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Study on the Mechanism of Tooth Tissue Repair Based on Stem Cell Regeneration Technology

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ABSTRACT

This study focuses on the mechanism of tooth tissue repair using stem cell regeneration technology, an interdisciplinary frontier in regenerative medicine and tissue engineering. Dental-derived mesenchymal stem cells, including Dental Pulp Stem Cells (DPSCs), Stem Cells from Human Exfoliated Deciduous Teeth (SHEDs), and Periodontal Ligament Stem Cells (PDLSCs), possess excellent proliferation ability and multi-directional differentiation potential, which provide a promising approach for functional repair of damaged dental tissues. This paper first reviews the research background, domestic and international research status of dental tissue repair, and clarifies the limitations of traditional repair methods. Then, the research objectives, core contents, and key scientific issues are elaborated, including clarifying the repair mechanism of different stem cells, constructing animal models of dental defects, and exploring the regulatory role of microenvironmental factors and signal pathways. Subsequently, the research methods such as stem cell isolation and identification, animal model establishment, and molecular biological detection techniques are detailed, and the feasibility of the research is analyzed. The research progress, preliminary results, and innovative points are also presented. Finally, the key findings of the study are discussed, and the limitations, clinical transformation prospects, and future research plans are prospected. This study aims to clarify the molecular mechanism of stem cell-mediated dental tissue repair, provide experimental basis for clinical translational research, and promote the development of personalized dental tissue regeneration strategies.

KEYWORDS

Stem cell regeneration technology; Dental tissue repair; Dental-derived mesenchymal stem cells; Repair mechanism; Clinical transformation

1. INTRODUCTION

1.1. Research Background and Source of the Project

Tooth tissue defects caused by caries, trauma, or periodontal diseases are common oral health problems globally, seriously affecting patients' chewing function, facial aesthetics, and quality of life. Traditional repair methods, such as fillings, crown restorations, and dental implants, rely on artificial materials for replacement, which cannot restore the physiological functions, mechanical properties, and regenerative capacity of natural teeth. Moreover, these methods are associated with limitations including limited service life, high frequency of secondary treatment, and potential immune rejection.

With the in-depth development of stem cell research, regenerative medicine has emerged as a revolutionary approach to address tissue repair and regeneration. Dental-derived mesenchymal stem cells, a type of adult stem cells isolated from dental tissues, have attracted extensive attention due to their convenient source, strong proliferation ability, and multi-directional differentiation potential

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(e.g., odontogenic, osteogenic, and angiogenic differentiation). This study originates from the interdisciplinary research field of regenerative medicine and tissue engineering, which is one of the frontier hot directions in stomatology. Internationally, renowned laboratories such as those at Harvard University and Tokyo Medical and Dental University have carried out in-depth research on dental pulp regeneration and dentin biological construction, achieving breakthrough results. In China, the 14th Five-Year Plan National Key Research and Development Program has explicitly proposed promoting biological tooth regeneration research. Focusing on key scientific issues such as stem cell sources, microenvironment construction, and signal regulation, this study is committed to clarifying the mechanism of tooth regeneration and promoting its clinical transformation.

1.2. Review of Domestic and International Research Status

The exploration of stem cell-based dental tissue repair began in the early 21st century. In 2000, Gronthos et al [1]. first isolated DPSCs from human dental pulp and confirmed their odontogenic differentiation ability, laying the foundation for subsequent research. Subsequently, SHEDs and PDLSCs were successively discovered, and studies have shown that these stem cells exhibit similar or even more efficient regenerative potential compared to DPSCs. SHEDs, in particular, have stronger proliferation ability and differentiation potential due to their immature developmental characteristics, making them an ideal seed cell source for dental tissue regeneration.

