Research Report **Open Access**

The Development and Clinical Transformation of Gene Therapy in Cardiovascular Diseases

Wei Wang, Lingfei Jin

Biotechnology Research Center, Cuixi Academy of Biotechnology, Zhuji, 311800, China

Corresponding author email: 3541865881@qq.com

International Journal of Molecular Medical Science, 2024, Vol.14, No.2 doi: 10.5376/ijmms.2024.14.0007

Received: 03 Mar., 2024

Accepted: 07 Apr., 2024

Published: 17 Apr., 2024

Preferred citation for this article:

Wang W., and Jin L.F., 2024, The development and clinical transformation of gene therapy in cardiovascular diseases, International Journal of Molecular Medical Science, 14(2): 48-55 (doi: 10.5376/ijmms.2024.14.0007)

Abstract Cardiovascular disease is one of the major causes of death worldwide, posing a huge burden on human health. Gene therapy, as an emerging treatment method, has the potential to change traditional treatment modes. This review aims to explore the development and clinical translation of gene therapy in cardiovascular diseases. This review systematically reviews the research progress of gene therapy related to cardiovascular diseases, including angiogenesis and repair, myocardial protection and reconstruction, as well as inflammation and immune regulation. In addition, the clinical trials of gene therapy that have been conducted were reviewed and their challenges and opportunities were discussed. The paper further prospects the prospects of gene therapy in cardiovascular diseases and explores the applications of personalized gene therapy and precision medicine. This review aims to provide a comprehensive overview and reference for the application and research of gene therapy in cardiovascular diseases.

Keywords Gene therapy; Cardiovascular disease; Clinical conversion; Personalized treatment

Cardiovascular disease is one of the most significant causes of death worldwide, having a significant impact on human health and quality of life. Although there are currently various traditional treatment methods to choose from, such as drug therapy, surgery, and interventional therapy, there are still many challenges and limitations. Therefore, it is particularly important to seek new treatment methods to improve the prognosis and quality of life of cardiovascular diseases.

In recent years, gene therapy has attracted widespread attention and research as an emerging therapeutic strategy. Gene therapy aims to treat and prevent cardiovascular diseases by introducing, modifying, or inhibiting the expression of specific genes (Cring and Sheffield, 2022). Its core principle is to restore or enhance the function of abnormal genes or inhibit the expression of harmful genes by delivering appropriate genes or RNA to the patient's body. Gene therapy has many advantages, such as targeting the cause directly, providing long-lasting therapeutic effects, reducing drug side effects, and improving patient resistance.

In the field of cardiovascular disease, gene therapy provides us with new treatment ideas and opportunities. Previous studies have shown that gene therapy can improve the development and prognosis of cardiovascular diseases by promoting angiogenesis and repair, protecting myocardial cells, regulating inflammation and immune responses, and other pathways. These studies provide strong evidence for the development and clinical translation of gene therapy in the field of cardiovascular disease. However, although gene therapy has achieved some encouraging results in the laboratory, its application in clinical practice still faces many challenges. For example, the effectiveness and safety of gene delivery technology, the persistence and consistency of therapeutic effects, the personalization of treatment plans, and ethical and regulatory issues are all important factors that affect the clinical translation of gene therapy.

Therefore, this review will comprehensively analyze the development and clinical translation of gene therapy in cardiovascular diseases. We will focus on the research progress in key areas such as angiogenesis and repair, myocardial protection and reconstruction, and inflammation regulation, and review the clinical trials of gene therapy that have been conducted. At the same time, discuss the prospects of gene therapy in cardiovascular diseases, as well as the application prospects of personalized therapy and precision medicine. Through these reviews, the aim is to provide a comprehensive understanding and understanding of the application and clinical translation of gene therapy in cardiovascular diseases, and to provide guidance for further research and development.

1 Research Progress in Gene Therapy Related to Cardiovascular Diseases

1.1 Gene therapy related to angiogenesis and repair

Cardiovascular disease is a kind of disease caused by atherosclerosis, hypertension, heart failure, etc. Its development is closely related to the limitation of angiogenesis and repair. In recent years, gene therapy has become a new field for improving the prognosis of cardiovascular diseases, including research on improving cardiovascular disease by promoting angiogenesis and repair. Angiogenesis and repair are important physiological processes in the cardiovascular system, which can restore blood supply and repair damaged tissues (Johnson et al., 2019). Gene therapy promotes the growth and repair of new blood vessels by targeting the activation or inhibition of specific gene expression, bringing hope for the treatment of cardiovascular diseases.

