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Stem-Cell Teeth Implant

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ABSTRACT: The primary objective of this research is to investigate the major advantages of stem cell dental implants alongside their role in tooth regeneration and their potential to replace the already existing dental implant method. Dental implants are considered the latest teeth replacement technology in the 20th century. Despite its obvious purpose, the treatments are still uncommon due to their extensive healing process and other potential risks regarding infections. On the account of these concerns, scientists are looking into new possibilities of teeth replacement treatment and therapy. Stem cell therapy is commonly used for treating diseases by replacing tissues that are damaged due to injuries or diseases. Stem cells are unspecialized cells and are capable of diving and regrowing themselves. Due to these properties, stem cell dental implants are now considered to be a new alternative to teeth implants.

KEYWORDS: Dental Implants, Oral Tissues Regeneration, Stem Cells, Stem Cells Therapy, Tooth Regeneration.

1. INTRODUCTION

1.1 Introduction to Stem Cells

Stem cells are distinct cells that can differentiate into numerous types of cells, as needed by the body [1]. Human bodies require a wide range of cells to survive and operate effectively, but not all of these cells are innately generated in their complete, mature state [2]. As a result, stem cells have the potential to proliferate and transform into other cell types that the body lacks. These operate as a body's recovery system [3]. The capability of stem cells to proliferate and specialize into different cell types degrades as they age [4]. However, once a stem cell's differentiation route has been determined, it can no longer transform into another type of cell on its own [5]. For example, in the embryo, stem cells divide and cause the formation of various organs of the body. With the ability to divide, stem cells are being studied for the treatment of various diseases called stem cell therapy.

Dental stem cells are a subset of mesenchymal stem cells found in specific dental tissues like the apical papilla, dental pulp, dental follicle, and periodontium [6]. Studies have found that mouth tissues are a source of stem cells. Tissue regeneration has been demonstrated in dental tissues to replace bone degradation caused by diseases such as severe cavities and fractures that cannot be addressed with dental implants. Therefore, dental regenerative medicine employs stem cell therapy [7].

1.2 Types of Stem Cells

Stem cells are grouped into three main types which include Adult Stem Cells (ASCs), Embryonic stem cells (ESCs), and Induced Pluripotent Stem Cells (iPSACs) [8].

- Segregated from properly matured tissues, Adult Stem Cells (ASCs) have the ability to convert into a wide range of cell types, although not all of them [9]. For instance, adult stem cells derived from the blood can only be altered into different types of blood cells [10].
- Embryonic Stem Cells (ESCs) can grow into any form of specialised cell or tissue in the body. This might lead to new medical technologies and systems that can develop tissues or organs to substitute decaying ones [11].
- Induced Pluripotent Stem Cells (iPSACs) are converted from a diversity of somatic and stem cells. It is important to note that this type of cell could be utilised to generate disease-specific tissues in individuals as well as medication evaluation [12].

1.3 Dental Implants

The substitution of tooth roots with screw-like posts, metallic, along with the replacement of injured or absent teeth with simulated teeth that appear and operate similarly to natural teeth are involved in dental implants. As a consequence, dental implant surgery can be a viable substitute for ill-fitting bridgework or dentures. When the genuine teeth roots are insufficient to construct

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bridgework or dentures teeth replacements, it can also be a useful alternative [13]. Surgeons will implant a screw-like component further into the jawbone, that will function as an anchor for a crown, which is a synthetic tooth [14]. Focusing on the advantages of dental implants, articles show that they function identically to natural teeth. Moreover, they help to avoid bone deterioration and maintain the stability of adjoining teeth [15]. On the other hand, there are disadvantages to dental implants, such as failures due to mechanical failure, fragments in the dental crown, and far more costly than other kinds of medication [16].

1.4 Role of Stem Cells in Dental Implants

The demand for cosmetic and functional dental implant treatments is on the rise at the present. In the field of prosthodontics, new technologies that allow for significant alveolar ridge augmentation are gaining a lot of interest.[17] To develop the osseointegration of load-bearing implants, various ceramic, metallic, and hybrid scaffolds have been utilized. Implant malfunction investigations, on the other hand, analyses a significant rate of interfacial failure due to inadequate implant tissue integration and osteolysis, as well as a mismatch in modulus. Currently, stem cells are being considered for implant site augmentations.[18] Teeth are integrated organs with two distinct particular hard tissues, enamel and dentine, which configure a unified attachment complex alongside bones via a particularised (periodontal) ligament. They are ectodermal organs that progress through reciprocal interactions among oral epithelial cells (ectoderm) and mesenchymal cells originating from the cranial neural crest. The epithelial cells create ameloblasts that make enamel, while the mesenchymal cells generate all other differentiated cells.[19] Elderlies are often prone to tooth loss. One-quarter of people aged 65 and over (26%) have 8 or lesser numbers of teeth. About one-sixth of adults aged 65 or older (17%) have lost all of their teeth. Total tooth loss between grown-ups aged 65 or older decreased by more than 30% from 27% in 1999–2004 to 17% in 2011–2016.[20] Tissue engineering treatments and stem cells have promise for accomplishing alveolar bone regeneration, repairing crucial periodontal tissue abnormalities, and eventually replacing a missing tooth. Salivary glands, tongues, skeletal muscles, and temporomandibular joint condylar cartilage are organs and tissues that will be applied in regenerative dental medicine [21].

