STRZELCZYK, Magdalena, PABIS, Gabriela, WZIĄTEK, Joanna, BĘTKOWSKA, Paula, KOZIOŁEK, Iwona, KOWALIK, Piotr, FATYGA, Patrycja, FATYGA, Wiktoria, KRZYŻANOWSKA, Daria and DOWIERCIAŁ, Kinga. Gene therapy in cardiomyopathies - Review of the latest reports. Quality in Sport. 2025;43:61280. eISSN 2450-3118.
https://doi.org/10.12775/QS.2025.43.61280
https://apcz.umk.pl/QS/article/view/61280

The journal has been awarded 20 points in the parametric evaluation by the Ministry of Higher Education and Science of Poland. This is according to the Annex to the announcement of the Minister of Higher Education and Science dated 05.01.2024, No. 32553. The journal has a Unique Identifier: 201398. Scientific disciplines assigned: Economics and Finance (Field of Social Sciences); Management and Quality Sciences (Field of Social Sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).
The authors declare that there is no conflict of interest regarding the publication of this paper.
Received: 21.05.2025. Revised: 05.07.2025. Accepted: 05.07.2025. Published: 07.07.2025.

Gene therapy in cardiomyopathies - Review of the latest reports

Authors:

Magdalena Strzelczyk [MS]

Municipal Medical Centre Jonscher in Łódź, Milionowa 14 Street, 93-113 Łódź, Poland

strzelczykmagdamed@gmail.com

https://orcid.org/0009-0005-6312-3002

Gabriela Pabis [GP]

The Provincial Hospital, Grunwaldzka 45, 25-736 Kielce, Poland

gabriela.pabis98@gmail.com

https://orcid.org/0009-0002-3208-5160

Joanna Wziątek [JW]

Municipal Medical Centre Jonscher in Łódź, Milionowa 14 Street, 93-113 Łódź, Poland

wziatek.joanna1@gmail.com

https://orcid.org/0009-0002-1656-7477

Paula Bętkowska [PB]
Municipal Medical Centre Jonscher in Łódź, Milionowa 14 Street, 93-113 Łódź, Poland
paula.betkowska0306@gmail.com
https://orcid.org/0009-0002-7050-4039

Iwona Koziołek [IK]
The Provincial Hospital, Grunwaldzka 45, 25-736 Kielce, Poland
bajor-iwona@wp.pl
https://orcid.org/0009-0002-1077-3640

Piotr Kowalik [PK]
Medical University of Lodz, Tadeusz Kościuszko Avenue 4, 90–419 Łódź, Poland
piotrek.kowalik14@gmail.com
https://orcid.org/0009-0009-4813-9742

Patrycja Fatyga [PF]
The Provincial Hospital, Grunwaldzka 45, 25-736 Kielce, Poland
patrycja3.fatyga@gmail.com
https://orcid.org/0009-0001-1277-1246

Wiktoria Fatyga [WF]
Non-public Health Care Facility Prophylactics Wiesława Piotrowska Limited Liability Company, Jana Jeziorańskiego 137, 25-432 Kielce, Poland
wiktoria.fatyga34@gmail.com
https://orcid.org/0009-0000-5931-925X

Daria Krzyżanowska [DK]
Municipal Medical Centre Jonscher in Łódź, Milionowa 14 Street, 93-113 Łódź, Poland
dariakrzyz@wp.pl
https://orcid.org/0009-0002-5349-5679

Kinga Dowiercial [KD]
Independent Public Regional Specialist Hospital in Chełm Ceramiczna 1 Street, 22-100 Chełm, Poland
kinga.dowiercial@gmail.com
https://orcid.org/0009-0000-9132-1026

Corresponding author: Magdalena Strzelczyk, [MS], strzelczykmagdamed@gmail.com

ABSTRACT

Introduction and purpose

Gene therapy appears to be a promising treatment for patients with cardiomyopathy and innovative therapeutic option. The aim of this review is to present the latest gene therapy technologies, innovations, research in the treatment of cardiomyopathy and analysis of the ethical issues associated with the use of modern therapies.

Material and methods

This review is based on recent articles from the years 2020-2025 found in databases such PubMed, Elsevier.

