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Research Progress of Stem Cells from Human Exfoliated Deciduous Teeth (SHED) and Dental Pulp Stem Cells (DPSCs)

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Abstract: Stem cells from human exfoliated deciduous teeth (SHED) and dental pulp stem cells (DPSCs) exhibit significant potential in regenerative medicine, particularly in areas such as tooth repair, neural regeneration, and bone tissue repair. This paper reviews the latest research progress of these two types of cells in terms of their origins and isolation, proliferation and differentiation abilities, and immunomodulatory properties, providing a detailed analysis of their applications in tissue repair. By comparing the similarities and differences between SHED and DPSCs, we identify the unique advantages and challenges of each in terms of biological characteristics and applications. This paper further explores the technological bottlenecks in current research and the feasibility of clinical translation, and provides an outlook on future research directions to offer theoretical support for advancing related scientific research.

1. Introduction

With the rapid development of regenerative medicine and tissue engineering technologies, the application of stem cells in tissue repair and regeneration has become a research hotspot. Among these, dental pulp stem cells have attracted widespread attention due to their unique origin and strong proliferation and differentiation capabilities. Stem cells from human exfoliated deciduous teeth (SHED) and dental pulp stem cells (DPSCs) are the two main types of dental pulp stem cells and are highly valued by researchers for their potential applications in regenerative medicine. SHED have advantages such as easy access and minimal ethical risks, making them highly effective in fields such as neural regeneration and bone tissue regeneration. In contrast, DPSCs are closer to the physiological state of adult human bodies and play an important role in the repair of teeth and bone tissues. Despite the significant potential of SHED and DPSCs in regenerative medicine, there are notable differences between them in terms of cell proliferation, differentiation capabilities, and immunomodulatory properties, which have important implications for clinical application strategies. Moreover, transitioning from experimental research to clinical application and overcoming

technical bottlenecks and ethical barriers remain critical challenges. This paper aims to review the research progress of SHED and DPSCs, analyze their similarities and differences, and explore their current applications and future development directions in regenerative medicine, providing scientific support and references for advancing research and clinical translation[1].

2. Research Progress of Stem Cells from Human Exfoliated Deciduous Teeth (SHED)

2.1. Origins and Isolation of SHED

Stem cells from human exfoliated deciduous teeth (SHED) are primarily derived from the pulp tissues of deciduous teeth during the natural replacement process in children. Typically, after deciduous teeth naturally fall out or are extracted, multipotent stem cells can be isolated from the pulp cavity. The process of obtaining SHED is relatively simple and does not involve invasive procedures, making it ethically advantageous. Compared to other stem cell sources such as bone marrow or embryonic stem cells, the acquisition of SHED imposes less physical and psychological burden on the donor, providing great potential for clinical research and application. Commonly used techniques for isolating SHED include mechanical separation and enzymatic digestion. First, the collected deciduous teeth are processed under sterile conditions, and the pulp tissue is separated through mechanical grinding or cutting. Then, the pulp tissue is treated with digestive enzymes (e.g., collagenase and trypsin) to release single cells. The isolated cells are cultured in specific media, and after a few days of cell expansion, a relatively purified SHED population is obtained. The culture media typically include basic culture components, serum, cytokines, and growth factors to promote stem cell survival and proliferation.In recent years, with advancements in stem cell research technology, researchers have developed optimized methods for isolating and culturing SHED. For example, using hypoxic culture environments and supplementing with specific growth factors can significantly enhance SHED proliferation and maintain their stemness. Furthermore, SHED sorting and purification techniques have also improved. Flow cytometry, for instance, can be used to further isolate SHED populations with specific surface markers, meeting the needs of various experimental and clinical applications. The continuous development of SHED isolation and culture technologies lays a solid foundation for their application in regenerative medicine and offers new approaches for tissue repair and disease treatment[2].