The focus of a gene therapy study is on the vascular endothelial growth factor (VEGF) family (Figure 1), which plays an important role in angiogenesis and repair. Research has shown that by using a vector that transduces the VEGF gene, overexpression of VGEF can be induced, promoting the growth of new blood vessels, and improving myocardial blood supply. Similarly, other growth factors and regulatory factors such as FGF (fibroblast growth factor), PDGF (platelet derived growth factor), and HGF (hepatocyte growth factor) have also been extensively studied. These gene therapy strategies can not only stimulate the formation of new blood vessels, but also improve the function and stability of existing blood vessels.

In addition to growth factors, gene therapy can also achieve therapeutic effects by altering negative regulatory factors of angiogenesis, such as vascular endothelial growth factor inhibitors (VEGF inhibitors). By inhibiting the expression of these negative regulatory factors, the inhibitory effect of angiogenesis can be reduced, thereby promoting the growth and repair of blood vessels.

In animal models and preliminary clinical trials, gene therapy related to angiogenesis and repair has achieved some encouraging results. However, further research is needed to address potential safety issues and ensure consistency in treatment outcomes. In addition, the personalization and precision of gene therapy plans are also the direction of future research to achieve better treatment outcomes and prognosis.

Gene therapy related to angiogenesis and repair has shown enormous potential in the field of cardiovascular diseases. By activating beneficial gene expression or inhibiting harmful gene expression, we can promote the growth and repair of new blood vessels, providing new ideas and methods for the treatment of cardiovascular diseases. However, further research is still needed to verify its efficacy and safety in order to achieve true clinical translation.

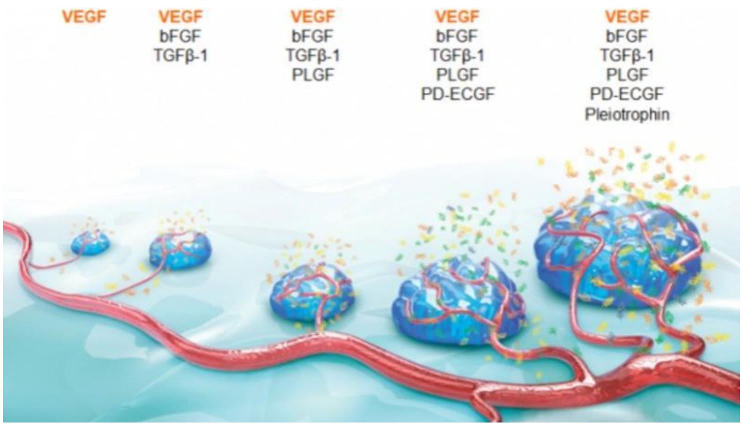

Figure 1 Vascular endothelial growth factor (VEGF)

1.2 Gene therapy related to myocardial protection and reconstruction

Gene therapy related to myocardial protection and reconstruction is one of the research hotspots in the field of cardiovascular diseases. By regulating the expression of myocardial protective genes and regeneration related genes, we can promote the survival and regeneration of myocardial cells, providing new pathways for the repair of myocardial tissue and the recovery of cardiac function. However, more research is still needed to achieve the clinical application of gene therapy.

Myocardial protection and reconstruction are important directions in the treatment of cardiovascular diseases, and gene therapy also has potential application prospects in this field. Gene therapy research on myocardial protection and reconstruction can promote the survival and regeneration of myocardial cells by activating protective genes, inhibiting harmful genes, etc., thereby reducing myocardial injury and promoting the recovery of cardiac function.

A common gene therapy strategy is to transduce protective genes such as heat shock protein (HSP), antioxidant enzymes (such as superoxide dismutase SOD), and anti apoptotic factors (such as Bcl-2). Overexpression of these genes can increase the antioxidant capacity of myocardial cells, reduce cell apoptosis, and promote cell survival and recovery of cardiac function.

Another strategy is to promote the regeneration and repair of myocardial cells by transducing regeneration related genes, such as genes that regulate myocardial cell proliferation and differentiation. Some studies have shown that by introducing cell cycle regulatory factors, fibroblast transdifferentiation genes, etc., the proliferation and differentiation of myocardial cells can be stimulated, thereby promoting the reconstruction and repair of myocardial tissue. In addition, gene therapy can also achieve myocardial reconstruction through stem cells and genetically modified cells. For example, by transducing specific genes in stem cells or genetically modified cells, targeted differentiation of these cells into cardiomyocytes can be promoted (Figure 2), thereby achieving myocardial regeneration and reconstruction.

