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Human Stems Cells Used in Tissue Regeneration

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In recent years stem cells have been the subject of many experiments and research projects. It has long been known that stem cells have the ability to differentiate into many different cells; but not much was known about where to obtain these miracle cells. The most immediate answer was Embryonic Stem Cells (ESC) however; recent discoveries have broadened our understanding of stem cells and the multiple tissues and organs that they can be harvested. The possibilities for uses of stem cells are seemingly endless, ranging from bone regeneration, treatments for many cancers and diseases, and many more (Estrela *et al.*, 2011). Much is still to be discovered about stem cells however, promising discoveries are being made in the field of tissue regeneration in the form of wound closure, dental regeneration, and bone regeneration. Stem cells are being used paired with special scaffolds that may soon be able to be used as replacements for lost teeth and bones. Tissue regeneration using stem cells shows promising implications in neurodegenerative diseases such as Parkinson's and Alzheimer's disease (Vakhrushev et al., 2012). Much research is still to be done as tissue regeneration has only been done on a small scale in labs, with little or no *in vivo* experiments being done yet.

Introduction

Chronic wounds have been a problematic ailment for both physicians and patients alike, but what if there was a solution that could be applied topically or injected into or near the wound that could finally heal the wound for good. For many reasons including injury and disease many people struggle with tooth lose, but what if dentures could be a thing of the past, if actual teeth could be grown in place of those lost. And what if vital tissues that are degenerated due to diseases such as heart attacks, Parkinson's or Alzheimer's could be regenerated and people cured. These are the problems that are being addressed with recent stem cell research. With the recent discoveries many innovative "therapeutic strategies" that are geared toward tissue regeneration are being developed. Stem cells provide the ideal cells for this research as they have the ability to self-renew and are capable to differentiating into many different cell types (Estrela *et al.*, 2011). There are however different sources of stem cells that all yield different types of stem cells all with their own regenerative possibilities, so the questions is which stem cells are the best to use in the clinical field in respect to tissue regeneration.

Multiple forms of stem cells

Many times when people think of stem cells the initial thought is embryonic stem cells. Embryonic stem cells were appealing to researchers because they are pluripotent which means that they can become almost any type of cell (Falanga). However legal and ethical difficulties arose from the method of harvesting these cells that often involved destroying an embryo. These problems would soon be resolved with the discovery of many different sources of human stem cells. It has been discovered that an easy to harvest, readily available source of stem cells could be found in human teeth. In fact like bone marrow, human teeth contain mesenchymal stem cells (MSC), which are multipotent cells that can generate into many different cell types depending on the environment in which they are grown (Estrela *et al.*, 2011). The stem cells are found more specifically in the dental pulp, or inner soft part of the tooth, and many of the teeth used are

naturally shed teeth stored in a special medium that will support the stem cells until harvesting. Stem cells have since been found to reside in nearly all living tissues, although not all sources have been utilized as harvesting sites (fig. 1), however, this paper will focus on the recent progress of using dental pulp stem cells (Inanc *et al.*, 2011).

Source of Stem Cell	Multipotent vs Pluripotent	Successfully Harvested for Research
Embryo	Pluripotent	Yes
Cord Blood	Pluripotent	Yes
Dental Tissue	Multipotent	Yes
Adipose Tissue	Multipotent	Limited
Bone Marrow	Multipotent	Yes

Table 1. Although many sources have been identified not all have been successfully harvested.