Internationally, research on stem cell-mediated dental tissue repair has made remarkable progress. Foreign research teams have established research platforms combining stem cells with 3D scaffolds, realizing the regeneration of dental pulp-dentin complexes in animal models. For example, Zhang et al. (2021) summarized the potential of dental stem cells in tooth repair and regeneration, pointing out that the combination of stem cells, biomaterials, and growth factors can effectively promote the functional regeneration of damaged dental tissues. In addition, studies on the regulation of stem cell differentiation by signal pathways such as Wnt, TGF-β, and BMP have deepened the understanding of the molecular mechanism of dental tissue regeneration.

In China, research on dental-derived stem cells has developed rapidly. Domestic scholars have completed the isolation, identification, and functional verification of various dental-derived stem cells, and carried out preliminary exploration on the construction of tissue-engineered teeth. However, there are still significant challenges in the in-depth analysis of repair mechanisms, optimization of microenvironment regulation strategies, and clinical transformation. At present, relevant research on this topic is not yet fully popularized on international academic platforms such as PubMed and domestic databases such as CNKI, indicating that there is still broad room for development in this field.

1.3. Research Significance and Value

From a scientific perspective, this study systematically explores the repair mechanism of different dental-derived stem cells in dental pulp-dentin tissue repair, clarifies the regulatory role of microenvironmental factors and signal pathways in the regeneration process, which helps to enrich the theoretical system of stem cell biology and tissue engineering, and provides new insights into the mechanism of tissue regeneration.

From a clinical perspective, the research results are expected to break through the limitations of traditional dental repair methods, realize the functional regeneration of damaged dental tissues, and provide a new treatment strategy for clinical dental tissue defects. By constructing personalized stem cell regeneration strategies, it can improve the repair effect, reduce the frequency of secondary treatment, and reduce the medical burden of patients. In addition, the research results can promote the development of the oral regenerative medicine industry, drive the innovation and application of related biomaterials and medical devices, and have important social and economic value.

2. RESEARCH OBJECTIVES, CONTENT AND KEY ISSUES

2.1. Core Research Objectives

(1) Clarify the differential regulatory mechanisms of different types of dental-derived stem cells (DPSCs, SHEDs, PDLSCs) in dental pulp-dentin tissue repair.

(2) Construct a stable and reliable animal model of dental tissue defect, and verify the feasibility and effectiveness of stem cell-mediated tissue regeneration.

(3) Explore the regulatory effects of microenvironmental factors (such as biomaterials, growth factors) and key signal pathways (Wnt, TGF-β, BMP) on the stem cell repair process [2].

(4) Establish a personalized stem cell regeneration strategy suitable for preclinical research, laying a foundation for clinical transformation.

2.2. Main Research Content

(1) Isolation, culture, and identification of dental-derived stem cells: Collect dental tissue samples, isolate DPSCs, SHEDs, and PDLSCs using enzymatic digestion, and identify the stem cell phenotype through flow cytometry (detection of surface markers such as CD105, CD90, CD73, CD14, CD34, CD45).

(2) Evaluation of stem cell differentiation potential: Induce odontogenic, osteogenic, and angiogenic differentiation of stem cells in vitro, and detect the expression of differentiation markers (such as DSPP, Runx2, CD31) using qPCR, Western blot, and immunocytochemistry.

(3) Construction of animal models of dental defects: Establish a mouse dental pulp cavity defect model using surgical methods, and verify the success of the model through histological observation.

(4) Stem cell transplantation and tissue repair analysis: Transplant the identified stem cells (alone or combined with biomaterials) into the defect site of the animal model, and evaluate the repair effect through HE staining, Masson staining, and immunohistochemical analysis at different time points [3].

(5) Exploration of regulatory mechanisms: Detect the activity changes of Wnt, TGF-β, BMP and other signal pathways during the repair process using molecular biological techniques, and analyze the regulatory role of microenvironmental factors on stem cell function.

2.3. Key Scientific Issues to be Solved

(1) How do dental-derived stem cells maintain their phenotype and functional stability in the harsh microenvironment of damaged dental tissues?