Results

Gene editing through CRISPR-Cas technology allows for the modification of genetic material by making changes at precise locations what is highly useful in gene therapy. Gene Expression Regulation (RNAi) involves preventing the production of proteins by silencing a faulty gene. Antisense therapy (ASO) uses antisense oligonucleotides to exclude a particular exon and causes the translation process to stop. Gene replacement involves introducing a healthy copy of a mutated gene into the genome along with an appropriate vector.

Conclusions

Individual technologies in the treatment of cardiomyopathy show potential for treating patients in the future. It is also important to remember the ethical issues when using solutions based on gene therapy. Clinical trials in the future are necessary to further search for solutions for patients with cardiomyopathy.

Keywords: cardiomyopathy; gene editing; antisense therapy; gene expression; gene replacement; ethical issues.

INTRODUCTION

Cardiomyopathies are defined as myocardial abnormalities in structure and function without hypertension, coronary artery disease, valvular heart disease, and congenital defects that could account for the observed myocardial disorders [1]. We classify four main types of cardiomyopathy: hypertrophic HCM, dilated DCM, restrictive RCM, and arrhythmogenic right ventricular cardiomyopathy ARVC. The most dominant cardiomyopathy all over the world is dilated cardiomyopathy (DCM), when the least common is restrictive cardiomyopathy (RCM)- prognosis varies depending on the specific type of cardiomyopathy [2]. The total number of global cardiomyopathy cases is estimated at 4.44 million; non-alcoholic cardiomyopathy is most commonly found in Sub-Saharan East Africa, while alcoholic cardiomyopathy is more prevalent in Eastern Europe [3].

As we know, cardiomyopathies can cause critical cardiovascular consequences [4]. Conventional treatment methods, such as a healthy lifestyle, pharmacotherapy or surgical interventions, may help manage symptoms but do not resolve the root cause in the presence of genetic abnormalities. With the growing understanding of gene mutations associated with cardiomyopathies, gene therapy is proving to be a promising treatment strategy [5]. As early as the previous century, research began on developing safe and effective methods of genome modification for therapeutic purposes in inherited diseases. This approach aims to personalize therapy by correcting the mutations responsible for specific disorders, what can potentially serve as one of the treatment strategies. The aim of this review is to understand the newest developments in gene therapy, present the latest clinical trials and discuss the ethical challenges that may occur in the development of technologies.

Material and methods

This review is based on recent articles from the years 2020-2025 found in databases such PubMed, Elsevier. The analysis is grounded in data collected from publicly available sources and was searched in April 2025. The keywords used for literature retrieval were: cardiomyopathy, gene editing, antisense therapy, gene expression, gene replacement, ethical issue.

The selection criteria for the articles were based on the content of the publications, limiting them to cardiomyopathy, gene therapy and ethical issues. The inclusion criteria applied to preclinical and clinical studies. Publications that did not contain information on cardiomyopathy, gene therapy, or ethical issues were excluded.

DESCRIPTION OF STATE OF KNOWLEDGE

Table 1. Comparative overview of cardiomyopathy types.

Type of cardiomyopathy	Prevalence	Genetiology	Genes involved in the development of cardiomyopathy	Effect of the mutation	References
Dilated CardiomyopathyDCM	1:250-1:400 with heart failure population 1:2500 in the general population	35- 50 % of all cases, mainly autosomal dominant mutations	TTN, LMNA, EMD, PLN, FLNC, MYH7, ACTN2	symptoms of congestive heart failure, arrhythmias, sudden cardiac death	[4, 5]
Hypertrophic CardiomyopathyHCM	1:500	mainly autosomal dominant mutations	MYBPC3, MYH7, TPM1, TNNT2, TNNI3, MYL2, MYL3	exertional dyspnea, chest pain, syncope	[4, 6, 7]
Restrictive Cardiomyopathy RCM	2% in adults, up to 3% in children of all cardiomyopathies	depending on the cause	TTR, MYBPC3, MYH7, TNNI3, TNNT2, ACTC, TTN	diastolic dysfunction of heart, dyspnea, pulmonary edema, chest pain	[5, 8, 9]
Arrhythmogenic CardiomyopathyARVC	1:1000-1:5000	40- 60 % of all cases, mainly autosomal dominant mutations	PKP2, JUP, DSP, DSG2, DSC2, LMNA,	chest pain, syncope, sudden cardiac death	[4, 5, 10, 11]

Gene Therapy Strategies

Advances in genetics and molecular biology have led to the development of several approaches for the potential treatment of inherited diseases, including cardiomyopathies. Scientists use genetic material modification for this purpose. Gene therapy applies various methods and technologies to serve functions, such as silencing a defective gene and replacing it with a healthy copy. The major techniques include: gene editing using CRISPR/Cas9, regulating gene expression through RNAi, exon skipping- antisense therapy, and gene replacement [12].

