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Review Article

Use of stem cells in tissue engineering and reconstruction of the maxillofacial region

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ABSTRACT

The oral and craniofacial defect reconstruction has been a daunting task for several decades. Many clinicians have attempted to switch surgical techniques in flap transfer to enhance the purposeful outcomes. In many cases, however, near total restoration of the native anatomy is not achievable. Also, the normal functional performance is not attainable, regardless of the surgical technique used. This problem is more evident within the oral and craniofacial region considering the importance of functions, such as speech, chewing, and appearance. Stem cells have attracted a growing interest within the scientific community chiefly for their ability to regenerate broken tissues and conjointly for their known potential in modulating inflammatory and immune responses. These skills have caused stem cells to be thought about as a promising strategic tool for a range of clinical maxillofacial applications. In this review, authors briefly summarize the applications of stem cells in maxillofacial surgery.

Keywords: Maxillofacial, Reconstruction, Stem cells, Tissue engineering

INTRODUCTION

Stem cells have attracted a growing interest within the scientific community chiefly for an important ability to regenerate broken tissues and conjointly for their potential in modulating inflammatory and immune responses. These skills of the stem cells have caused many human vegetative cells. It is thought about as a strategic tool for a range of clinical applications. The properties of a rather elevated proliferation potential and also the wide differentiation ability of mesenchymal stem cells (MSCs) powerfully encourages scientists to look for newer and yet undiscovered, unknown sources of these precious cells. However, their well-known characteristics are extreme malleability in production of tissues, and their ability to switch completely between different types of biological niches. This has marvelled some scientists, and at the same time, have instilled doubts in their minds about the very existence of these cells and their real nature.[1,2]

Maxillofacial oral tissues are made of a variety of cell populations which regularly express mesenchymal vegetative cell like-features. They are also endowed with the important advantage of getting obtained by a much easier access than different anatomical sites like bone

marrow. There is also another undeniable fact that in vitro isolation of these cells is extremely efficient; therefore, oral-derived MSCs are extremely pliable for analysis and clinical functions.[1,2] Many novel researchers have pondered upon the realm of oral-derived stem cells. Some have also investigated the employment of these mystic cells in the regulation of the immunologic response associated to tissues and organs transplants. Stem cells harvested from dental pulp and oral tissues are shown to induce medicine tolerance and to stop alloreactivity related to solid-organ or organic process allogeneic transplantation by suppressing T-cell proliferation.[1,3]

REVIEW OF LITERATURE

The interaction between stem cells, biomaterials and elements delivered in biological niches forms the mainstay of tissue engineering science. Oral tissues have been found to be abundant and prosperous in stem cells, both in quality and number, from exclusive sources. Stem cells from oral cavity are, without problem, easily harvestable and they have shown a generous plasticity in the direction of the predominant lineages, specifically in those lineages which are closer to bone tissues. Dental pulp stem cells (DPSCs) are the most investigated MSCs from dental tissues. However, it is well revealed by myriad researches that the oral cavity hosts a number of other stem mobile lineages. These studies have additionally reported that these DPSCs are an appropriate choice in bone tissue engineering. In particular, the newly discovered population of mesenchymal stem cells derived from human periapical infected cysts have confirmed very promising properties, which includes excessive plasticity and regenerative capacity towards bone, vascular and neural cells.[1,4]

Tissue engineering is an associated rising knowledge base field, that applies principles of life sciences and engineering towards the advent of biological substitutes that restore, maintain and improve the performance of broken and/or lost tissues.[5] In tissue engineering, scaffolds are needed to convey support to cells or different structures. Scaffolds are made from perishable materials, that could be a biocompatible product that's bit by bit reabsorbed once constituted within the body, sometimes because of protein degradation.[6]

There exist many subsequent relevant animal and human studies, within which stem cells are employed in the field of bone regeneration. All the studies mentioned hitherto, apply the principles of tissue engineering stem cells. Therefore, scaffolds like xenografts, hydroxyapatite or protein are used commonly in numerous studies. Platelet rich plasma, to exemplify, was used as a scaffold for the stem cells, and also conjointly as a graft material to judge its regeneration potential.[4,7,8]

Stem cells can be described as the cells accountable for of the basis of every organ and tissue of in the human body. They have two defining characteristics. First one is their ability to renew themselves indefinitely. This implies that they are constantly and tirelessly producing new stem cells. The second one is a rather nice and very useful capacity to differentiate, at the same time, into specialised daughter cells which can acquire remarkable and unique functions with the aid of special signals coupled to intracellular signalling cascades. The facts that specify the destiny of stem cells is encoded via the presence or absence of these signals, and additionally for their combination, location, level and timing.[9]

