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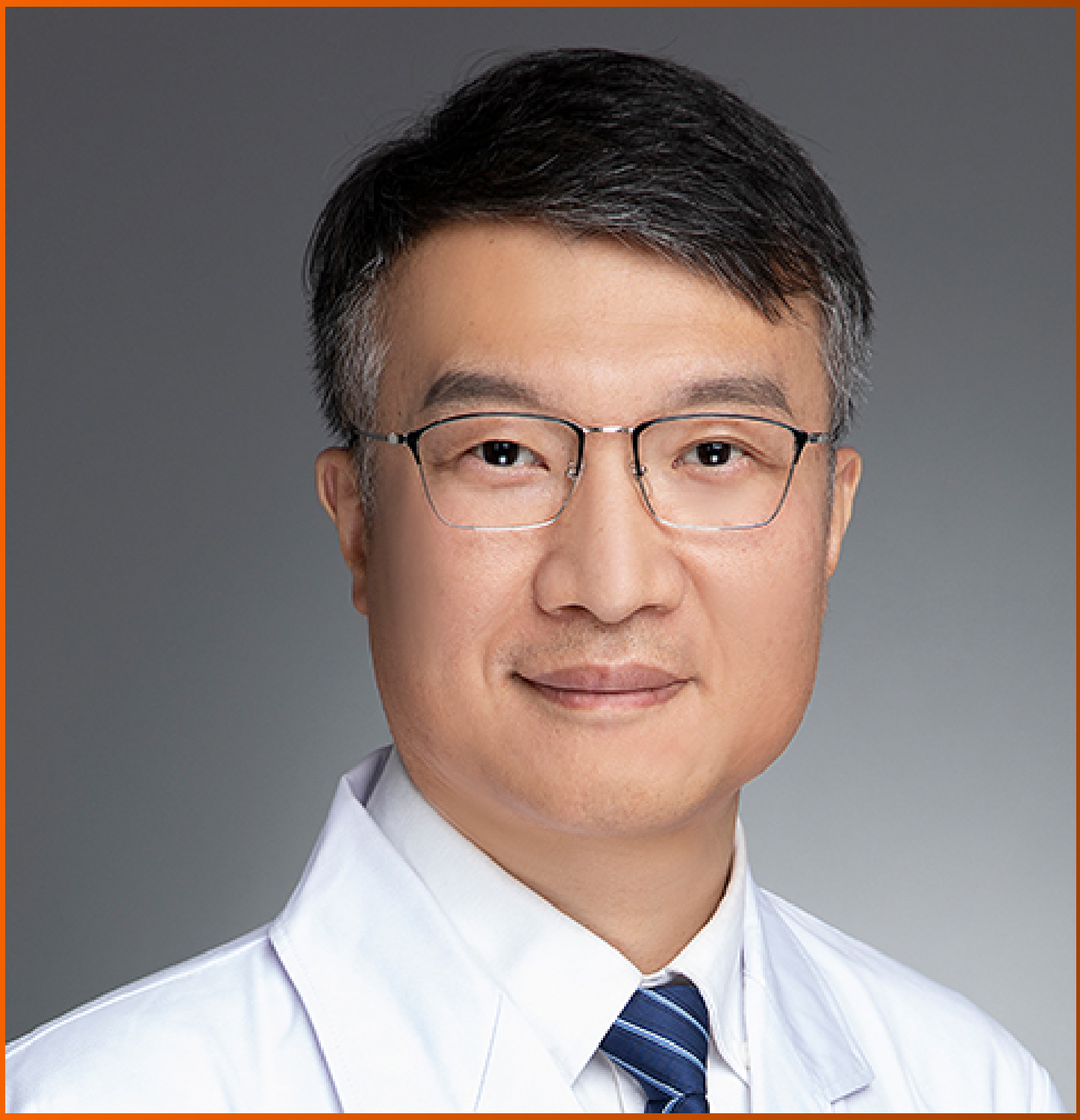

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The primary aim of *World Journal of Cardiology* (*WJC*, *World J Cardiol*) is to provide scholars and readers from various fields of cardiology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

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EDITORIAL

Facing ethical concerns in the age of precise gene therapy: Outlook on inherited arrhythmias