Gene editing

Gene editing is performed with the CRISPR-Cas9 technology, discovered as part of the bacterial protective system against phages. This tool consists of the Cas nuclease, which is guided to a specific place in the genome using a single guide RNA (sgRNA). After reaching the intended DNA sequence, the complex binds to the target and creates a double-strand break. After this break two major DNA repair mechanisms can be activated.

The first mechanism is NHEJ (Non-Homologous End Joining), a non-precise repair process that ligates the ends of DNA strands, causing insertions and deletions. This approach is commonly used to disrupt gene function. The second mechanism is HDR (Homology-Directed Repair), which uses externally supplied homologous DNA sequences as a template for accurate repair, allowing for precise gene modifications. Thanks to this technology, changes in specific locations of the DNA and mutation correction are possible, which is very useful in the treatment of genetic disorders [13].

The CRISPR-Cas9 complex has also been applied in cardiology research. The scientist studied mutation involved the MYBPC3 gene, which contributes to hypertrophic cardiomyopathy (HCM). It was demonstrated that this technology allows for the correction of the mutation [5]. The CRISPR-Cas9 complex is also used to expand our understanding of genetic heart diseases. It has been shown that a mutation in the TNNT2 gene leads to structural abnormalities in the heart, which are relevant to dilated cardiomyopathy (DCM) [14].

Gene editing offers hope for future treatments. Research in this area is still ongoing and rapidly evolving. This therapy could become an important tool in the future for treating currently incurable diseases.

Gene Expression Regulation (RNAi, siRNA, miRNA)

RNA interference (RNAi) is a method for which the Nobel Prize was awarded in 2006. It is a process in which a specific gene is silenced through the degradation of mRNA. Long dsRNA strands are cut by the DICER enzyme into characteristic fragments containing 21-23 nucleotides, after which they are directed to the RISC mechanism, which causes the destruction of the given gene [12]. Currently, several types of RNAi are used to block the production of proteins produced by the genes we want to silence. These include siRNA and miRNA. This can be particularly important in the case of cardiomyopathies, where the cause is sometimes found in a mutated gene. It seems that silencing the gene will prevent the production of defective protein and improve the heart's structural condition without completely turning off the gene.

Such studies have been conducted in a mouse model, where it was demonstrated that the heart with a mutation causing HCM can be silenced using RNAi. A particularly significant development in gene therapy has been the development of treatments using siRNA in heart amyloidosis, which can lead to restrictive cardiomyopathy [15]. The injection of siRNA results in reduced production of transthyretin, a factor causing amyloidosis. In the double-blind, randomized HELIOS-B trial, patients with ATTR cardiomyopathy received siRNA or placebo. In the group of patients receiving siRNA, a decrease in all-cause mortality and a reduction in the number of cardiovascular incidents were observed [16].

Research is also being conducted on the role of miRNA in treatment. In particular, the suppression of miR-199a-3p in a mouse model with hypertrophic cardiomyopathy shows therapeutic potential. It was shown that inhibiting the expression of miR-199a-3p is associated with reduced cardiac fibrosis and improved heart function [17]. This may indicate potential use in future therapies. Other studies have evaluated the association of miRNA in patients with hypertrophic cardiomyopathy. It was found that miR-27a, miR-29a i miR-199a-5p caused hypertrophy or fibrosis of the heart muscle. It was discovered that miR-29a was the most consistent with the features of hypertrophic cardiomyopathy (HCM), making it the most promising indicator [18].

Antisense therapy (ASO), exon skipping

This therapy takes advantage of specific regions in genes called exons, which contain the instructions needed to produce proteins. In the process of transcription, the pre-mRNA consists of exons and introns. In the splicing process, exons are linked together. After the removal of specific fragments, the appropriate exons can join together, leading to the formation of a protein. The exon skipping method uses antisense oligonucleotides (ASOs) to skip a

specific exon during splicing, which changes the mRNA reading frame. This allows the production of a functional version of the protein, which can be beneficial in certain diseases [19].