2. STEM CELLS SOURCES AND THEIR LABORATORY GROWTH

Stem cells were established to have the ability to grow promptly and have the potential to form specialized bones, neuronal cells, and even dentin. Dental therapies regularly use neuronal stem cells for treatments. These stem cells-based dental treatments focus on healing damaged teeth, urging bone regeneration, and also treating various neural injuries. Even though a wide variety of stem cells have been categorised, stem cells still narrow down into two main types: embryonic stem cells and adult stem cells. As discussed in the introduction, stem cells have three main competences-being able to go through self-renewal, being able to generate daughter cells that have more specialized properties and being able to repopulate in a host. There are three main sources for stem cell extraction. The human umbilical cord, bone marrow, and adipose tissue. The stem cells that are normally found in human umbilical cords are hematopoietic stem cells and mesenchymal human stem cells. These stem cells can be found in the baby's umbilical cord after its birth. Hematopoietic stem cells function as red blood cells and as an immune system cell generator. Even though the mesenchymal cells are also found in the same source, their function is different. The mesenchymal cells act as a generator for bone, cartilage, and other types of tissues. It can be said that the bone marrow is the most common source of stem cells. Much like the umbilical cord, the hematopoietic stem cells and the mesenchymal stem cells can be found in the bone marrow [22]. Since the bone marrow houses the most concentrated stem cell blood, the bone marrow is considerably the best candidate for regenerative medicine and therapeutic purposes [23].

The method of growing cells in a laboratory environment is called cell culture [24]. Its clinical purpose is to introduce and create model systems that cover basic cell biology, investigate drug toxicity, and duplicate disease mechanisms. Cell culture makes it possible for scientists to manipulate molecular pathways and sample genetic substances. By these utilities, the process of growing stem cells also relies on the cell culture method [25]. Starting by isolating the human embryonic cells using the separation of its inner cell mass- the cellular mass on one side of the round embryo hollow interior forms in the blastocyst- and putting it in a laboratory dish containing culture medium [26]. A culture medium is a substance created to support the growth of microorganisms and cells, this medium is in solid, liquid, or semi-solid form [27]. Then, the cells in the dish will divide themselves, spreading all over the dish forming clonogenic adherent cell clusters with a fibroblastic morphology in vitro. The mouse cells, which are feeder cells, coat the inner surface of the dish. These cells release nutrients into the culture medium and also assist the cell's mass in attaching themselves to the dish [28].

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3. A PRECLINICAL STUDIES OF COMPLEX ORAL TISSUE AND ORGAN REGENERATION

A preclinical trial had been performed using animals since it is not yet possible to perform a clinical trial on human tissues and organs due to its complexity. These preclinical trials include the study in the field of tooth or root regeneration, salivary glands regeneration, and mandible condyle regeneration

3.1 Root or Tooth Regeneration

This preclinical trial is conducted with the goal to collect a functional tooth. This tooth will replace the tooth that had been lost and extracted out. Unlike other preclinical trials, tooth regeneration has become possible to perform clinically on humans.

3.2 Salivary Gland Regeneration

The salivary gland is an exocrine gland that contains a duct system, acini, and myoepithelial cells. Myoepithelial can be found in a thin layer in the glandular epithelium. The salivary glands are differentiated into three major types- the parotid, submandibular, and sublingual glands. Xerostomia, Sjögren's syndrome, radiotherapy, and aging are factors that can lead to the dysfunction of salivary glands [29]. With this concern in mind, scientists aim to find a way to generate stem cells. The expression of proteins and enzymes allows scientists to identify progenitor stem cells. The progenitor cells are discovered by using genetic application methods including, DNA label application to mark label-retaining quiescent cells, lineage tracing in mice, vitro floating sphere assays, and using 2-dimensional and 3-dimensional cultures of humans and rodents. The cells are capable of organ formation that can be used in salivary gland generation.