Federico Carbone, Fabrizio Montecucco

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Abstract

This editorial, comments on the article by Spartalis *et al* published in the recent issue of the *World Journal of Cardiology*. We here provide an outlook on potential ethical concerns related to the future application of gene therapy in the field of inherited arrhythmias. As monogenic diseases with no or few therapeutic options available through standard care, inherited arrhythmias are ideal candidates to gene therapy in their treatment. Patients with inherited arrhythmias typically have a poor quality of life, especially young people engaged in agonistic sports. While genome editing for treatment of inherited arrhythmias still has theoretical application, advances in CRISPR/Cas9 technology now allows the generation of knock-in animal models of the disease. However, clinical translation is somehow expected soon and this make consistent discussing about ethical concerns related to gene editing in inherited arrhythmias. Genomic off-target activity is a known technical issue, but its relationship with ethnical and individual genetical diversity raises concerns about an equitable accessibility. Meanwhile, the cost-effectiveness may further limit an equal distribution of gene therapies. The economic burden of gene therapies on healthcare systems is is increasingly recognized as a pressing concern. A growing body of studies are reporting uncertainty in payback periods with intuitive short-term effects for insurance-based healthcare systems, but potential concerns for universal healthcare systems in the long term as well. Altogether, those aspects strongly indicate a need of regulatory entities to manage those issues.

Key Words: Ethics; Inherited arrhythmias; CRISPR/Cas9; Gene therapy; Equitable accessibility

Core Tip: As for other diseases, inherited arrhythmias may take advantage from gene editing. Even we are still far from clinical translation, ethical issues need to be considered in order to proceed in this research field avoiding any misconduct. Off-target effects, equitable accessibility of life-saving gene therapies and economic burden for healthcare systems are key issues that need to addressed by regulatory entities.

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INTRODUCTION

The manuscript "Inherited arrhythmias and gene therapy: Are there any ethical considerations to take into account?", summarizes current evidence regarding potential application of gene therapy in the context of inherited arrhythmias[1]. This class of diseases aligns well with the application field of gene therapy meeting the clinical needs of monogenic disease with no or few therapeutic options available through standard care[2,3]. The quality of life for patients with inherited arrhythmias remains an unmet clinical need[4]. Young individuals engaged in agonistic sports often find themselves compelled to cease any practice following diagnosis. Despite a general consensus from the European Society of Cardiology and American Heart Association to continue sport activities, local laws usually restrict them from any competition[5,6]. Even a life-saving device like International Classification of Diseases is burdened by the negative effects of recurrent shocks, leading to the occurrence of electrical storms triggered by the catecholamines release after each shock [7].

OVERVIEW AND OUTLOOK ON GENOME EDITING FOR INHERITED ARRHYTHMIAS

Throughout the manuscript the authors review the theoretical applications of genome editing for the treatment of inherited arrhythmias. Advances in CRISPR/Cas9 technology have broadened the potential for generating knock-in animal models[8,9]. However, current challenges lie in the development of delivery methods and ensuring editing efficiency while minimizing off-target effects[10]. In addition to technical limitations, ethical concerns are worth considering. One such concern arises from genomic off-target activity which is actively being addressed through the development of prediction assays capable of identifying unwanted editing events[11]. Furthermore, on- and off-target effects may be influenced by the individual genetical diversity, potentially limiting the equitable accessibility of life-saving gene therapies. Similarly, the cost-effectiveness may further limit the equal distribution of gene therapies. While this impact is intuitive for insurance-based healthcare systems, a similar effect is anticipated for universal healthcare systems in the long term[12-14]. In the real word, this is a poignant aspect as many patients may have to put their homes and life savings at risk[13]. This underscores the need for a regulatory entity to prevent misconduct. Leading scientists, politicians and economists are called upon to promptly update the first genome editing-specific guidance documents release by the United States Food and Drug Administration and European regulators in 2022[15,16].

CONCLUSION

In this context, the research of gene therapies for inherited arrhythmias is still in its infancy and lacks translation into a clinical setting. However, it must continue on a well-established track that adheres to defined ethical standards.