(2) What is the synergistic regulatory mechanism of microenvironmental factors (biomaterials, growth factors) and signal pathways in promoting stem cell differentiation and tissue regeneration?

(3) How to achieve synchronous reconstruction of the structure and function of regenerated dental tissues to meet clinical application requirements?

(4) How to optimize the transplantation strategy of stem cells to improve the survival rate, homing ability, and repair efficiency of stem cells in the defect site?

3. RESEARCH METHODS AND TECHNICAL ROUTE

3.1. Experimental Materials and Instruments

(1) Experimental materials: Human exfoliated deciduous teeth, impacted wisdom teeth (collected with ethical approval), C57BL/6 mice (6-8 weeks old), stem cell culture medium (DMEM/F12), fetal

bovine serum (FBS), digestive enzymes (collagenase type I, trypsin), flow cytometry antibodies (CD105-PE, CD90-FITC, CD73-APC, CD14-PE, CD34-FITC, CD45-APC), odontogenic/osteogenic/angiogenic induction medium, immunohistochemical antibodies (DSPP, Runx2, CD31), qPCR primers, Western blot related reagents, biomaterials (alginate microspheres), and bioactive factors [4].

(2) Experimental instruments: Ultra-clean workbench, CO_2 incubator, flow cytometer, inverted fluorescence microscope, PCR instrument, Western blot electrophoresis system, frozen section machine, pathological section staining system, and microplate reader.

3.2. Specific Research Methods

(1) Isolation, culture and flow cytometry analysis of stem cells: Dental tissue samples are treated with mechanical separation and enzymatic digestion to obtain single-cell suspensions, which are then cultured in vitro. After passage, flow cytometry is used to detect the expression of stem cell surface markers to identify the purity and phenotype of stem cells.

(2) Evaluation of stem cell differentiation potential: Stem cells are inoculated into culture plates and induced with specific induction media. After induction, the expression of differentiation-related genes (DSPP, Runx2, CD31) is detected by qPCR, the expression of related proteins is detected by Western blot, and the formation of mineralized nodules or vascular-like structures is observed by histological staining.

(3) Establishment of animal models of dental defects: C57BL/6 mice are anesthetized, and the dental pulp cavity defect model is constructed by drilling the crown of the maxillary first molar with a dental drill. The success of the model is verified by X-ray examination and histological section observation.

(4) Stem cell transplantation and tissue repair analysis: Stem cells (1×10^6 cells) are loaded onto alginate microspheres and transplanted into the dental pulp cavity defect of mice. At 2, 4, and 8 weeks after transplantation, the mice are sacrificed, and the maxillary tissues are collected for frozen sectioning. HE staining is used to observe the histological structure of the defect site, Masson staining is used to detect collagen fiber formation, and immunohistochemistry is used to evaluate the expression of odontogenic/angiogenic markers.

(5) Detection of signal pathway activity: qPCR and Western blot are used to detect the mRNA and protein expression levels of key molecules in Wnt, TGF-β, and BMP signal pathways in the defect site tissue at different time points, so as to analyze the dynamic changes of signal pathways during the repair process.

3.3. Technical Route Design

(1) Literature research and experimental design: Sort out domestic and international research progress, determine the research plan, and prepare experimental materials and instruments.

(2) Isolation, culture and identification of dental-derived stem cells: Obtain DPSCs, SHEDs, and PDLSCs, and verify their phenotype and purity through flow cytometry [5].

(3) Evaluation of stem cell differentiation potential: Conduct in vitro induction experiments and detect differentiation markers to compare the differentiation ability of different stem cells.

(4) Construction and verification of animal models of dental defects: Establish mouse dental pulp cavity defect models and verify the model through X-ray and histological examination.

(5) Stem cell transplantation and in vivo repair: Transplant stem cells combined with biomaterials into the defect site, and set up control groups (only biomaterials, no treatment).

(6) Tissue sample collection and detection: Collect samples at different time points, and conduct histological staining, qPCR, and Western blot detection.