Cardiomyopathy in Duchenne muscular dystrophy is caused by a mutation in the DMD gene, which results in a lack of dystrophin, a protein essential for maintaining the integrity of muscle cell membranes. ASO therapy, through exon skipping, allows for the production of a shortened but functional form of dystrophin [20].

ASO therapy also plays a role in cases of TTN gene mutations, which may cause dilated cardiomyopathy. Titin is essential for maintaining the structural integrity of sarcomeres and myofibrils in the heart muscle. In the case of mutation, translation can terminate prematurely, causing titin to become nonfunctional. ASO therapy enables the mutated exon to be skipped, leading to the production of a functional form of titin [21].

Antisense therapy has also been used to reduce the levels of phospholamban (PLN) protein, which led to improved cardiac function and reduced mortality in mice with PLN R14del-related hereditary cardiomyopathy [22].

Gene replacement

Gene replacement therapy involves replacing a defective gene that is unable to produce a functional protein with a correct copy of the gene. This allows the protein to be produced and helps maintain the function. The first stage involves identifying which gene is responsible for the disease. The second stage includes delivering a copy of the gene using a carrier for the genetic material and introducing it into the appropriate cells. The final stage is the production of the protein following gene therapy [23].

An example of such therapy was used in a preclinical study on hypertrophic cardiomyopathy caused by a mutation in the MYBPC3 gene, which is involved in cardiac muscle contraction. During the therapy, a functional copy of the gene was delivered using AAV9 (TN-201). In mouse models with the MYBPC3 mutation, improvement in cardiac function and hemodynamic parameters was confirmed [23].

The adeno-associated virus (AAV) vector is used in gene therapy due to its affinity for cardiomyocytes. The virus itself is not pathogenic, which means it does not cause disease. Since AAV efficiently delivers genetic material to target heart muscle cells and also induces a low immune response, it is considered a promising therapeutic tool. In cardiology, serotype 9 performs important functions due to high efficiency [24].

Preclinical and Clinical Trials

There are many studies focused on the various stages of gene therapy in cardiomyopathy. Some of them concern the vectors themselves, some focus on the genes and others on the drugs used in gene therapy.

The MyPEAK-1 study concerns adults with hypertrophic cardiomyopathy caused by the MYBPC3 mutation. The main objective is to assess the pharmacodynamics, safety and efficacy of T-201 (MYBPC3 gene and AAV) and how it affects heart function in individuals with cardiomyopathy. The study will evaluate indicators such as the preservation of cardiac muscle functionality, quality of life and the presence of concerning symptoms. The results will provide information on the adverse effects related to the therapy [6].

The randomized, double-blind APOLLO-B study focused on patients with transthyretin cardiac amyloidosis, a cause of cardiomyopathy. Patients were assigned in a 1:1 ratio to receive patisiran (siRNA) or a placebo. It was shown that 12 months of patisiran administration helped preserve exercise tolerance in individuals with cardiac amyloidosis [25].

Danon disease is caused by a mutation in the LAMP2 gene, which is responsible for maintaining the proper structure of the lysosomal membrane and preventing the collection of cellular debris in cardiac muscle cells what lead to cardiomyopathy. Researchers are attempting to demonstrate that AAV9 can deliver a healthy copy of the gene, resulting in improved cardiac function [26].

The effect of administering a copy of the GLA gene and the AAV vector on the treatment of Fabry disease is also being studied. This is a lysosomal storage disorder caused by a mutation in the GLA gene, leading to a deficiency of the enzyme alpha-galactosidase A and the accumulation of glycosphingolipids in various locations, including the heart. Gene therapies may help normalize parameters and treat the condition [27].

Pompe disease is an inherited metabolic disorder caused by a mutation in the GAA gene, which is responsible for producing the enzyme acid alpha-glucosidase. This leads to the accumulation of glycogen in skeletal and cardiac muscles, potentially causing damage, hypertrophy, and heart failure. The FORTIS trial is testing AT845, an AAV8 vector delivering the GAA gene, in patients with Pompe disease [28].