FOOTNOTES

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REFERENCES

1 **Spartalis M**, Spartalis E, Siasos G. Inherited arrhythmias and gene therapy: Are there any ethical considerations to take into account? *World J Cardiol* 2023; **15**: 623-626 [PMID: 38173906 DOI: 10.4330/wjc.v15.i12.623]
2 **Schambach A**, Buchholz CJ, Torres-Ruiz R, Cichutek K, Morgan M, Trapani I, Büning H. A new age of precision gene therapy. *Lancet* 2023 [PMID: 38006899 DOI: 10.1016/S0140-6736(23)01952-9]
3 **Bezzerides VJ**, Prondzynski M, Carrier L, Pu WT. Gene therapy for inherited arrhythmias. *Cardiovasc Res* 2020; **116**: 1635-1650 [PMID: 32321160 DOI: 10.1093/cvr/cvaa107]
4 **Offerhaus JA**, Bezzina CR, Wilde AAM. Epidemiology of inherited arrhythmias. *Nat Rev Cardiol* 2020; **17**: 205-215 [PMID: 31582838 DOI: 10.1038/s41569-019-0266-2]
5 **Ackerman MJ**, Zipes DP, Kovacs RJ, Maron BJ. Eligibility and Disqualification Recommendations for Competitive Athletes With Cardiovascular Abnormalities: Task Force 10: The Cardiac Channelopathies: A Scientific Statement From the American Heart Association and American College of Cardiology. *J Am Coll Cardiol* 2015; **66**: 2424-2428 [PMID: 26542662 DOI: 10.1016/j.jacc.2015.09.042]
6 **Heidbuchel H**, Arbelo E, D'Ascenzi F, Borjesson M, Boveda S, Castelletti S, Miljoen H, Mont L, Niebauer J, Papadakis M, Pelliccia A, Saenen J, Sanz de la Garza M, Schwartz PJ, Sharma S, Zeppenfeld K, Corrado D; EAPC/EHRA update of the Recommendations for participation in leisure-time physical activity and competitive sports in patients with arrhythmias and potentially arrhythmogenic conditions. Recommendations for participation in leisure-time physical activity and competitive sports of patients with arrhythmias and potentially arrhythmogenic conditions. Part 2: ventricular arrhythmias, channelopathies, and implantable defibrillators. *Europace* 2021; **23**: 147-148 [PMID: 32596731 DOI: 10.1093/europace/euaa106]
7 **Schwartz PJ**, Ackerman MJ. The long QT syndrome: a transatlantic clinical approach to diagnosis and therapy. *Eur Heart J* 2013; **34**: 3109-3116 [PMID: 23509228 DOI: 10.1093/eurheartj/eht089]
8 **Shen B**, Zhang J, Wu H, Wang J, Ma K, Li Z, Zhang X, Zhang P, Huang X. Generation of gene-modified mice *via* Cas9/RNA-mediated gene targeting. *Cell Res* 2013; **23**: 720-723 [PMID: 23545779 DOI: 10.1038/cr.2013.46]
9 **Song Y**, Guo T, Jiang Y, Zhu M, Wang H, Lu W, Jiang M, Qi M, Lan F, Cui M. KCNQ1-deficient and KCNQ1-mutant human embryonic stem cell-derived cardiomyocytes for modeling QT prolongation. *Stem Cell Res Ther* 2022; **13**: 287 [PMID: 35765105 DOI: 10.1186/s13287-022-02964-3]
10 **Moore OM**, Ho KS, Copeland JS, Parthasarathy V, Wehrens XHT. Genome Editing and Cardiac Arrhythmias. *Cells* 2023; **12** [PMID: 37408197 DOI: 10.3390/cells12101363]
11 **Turchiano G**, Andrieux G, Klermund J, Blattner G, Pennucci V, El Gaz M, Monaco G, Poddar S, Mussolino C, Cornu TI, Boerries M, Cathomen T. Quantitative evaluation of chromosomal rearrangements in gene-edited human stem cells by CAST-Seq. *Cell Stem Cell* 2021; **28**: 1136-1147.e5 [PMID: 33626327 DOI: 10.1016/j.stem.2021.02.002]
12 **Wong CH**, Li D, Wang N, Gruber J, Lo AW, Conti RM. The estimated annual financial impact of gene therapy in the United States. *Gene Ther* 2023; **30**: 761-773 [PMID: 37935855 DOI: 10.1038/s41434-023-00419-9]
13 **Harrison PT**, Friedmann T. Cost of gene therapy. *Gene Ther* 2023; **30**: 737 [PMID: 37938351 DOI: 10.1038/s41434-023-00408-y]
14 **Zemplenyi A**, Leonard J, DiStefano MJ, Anderson KE, Wright GC, Mendola ND, Nair K, McQueen RB. Using Real-World Data to Inform Value-Based Contracts for Cell and Gene Therapies in Medicaid. *Pharmacoeconomics* 2023 [PMID: 37989969 DOI: 10.1007/s40273-023-01335-x]
15 **Administration UFaD**. Human gene therapy products incorporating human genome editing. US Food and Drug Administration. March, 2022
16 **Anliker B**, Childs L, Rau J, Renner M, Schüle S, Schuessler-Lenz M, Sebe A. Regulatory Considerations for Clinical Trial Applications with CRISPR-Based Medicinal Products. *CRISPR J* 2022; **5**: 364-376 [PMID: 35452274 DOI: 10.1089/crispr.2021.0148]

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