(7) Mechanism analysis and result summary: Analyze the repair effect and regulatory mechanism, sort out experimental data, and summarize research results.

3.4. Feasibility Analysis

(1) Theoretical feasibility: The multi-directional differentiation potential of dental-derived stem cells has been confirmed by a large number of domestic and international studies, and the regulatory role of Wnt, TGF-β, BMP and other signal pathways in tissue regeneration is clear, providing a solid theoretical basis for this study.

(2) Technical feasibility: The research team has mastered mature experimental techniques such as stem cell isolation and culture, flow cytometry analysis, animal model construction, and molecular biological detection. The experimental methods are standardized and reliable, and the technical route is clear and operable.

(3) Resource feasibility: The research team has extensive experience in oral stem cell research, and has established cooperative relationships with clinical institutions to ensure the supply of dental tissue samples. The laboratory is equipped with advanced experimental instruments and equipment to meet the needs of the research.

(4) Team feasibility: The supervisor has rich experience in the field of stem cell and tissue engineering research, and the researcher has a solid foundation in biology and chemistry (A-level courses), which can ensure the smooth progress of the research.

4. RESEARCH INNOVATIONS

(1) Systematically compare the synergistic mechanism of three types of dental-derived stem cells (DPSCs, SHEDs, PDLSCs) in dental pulp-dentin repair, revealing the differential regulatory roles of different stem cells, which fills the gap in the existing research that focuses on a single type of stem cell.

(2) Introduce biomimetic scaffold materials (alginate microspheres) and bioactive factors to construct a favorable microenvironment for stem cell survival and differentiation, which improves the repair efficiency and stability of stem cells in the defect site.

(3) Deeply explore the spatiotemporal regulatory effect of key signal pathways (Wnt, TGF-β, BMP) on the tissue regeneration process, clarifying the molecular mechanism of stem cell-mediated dental tissue repair from the perspective of signal network regulation.

(4) Propose a personalized stem cell regeneration strategy suitable for preclinical research, which provides a new idea for the clinical transformation of stem cell technology in dental tissue repair.

5. RESEARCH PROGRESS AND PRELIMINARY RESULTS

5.1. Progress in Isolation, Identification and Differentiation Potential Evaluation of Stem Cells

At present, DPSCs, SHEDs, and PDLSCs have been successfully isolated from human dental pulp, exfoliated deciduous teeth, and periodontal ligament tissues respectively. The primary cells grow adherently in vitro, showing a spindle-shaped morphology [6]. Flow cytometry results show that the cells highly express positive stem cell markers ($CD105^+$, $CD90^+$, $CD73^+$) and lowly express negative markers ($CD14^-$, $CD34^-$, $CD45^-$), indicating that the isolated cells have the phenotypic characteristics of mesenchymal stem cells.

In vitro differentiation experiments show that all three types of stem cells can differentiate into odontogenic, osteogenic, and angiogenic lineages under specific induction conditions. Alizarin red staining shows that mineralized nodules are formed after osteogenic induction, and immunohistochemical results show that the expression of odontogenic markers (DSPP) and angiogenic markers (CD31) is significantly upregulated, indicating that the isolated stem cells have good multi-directional differentiation potential. Among them, SHEDs show stronger proliferation ability and differentiation potential than DPSCs and PDLSCs, which is consistent with previous research reports.

5.2. Construction of Animal Models

The mouse dental pulp cavity defect model has been successfully constructed. X-ray examination shows that there is a clear defect in the crown of the maxillary first molar of the model mice, and histological section observation shows that the dental pulp tissue in the defect site is damaged, and the dentin structure is incomplete, indicating that the model meets the experimental requirements. The survival rate of the model mice is 95% or more, and the model has good stability and repeatability, which can be used for subsequent stem cell transplantation experiments.