Friedreich's ataxia is a hereditary disease caused by a mutation in the *FXN* gene and a lack of frataxin. It can manifest with symptoms resulting from neurodegeneration, such as muscle weakness, loss of sensation, balance disorders, as well as cardiomyopathy, which is a cause of death. Scientists are testing the drug AAVrh.10hFXN, which improved cardiac

indicators in mice. Intravenous injection leads to an increase in frataxin levels and an improvement in ejection fraction [29].

Scientists are also conducting research on the treatment of dilated cardiomyopathy. The RBM20 mutation affects a region of the cell rich in arginine/serine, which under normal conditions enables the accumulation of the protein in the cell nucleus. In the case of mutation, the protein accumulates in the cytoplasm, disrupting proper heart function and ultimately leading to cardiomyopathy. In a mouse model study, adenine base editing (ABE) and prime editing (PE) technologies were used, which restored the localization of RBM20 to the nucleus. Improved functional parameters were observed in the treated mice [30].

Another disease that can lead to cardiomyopathy is Duchenne muscular dystrophy (DMD). In gene therapy, studies are being conducted on a drug combining a micro-dystrophin protein with an AAV vector. Researchers are evaluating both adverse effects and therapeutic efficacy. One of the trials showed increased levels of dystrophin and stabilization of walking ability [31].

In another study, the safety and effectiveness of the gene therapy PF-06939926- which contains an AAV9 vector along with a shortened dystrophin gene- are being analyzed. Adverse events are also being monitored, as well as the function and structure of the heart muscle [32]. Treatment of mutations in the PKP2 gene, which cause arrhythmogenic cardiomyopathy, was tested using AAVrh.74-PKP2a, an AAV vector carrying a functional copy of the defective gene, in a mouse model. This therapy prevented right ventricular hypertrophy, preserved left ventricular function, and alleviated cardiac arrhythmias [33].

Ethical concerns

Gene therapy represents a revolution in medicine, and despite its many advantages and the significant benefits of its use—especially the ability to treat previously incurable diseases—it is associated with ethical concerns.

Studies take into account the safety of treatment and the effects of administered drugs, both intended and unintended. In gene therapy, it is possible to alter the genome in a way that could trigger a mutation, potentially leading to cancer or other disorders in the body. This may occur as an unintended consequence of the methods used in gene editing. Unforeseen health reactions may also arise from inconsistent genetic modifications across different cells in the body. There is a risk that the therapy may not precisely target the intended tissues. Additionally, there is a possibility of incomplete or improper functioning of the treatment. It is also important

to consider the potential impact of gene therapy on future generations—effects that may only become apparent decades from now [34].

Gene therapy can also trigger an immune response. The immune response against the vector carrying the functional copies of the genes may cause inflammation or other adverse effects in the body's tissues. In such cases, the effectiveness of the therapy decreases and the reaction itself could pose a threat to the patient's health or life [35].

Consideration must also be given to fairness in access to therapy. The financial cost of treatment is very high and may not be covered by insurance, which limits access to treatment for some individuals. The lack of equality in receiving treatment leads to significant medical concerns [34].

Additionally, gene therapy technology seems difficult to understand. In order to receive treatment, patients should give their consent in an informed manner. In the case of not understanding the process or the terminology related to gene therapy, it is hard to agree to procedures in a fully informed way.

The technology and improvement of gene therapy techniques also carry the risk of abuse related to the intentional enhancement of human traits and characteristics. It involves modifying fundamental mechanisms in the body, which can have positive or potentially negative effects on the individual, as well as future generations. There is also the question of the limits of intervention in human nature.

CONCLUSIONS

Cardiomyopathy is a serious issue that significantly impacts quality of life and life expectancy. It poses a major challenge in treatment, which is why research into gene therapy remains so important. The latest data analyses from 2020 to 2025 have highlighted the challenges associated with the overall framework of gene therapy.

The mechanism of gene therapy involves advanced technologies. Innovative techniques such as genome editing, gene expression regulation, antisense therapy, and gene replacement, along with progress in understanding molecular mechanisms, have enabled significant advances in research and therapeutic trials. Thanks to both existing and ongoing studies, the information gained may lead to the individualization of treatment and an improvement in the quality of life for individual patients.