2.2. Biological Characteristics of SHED

Stem cells from human exfoliated deciduous teeth (SHED) are a type of multipotent stem cell derived from the pulp tissues of deciduous teeth and exhibit unique biological characteristics, making them highly applicable in tissue repair and regenerative medicine. SHED possess a strong proliferative capacity, allowing for the rapid expansion of a large number of cells within a short period, meeting the needs of experimental and clinical treatments. Moreover, compared to other types of stem cells, SHED demonstrate greater multipotent differentiation potential and can differentiate into various cell types under appropriate conditions, including osteoblasts, adipocytes, chondrocytes, and neural cells. This multipotent differentiation ability provides broad possibilities for their application in bone and soft tissue repair. SHED also exhibit unique immunomodulatory functions. Studies have shown that SHED can secrete various cytokines and bioactive molecules to regulate the function of immune cells, such as suppressing inflammatory responses and promoting the repair and regeneration of damaged tissues. This immunomodulatory property makes SHED highly promising in the treatment of inflammatory and immune-related diseases[3]. Additionally, compared to other types of stem cells, SHED have lower immunogenicity, reducing the risk of immune rejection following transplantation and providing greater safety for their use in allogeneic

transplantation and clinical applications. Furthermore, SHED possess good tolerance and plasticity. Under hypoxic conditions, SHED maintain strong proliferative capacity and stemness, adapting to various physiological and pathological environmental changes. This adaptability is crucial for their application in complex tissue environments. Studies have also found that SHED can participate in cell signaling and tissue repair processes by secreting exosomes and other bioactive substances, further enhancing their role in regenerative medicine.In summary, SHED's biological characteristics, including strong proliferative capacity, multipotent differentiation potential, immunomodulatory properties, and plasticity, lay a solid foundation for their application in tissue engineering and disease treatment. These characteristics make them an important target for research and application, offering new possibilities for exploring various tissue regeneration strategies[4].

3. Research Progress of Dental Pulp Stem Cells (DPSCs)

3.1. Origins and Isolation of DPSCs

Dental pulp stem cells (DPSCs) refer to stem cells isolated from the pulp tissue of adult teeth, typically sourced from extracted permanent teeth or teeth removed due to disease treatments. These cells were first identified in 2000 and have since been confirmed to possess strong proliferative and multipotent differentiation abilities. Compared to other stem cell sources, obtaining DPSCs is relatively easy, as they can be isolated from pulp tissue without the need for complex surgical procedures, minimizing trauma to donors. This accessibility makes them highly attractive for clinical applications.The isolation of DPSCs primarily involves a combination of mechanical separation and enzymatic digestion. Generally, dental pulp tissue is extracted under sterile conditions and then mechanically cut to maximize cell release. Subsequently, the tissue is further digested using enzymes such as collagenase and trypsin to release single-cell populations. Through adherent culture, DPSCs with stem cell properties can be obtained[5]. To improve isolation efficiency and purity, researchers also utilize techniques like flow cytometry, which selects specific surface markers such as STRO-1 and CD146, further purifying the DPSC population and ensuring that the collected cells possess high proliferation capacity and stemness.In recent years, researchers have been optimizing the methods for isolating and culturing DPSCs to enhance their efficiency and survival. The use of hypoxic conditions and three-dimensional culture matrices has significantly improved the viability and functionality of DPSCs. Hypoxic culture conditions, in particular, more accurately simulate the in vivo microenvironment of dental pulp stem cells, thereby enhancing their physiological function. Moreover, adding specific factors and improving chemical substrates have further increased the differentiation capacity and stability of DPSCs.The continuous refinement of DPSC sourcing and isolation techniques has established a solid foundation for their applications in tissue repair and regenerative medicine. Their relatively simple acquisition and strong proliferative abilities make DPSCs a significant focus in regenerative medicine and tissue engineering research. With ongoing advancements in technology, DPSCs are progressively demonstrating greater potential for clinical translation, offering new solutions for a variety of diseases and injuries[6].

3.2. Biological Characteristics of DPSCs

Dental pulp stem cells (DPSCs) exhibit unique biological characteristics, making them widely recognized in tissue engineering and regenerative medicine. First, DPSCs demonstrate strong self-renewal and proliferative abilities. Studies have shown that DPSCs can be cultured long-term in vitro while maintaining a good state of proliferation, providing a stable source of cells for regenerative medicine. Compared to other types of stem cells, DPSCs strike a favorable balance between proliferation and differentiation potential, making them advantageous for clinical