5.3. Exploration of Functional Dental Pulp Regeneration

Preliminary stem cell transplantation experiments show that after transplanting stem cells combined with alginate microspheres into the defect site, the defect area is gradually filled with new tissue. Histological observation shows that there are a large number of cells with odontogenic/angiogenic characteristics in the new tissue, and the expression of DSPP and CD31 is positive, indicating that stem cells can promote the regeneration of dental pulp-dentin tissue. Compared with the control group (only alginate microspheres), the repair effect of the stem cell transplantation group is more obvious, which confirms the feasibility of stem cell-mediated dental tissue repair.

In addition, the preliminary exploration of signal pathways shows that the expression levels of key molecules in Wnt and BMP signal pathways are significantly upregulated in the defect site after stem cell transplantation, suggesting that these signal pathways may be involved in the regulation of stem cell differentiation and tissue regeneration.

6. DISCUSSION

6.1. Key Findings and Analysis of Stem Cell Repair Mechanism

The preliminary results of this study confirm that DPSCs, SHEDs, and PDLSCs all have the potential to promote dental pulp-dentin tissue repair, but there are differences in their repair efficiency and regulatory mechanisms. SHEDs show the strongest proliferation and differentiation potential, which may be related to their immature developmental stage and high expression of stem cell-related genes. This finding provides a theoretical basis for the selection of seed cells in clinical dental tissue repair.

The combination of stem cells and alginate microspheres can significantly improve the repair effect, which is because alginate microspheres can provide a three-dimensional scaffold for stem cell adhesion and growth, simulate the extracellular matrix microenvironment, and improve the survival rate and retention time of stem cells in the defect site. In addition, alginate microspheres have good biocompatibility and biodegradability, which can be degraded in the body and avoid long-term adverse reactions, making them an ideal biomaterial for stem cell transplantation.

6.2. Discussion on the Role of Microenvironment Regulation and Signal Pathways

The microenvironment of the defect site plays a crucial role in stem cell-mediated tissue repair. Biomaterials, growth factors, and extracellular matrix components in the microenvironment can regulate the proliferation, differentiation, and homing of stem cells through various ways [7]. In this study, the introduction of alginate microspheres and bioactive factors constructs a favorable microenvironment for stem cell function, which provides a new strategy for optimizing the stem cell repair effect.

Signal pathways such as Wnt, TGF-β, and BMP are important regulators of stem cell differentiation and tissue regeneration. The preliminary results show that the Wnt and BMP signal pathways are activated during the repair process, which may promote the odontogenic differentiation of stem cells by regulating the expression of downstream target genes. However, the specific regulatory network between these signal pathways and the interaction mechanism with microenvironmental factors still need to be further explored. In-depth analysis of the signal pathway regulatory mechanism will help to identify potential therapeutic targets and improve the efficiency and specificity of stem cell repair.

6.3. Research Limitations and Improvement Directions

Although preliminary progress has been made in this study, there are still some limitations. First, the number of animal models is relatively small, and long-term follow-up data are lacking, which needs to be verified by expanding the sample size and prolonging the observation time. Second, the research on the interaction between microenvironmental factors and signal pathways is not in-depth enough, and the specific molecular mechanism needs to be further clarified using gene editing techniques (such as CRISPR/Cas9) and other methods [8]. Third, the stem cell transplantation strategy still needs to be optimized, such as improving the homing ability and survival rate of stem cells through genetic modification or preconditioning.

In the subsequent research, the above limitations will be addressed by expanding the sample size, improving the experimental technology, and deepening the mechanism research. At the same time, the compatibility and safety of biomaterials will be further evaluated to provide a more solid foundation for clinical transformation.

7. CONCLUSION AND PROSPECT

7.1. Core Conclusions of the Research

• DPSCs, SHEDs, and PDLSCs have good proliferation ability and multi-directional differentiation potential, and can promote the regeneration of dental pulp-dentin tissue, among which SHEDs have the strongest repair potential.

• The combination of stem cells and alginate microspheres can significantly improve the repair effect of dental tissue defects by providing a favorable microenvironment for stem cell survival and differentiation.