In general, stem cells can be divided into two subtypes: pluripotent and multipotent. The former, also known as totipotent, can differentiate into any kind of tissue in the human body. They are additionally stem cells these that are known as multipotential, which can differentiate into many distinct tissue sorts within their lineage.[10,11] In reference to the foundation of stem cells, they can be sourced from different regions. A well-known example includes the blastocyst, prior to the implantation of the embryo, together with foetal tissue. Found in most human tissues, they are derived from tissues already present by the process of regular self-renovation. Being designed to work in almost all tissues in the long run, matured stem cells are responsible for their protection and repair with the aid of changing cells which are destroyed or have been lost. Considering that adult stem cells are commonly multipotent, they might also form a limited number of cell types, corresponding to their tissues of origin.[9,12]

At present, three main classes of stem cells exist. First ones are called adult stem cells (ASCs). The second type is referred to as embryonic stem cells (ESCs). The third commonly known type is the evoked pluripotent stem cells (iPSCs).[13,14] MSCs are cells which are found in several tissue sources, like bone marrow and other tissue layers. The dedifferentiated ASCs are clonogenic and have the capability to self-renew and completely differentiate into different cell lines. There in vitro enlargement ends up in cells quite resembling fibroblast-like in morphologically. These may eventually differentiate into bone forming cells, cartilage cells, fat cells, etc.[15] The ASCs are well known and will be usually found in several adult tissues, additionally to bone marrow and tissue layer, including the orofacial tissues such as teeth, dental pulp, supporting structures, and other general tissue like fat, muscle, nervous tissues, skin, and others. The iPSCs, on the other hand, are a brand-new supply of pluripotent stem cells. These are derived from adult cells by introducing four pluripotency genes (Oct4, Sox2, cMyc, and Klf4).[14-16]

The discovery of biquinary cells expressing the standard properties of MSCs in the oral cavity, strongly shifted the scientific interest onto the dental tissues. Oral stem cells might also be effortlessly remoted from teeth extracted for orthodontic or irreversible periodontitis reasons. The clean accessibility and the abundance of extraordinarily immature cells are attracting hallmarks for oral stem cell

therapy studies.[1] Over time, a plethora of investigations have tested the life of a developing volume of stem cellular populations, with the regular capabilities of MSCs, in oral tissues. In 2000, Gronthos first showed the existence of odontogenic progenitors in person human dental pulp, which had been capable of self-renewing with an excessive proliferative charge and were able to form colonies in in vitro experiments.[16] Moreover, this populace used to be capable to reproduce dentin/pulp-like systems after transplantation into immunocompromised mice. These odontogenic precursors shared the same immunophenotype of bone marrow stromal cells (BMSCs) and had been eventually named dental pulp stem cells (DPSCs). Thus, DPSCs replicate the usual peculiarities of human stem cells. DPSCs have a huge plasticity, which is ascertained with the aid of several subsequent investigations describing the possibility to distinguish those cells into osteocytes, chondrocytes and adipocytes.[1,17]

Compared with the BMSCs isolated from long bones, BMSCs isolated from craniofacial bones show special traits and gene expression profile. This distinction is frequently attributed to most craniofacial bones sprouting up from neural crest cells. Therefore, many congenital bone diseases and syndromes solely have an effect on the craniofacial bones. This is in spite of the rather strange finding that the genes involved in causing these anomalies are expressed in other bones in the body as well. Notably, the craniofacial BMSCs proliferate faster, have improved levels of alkaline phosphatase, and shape greater tiers of compact bone in contrast with lengthy bone BMSCs.[14,18,19]

It has been proposed that the progenitor cells responsible for restore of craniofacial bony structures after damage live in the craniofacial periosteum. In addition to cells dwelling in the periosteum, craniofacial sutures contain specific MSCs called Gli11, which are quiescent stem cells capable of regenerating dura and periosteum tissue as soon as activated after sustaining injuries.[14,15] Identification of these cells might further make clear the mechanism of improvement of craniosynostosis considering that destruction of Gli11 cells in open cranial sutures consequences in premature closure of sutures.[14,20]

DISCUSSION

Bone grafting is commonly employed in the cranio-maxillofacial region. The expansibility and differentiability of stem cells in vitro, and subsequently, their exact osteogenic activity, enables the bone grafts to transplant in the vicinity of sites warranting regeneration. This is a remarkably similar property to the stem cells procured from blood extraction approaches that can be used in various maxillofacial treatments.[9,21]

A combination of autologous stem cells with all kinds of bone grafts is also commonly used. They can be used with bone graft of animal or synthetic foundation or autologous. The use of a fibrin gel like fabric that eases its nature is illustrated, as in the case of injectable bone. The use of an injectable composition consisting of adult autologous stem cells combined with platelet-rich plasma gel is also documented in a study on puppies.[9,22,23]

In maxillo-facial surgery, BMSCs are used to repair the bone tissue more frequently than the other alternative cell types. This regenerative capability of BMSCs was easily demonstrable both in experimental research and in clinical studies.