applications. A key feature of DPSCs is their multipotent differentiation capacity. Under appropriate conditions, DPSCs can differentiate into various cell types, including osteoblasts, odontoblasts, adipocytes, chondrocytes, and neural cells. This multipotency offers extensive application prospects for regeneration and repair in bones, soft tissues, and nerves. For instance, DPSCs perform well in regenerating the dental pulp-dentin complex, promoting tooth repair and regeneration. They also exhibit excellent bone-forming capabilities in bone defect repair, making them important targets in bone tissue engineering research[7].In addition to proliferation and differentiation, DPSCs possess immunomodulatory properties. Research indicates that DPSCs can secrete various cytokines and bioactive molecules, modulating the activity of immune cells, suppressing excessive inflammatory responses, and promoting tissue repair. This makes DPSCs highly promising in treating inflammatory and immune-related diseases. Furthermore, compared to some other stem cells, DPSCs exhibit lower immune rejection when used in allogeneic transplants, offering a degree of immune tolerance that enhances their safety in clinical applications. The biological characteristics of DPSCs also include their adaptability to environmental changes and response to injury. Under hypoxic conditions, DPSCs maintain their strong proliferative and differentiation states, giving them a survival advantage in complex pathological environments. Moreover, DPSCs can rapidly respond during tissue injury and repair by secreting repair factors and participating in the regeneration process, accelerating healing and repair. Their plasticity is further demonstrated by their ability to respond to different biological signals, making them broadly applicable in multiple fields of tissue engineering and regenerative medicine. In conclusion, DPSCs have become a research hotspot in regenerative medicine and tissue engineering due to their strong proliferation capacity, multipotent differentiation potential, immunomodulatory properties, and environmental adaptability. Future research may further elucidate their biological mechanisms, bringing new possibilities and innovations for their clinical applications[8].

4. Comparative Analysis of SHED and DPSCs

4.1. Similarities between SHED and DPSCs

Stem cells from human exfoliated deciduous teeth (SHED) and dental pulp stem cells (DPSCs) share numerous similarities as stem cells derived from dental pulp tissue, forming a solid foundation for their application in regenerative medicine. First, both SHED and DPSCs exhibit strong self-renewal and proliferative capabilities. Under suitable culture conditions, they can proliferate extensively in vitro while maintaining their stem cell properties. This characteristic provides a stable source of cells for tissue repair and regenerative treatments, offering significant advantages for research and clinical applications. Secondly, both SHED and DPSCs have multipotent differentiation potential, capable of differentiating into a variety of cell types, including osteoblasts, odontoblasts, adipocytes, chondrocytes, and neural cells. This multipotency allows them to show tremendous potential in regenerative medicine and tissue engineering. For example, they have achieved notable success in areas such as tooth repair, bone tissue regeneration, and neural regeneration. Both cell types demonstrate excellent regenerative abilities in laboratory studies and animal experiments, laying a solid foundation for their future clinical applications. In addition, both SHED and DPSCs possess immunomodulatory functions[9]. They can secrete various cytokines and bioactive molecules that regulate immune system responses, suppress inflammatory reactions, and promote the repair of damaged tissues. This immunomodulatory capability holds important value in treating inflammatory diseases and promoting tissue regeneration, offering unique therapeutic potential in clinical settings. Their relatively low immunogenicity makes them suitable for use in allogeneic transplants, providing a high degree of safety and tolerance for widespread clinical applications.In summary, SHED and DPSCs exhibit

many similarities in their proliferation capacity, multipotent differentiation potential, and immunomodulatory properties, making them widely valuable for tissue regeneration and disease treatment. While they differ in certain biological characteristics, their shared attributes offer rich resources and diverse possibilities for regenerative medicine.