Recent Progress

Now that stem cells were readily available, the research could be expanded and ideas could really start. Of the many types of stem cells perhaps the most utilized is stem cells from dental tissue. Many things including the accessibility and multipotent ability make the stem cells from dental pulp an "attractive source" for research in tissue regeneration. Dental pulp stem cells (DPSC) are able to be reprogrammed into many different cell types including myocytes, neurocytes, and osteoblast (Estrela *et al.*, 2011). Another type of stem cells called SHED cells harvested from exfoliated human deciduous teeth have a promising future in tissue regeneration as they have recently been used paired with a polylactoglycolide scaffold to engineer bone tissue that will in the future have implications for replacing bones lost to injury or disease. This was done by a process of first harvesting the cells from naturally shed human teeth, fixing the cells to the polylactoglycolide scaffold material by incubating in a carbon dioxide incubator for 45 minutes then the newly fixed cells were immersed in growth medium for 2 weeks. After two short weeks the cells showed signs of osteogenic differentiation. This experiment was transferred to an *in vitro* experiment when the scaffold were placed subcutaneously in mice and analyzed after one month. The findings were that not only did the stem cells again show osteogenic differentiation but the surrounding cells showed a change in the osteocalcin expression. Osteocalcin, being a protein involved in the formation of bone (Vakhrushev *et al.*, 2012).

Chronic wound healing is another field that is set to advance from stem cell research. Many patients have problems with wounds that for one reason or another will not heal despite traditional treatments. This field focuses on using multipotent stem cells harvested from multiple sources that can differentiate into different cell types when cultured in specific conditions. These cells are showing promising potential in the field of wound healing and may even decrease scarring. By applying the cells topically to the wound the thought is that the stem cells may "teach" the damaged tissue how to properly differentiate until the wound is healed. It is also believed that after application to the wound that the newly applied stem cells may recruit stem cells tissue differentiating cells that are naturally circulating throughout the body (Falanga). Although the exact method of how the stem cells are aiding in tissue repair is not known it is apparent that multipotent stem cells have a promising future in the world of wound healing.

Discussion

Problems with research in tissue regeneration

Although the thought of being able to "grow" tissue or even organs in a laboratory is a dream of many physicians and patients alike, realistically there are still much more research that needs to be done and much more progress that must be made before this dream can be a reality. Even though researchers have found multiple sources for stem cells such as dental pulp, adipose tissues, or even embryonic there is still a great problem in obtaining the quantities needed to do the large scale research that is necessary to make progress. It is also apparent that in one study with chronic wound repair using stem cells that it may be necessary to apply "at least one million autologous stem cells per cm^2 of wound surface" which is a large amount of cells for one treatment to one patient (Falanga). There is also an issue with ensuring that once stem cells are implanted into a certain area that they will indeed differentiate into the desired tissue. One researcher states that "the efficacy of the implanted stem cell-derived populations…is less tangible and remains a controversial issue" (Inanc). Controversial because some of the areas that are prospects for repair by stem cells are tissues that are vital to survival such as the heart or even the brain of accident victims or Alzheimer's patients. So potential patients and their families, as it stands right now, would have to decide if it is worth the risk of having the implanted stem cells differentiate into the wrong tissue type which could potentially cause death. Along with these problems there is a large cost associated with stem cell research, a cost that is not likely to lessen as these treatments are transferred from experimental to actual clinical use, then the cost will be transferred to the public and to insurance companies should they chose to cover such sometimes unconventional treatment option.

Future clinical uses of stem cells in tissue regeneration

Although there are many grandiose ideas associated with the many uses of stem cells, many are still just that, ideas. There are many *in vitro* studies going on today that show promising outcomes however, when these studies are transferred into animal *in vivo* studies there has been some difficulty assessing the effectiveness of stem cell treatments. The field of stem cell research is a young field that has yet to be even mildly explored and there will be much to see from this research. There is hope that in the future stem cells may be used to "grow" replacement organs for transplant into diseased or injured patients. With this hope however, one has to question what type of ethical and legal issues associated with this idea. Who would be eligible for these transplants, would say a 100 year old patient be given a new heart or the town drunk who has many tickets for drunk driving be given that new liver. How would you price these things and would insurance cover the cost, or is it something that would be reserved for the wealthy. These are just some questions that can arise with such medical advances. But perhaps the big question is although the thought of being able to replace any organ that threatens to fail would it create more problems than solutions.

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