Although gene therapy related to myocardial protection and reconstruction has shown great potential in laboratory and animal models, its application in clinical trials still faces some challenges. For example, the delivery system of gene therapy, gene selection, and regulation of expression levels still need further research and optimization. In addition, the evaluation of long-term effectiveness and safety is also an important issue.

1.3 Gene therapy related to inflammation and immune regulation

Gene therapy related to inflammation and immune regulation is a new field in the treatment of cardiovascular diseases. By regulating the expression of genes related to inflammation and immune response, we can suppress the degree of inflammation and immune response, thereby improving the prognosis of cardiovascular disease. However, further research is still needed to validate the safety and efficacy of gene therapy in order to realize its potential in clinical applications.

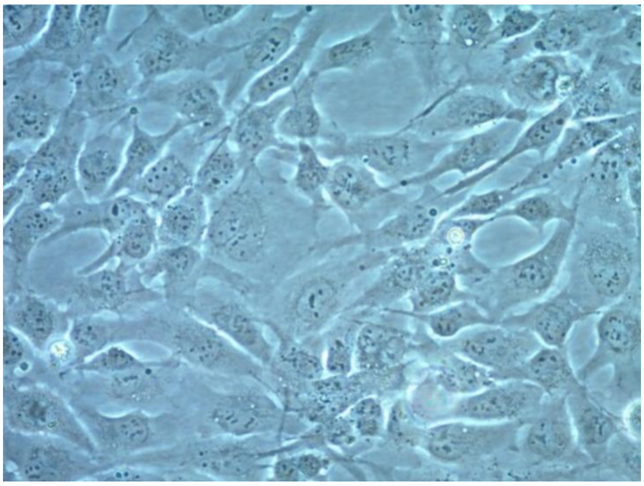

Figure 2 Myocardial cells

Inflammation and immune regulation play important roles in the development and progression of cardiovascular diseases (Li and Yang, 2020). Gene therapy has also shown potential in regulating inflammation and immune responses, providing new directions for the treatment of cardiovascular diseases. Inflammation and immune response often manifest as vascular wall inflammation and elevated levels of inflammatory markers such as C-reactive protein and tumor necrosis factor in cardiovascular diseases. Gene therapy strategies can suppress the degree of inflammation and inflammation related damage by regulating the expression of genes related to inflammation and immune response, thereby improving the prognosis of cardiovascular diseases.

A common gene therapy method is to inhibit the inflammatory response by transducing anti-inflammatory factor genes. For example, Transduction of genes that inhibit tumor necrosis factor or chemokine expression inhibitors can reduce inflammation of vascular wall and the release of inflammatory mediators, thereby reducing the occurrence and progression of atherosclerosis.

Another strategy is to regulate immune responses by transducing genes of immune regulatory factors. For example, genes that transduce the surface molecules of antigen presenting cells can enhance the specificity and function of antigen presenting cells, thus regulating the occurrence and degree of immune response and inhibiting the development of cardiovascular diseases such as atherosclerosis.

In addition, some studies have explored gene therapy for immune cells, such as transducing T cell surface receptor genes to enhance their anti-inflammatory function, or transducing stem cells into immunosuppressive cells to regulate immune responses and alleviate inflammatory responses. Although gene therapy related to inflammation and immune regulation has shown potential in laboratory and animal models, there are still some challenges in clinical application. For example, further research and optimization are needed on issues such as appropriate genome selection, delivery system selection, and gene regulation. In addition, evaluating the long-term efficacy and safety of gene therapy is also a challenging issue.

2 Clinical Practice and Translation of Gene Therapy

2.1 Overview of clinical trials of gene therapy in cardiovascular diseases

The core idea of gene therapy is to repair or regulate abnormal gene functions in patients by introducing exogenous genetic materials. In the field of cardiovascular disease, clinical practice and translation of gene therapy are constantly evolving, and have already involved multiple clinical trials. Some clinical trials of gene therapy related to cardiovascular diseases have been conducted or are currently underway.

At present, some experiments have been conducted on myocardial ischemia and myocardial infarction, such as gene therapy using angiogenic factors (such as VEGF and FGF) to promote new blood vessel growth and myocardial protection (Deng et al., 2020). Other experiments involve using stem cells to transduce specific genes to promote myocardial repair and regeneration. In the aspect of atherosclerosis, some experiments are under way to inhibit inflammation of arterial wall, promote plaque stability and enhance the function of vascular smooth muscle cells through gene therapy. For example, in trials, genes that inhibit inflammatory factors or stabilize plaque are used to treat atherosclerosis.