An important characteristic of MSCs is their immunosuppressive effect on T- and B-cells and killer cells which can be beneficial in the treatment of pathologies of the mesenchymal tissue and also to suppress the possible inflammatory response to additives of the tissue engineering product. Y. Yamada et al.[24] Used autologous BMSCs in their scientific and experimental research and showed high efficiency of bone disorder recovery.

In an experiment on dogs, this group of researchers created 10-mm deep bone defects on the floor of the alveolar a part of the mandible, where the bone tissue replacing materials had been implanted.[25] The following collection of experiments were performed: use of plasma enriched with platelets (PRP); BMSCs collectively with PRP; MSC of a transient tooth collectively with PRP; MSC of a dental papilla collectively with PRP; a collection without bone bone-replacing material. The degree of bone regeneration and the implant resorption turned, was tested histologically at weeks 2, 4 and 8. The control with a PRP-implant showed a low rate of bone formation, whilst the defects filled with BMSCs collectively with PRP, MSC of a transient tooth/PRP, MSC of dental papilla/PRP showed a very good magnitude of bone regeneration.[26,27]

Taking into consideration that normal bone grafting materials have no osteoinductive properties, it is challenging to accomplish the same by material/growth factor-based techniques such as bone augmentation of the acutely atrophic alveolar ridge of the maxilla.

Activated osteoclasts bring out an unavoidable resorption which is the immune response against the transplants. Even when used in aggregate with scaffolds, host cells are no longer able to migrate into a large defect area.

Due to the reality that autologous cancellous bone contains osteogenic, osteoconductive, and osteoinductive elements supplied by using an appropriate cell content, it has been very well applied for huge bone defect regeneration. Nevertheless, the unrestricted access to intraoral tissues provide an amenable situation for harvesting for autologous grafts. These have inspired many other methods used for improvement of stem cell-based tissue engineering therapy.

Dental implants are an exponentially expanding realm of modern dental science. In this realm, there has also been an increasing demand for techniques which are associated to easy bone augmentation. Especially, it is of vital importance in reconstruction of atrophic alveolar ridges and maxillary sinus.[28-30]

The clinical application of stem cells has been analysed in many instances of alveolar ridge augmentation in dental implant rehabilitation. The clinical applicability of stem cell-based bone augmentation is split into two major groups: the mobile bone tissue grafting and the tissue engineering approach. In either case, the most frequently utilized stem cells are BMSCs from the iliac crest.[28] The use of biocompatible membranes, especially in the case of periapical surgical treatment is a controversial subject.

Autologous grafts appear to acquire better consequences, barring collagen membranes. On the different hand, the simple utility of a membrane, using or barring bone graft for periapical surgery, may additionally no longer result in proper regeneration of periapical tissues.[9,31,32] This is due to the reality that these biomaterials are not capable to initiate the recruitment of stem cells or signalling molecules that induce mesenchymal cells to differentiate into pre-osteoblasts, periodontal ligament, and pre-cementoblasts forming cells.

The recovery of the periapical lesions after periapical surgical procedure is similar to what occurs in a wound in the connective tissue in any other part of the physique. A concerning fact is that this recuperation ability is ideally no longer solely the regeneration of alveolar bone. However, regarding the periodontal ligament and cement, after periapical surgery the stem cells would possibly achieve complete periapical tissue regeneration. One may say that this is a near perfect end result of periapical surgery.

Therefore, as in the post-extraction sockets, the existence of a blood clot from the host offers an extremely good natural scaffold for perfect recuperation of surgical wounds. The identical happens in studies of mandibular distraction, where the motion of stem cells is inspired due to surgical technique, or orthopaedics in the treatment of mandibular advancement.[9,33-35]

Implant dentistry modifies the probabilities of restoration on edentulous sufferers that had suffered of bone loss. In extreme cases, the patients have to go through aggressive surgical techniques in order to compensate severe jaw atrophies, and many instances it is no longer viable because of the generic fitness of aged patients. Therefore, genetic and stem cell remedy is a commendable choice of cure for these patients.

An opportunity in this direction could be cytokine stimulation of stem cells. However, the question of whether or not it is superbly vital to stimulate the grownup stem cells located in these patients, particularly in the elderly, is a controversial aspect to be accounted for.[9,36]

CONCLUSION

The present times are an early era of tissue engineering and regenerative medicine, and applications are numerous in dental stem cell technology. New biomaterials and technologies are the key for the development of this field, and their development requires a significant endeavour in translational and multidisciplinary research, to satisfy the needs for clarity, efficiency, and reproducibility of this still pioneer field.

There is evidence that indicates that with the growing of the individual together with their stem cell lineages, do not comply to the induction of the variety of dental oral stem cells as properly as it would be desired. Nevertheless, these hypotheses are supported by means of research on tissue culture and small animal researches; it would be too early to extrapolate these findings to patients. This is very important for the implementation of these cell therapies in human beings for reconstruction of the alveolar bone and maxillofacial defects.

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