3.3 Regeneration of Mandibular Condyle

There has been a report on the regeneration of a rabbit condyle with the help of joint ultrasound. 36 rabbits are used as test subjects for this study [30]. This tissue regeneration can be one of the factors to resolve temporomandibular joint condyle defects or trauma. Due to this discovery along with future successful research, scientists are hoping to develop stem-cell-based tissue engineering for condyle [28].

4. TOOTH REGENERATION

4.1 Signaling Centers in Tooth Development

Signaling centers, necessary components of tooth development, help regulate the morphogenesis of teeth. Thus, they affect the shape and size of teeth. Initially, the molar initiation knot (IK) is required for the progression of tooth development. A study has reported that the initiation knot is an integral component of the molar development and does not contribute cells to the PEK, which proceed independently [31]. Consequently, the primary enamel knot (PEK) and the secondary enamel knot (SEK) appear, controlling the tooth crown development and determining the cusp pattern, respectively [32].

4.2 Dental Stem Cells

A study in mouse incisors found that stem cells divide slowly to form daughter cells, one remains in the cervical loop and one enters the zone of rapidly dividing inner enamel epithelial cells. In later cell division, the latter cells move and differentiate into ameloblasts that form the enamel matrix [33]. Ameloblasts regulate the enamel development and mineralization. These cells maintain intercellular connections by creating a semi-permeable barrier which can receive nutrients and ions, and also form extracellular crystals in specified conditions. Following the enamel maturation, many of them will go through apoptosis and regression [34]. The loss of ameloblasts and neighboring environment resulted in the cells incapable of repair or renewal [35].

4.3 Tooth Generation De Novo

A successful bioengineered tooth germ was reported in 2007 by recombining dissociated tooth germ cells [36]. Yet, the method was not applicable in humans since those germ cells are not accessed easily [32]. Another method, induced pluripotent stem cells or iPSCs, is then suggested. By human iPSCs pre-differentiating into epithelial sheets and responding to odontogenic signals from embryonic dental mesenchyme, iPSCs in humans are able to contribute to tooth generation. The resulting teeth contain cells that are similar to human enamel and ameloblast [37].

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CASE STUDY

A study in 2016, including 8 patients with 3 men and 5 women aged 45 to 67, evaluated the effectiveness and harmlessness of MSC-CM in a human clinical trial for alveolar bone regeneration. The patients were partially edentulous but incapable of conventional removable dentures. The procedures included maxillary sinus floor elevation or SFE, socket preservation or SP, and guided bone regeneration or GBR. Cases were reported with newly formed bone, and the bone ingrowth into the metal implant was good. No patient had abnormal swelling or delayed healing after the surgery, but infiltration of inflammatory cells was spotted. The study showed the potential of transplantation of stem cells for treating both periodontal regeneration and other systemic diseases. However, another clinical trial with a larger patient group is still required since the study had a limited number of patients [38].

CONCLUSION

Stem cells are capable of differentiating into a range of cell types as the body requires. Although there are some limitations to stem cells, they are the body's recuperation system. Stem cells are extracted from various sources including the umbilical cord, the bone marrow, and the adipose tissues. The properties of stem cells' tissue regeneration will be applied to the treatment of a variety of oral disorders caused by irreversible bone degradation. Stem cells are mainly divided into three major types, consisting of, adult stem cells, embryonic stem cells, and induced pluripotent stem cells. After stems cells are extracted from their sources, scientists often manipulate them to regenerate before they are ready for medical applications. The process of regenerating stem cells, also known as culture, is done in the laboratory. Culture allows scientists to manipulate molecular pathways and sample genetic substances. Through the process of isolating the human embryonic cells, the self-division of the cells, and the cells spreading vastly over the dish, scientists are able to regenerate new stem cells. Even though stem cells regeneration is well familiar within the scientific field, organ and oral tissue regeneration are not. However, some have already been tested in animals, these two methods are still in their preclinical studies stage, root or tooth, salivary gland, mandibular condyle are the main subjects of these preclinical studies. A recent clinical trial had been successful in testing tooth regeneration in humans. In spite of the low regeneration potential of human teeth, humans have successfully reconstructed teeth. Many experiments and research have been done to overcome drawbacks in addition to further improving the promising methods. As a result, many methods are now available for tooth regeneration. Due to this reason, scientists see the potential in using stem cells as a new alternative for dental implants. Dental implants are currently using screw-like posts and metallic which have some disadvantages. However, tissue engineering and stem cell treatments have the potential to regenerate alveolar bone, cure critical periodontal tissue defects, and eventually replace a missing tooth. Further research is suggested to use Stem Cell dental implants instead of metallic ones. A study conducted to evaluate the harmlessness and effectiveness of alveolar bone regeneration had shown the potential of transplantation of stem cells for treating periodontal regeneration and other systemic diseases.

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