In addition, some clinical trials have been conducted to investigate the use of gene therapy to correct genetic mutations associated with congenital heart disease. For example, gene repair techniques targeting specific mutated genes are used to treat some congenital heart diseases. In the treatment of heart failure, some gene therapies in trials aim to enhance myocardial contractility and metabolic function. For example, in the experiment, carriers were used to deliver specific genes to enhance the contractile proteins of myocardial cells.

Clinical trials of gene therapy in cardiovascular diseases have made progress, but still face some challenges. This includes the selection of delivery systems, regulation of gene expression, and evaluation of the persistence and safety of treatment. In addition, the high cost and large-scale production of gene therapy are also one of the factors that restrict its transformation. Nevertheless, clinical trials of gene therapy in the field of cardiovascular disease continue, and it may provide more promising therapies for the treatment of cardiovascular disease in the future.

2.2 Challenges and opportunities for clinical translation of gene therapy

The clinical translation of gene therapy in cardiovascular diseases faces some challenges and opportunities. In terms of challenges, the selection of delivery systems is one of them. The cardiovascular system is complex, and accurately delivering genetic materials to specific areas is one of the key challenges. Effectively delivering therapeutic genes to the heart, blood vessels, or other related tissues to achieve therapeutic effects requires overcoming tissue wall barriers and stably delivering genetic materials to the target location.

In addition, gene therapy may encounter safety issues, such as immune reactions, toxic reactions, or adverse events. The side effects during treatment are an important consideration factor that needs to ensure treatment safety and reduce the potential risk of adverse reactions. The persistence of gene therapy is a key issue. In cardiovascular disease, it is necessary to ensure that the introduced genes can exist for a long time and continue to exert therapeutic effects, in order to achieve the goal of long-term disease improvement and disease management.

At the same time, there are also certain challenges in map diversity and individual differences. Cardiovascular diseases have a wide range of types and complex genetic backgrounds, and there are genetic and environmental differences among different patients. In gene therapy, it is necessary to consider individual differences and provide personalized treatment strategies for different types of cardiovascular diseases.

On the other hand, there are also opportunities for gene therapy in cardiovascular diseases. With the continuous development of technology, such as the emergence and continuous improvement of gene editing technology, gene therapy has more opportunities in the field of cardiovascular disease. These new technologies make gene therapy more precise, efficient, and provide more treatment options.

The development of gene therapy provides new opportunities for early intervention in cardiovascular diseases (Wang and Kuang, 2023). Individualized care through early detection and gene therapy can provide more precise treatment strategies, reduce the risk of disease progression and complications. Gene therapy involves interdisciplinary collaboration, including basic scientific research, clinical medicine, genetics, biotechnology, and other fields. Multidisciplinary collaborative research will promote the exchange of knowledge and technology, and promote the clinical translation of gene therapy in cardiovascular diseases.

Developing appropriate regulations and ethical frameworks is also crucial for the clinical translation of gene therapy in cardiovascular diseases. Appropriate regulation and ethical guidance will ensure the safety and effectiveness of clinical practice, and provide support for the development and application of gene therapy. Overall, despite facing challenges, gene therapy has many opportunities that can be fully utilized in cardiovascular disease.

3 The Prospects of Gene Therapy in Cardiovascular Diseases

3.1 Future application scenarios and potential benefits

Gene therapy in cardiovascular diseases has broad prospects. Gene therapy can intervene in mutated genes in inherited cardiovascular diseases to restore abnormal gene function or repair gene defects, thereby achieving disease treatment and prevention. Gene therapy can promote myocardial regeneration and repair, increase the proliferation and regeneration ability of myocardial cells, and provide new treatment strategies for heart diseases such as myocardial infarction and heart failure. In addition, gene therapy can promote angiogenesis and repair damaged blood vessels, improve blood supply and circulatory function, which is of great significance for ischemic cardiovascular disease.

The future application scenarios and potential benefits of gene therapy in cardiovascular diseases are expected. In terms of future applications, gene therapy can be used for early detection and intervention, early detection of cardiovascular disease risk factors and genetic tendencies, and personalized gene therapy to reduce the risk of disease development and complications. For patients with drug-resistant cardiovascular diseases, such as patients who have failed to receive antiarrhythmic drug therapy, gene therapy can provide alternative treatment options to improve their symptoms and quality of life. Genetic cardiovascular disease may involve multiple mutated genes, and gene therapy can provide personalized treatment strategies based on the genotype of different patients to maximize the recovery of abnormal gene function.

