Series of Cardiology Research

Open Access
Review Article
Vol 7 Iss 1

The Role of Piezo1 Channels in Cardiovascular Function: Mechanotransduction in the Heart and Blood Vessels

Chi S*

School of Biomedical Engineering, The University of Sydney, Darlington, Australia

***Correspondence:** Shaopeng Chi, School of Biomedical Engineering, The University of Sydney, Darlington, Australia

Received on 08 February 2025; Accepted on 21 March 2025; Published on 25 March 2025

Abstract

Piezo1 channels are mechanosensitive ion channels critical for translating mechanical forces into cellular signals in the cardiovascular system. They regulate heart function by influencing cardiomyocyte contractility and arrhythmogenesis and play a key role in vascular function by modulating endothelial and smooth muscle cell responses to mechanical stimuli. Dysregulation of Piezo1 can contribute to conditions such as arrhythmias, heart failure, and vascular diseases. Despite advancements in understanding Piezo1, challenges remain in studying their mechanisms and developing targeted therapies. Future research into Piezo1's signaling pathways, the development of selective modulators, and exploring neurovascular interactions hold promise for therapeutic innovations.

Keywords: Piezo1, mechanotransduction, cardiomyocytes, arrhythmogenesis, vascular function

Abbreviations: AF: atrial fibrillation

Introduction

Piezo channels, a family of mechanosensitive ion channels, are essential for translating mechanical forces into cellular signals. These channels are involved in various physiological processes, such as touch sensation, blood flow regulation, and cell migration, and are critical for proper tissue function across several systems, including the cardiovascular system. Among the Piezo family, Piezo1 has garnered attention for its widespread expression in endothelial cells, smooth muscle cells, and cardiomyocytes. In the cardiovascular system, Piezo1 channels mediate cellular responses to mechanical forces such as stretch, shear stress, and pressure. These processes are crucial for maintaining vascular tone, regulating cardiac contractility, and influencing arrhythmogenesis [1–3].

Recent research has revealed the significant role Piezo1 plays in heart function and vascular health, and its contribution to diseases like arrhythmias, heart failure, and vascular dysfunction. This review explores the current understanding

of Piezo1 in the cardiovascular system, with a focus on its impact on mechanotransduction, heart function, and vascular homeostasis [4–6].

Piezo1 in Cardiomyocytes: Bridging Mechanical Forces and Cardiac Rhythm

Piezo1 channels in cardiomyocytes are involved in sensing mechanical forces during the cardiac cycle. These channels activate in response to stretch and pressure, leading to ion influx that influences cardiac contractility and rhythm. Piezo1's role in heart function is particularly crucial under mechanical stress, as dysregulation of its activation can contribute to pathological conditions, including arrhythmias and heart failure [2, 5, 7].

A critical example is atrial fibrillation (AF), a common arrhythmia exacerbated by mechanical stress. Piezo1 channels contribute to the initiation and propagation of arrhythmic signals in the heart, making them important players in the development and progression of AF. Understanding the role of Piezo1 in arrhythmogenesis is essential for developing targeted therapies for this and other arrhythmias [8].

Piezo1 in Vascular Function: Maintaining Blood Flow and Vessel Integrity

Piezo1 channels also play a central role in vascular homeostasis. In endothelial cells and smooth muscle cells, Piezo1 mediates the response to mechanical forces, such as shear stress and blood pressure, which regulate vascular tone and blood flow. Dysfunctional Piezo1 signaling in endothelial cells is linked to vascular diseases such as hypertension and atherosclerosis, as it impairs normal blood vessel function [3, 9].

Similarly, in smooth muscle cells, Piezo1 regulates vascular tone and blood pressure by influencing their contraction and relaxation in response to mechanical cues. The coordinated activity of Piezo1 channels in both endothelial and smooth muscle cells is vital for maintaining vascular function and preventing diseases associated with vascular remodeling, such as hypertension and atherosclerosis [9, 10].

Challenges in Studying Piezo1 Channels: Unraveling Mechanotransduction Complexity

Despite the growing recognition of Piezo1's importance in the cardiovascular system, several challenges remain in fully understanding its functions and mechanisms [11–13]. One primary hurdle is selectively manipulating Piezo1 channels in vivo. While genetic knockout models have provided valuable insights, they fail to capture the dynamic activation of Piezo1 in response to mechanical forces. Moreover, real-time imaging techniques capable of monitoring Piezo1 activation are still in the early stages of development.

Piezo1 channels have complex gating mechanisms and ion permeation pathways that are not yet fully understood [12, 13]. Advanced imaging techniques, such as cryo-electron microscopy, have provided some structural insights, but much remains to be discovered regarding the molecular mechanisms governing mechanosensitivity and ion conduction in Piezo1 channels [11, 13].

Therapeutic Potential and Future Directions: Targeting Piezo1 for Cardiovascular Diseases

Piezo1 channels hold significant therapeutic potential due to their central role in cardiovascular function. Modulating Piezo1 activity could provide a novel approach to treating arrhythmias, heart failure, and vascular diseases. For example, selectively enhancing or inhibiting Piezo1 in a tissue-specific manner could offer a targeted therapeutic strategy to restore normal mechanotransduction and prevent pathological remodeling of the heart and vasculature [14–16].

