Journal of Cardiovascular Translational Research (2022) 15:441–443
https://doi.org/10.1007/s12265-022-10270-9

EDITORIAL

Cellular and Extracellular Non-coding RNAs in Cardiac Physiology and Diseases

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Received: 28 April 2022 / Accepted: 29 April 2022 / Published online: 16 May 2022

Despite considerable advances over the past 20 years, cardiovascular diseases (CVDs) have persisted as the leading global cause of illnesses and deaths. CVDs trigger adverse cardiac remodeling, manifested by hypertrophy, inflammation, fibrosis, and apoptosis, leading to heart failure (HF) [1]. Accumulating evidence has shown that cellular and extracellular non-coding RNAs (ncRNAs) participate in regulating normal physiological processes of the heart and various pathological processes of CVDs. A continued and deeper understanding of the molecular mechanisms of cellular and extracellular ncRNAs in CVDs may contribute to the development of early diagnosis and novel RNA-based therapy [2].

This special issue entitled "Cellular and Extracellular Non-coding RNAs in Cardiac Physiology and Diseases" contains ten selected papers dedicated to the role of cellular and extracellular ncRNAs on cardiovascular physiology, pathophysiology, and diseases such as ischemic heart disease, hypertension, diabetic cardiomyopathy, atherosclerosis, and vascular diseases. The roles of cellular and extracellular ncRNAs have been carefully reviewed and discussed concerning clinical diagnosis, treatment, and prognosis assessment of cardiovascular diseases.

In this issue, the functions of cellular ncRNAs in CVDs were described by two groups. Zhong and Jin et al. investigated the role of microRNA (miR)-122-5p in hypertension. They proved that miR-122-5p aggravated angiotensin II-induced myocardial fibrosis and dysfunction in rats by modulating the elabela/apelin-ACE2-GDF15 signaling. Inhibition of miR-122-5p could rescue angiotensin II-induced cellular oncosis, migration, inflammation, and oxidative stress in rat cardiac fibroblasts [3]. Shan and Fang et al. investigated the function and mechanism of circular RNAs (circRNAs) in cardiac remodeling. They found that circ_0036176 inhibited mCF proliferation by translating Myo9a-208 protein to suppress the cyclin/Rb pathway [4]. This work broadened our understanding of the mechanisms underlying ncRNAs' function in CVDs.

A series of articles were then dedicated to introduce the role of extracellular ncRNAs in diabetic cardiomyopathy, atherosclerosis, vascular remodeling, and myocardial infarction. Chen et al. provided a comprehensive review of the present knowledge of how extracellular ncRNAs function in diabetic cardiomyopathy (DCM), mainly focusing on their physio-pathological properties and offering critical perspectives with respect to potential clinical translation for biomarkers and therapies [5]. Tang and Peng et al. systemically reviewed the participation of different ncRNAs in atherosclerosis (AS) in various carrier forms. They also focused on the role and potential mechanisms of extracellular ncRNAs in AS and introduced their potential implications for clinical treatment [6]. Dai et al. summarized the latest advances of extracellular ncRNAs in pathological vascular remodeling-associated diseases and described vessel-associated extracellular ncRNAs and their mechanisms of action [7]. Wang and Ding et al. provided updated information about the crosstalk mediated by extracellular circRNAs in pathological processes. They reviewed the modulation of extracellular circRNAs in ischemic myocardial injury and remodeling [8]. These articles provide the latest picture about extracellular ncRNAs as potential therapeutic targets for myocardial injury and dysfunction.

Editor-in-Chief Enrique Lara-Pezzi oversaw the review of this article

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Most extracellular ncRNAs are present in extracellular vesicles (EVs), including exosomes and microvesicles. EVs are emerging as crucial mediators of cell-to-cell communication in multiple organs or tissues. EV-associated ncRNAs derived from cardiovascular or non-cardiac cells regulate cardiovascular pathophysiology in heart development and diseases. The functional relevance of the EV-associated ncRNAs in heart diseases provides an avenue to develop novel diagnostic tools and therapies for heart diseases. Wang and Chen et al. summarized the recent progress of EV-associated ncRNAs in multiple cardiovascular diseases, including myocardial infarction, arrhythmias, cardiac hypertrophy, and heart failure, emphasizing the underlying molecular mechanisms [9]. Wang et al. compared the difference between circulating exosomes and the rostral ventrolateral Medulla (RVLM) in chronic heart failure (CHF) rats by miRNA microarray. They found that circulating exosomes enhanced inflammatory response in the RVLM through the packaged miRNAs, which may further contribute to sympathetic hyperactivity in CHF [10].

Targeting-regulated exosomal miRNAs from stem cells have beneficial effects on ischemic heart disease. Stem cell-derived exosomes have been considered an efficient and safe transporter for ncRNAs and a central mediator of the cardioprotective potentials of the parental cells [11, 12]. Liu et al. overviewed the function of exosomal miRNAs from bone marrow mesenchymal stem cells (BMSCs), cardiac progenitor cells (CPCs), and induced pluripotent stem cells (iPSCs) in improving myocardial injury with various biological effects, including pro-angiogenesis, regulation of autophagy, apoptosis, fibrosis, and hypertrophy. They also enumerated the current strategies of bioengineering methods to modify miRNA content and exosomal membrane protein components to promote their therapeutic efficiency in ischemic heart disease (IHD) [11]. Li and Song et al. reviewed the downstream targets and signal pathways of exosomal ncRNAs derived from stem cells. They summarized the recent advances in specific nanomaterials that are used to encapsulate exosomes and promote ischemic tissue repair. Importantly, they also highlighted the inflammasome pathways that could be targeted for developing a novel therapy against ischemic diseases [12].

This special issue provides an overview and updated knowledge of cellular and extracellular ncRNAs in CVDs. More studies, including clinical trials and animal experiments, will be needed to elucidate further the diagnostic and therapeutic effects of EV-associated ncRNAs in CVDs. In the coming years, extracellular ncRNAs should be paid more attention, especially for evaluating and managing patients with CVDs.

Funding This work was supported by the grants from National Key Research and Development Project (2018YFE0113500 to JJ Xiao), the National Natural Science Foundation of China (82020108002 to J Xiao), the grant from Science and Technology Commission of Shanghai Municipality (20DZ2255400 and 21XD1421300 to J Xiao), the "Dawn" Program of Shanghai Education Commission (19SG34 to J Xiao).

Declarations

Research Involving Human Participants and/or Animals This article does not contain any studies with human participants or animals performed by any authors.

Informed Consent This article does not contain any studies with human participants.

Conflict of Interest The authors declare no competing interests.

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