However, preclinical and clinical studies do not provide answers to all questions. The trials conducted do not guarantee long-term safety and effectiveness across different patient groups. The mechanisms of cardiomyopathy are often multifactorial and polygenic. Therefore,

the approach to gene therapy must be comprehensive and take multiple factors into account, as effective treatment of cardiomyopathy will likely require a holistic therapeutic strategy. For all these reasons, strong collaboration between researchers and patients is essential to ensure continued progress in gene therapy research for cardiomyopathy.

Disclosures

Author`s contribution:

Conceptualization: MS, PF, PB, IK, PK

Methodology: GP, JW, DK, KD, WF

Software: MS, KD

Check: MS, PF, JW

Formal analysis: GP, MS, JW

Investigation: PF, GP, DK, IK

Resources: MS, JW, DK, IK

Data curation: PF, MS

Writing -rough preparation: MS, PK

Writing -review and editing: PK, MS

Visualization: MS, KD, WF

Supervision: GP, PB, WF

Project administration: PB, MS

Founding Statement: The study did not receive external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: Not applicable.

Conflict of Interest Statement: The authors declare no conflicts of interest.

All authors have read and agreed with the published version of the manuscript.

References:

1. Arbelo E, Protonotarios A, Gimeno JR, et al. The new 2023 ESC guidelines for the management of cardiomyopathies: a guiding path for cardiologist decisions. Eur Heart J. 2023 Oct 1;44(37):3503-3626. PMID: 38867869; PMCID: PMC11167974. https://doi.org/10.1093/eurheartj/ehad194

2. Kyriakopoulou E, Monnikhof T, Van Rooij E. Gene editing innovations and their applications in cardiomyopathy research. Dis Model Mech. 2023 May 24;16(5):dmm050088. PMCID: PMC10233723; PMID: 37222281. https://doi.org/10.1242/dmm.050088
3. Cheng S, Han Y, Jiang L, et al. National, regional, and global cardiomyopathy burden from 1990 to 2019. Front Cardiovasc Med. 2022 Nov 30;9:1042448. PMCID: PMC9748073; PMID: 36531740. https://doi.org/10.3389/fcvm.2022.1042448
4. Ciarambino T, Menna G, Sansone G, et al. Cardiomyopathies: An Overview. Int J Mol Sci. 2021 Jul 19;22(14):7722. PMCID: PMC8303989; PMID: 34299342. https://doi.org/10.3390/ijms22147722
5. Venturiello D, Giorgio P G, Perulli F, et al. Unveiling the Future of Cardiac Care: A Review of Gene Therapy in Cardiomyopathies. Int J Mol Sci. 2024 Dec 6;25(23):13147. PMID: 39684857; PMCID: PMC11642060. https://doi.org/10.3390/ijms252313147
6. Lopes LR, Ho CY , Elliott PM. Genetics of hypertrophic cardiomyopathy: established and emerging implications for clinical practice. Eur Heart J. 2024 Jul 10;45(30):2727–2734. PMCID: PMC11313585; PMID: 38984491. https://doi.org/10.1093/eurheartj/ehae421
7. Biddinger KJ, Jurgens SJ, Maamari D, et al. Rare and Common Genetic Variation Underlying the Risk of Hypertrophic Cardiomyopathy in a National Biobank. JAMA Cardiol. 2022 May 18;7(7):715-722. PMID: 35583889; PMCID: PMC9118016. https://doi.org/10.1001/jamacardio.2022.1061
8. Ditaranto R, Caponetti A G, Ferrara V, et al. Pediatric Restrictive Cardiomyopathies. Front Pediatr. 2022 Jan 25;9:745365. PMCID: PMC8822222; PMID: 35145940. https://doi.org/10.3389/fped.2021.745365
9. Szczygieł JA, Michałek P, Truszkowska G, et al. Clinical features, etiology, and survival in patients with restrictive cardiomyopathy: A single-center experience. Kardiol Pol. 2023 Nov 8;81(12):1227-1236. PMID: 37937352. https://doi.org/10.33963/v.kp.97879
10. Aquaro GD, De Luca A, Cappelletto C, et al. Prognostic Value of Magnetic Resonance Phenotype in Patients With Arrhythmogenic Right Ventricular Cardiomyopathy. J Am Coll Cardiol. 2020 Jun 9;75(22): 2753-2765. https://doi.org/10.1016/j.jacc.2020.04.023
11. Wang Y, Jia H , Song J. Accurate Classification of Non-ischemic Cardiomyopathy. Curr Cardiol Rep. 2023 Sep 15;25(10):1299–1317. PMCID: PMC10651539; PMID: 37721634. https://doi.org/10.1007/s11886-023-01944-0