In terms of potential benefits, gene therapy has the potential to become a curative treatment for cardiovascular diseases, achieving complete cure by repairing abnormal genes or increasing the repair ability of damaged tissues. Gene therapy can reduce the occurrence and progression of complications in cardiovascular diseases, improve the quality of life of patients, and lower long-term care and treatment costs. Gene therapy can provide personalized treatment strategies based on an individual's genotype and phenotype, improving the accuracy and effectiveness of treatment.

3.2 The impact of the development of new technologies and strategies on gene therapy for cardiovascular diseases

The development of new technologies and strategies has a profound impact on gene therapy for cardiovascular diseases, which can improve the effectiveness and safety of treatment, and expand the feasibility of treatment. The emergence of gene editing techniques such as CRISPR-Cas9 has made gene therapy more precise and efficient (Liao and Guo, 2021). By using gene editing technology, abnormal gene sequences can be directly modified, defects or functional disease-related genes can be repaired, thereby achieving the goal of treatment. This will bring more opportunities for gene therapy for cardiovascular diseases.

The delivery system is a crucial part of gene therapy, affecting the accurate delivery of genetic materials to the lesion site. With the development of nanotechnology and carrier technology, the design and improvement of delivery systems have improved the delivery efficiency and stability of genetic materials, effectively overcoming the challenges brought by the complexity of the cardiovascular system.

In addition, cell therapy and stem cell technology can utilize the self-renewal and differentiation ability of stem cells for the treatment and regeneration of cardiovascular diseases. For example, the regeneration and transplantation of myocardial cells can promote the repair of the heart. Cell therapy and stem cell technology provide new approaches and strategies for gene therapy.

One important challenge of gene therapy is to ensure that the introduced genes can exist for a long time and continue to exert therapeutic effects. In recent years, scientists have developed a series of gene expression regulation strategies, such as using specific promoters and regulatory elements, as well as RNA interference technology, to achieve precise regulation and long-term expression of genes, thereby improving treatment efficacy (Lu and Thum, 2019). Gene therapy for cardiovascular diseases requires interdisciplinary collaborative research and the support of appropriate regulatory and ethical frameworks. This helps to enhance the safety of gene therapy research and the feasibility of clinical translation, promoting the development of technology and strategies.

In summary, the development of new technologies and strategies has a significant impact on gene therapy for cardiovascular diseases. The advancement of these technologies and strategies will improve the effectiveness and safety of gene therapy, and expand its application scope in the treatment of cardiovascular diseases.

3.3 Application of personalized gene therapy and precision medicine in cardiovascular diseases

The application of personalized gene therapy and precision medicine in cardiovascular diseases is changing the traditional one size fits all treatment model, providing patients with more precise and effective treatment strategies. By analyzing an individual's genotype and genetic variation, the risk of developing a certain cardiovascular disease can be evaluated. This personalized risk assessment can help doctors and patients develop targeted preventive measures and monitoring plans to reduce the occurrence and progression of diseases.

In addition, individual genomic information can affect drug absorption, metabolism, and response. By detecting the genotype of patients, it is possible to identify whether there are genetic variations related to drug metabolism, thereby guiding appropriate drug selection and dosage, and improving the effectiveness and safety of drug treatment. Gene therapy in cardiovascular diseases can provide personalized treatment strategies based on the patient's genotype and phenotype. For example, developing corresponding gene therapy methods for different gene mutations, or adjusting treatment plans based on individual gene expression patterns to maximize gene function restoration and disease improvement.

The microbiome is a collection of microorganisms such as bacteria, fungi, and viruses in the human body, which has a significant impact on cardiovascular health. Personal microbial composition can predict the risk of cardiovascular disease by analyzing gut microbiota, and may be managed through microbial preparations or dietary adjustments to cardiovascular health (Witkowski et al., 2020). The use of genomic and biomarker information can help predict the progression and prognosis of cardiovascular disease in patients. This helps with early intervention and effective treatment, reducing the occurrence of complications.

The application of personalized gene therapy and precision medicine enables doctors to develop personalized treatment plans based on the patient's genetic characteristics, biomarkers, and environmental factors (Zhang et al., 2021). This personalized treatment method is expected to improve treatment effectiveness, reduce adverse reactions, and bring better results for the prevention and treatment of cardiovascular diseases.

4 Summary and Outlook

Significant progress has been made in the development and clinical translation of gene therapy in the field of cardiovascular diseases. Gene therapy provides new means for the treatment and prevention of cardiovascular diseases by repairing, replacing, or regulating abnormal genes. In recent years, research has discovered genes related to cardiovascular disease, laying the foundation for the development of treatments targeting these genes. In addition, the application of gene editing techniques such as CRISPR-Cas9 makes gene therapy more precise and efficient. These technologies enable us to directly modify the patient's genes to achieve therapeutic effects. In order to accurately deliver genes to cardiovascular tissues, a reliable delivery system is also needed. The development of nanotechnology and carrier technology has significantly improved the delivery efficiency and stability of gene therapy. Personalized gene therapy strategies are also very important. Developing personalized gene therapy strategies based on an individual genotypes and phenotypes can help improve treatment effectiveness and safety, and provide better healthcare for patients.

However, despite these advances, gene therapy still faces challenges in the field of cardiovascular disease. On the one hand, it is necessary to further improve the delivery system to enhance the efficiency and stability of gene delivery. On the other hand, the safety of gene therapy needs to be validated, including in-depth research and validation of gene editing techniques that may cause mutations or other adverse effects. In addition, the long-term effectiveness and persistence of gene therapy also require more systematic and long-term research to verify its feasibility and reliability in cardiovascular disease.

Despite these challenges, gene therapy still has enormous potential in the field of cardiovascular disease. With the continuous advancement of technology and the advancement of clinical trials, gene therapy is expected to provide more precise, effective, and personalized treatment strategies for cardiovascular disease patients. Further research and exploration will promote the widespread application of gene therapy in the field of cardiovascular disease, bringing greater improvements to the quality of life and health status of patients.

Acknowledgments

Thank you to Ms. Fang Keyan for her guidance and review of the paper. Their many constructive suggestions have enabled the research to be improved. The accompanying images in the paper are sourced from the internet. I respect and uphold the rights of each image owner. If there is any infringement of the images, please feel free to contact me at any time.

References

Cring M.R., and Sheffield V.C., 2022, Gene therapy and gene correction: targets, progress, and challenges for treating human diseases, Gene Ther., 29: 3-12.
https://doi.org/10.1038/s41434-020-00197-8
PMid:33037407

Deng J., Guo M., and Li G., 2020, Junjie Xiao Gene therapy for cardiovascular diseases in China: basic research, Gene Ther., 27: 360-369.
https://doi.org/10.1038/s41434-020-0148-6
PMid:32341485

Johnson T., Zhao L., Manuel G., Taylor H., and Liu D., 2019, Approaches to therapeutic angiogenesis for ischemic heart disease, J. Mol. Med. 97: 141-151.
https://doi.org/10.1007/s00109-018-1729-3
PMid:30554258 PMCid:PMC6417498

Liao M.Q., and Guo S.X., Adeno-associated virus-based gene therapy for cardiovascular diseases, Shengming Kexue (Chinese Bulletin of Life Sciences), 3: 392-399.

Li H.M., Yang C., 2020, Research progress of function and molecular mechanism of interleukin-37 in cardiovascular disease, Yixue Zongshu (Medical Recapitulate), 26(19): 3780-3784.

Lu D., and Thum T., 2019, RNA-based diagnostic and therapeutic strategies for cardiovascular disease, Nat. Rev. Cardiol. 16: 661-674.
https://doi.org/10.1038/s41569-019-0218-x
PMid:31186539

Wang J., Kuang S.Q., 2023, The role of molecular biogenes in essential hypertension, Linchuang Yixue Jinzhan (Advances in Clinical Medicine), 13(7): 11036-11042.
https://doi.org/10.12677/ACM.2023.1371539

Witkowski M., Weeks T.L., and Hazen S.L., 2020, Gut microbiota and cardiovascular disease, Circulation Research, 127(4): 553-570.
https://doi.org/10.1161/CIRCRESAHA.120.316242
PMid:32762536 PMCid:PMC7416843

Zhang F., Xu D.D., Jiao X.D., Tao X., Wei H., Gao S.H., Hou X.Y., Li M.M., Wang Z.P., and Chen W.S., 2021, Advances of research on technologies for individualized treatment in clinical drug therapy, Yaoxue Jinzhan (Progress in Pharmaceutical Sciences), 45(2): 91-99.