factors, which allows for their calcium ion handling and interaction properties (Upon, 2011). Normally, these adult cardiomyocytes cannot regenerate once damaged (Upon).

This leads to the malfunction or loss of function within the heart, causing many of the heart conditions prevalent in society. Studies show that induced pluripotent stem cells can differentiate into the three electroencephalographic

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phenotypes of cardiologists: nodal, atrial, and ventricular (Upon, 2011). In a functioning human heart, nodal cardiologists are found at the bottom, atrial cardiologists pump blood in, and ventricular cardiologists pump blood out to the lungs and the rest of the body.

Each phenotype shows that suppositories can successfully increase the rate of contraction while ceremonially can decrease the rate of contraction (Upon). Ellen Peon's review paper explains that the function of cardiologists in the heart is to perform the contraction for blood flow. More importantly, it explains that the presence of specific chemicals, suppositories and ceremonially, effects the speed of contraction.

Peon's findings about the specifics of heart contractions are extremely beneficial information in terms of regenerative medicine applied to cardiovascular diseases because a heart that is uncontrollably pumping too fast or too slow has the potential to be regulated simply by adding either suppositories or ceremonially concentrations to the environment. Both chemicals could be studied further to determine if a drug design involving the two is reasonable for treatment. Even though using induced pluripotent stem cells to generate heart tissue is less invasive, there are drawbacks to be looked into further by researchers. In the review paper, Upon notes that cardiologists derived from induced pluripotent cells are immature functionally and structurally. This is problematic because at immature stages, the electrical properties of the cardiologists are similar to that of those of heart failure. It was also observed that the induced cardiologists were about ten times smaller than the normal adult cardiologists. Most importantly, the safety and practical worth of the induced cardiologists is unknown because

there is not a lot of information about the amphibology of these cells.

Downsides noted in Samurai's paper include the large-scale preparation that goes into creating these induced cardiologists and the elimination of undifferentiated induced allurements stem cells from generating the cardiologists.

With all that being said, there is promising potential for using regenerative medicine as a less invasive means to treat cardiovascular diseases. An alternate method used to bypass these downfalls is the cell-sheet technique. This technique involves harvesting a sheet of undamaged cells and transplanting them directly on top of the injured organ. The idea is that the undamaged cells will essentially promote recovery of the organ's wounded cells. Kumara and others illustrate the efficacy of induced plenteous stem cell derived cardiologists whets.

After chemic cardiopulmonary, the induced cardiologists sheets were able to improve cardiac function (Kumara, 2011 Chemic cardiopulmonary is when there is a lack of oxygen supply to the heart muscle tissue, causing measurable deterioration of it function. Sheets of cardiologists capable of restoring tissue after being deteriorated is a feasible option for treating chemic cardiopulmonary. However, this is still invasive for the patient and tissue is still be removed from one location and transplanted to another.

Inducing regenerative cardiologists is still a much sees invasive option to restore cardiac tissue. As previously mentioned, there is not a lot of regenerative potential for heart tissue once it has been wounded. One of the reasons for this is due to the activation of cardiac fibroblasts (Song 2012). A

cardiac fibroblast is a particular heart cell type that is responsible for maintaining the structural integrity of connective tissues. Activation of these fibroblasts leads to cardiac fibrosis (Song, 2012), which is simply the formation of excess connective tissue in the hearts.

It is the fibrosis that interferes with regeneration of cardiac cells causing a number of problems like the loss of contractile function and the increased susceptibility to arrhythmias (Song 2012). But because most of the cells of the heart are in fact cardiac fibroblasts, they are a potential regenerative medicinal source of cardiac function restoration. One major success of regenerative medicine as it relates to cardiovascular medicine is the repair of heart tissue by reprogramming. This was first performed by Kohn and Song along with other researchers. Song's paper shows that GATA, Hand, ME-FCC, and TPTB are able to reprogram mouse cardiac fibroblasts into contracting cardiac-like cells in vitro and in vivo. The discovery of these essential cardiac inducing factors can act as the platform for answering more fundamental research questions in the future.

Data from Song's research illustrate that the expression of these four transcription factors enhances cardiac function while decreasing adverse ventricular remodeling following infarction. Findings from this study shows that the efficiency of reprogramming to induced cardiac-like cells using GATA, Hand, MFC, and TPTB is comparable to the reprogramming of induced pluripotent stem cells by the Yamanaka factors (Song). The method of retrovirus transduction was used to incorporate the transcription factors into the genome of the non-mouse in order to bring the cells back to a pluripotent state. Although viral and retrovirus transduction is a convenient

method to incorporate new DNA sequences, there are drawbacks that may be adversely affecting outcomes of the induced pluripotent cells. There are a couple of key disadvantages using viruses and vectors to incorporate DNA into a host's genome. One disadvantage is the genomic integration that occurs with retrovirus vectors. Genomic integration involves inserting DNA sequences directly into the host's cell's DNA. The problem is that vectors integrate near the starting point of transcription causing either enhanced transcription more than normal or this can disrupt transcriptions.

The results from both outcomes are altered expression due to the technique used rather than the genetic information present. The likelihood of residual transgene expression is another disadvantage to using vectors as a means of incorporating new DNA sequences. Residual transgene expression is when genetic material from one organism remains after it is transferred leading to the protein synthesis with the contents of the lingering DNA.

Because of drawbacks to using vector methods, such as genomic integration and residual transgene expressions, research has been done to find alternative methods that are as practical in a clinical setting. A successful alternative to retrovirus transduction involves virus-free integration methods.

In relation to cardiovascular medicinal applications, cardiologists have been successfully derived from virus-free induced pluripotent cells. Shih et al. and others demonstrate that virus-free induced pluripotent stem cells are able to differentiate into cardiologists with the characteristic cardiac-specific properties. The induced cardiologists showed thick and thin filaments of muscle proteins, as expected to be seen in normal adult cardiologists (Shih et al., 2001). Additionally, the induced cardiologists expressed calcium ion

handling and ion channel proteins, which further confirms the heart tissue development. Overall, the virus-free methods are preferred over retrovirus vector methods in clinical settings because the outcomes have less harmful potential in vivo.

Despite some of the critical downfalls discussed, it is clear that the use of induced pluripotent stem cells for regenerative medicine is ultimately useful to the field of cardiovascular medicine because it is a less invasive option that effectively restores wounded cardiac tissue by inducing cardiologists and reducing occurrences of fibrosis (Upon, 2012). Peon's paper shows that in the presence of suppositories and ceremonially, cardiologists contraction rates are affected. Drug designers working to create heart-regulatory drugs to control abnormalities in heartbeats now have more information to work with.