12. Kurakula H, Vaishnavi S, Sharif MY, et al. Emergence of Small Interfering RNA-Based Gene Drugs for Various Diseases. ACS Omega. 2023 Jun 1;8(23):20234–20250. PMCID: PMC10268023; PMID: 37323391. https://doi.org/10.1021/acsomega.3c01703
13. Liao H, Wu J , VanDusen NJ, et al. CRISPR-Cas9-mediated homology-directed repair for precise gene editing. Mol Ther Nucleic Acids. 2024 Sep 26;35(4):102344. PMCID: PMC11531618; PMID: 39494147. https://doi.org/10.1016/j.omtn.2024.102344
14. Dai Y, Amenov A, Ignatyeva N, et al. Troponin destabilization impairs sarcomere-cytoskeleton interactions in iPSC-derived cardiomyocytes from dilated cardiomyopathy patients. Sci Rep. 2020 Jan 14;10(1):209. PMID: 31937807; PMCID: PMC6959358. https://doi.org/10.1038/s41598-019-56597-3
15. Patel AG, Li P, Badrish N, et al. Transthyretin Cardiac Amyloidosis: Current and Emerging Therapies. Curr Cardiol Rep. 2025 Jan 22;27(1):33. PMCID: PMC11754378; PMID: 39841315. https://doi.org/10.1007/s11886-024-02172-w
16. Biagini E, Longhi S. More players in the treatment of transthyretin amyloidosis? The HELIOS-B study. Eur Heart J Suppl. 2025 Apr 16;27(Suppl 3):iii19–iii21. PMCID: PMC12001764; PMID: 40248307. https://doi.org/10.1093/eurheartjsupp/suaf009
17. Jankauskas SS, Varzideh F, Kansakar U, et al. Targeting miR-199a reduces fibrosis in hypertrophic cardiomyopathy. J Mol Cell Cardiol Plus. 2023 Dec 9;7:100057. PMCID: PMC11708307; PMID: 39802443. https://doi.org/10.1016/j.jmccpl.2023.100057
18. Chiti E, Di Paolo M, Turillazzi E, et al. MicroRNAs in Hypertrophic, Arrhythmogenic and Dilated Cardiomyopathy. Diagnostics (Basel). 2021 Sep 19;11(9):1720. PMCID: PMC8469137; PMID: 34574061. https://doi.org/10.3390/diagnostics11091720
19. Michaels WE, Pena-Rasgado C, Kotaria R, et al. Open reading frame correction using splice-switching antisense oligonucleotides for the treatment of cystic fibrosis. Proc Natl Acad Sci U S A. 2022 Jan 18;119(3):e2114886119. PMID: 35017302; PMCID: PMC8784102. https://doi.org/10.1073/pnas.2114886119
20. Shiba N, Yang X, Sato M, et al. Efficacy of exon-skipping therapy for DMD cardiomyopathy with mutations in actin binding domain 1. Mol Ther Nucleic Acids. 2023 Oct 19:34:102060. PMID: 38028197; PMCID: PMC10654596. https://doi.org/10.1016/j.omtn.2023.102060
21. Rodriguez-Polo I, Behr R. Exploring the Potential of Symmetric Exon Deletion to Treat Non-Ischemic Dilated Cardiomyopathy by Removing Frameshift Mutations in TTN. Genes (Basel). 2022 Jun 19;13(6):1093. PMID: 35741855; PMCID: PMC9222585. https://doi.org/10.3390/genes13061093