However, several challenges must be addressed before Piezo1-targeted therapies can be developed. A more profound understanding of the mechanotransduction pathways involving Piezo1 is essential, including how Piezo1 interacts

with other signaling molecules, such as G-protein-coupled receptors [15, 17]. Furthermore, developing selective Piezo1 modulators will be necessary to minimize off-target effects and maximize therapeutic efficacy.

The role of Piezo1 in neurovascular interactions, particularly in diseases affecting both the cardiovascular and nervous systems, such as stroke and cardiac arrhythmias, should also be explored. Recent research on Piezo1 in astrocytes suggests that Piezo1 channels in the brain may influence cardiovascular function, providing further insight into the potential cross-talk between the cardiovascular and nervous systems [18].

Advances in technologies such as gene-editing tools, real-time imaging, and in vivo sensor systems will be instrumental in advancing Piezo1 research. These tools will allow for more precise manipulation and real-time study of Piezo1 channel activity in both physiological and pathological conditions [18].

Conclusion: Unlocking the Therapeutic Potential of Piezo1 in Cardiovascular Medicine

Piezo1 channels play a pivotal role in cardiovascular health, influencing cardiac contractility, arrhythmogenesis, and vascular function. Their involvement in mechanotransduction pathways highlights their importance in maintaining cardiovascular homeostasis. While advancements have been made in understanding Piezo1, challenges remain in fully elucidating its mechanisms and developing targeted therapies. Future research focused on mechanotransduction pathways, the development of selective modulators, and the exploration of neurovascular interactions will be key in harnessing the therapeutic potential of Piezo1 channels for treating cardiovascular diseases [5].

Author Contributions

Chi S wrote the manuscript.

Acknowledgments

This work was supported by the Australian Research Council (ARC, DE230101128).

References

1. Coste B, Mathur J, Schmidt M, et al. Piezo1 and Piezo2 are essential components of distinct mechanically activated cation channels. Science. 2010;330(6000):55-60.

2. Su SA, Zhang Y, Li W, et al. Cardiac Piezo1 Exacerbates Lethal Ventricular Arrhythmogenesis by Linking Mechanical Stress with Ca2+ Handling After Myocardial Infarction. Research (Wash D C). 2023;6:0165.

3. Lim XR, Abd-Alhaseeb MM, Ippolito M, et al. Endothelial Piezo1 channel mediates mechano-feedback control of brain blood flow. Nat Commun. 2024;15(1):8686.

4. Jiang F, Yin K, Wu K, et al. The mechanosensitive Piezo1 channel mediates heart mechano-chemo transduction. Nat Commun. 2021;12(1):869.

5. Beech DJ. Are PIEZO1 channels a potential therapeutic target for heart failure? Getting to the heart of the matter. Expert Opin Ther Targets. 2023;27(6):409-11.

6. Li J, Hou B, Tumova S, et al. Piezo1 integration of vascular architecture with physiological force. Nature. 2014;515(7526):279-82.

7. Ihara T, Kira S, Miyamoto T, et al. 316 Clock genes regulate circadian rhythm of Piezo1 and TRPV4 expressions and intracellular Ca2+ influx after stretch stimulation in the cultured urothelial cells. Eur. Urol. Suppl. 15, e316.

8. Jakob D, Klesen A, Allegrini B, et al. Piezo1 and BKCa channels in human atrial fibroblasts: Interplay and remodelling in atrial fibrillation. J Mol Cell Cardiol. 2021;158:49-62.

9. Xu H, He Y, Hong T, et al. Piezo1 in vascular remodeling of atherosclerosis and pulmonary arterial hypertension: A potential therapeutic target. Front Cardiovasc Med. 2022;9:1021540.

10. Abello J, Yin Y, Zhao Y, et al. Endothelial cell Piezo1 promotes vascular smooth muscle cell differentiation on large arteries. Eur J Cell Biol. 2025;104(1):151473.

11. Zhao Q, Zhou H, Chi S, et al. Structure and mechanogating mechanism of the Piezo1 channel. Nature. 2018;554(7693):487-92.

12. Zhao Q, Wu K, Chi S, et al. Heterologous Expression of the Piezo1-ASIC1 Chimera Induces Mechanosensitive Currents with Properties Distinct from Piezo1. Neuron. 2017;94(2):274-77.

13. Zhao Q, Wu K, Geng J, et al. Ion Permeation and Mechanotransduction Mechanisms of Mechanosensitive Piezo Channels. Neuron. 2016;89(6):1248-263.

14. Wang Y, Chi S, Guo H, et al. A lever-like transduction pathway for long-distance chemical- and mechano-gating of the mechanosensitive Piezo1 channel. Nat Commun. 2018;9(1):1300.

15. Zhang T, Chi S, Jiang F, et al. A protein interaction mechanism for suppressing the mechanosensitive Piezo channels. Nat Commun. 2017;8(1):1797.

16. Wang Y, Chi S, Zhao Q, et al. A lever-like transduction pathway for long-distance chemical- and mechano-gating of the mechanosensitive Piezo1 channel. Biophys J. 2018;114(3):113a–114a.

17. Komuro J, Takeda N, Komuro I. PIEZO1 as a potential therapeutic target in Marfan syndrome. Eur Heart J. 2025;46(10):975-77.

18. Chi S, Cui Y, Wang H, et al. Astrocytic Piezo1-mediated mechanotransduction determines adult neurogenesis and cognitive functions. Neuron. 2022;110(18):2984-999.e8.

To access the full-text version of this article, please scan the QR code: