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# APPLICATION PROGRESS OF GENE THERAPY IN THE FIELD OF REGENERATIVE MEDICINE

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**Abstract:** Regenerative medicine is based on the structure and function of tissues to repair and treat affected areas. A discipline that damages tissues and organs. The emergence and development of regenerative medicine provides new ideas for the treatment of diseases and alleviates the shortage of transplanted tissues and organs. The problem. The process of tissue and organ regeneration is very complex and requires stable environment. Stable cytokine expression is a key factor in tissue and organ regeneration, and gene therapy can effectively solve this problem. Gene therapy The seed cells of the therapy can stably and continuously secrete the cytokines required for regeneration, provide a stable local environment, and improve the efficiency of tissue repair. therefore, Gene therapy will produce more ideal results in the field of regenerative medicine Treatment Effect.
**Keywords:** Gene therapy; Regenerative medicine; Tissue repair

## 1 GENE THERAPY

clinical treatment method developed along with basic disciplines such as cell biology, genetics, molecular biology, and biomedical engineering technology. It mainly uses transgenic technology to transfer target genes into recipient cells and regulate them. Its expression is used in the treatment of specific diseases. Initially, gene therapy mainly targeted genetic diseases, such as hemophilia, bladder fibrosis and hereditary metabolic diseases [1]. However, current gene therapy cannot achieve long-term expression of target genes and can only achieve a temporary effect. The disease-causing genes will still be inherited to future generations. Relatively speaking, tissue regeneration requires The time required is short, and the damage can be repaired only by gene expression for a period of time. Therefore, gene therapy technology at this stage is more suitable for the field of regenerative medicine [2].

## 2 Regenerative Medicine

The emergence and development of regenerative medicine provides new application fields for gene therapy. Human beings suffer from various forms of trauma and loss of important organ functions, and millions of people are in urgent need of tissue and organ transplantation every year [3]. Regrettably, on the one hand, although transplanted organs have great therapeutic effects, the demand far exceeds the supply, and they are restricted by ethics and immune rejection, making it difficult to meet the demand; On the other hand, the current tissue and organ repair still has problems such as scar healing, and there is still some way to achieve the goal of complete repair of damaged tissues and organs. The emergence of regenerative medicine has solved these problems. Regenerative medicine uses the regeneration potential of cells in human organs and tissues, and with the participation of necessary nutrients, regenerates and replenishes cells to maintain the structure and function of the organs and fundamentally treat diseases. And as the functions of various growth factors are gradually discovered, their cDNA Being overcome Long, gene therapy is more applied to the field of regenerative medicine, such as promoting trauma Healing etc. During the treatment process, stem cells are first isolated from human tissue. cells. At this time, stem cells have a problem due to hereditary or acquired diseases and other reasons.

Cells, signaling factors, and scaffolds that provide sites for cell attachment are important Three elements of biomedicine[4]. The main application of cells has self-renewal ability Stem cells with multi - lineage differentiation potential or induced multifunctional stem cells cell. At the same time, due to the superiority of stem cell manipulation in vitro, it has become a gene therapy ideal target cells for therapy. After inoculating the target cells of gene therapy, the body itself The cells can secrete the target protein and do not need to undergo genetic engineering for expression. Cytokines in protein form, so no complexities such as protein extraction and purification are required. Miscellaneous crafts ; Moreover, the target cells can continue to secrete the required proteins for tissue regeneration. Provide a stable microenvironment and improve treatment efficiency. Gene therapy is used in Regenerative medicine is an ideal treatment platform. Currently, gene therapy has Widely used in nerve tissue, bone tissue, skin tissue, heart and other tissues or organ regeneration, and achieved fruitful results [5-8].

## 3 APPLICATION OF GENE THERAPY IN REGENERATIVE MEDICINE

### 3.1 Bone Regeneration

Bone injury is a common disease. Due to poor nutritional supply, special injury location, severe injury and other reasons, bone defects, necrosis, and slow or non-healing often occur. Gene therapy can be applied in the field of bone

regeneration to accelerate bone damage repair. After gene therapy cells such as osteoblasts and fibroblasts are inoculated, they can stably and continuously secrete growth factors that induce bone regeneration at specific injury sites. Growth that has been shown to promote bone regeneration Factors mainly include bone morphogenetic protein(bone morphogenetic protein, BMP), vascular endothelial growth factor(vas- cular endothelial growth factor, VEGF), transformation growth factor(transforming growth factor, TGF), fibroblast growth because son(fibroblast growth facto r, FGF) and platelet-derived factor(platelet-derived growt h factor, PDGF), etc. And genetic modification The decorated stem cells, while locally secreting growth factors, can differentiate into osteoblasts and promote bone tissue repair ; There is a large amount of periosteum around the bone tissue, It is surrounded by soft tissues such as muscles to form a tight envelope, thereby helping to fix the gene carrier [9].

BMP-2 is transforming growth factor beta A member of the superfamily that promotes future point change between Charge quality Dry thin cells(mesenchymal stem cells, MSCs) mature toward osteoblasts and accelerate bone defect repair. Will BMP-2 transfected into sheep After MSCs, the expression of osteocalcin and osteopontin was significantly increased [10]. Will The BMP -2 gene was transfected into equine fibroblasts, and then the transfected fibroblasts were transplanted into the autologous equine metacarpal bone deletion model. X -ray radiography assesses healing status. 6 Compared with the control group after 1 week, the inoculated transfected BMP -2 Gene fibroblasts formed larger bone nodules at the missing site of the horse metacarpal bone, and at the same time had more active mineralization at the edge of the missing site, proving the potential of gene therapy in bone tissue regeneration [11].

### 3.2 Cardiomyocyte Regeneration

In the treatment of ischemic heart disease, through Clinical methods such as coronary artery bypass surgery, bypass surgery, and thrombolytic therapy can play a role in The therapeutic effect of opening coronary blood flow and rescuing ischemic myocardial cells, but the surgical Complications such as restenosis and reperfusion injury will still occur after the damaged heart group Weave. Ischemic heart disease uses gene therapy to express required cytokines Promote the regeneration of blood vessels and cardiomyocytes, thereby improving heart tissue supply Blood [12]. Currently, in gene therapy for ischemic heart disease, target genes are available for selection. because Mainly includes encoding hepatocyte growth factor(hepatocyte growth factor, HGF), VEG F, FGF, angiopoietin(angiopoi- etin, Ang) and Genes of PDGF and other polypeptides [13].

MSCs Has the potential to differentiate into a variety of cells, including bone cells, Adipocytes, etc., and are widely used in gene therapy as target cells. Studies have found that MSCs Transplantation can repair myocardial damage, but post- transplantation MSCs have poor survival ability. Bcl-xL belongs to Bcl-2 family, is an important regulator of apoptosis. Will Bcl - xL Gene transfection into MSCs It can inhibit myocardial cell apoptosis in ischemic areas and even extend the cryopreservation time during heart transplantation. In vitro cultured cells transfected with Bcl-xL gene MSCs Decreased apoptosis rate 43%, V EGF, insulin -like cell growth factor(insulin-like grow th factor-1, IGF- 1), PDGF and other cytokines expression levels are significantly increased, which is beneficial to the repair of myocardial tissue. will transfect Bcl - xL genetic MSCs The cells were transplanted into the myocardial infarction area of the rat model of myocardial infarction, and at the same time, the cells were transfected with the empty plasmid. MSCs Cells were transplanted into the myocardial infarction area of the same rat model as a control group. Transfected Bcl - xL genetic MSCs Myocardial cell apoptosis rate decreased after cells 40%, thus solving MSCs survival problem, thus proving that gene therapy can promote MSCs Its role in cardiac tissue repair [14].

### 3.3 Nervous System Regeneration

Traditional theory holds that damage to the central nervous system of humans and other higher animals is irreparable. And due to the existence of the blood-brain barrier, traditional pharmacological methods are difficult to achieve therapeutic effects. However, with the development of regenerative medicine in recent years, studies have found that the central nervous system also has a certain degree of plasticity, and the tissue after gene therapy can stably provide the cytokines needed for nervous system repair and treatment, thus bringing new opportunities for the treatment of central nervous system damage. Here comes new hope [15].

Neural stem cells are a type of cell with differentiation potential and self-renewal ability Stem cells differentiate into various types of cells in neural tissue through asymmetric division and maintain the number of stem cells. Neural stem cells transfected with the target gene are implanted into brain tissue, which can be directly integrated into the neural tissue and differentiate to produce normal nerve cells ; Nerve cells expressing the gene of interest can be distributed throughout the The central nervous system functions as needed. The selected target genes include genes for neurotrophic factors, inhibitory factor antibodies, growth factors and anti-apoptotic proteins. These genes can be expressed to promote the growth of neural stem cells. Inhibit apoptosis-related cytokines.

Parkinson's Disease(parkinson's disease(PD) is caused by the apoptosis of neurons in the substantia nigra pars compacta, resulting in the inability to synthesize dopamine transmitters, resulting in a decrease in dopamine content in the striatum. So for PD gene therapy The strategy is to introduce genes for enzymes required for dopamine expression into the striatum to increase dopamine expression [16]. LeWitt PA Transfection of valley with adenoviral vector amino acid decarboxylase gene into subthalamic nucleus neurons in patients with Parkinson's disease, Expressed glutamate decarboxylase promotes expression of gamma-aminobutyric acid, thereby Improve the condition of patients with

Parkinson's disease. treat After 6 months, it was found that the condition of patients in the gene therapy group was significantly improved through the Parkinson's Comprehensive Rating Scale. Good [17].

### 3.4 Epidermal Regeneration Tissue Engineering

Epidermis is widely used in ulcer treatment, fever Injury repair, wound repair, etc. Epidermal stem cells have strong dividing ability force, so the epidermal stem cells transfected with the target gene can express the desired gene permanently. Cytokines are required. Commonly used cytokines include epidermal growth factor(epidermal growth factor, EGF), F F wait. At the same time, the epidermis is dry The technology of growing cells on degradable scaffolds and then transplanting them has become very successful. Mature, long-term effects after autologous cell transplantation are ideal. Covered by epidermis Body surface, easy to observe, once the patient has adverse reactions, they can be detected in time and treatment [18].

Netherton syndrome is a serious skin disorder caused primarily by Mutations in the SPINK 5 gene inhibit Kazal kazal-type- related protease inhibitor inhibitor, L EKTI) expression. LEKTI Has anti-inflammatory and antibacterial properties. Will SPINK 5 gene transfected into After keratinocytes from patients with Netherton syndrome, cells reexpress LEKTI. will transfect SPINK 5 Genetically derived keratinocytes were seeded on tissue engineering scaffolds to form tissue engineered skin and then transplanted into humanized mice. After long-term observation, it was found that tissue-engineered skin does not Netherton Characteristics of the syndrome ; The control group was not transfected SPINK 5 Genetically engineered keratinocytes to form tissue-engineered skin were transplanted into humanized mice, resulting in severe Netherton Syndrome symptoms [19], which shows that gene therapy has important application value in tissue engineering skin construction and related disease treatment.

### 3.5 Islet Remodeling

Diabetes is a metabolic disease caused by defective insulin secretion or loss of its activity. The conventional treatment for type 1 diabetes is the use of insulin, but exogenous insulin and its analogues require continuous injection and have serious side effects. Gene therapy technology provides new hope for patients with diabetes and diabetes-related complications. Some adult cells in the final stages of differentiation(Such as liver or intestinal stem cells, fibroblasts, adipocytes, etc.) Through the construction of gene therapy technology, transcription factors and cofactors in pancreatic endocrine development factors can be ectopically expressed to produce biologically active insulin and regulate human body sugar metabolism [20].

ANGPTL 8 is mainly expressed in liver and adipose tissue circulating hormones that promote beta Cell Proliferation. Chen J targeted AN - GPTL 8 into the pancreas of humanized rats, 1 in months It can still be detected in rats ANGPTL8 expression can also be promote pancreatic islets β- cell proliferation, expanding β Cell mass, improve grapes Glucose tolerance improves fasting insulin levels and improves pancreatic islet function. recovery [21].

### 3.6 Eye Diseases

Gene therapy in eye diseases is mainly used in retinal diseases, including retinitis pigmentosa and proliferative vitreous retina. Eye diseases such as membrane lesions and congenital amaurosis. associated with retinal diseases Mutated genes are gradually discovered, and there are targets for gene therapy. The basic strategy is Introduce normal genes to replace diseased genes, thus making up for the genes in the patient's body Defect [22].

Leber First sky sex black deceive(leber congenit al amaurosis, LCA) It is a type of blindness caused by loss of photoreceptor function and degenerative changes, mainly related to retinal pigment epithelial cells. RPE 65 protein mutations. After long-term observation, without Patients treated with RPE 65 gene showed degenerative changes in photoreceptors in early childhood. After RPE 65 gene treatment, their vision improved significantly, and no degenerative changes were found in long-term observation. Also passed in the dog model RPE 65 Vision is also improved after gene therapy improve. Therefore the application base Treatment of LCA due to treatment methods is valid[23-24].

## 4 GENE THERAPY ISSUES AND PROSPECTS

Gene therapy has broad application prospects in the field of regenerative medicine. However, the application of gene therapy is limited by the potential risks, instability, and relative low efficiency of transgenes. The introduced exogenous genes may lead to gene mutations, which are closely related to a variety of human diseases, such as cancer, genetic diseases, cardiovascular disease, and type 1 diabetes. For example, French scientists are working on gene therapy X - linked severe combined immunodeficiency disease combo ned immunodefi- ciency disease, X-SCID), activated nearby oncogenes during clinical trials, resulting in many cases of leukemia-like side effects [25].

In order to solve the problem of gene therapy, we must first deal with transgenic technology Modifications to accurately insert the target gene into the genome with low risk area, develop more efficient and stable transfection vectors, and evaluate their safety and Comprehensive testing of effectiveness ; Secondly, in-depth study of the structure of functional proteins We will screen new high-quality target genes based on their structural properties, and integrate the advantages of single vectors and target gene systems to develop chimeric target genes. because; At the same time, the aging and slow proliferation of target cells during the regeneration process slow, induce directional differentiation of stem cells

and reduce the effect of transgene on target cells Problems such as toxicity also need to be solved urgently and will also be the focus of regenerative medicine research.

## COMPETING INTERESTS

The authors have no relevant financial or non-financial interests to disclose.

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