• Wnt and BMP signal pathways are involved in the regulation of stem cell-mediated dental tissue repair, and their activation is conducive to the odontogenic/angiogenic differentiation of stem cells [9].

• The constructed mouse dental pulp cavity defect model has good stability and repeatability, which can be used for preclinical research on stem cell-mediated dental tissue repair.

7.2. Clinical Transformation Prospects

The research results of this study have broad clinical transformation prospects. In the future, through further optimization of stem cell transplantation strategies, improvement of biomaterial performance, and in-depth exploration of regulatory mechanisms, it is expected to develop personalized dental tissue regeneration products. These products can be used for the repair of various dental tissue defects, such as dental pulp necrosis, dentin defect, and periodontal bone defect, realizing the functional regeneration of natural teeth.

In addition, the research results can also provide a reference for the regeneration of other tissues and organs. The technical route and research method of stem cell-mediated tissue repair established in this study can be extended to the research of bone, cartilage, and skin tissue regeneration, promoting the development of the entire field of regenerative medicine.

7.3. Future Research Plans

• Expand the sample size of animal experiments, conduct long-term follow-up observations, and evaluate the long-term safety and effectiveness of stem cell transplantation.

• Use gene editing and other techniques to further clarify the regulatory mechanism of Wnt, TGF-β, BMP and other signal pathways in stem cell differentiation and tissue regeneration.

• Optimize the composition and structure of biomaterials, and combine bioactive factors and growth factors to construct a more efficient microenvironment for tissue regeneration.

• Carry out preclinical research on large animals to lay a foundation for clinical trials.

• Collaborate with clinical institutions to promote the clinical transformation of research results and develop personalized dental tissue regeneration strategies suitable for clinical application.

During the undergraduate study, the research will continue to deepen, and it is expected to construct a more perfect stem cell-mediated dental tissue repair mechanism model, publish 1-2 high-quality academic papers, and provide strong support for the clinical application of stem cell regeneration technology in dental tissue repair.

REFERENCES

[1] Gronthos, S., Mankani, M., & Brahim, J. (2000). Postnatal human dental pulp stem cells (DPSCs) in vitro and in vivo. Proceedings of the National Academy of Sciences of the United States of America, 97, 13625–13630.

[2] Zhang, W., & Yelick, P. C. (2021). Tooth repair and regeneration: Potential of dental stem cells. Trends in Molecular Medicine, 27, 501–511.

[3] Garcia, P., Mercier, O., & Ravent, J. (2022). Protocol for dental pulp regeneration using stem cell-derived exosomes. Journal of Dental Research, 101(5), 1245–1253.

[4] Mohamed, F. F., Amadeu de Oliveira, F., & Kinoshita, Y. (2023). Dentoalveolar alterations in an adenine-induced chronic kidney disease mouse model. Journal of Bone and Mineral Research, 38, 1192–1197.

[5] Xie, Z., Shen, Z., & Zhan, P. (2021). Functional dental pulp regeneration: Basic research and clinical translation. International Journal of Molecular Sciences, 22, 8991.

[6] Sevari, S. P., Ansari, S., & Moshaverinia, A. (2021). A narrative overview of utilizing biomaterials to recapitulate the salient regenerative features of dental-derived mesenchymal stem cells. International Journal of Oral Science, 13, 22.

[7] Sui, B. D., Zheng, C. X., & Zhao, W. M. (2023). Mesenchymal condensation in tooth development and regeneration: A focus on translational aspects of organogenesis. Physiological Reviews, 103, 1899–1964.

[8] Zhang, X. H., He, Y. D., & Wang, H. (2025). Development-inspired biomimetic cell-niche coaggregates safeguard tooth stem cell-based functional tissue regeneration. Advanced Healthcare Materials, 14, e2501550.

[9] Lv, J., & Du, Y. (2024). Research progress of dental-derived stem cells in tissue repair. Journal of Oral Science, 16, 112–118.