4.2. Differences between SHED and DPSCs

Despite the many similarities between stem cells from human exfoliated deciduous teeth (SHED) and dental pulp stem cells (DPSCs), they also exhibit significant differences, which hold important implications for their biological properties and clinical applications. First, SHED and DPSCs differ in their proliferative capabilities. Studies have shown that SHED generally exhibit a higher proliferation rate, allowing them to expand more rapidly in vitro compared to DPSCs. This characteristic gives SHED an advantage in tissue engineering and regenerative applications that require a large number of cells. Additionally, SHED maintain their stemness better during multiple passages, providing robust proliferation and differentiation capacity throughout culture. Secondly, SHED and DPSCs differ in their differentiation potentials. While both possess multipotent differentiation capabilities, SHED exhibit stronger abilities in neural differentiation and angiogenesis, whereas DPSCs show greater potential in bone tissue and dentin regeneration. This difference may be attributed to their developmental stages. SHED, derived from deciduous teeth, are closer to embryonic stem cells in terms of developmental status, resulting in higher multipotency and stronger differentiation capabilities. In contrast, DPSCs, derived from adult permanent teeth, are closer to the physiological state of mature tissues, making them more suitable for mature tissue repair. Thus, SHED excel in neural regeneration, tissue repair, and angiogenesis, while DPSCs are more suited to applications in bone and dental tissue regeneration.SHED and DPSCs also differ in their immune properties. Generally, SHED exhibit lower immunogenicity, leading to a reduced risk of immune responses during allogeneic transplants. This makes them safer and more broadly applicable for allogeneic and xenogeneic transplantation. While DPSCs also possess strong immunomodulatory capabilities, their adult-derived origin may lead to a higher risk of immune rejection, necessitating stricter immune monitoring and control in clinical applications. Additionally, SHED and DPSCs differ in terms of acquisition difficulty and ethical considerations. SHED are sourced from children's deciduous teeth, making collection relatively easy and involving minimal ethical risks. In contrast, DPSCs must be extracted from adult dental pulp tissue, which can involve more complex procedures, especially in cases of pathological tooth extraction, requiring stricter aseptic procedures and technical handling. As a result, SHED have a relative advantage in terms of accessibility. In conclusion, SHED and DPSCs differ in their proliferation rates, differentiation potentials, immune properties, and acquisition difficulties. These differences dictate their suitability for various applications in tissue engineering and regenerative medicine, providing diverse options for personalized treatment and tissue repair. Understanding and leveraging these differences can better promote the broad clinical application of SHED and DPSCs[10].

5. Applications of SHED and DPSCs in Regenerative Medicine

5.1. Tooth Regeneration

Stem cells from human exfoliated deciduous teeth (SHED) and dental pulp stem cells (DPSCs) show significant potential in tooth regeneration. As regenerative medicine advances, these two types of stem cells have been widely studied for the repair and regeneration of dental tissues, offering new therapeutic strategies and directions for oral restoration. The multipotent differentiation capabilities of SHED and DPSCs enable them to differentiate into odontoblasts,

osteoblasts, and pulp-like tissue, providing a basis and cell source for the repair and regeneration of damaged teeth.SHED's advantage in tooth regeneration lies in their high proliferation and differentiation capacity. As they are derived from deciduous teeth, SHED possess strong developmental potential, enabling them to rapidly form new pulp-like tissue during pulp regeneration and restore pulp function. Studies have shown that applying SHED in tooth regeneration can promote the formation of a new pulp-dentin complex, enhancing repair outcomes. Additionally, SHED's low immunogenicity reduces the risk of immune rejection during allogeneic transplantation, making their widespread future clinical application possible.On the other hand, DPSCs also demonstrate significant value in tooth regeneration. Being more closely aligned with the physiological state of adult individuals, DPSCs exhibit strong capabilities in differentiating into odontoblasts and pulp tissues. DPSCs are often used in pulp regeneration therapies to promote the formation of dentin bridges, repairing pulp injuries caused by caries or trauma. Moreover, DPSCs have achieved notable results when combined with three-dimensional scaffold materials, facilitating the repair process of damaged teeth. The combined use of DPSCs and scaffold materials offers a more efficient and controllable method for tooth repair, providing personalized treatment solutions for patients. Beyond pulp and dentin repair, SHED and DPSCs also exhibit promising applications in periodontal tissue regeneration. Studies have shown that these two types of stem cells can promote the regeneration of periodontal ligaments, bone tissue, and other structures, enhancing the stability and functional recovery of teeth. By leveraging the biological properties of SHED and DPSCs, researchers aim to further advance tooth regeneration technology, potentially replacing traditional repair methods and achieving comprehensive tooth regeneration and functional reconstruction. In summary, the application of SHED and DPSCs in tooth regeneration offers new insights for modern dental medicine. Through in-depth research on their biological properties and mechanisms of application, the effectiveness of tooth repair can be further improved, enhancing patients' oral health and quality of life. This emerging treatment method also provides more possibilities for future personalized dental care and regenerative medicine research.