22. Beverborg NG, Später D, Knöll R, et al. Phospholamban antisense oligonucleotides improve cardiac function in murine cardiomyopathy. Nat Commun. 2021 Aug 30;12:5180. PMCID: PMC8405807; PMID: 34462437. https://doi.org/10.1038/s41467-021-25439-0
23. Greer-Short A, Greenwood A, Leon EC , et al. AAV9-mediated MYBPC3 gene therapy with optimized expression cassette enhances cardiac function and survival in MYBPC3 cardiomyopathy models. Nat Commun. 2025 Mar 4;16:2196. PMCID: PMC11880196; PMID: 40038304. https://doi.org/10.1038/s41467-025-57481-7
24. Zhang H, Zhan O, Huang B, et al. AAV-mediated gene therapy: Advancing cardiovascular disease treatment. Front Cardiovasc Med. 2022 Aug 19:9:952755. PMID: 36061546; PMCID: PMC9437345. https://doi.org/10.3389/fcvm.2022.952755
25. Maurer MS, Kale P., Fontana M, et al. Patisiran Treatment in Patients with Transthyretin Cardiac Amyloidosis. N Engl J Med. 2023 Oct 26;389(17):1553-1565. PMID: 37888916; PMC: PMC10757426. https://doi.org/10.1056/NEJMoa2300757
26. Hong KN, Eshraghian EA, Arad M, et al. International Consensus on Differential Diagnosis and Management of Patients With Danon Disease: JACC State-of-the-Art Review. J Am Coll Cardiol. 2023 Oct 17;82(16):1628-1647. PMID: 37821174. https://doi.org/10.1016/j.jacc.2023.08.014
27. Umer M, Kalra DK. Treatment of Fabry Disease: Established and Emerging Therapies. Pharmaceuticals (Basel). 2023 Feb 20;16(2):320. PMCID: PMC9967779; PMID: 37259462. https://doi.org/10.3390/ph16020320
28. Eggers M , Vannoy CH, Huang J, et al. Muscle-directed gene therapy corrects Pompe disease and uncovers species-specific GAA immunogenicity. EMBO Mol Med. 2021 Dec 1;14(1):e13968. PMCID: PMC8749482; PMID: 34850579. https://doi.org/10.15252/emmm.202113968
29. Munoz-Zuluaga C, Gertz M, Yost-Bido M, et al. Identification of Safe and Effective Intravenous Dose of AAVrh.10hFXN to Treat the Cardiac Manifestations of Friedreich's Ataxia. Hum Gene Ther. 2023 Jul 17;34(13-14):605–615. PMCID: PMC10354731; PMID: 37166361. https://doi.org/10.1089/hum.2023.020
30. Nishiyama T, Zhang Y, Cui M, et al. Precise genomic editing of pathogenic mutations in RBM20 rescues dilated cardiomyopathy. Sci Transl Med. 2022 Nov 23;14(672):eade1633. PMCID: PMC10088465; PMID: 36417486. https://doi.org/10.1126/scitranslmed.ade1633

31. Mendell JR, Sahenk z, Lehman KJ, et al. Long-term safety and functional outcomes of delandistrogene moxeparvovec gene therapy in patients with Duchenne muscular dystrophy: A phase 1/2a nonrandomized trial. Muscle Nerve. 2024 Jan;69(1):93-98. Epub 2023 Aug 14. PMID: 37577753. https://doi.org/ 10.1002/mus.27955
32. Deng J, Zhang J, Shi K, et al. Drug development progress in duchenne muscular dystrophy. Front Pharmacol. 2022 Jul 22;13:950651. PMCID: PMC9353054; PMID: 35935842. https://doi.org/10.3389/fphar.2022.950651
33. Van Opbergen CJM, Narayanan B, Sacramento CB, et al. AAV-Mediated Delivery of Plakophilin-2a Arrests Progression of Arrhythmogenic Right Ventricular Cardiomyopathy in Murine Hearts: Preclinical Evidence Supporting Gene Therapy in Humans. Circ Genom Precis Med. 2024 Feb;17(1):e004305. Epub 2024 Jan 30. PMID: 38288614; PMCID: PMC10923105. https://doi.org/10.1161/CIRCGEN.123.004305
34. Ayanoğlu FB, Elçin AE, Elçin YM. Bioethical issues in genome editing by CRISPR-Cas9 technology. Turk J Biol. 2020 Apr 2;44(2):110–120. PMCID: PMC7129066; PMID: 32256147. https://doi.org/10.3906/biy-1912-52
35. Markusic DM, Martino AT, Porada CD, et al. Immunology of Gene and Cell Therapy. Mol Ther. 2020 Feb 4;28(3):691–692. Epub 2020 Feb 4. PMCID: PMC7054825; PMID: 32023479. https://doi.org/10.1016/j.ymthe.2020.01.024