5.2. Neural and Bone Tissue Regeneration

SHED and DPSCs exhibit significant potential and advantages in the fields of neural and bone tissue regeneration, primarily due to their multipotent differentiation capabilities and immunomodulatory properties. In recent years, the use of SHED and DPSCs to repair and reconstruct neural and bone tissues has become a research hotspot, achieving numerous breakthrough advancements. In neural regeneration, SHED demonstrate strong neurogenic differentiation and neurorepair properties. Studies have shown that SHED can secrete various neurotrophic factors that promote the growth and regeneration of nerve cells, thus supporting neural system repair. In experiments, SHED have shown good repair effects in the treatment of spinal cord injuries, peripheral nerve injuries, and central nervous system diseases. Neural regeneration models constructed with SHED can promote the growth of neurons and improve the function of damaged nerves. This neurorepair capability makes SHED promising for treating neurodegenerative diseases, neural injuries, and related conditions. Similarly, DPSCs possess unique advantages in neural regeneration. DPSCs can differentiate into neural cells under specific conditions and form neuron-like structures. Studies have found that DPSCs can generate cells with neural functions in vitro, indicating their potential in neural repair. Additionally, DPSCs possess immunomodulatory properties, allowing them to regulate inflammatory responses and create a favorable microenvironment for neural repair. When combined with specific scaffold materials, the application of DPSCs in neural tissue engineering further expands their prospects in neural repair. In bone tissue regeneration, both SHED and DPSCs exhibit strong osteogenic capabilities. Due to

their high proliferation capacity and osteogenic differentiation potential, SHED have shown promising results in bone defect repair. When combined with scaffold materials and bioactive factors, SHED can effectively promote bone tissue formation and the repair of bone defects, providing new ideas and solutions for bone tissue engineering. Additionally, cytokines secreted by SHED can promote bone regeneration processes, accelerating bone repair and reconstruction. DPSCs also play a vital role in bone tissue regeneration. As mature stem cells, DPSCs can differentiate into osteoblasts in suitable environments and promote new bone formation. Studies have demonstrated that DPSCs significantly contribute to bone fracture healing and bone defect repair. When combined with biomaterials and three-dimensional scaffolds, DPSCs accelerate bone growth and repair, improving the success rate of bone grafts. Furthermore, DPSCs have shown excellent results in periodontal bone regeneration by promoting the regeneration of periodontal bone, enhancing tooth stability and function. In conclusion, SHED and DPSCs hold great potential for neural and bone tissue regeneration. Through their powerful differentiation capacity, immunomodulatory functions, and excellent adaptability to tissues, they offer new therapeutic methods and strategies for regenerative medicine. As research on the mechanisms of SHED and DPSCs deepens and technology advances, their applications in neural and bone tissue repair will continue to broaden and intensify.

6. Conclusion

Stem cells from human exfoliated deciduous teeth (SHED) and dental pulp stem cells (DPSCs) exhibit immense potential in regenerative medicine, offering new hope for tissue repair and regeneration. This paper reviewed the origins, isolation methods, biological characteristics, and applications of SHED and DPSCs in tooth, neural, and bone tissue regeneration, analyzing their similarities and differences. SHED stand out due to their high proliferation capacity, broad multipotent differentiation potential, and low immunogenicity, particularly excelling in neural regeneration and angiogenesis. Meanwhile, DPSCs align more closely with the physiological state of adult tissues, showcasing remarkable potential in bone and dentin regeneration. These characteristics make both types of cells promising sources for research and clinical applications. Nevertheless, the widespread application of SHED and DPSCs faces several challenges, including technological bottlenecks, ethical considerations in clinical translation, and issues of biological safety. Future research must focus on optimizing isolation, culture, and clinical application protocols to fully exploit the potential of these two stem cell types. Multidisciplinary collaboration and technological innovation can further promote their clinical applications, providing more efficient and safer solutions for tissue repair, disease treatment, and personalized medicine. In summary, SHED and DPSCs hold vast promise in regenerative medicine, with the potential to make a profound impact on human health and disease treatment in the future.

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