Editorial

New Therapetic Approaches in the Management of Ischemia Reperfusion Injury and Cardiometabolic Diseases: Opportunities and Challenges

Cardiovascular diseases rank the number one cause of death in both developed and developing countries with cardiometabolic syndrome and myocardial ischemia reperfusion (I/R) injury being the most important risk factors [1-3]. Both ischemia-reperfusion injury and cardiometabolic syndrome (or diseases) may result in cardiac remodeling, arrhythmias, cardiomyocyte death, heart failure and ultimately mortality [3]. Research over the past decades has greatly broadened our understanding of the molecular mechanisms underlying ischemic reperfusion injury and cardiometabolic diseases. Despite recent advances in diagnostic and therapeutic approaches, the incidence of cardiovascular disease is still rising thus warranting alternative favorable treatment. Up-to-date, a number of theories have been postulated for the pathogenesis of cardiac dysfunction in patients with ischemic heart or cardiometabolic diseases including hypoxia, volume or pressure overload, overactivation of sympathetic system, apoptosis, mitochondrial damage, and inflammation [4-6]. Here we present this special issue of "Current Drug Targets" on "Drug discovery and development in the management ischemia reperfusion injury and cardiometabolic diseases". Our enthusiasm for this topic rooted from the profound opportunities for novel drug targets or therapeutic concepts in ischemia-reperfusion injury and cardiometabolic diseases. To this end, it is pertinent to better our understanding for the precise mechanisms underlying the onset and pathogenesis of cardiac dysfunction in these comorbidities.

In the first review article of this special series, Chin and colleagues discussed various manifestations of reperfusion injury including arrhythmias, myocardial stunning and micro-vascular dysfunction, as well as cardiomyocyte death, and the pharmacological options to combat myocardial reperfusion injury such as the antioxidant flavonols, hydrogen sulfide, adenosine, opioids, incretin-based therapies and cyclosporin A [7]. In the second article, Chi and associates reviewed recent proof-of-concept trials to demonstrate the importance of reperfusion injury as a therapeutic target. They summarized the promising therapies and future perspectives on various clinical techniques to reduce myocardial reperfusion injury [8]. In the third article of this series, Rocic described various micro RNAs associated with the most common manifestations of cardiovascular diseases, including atherosclerosis, angina pectoris, myocardial infarction and myocardial reperfusion through arteriogenesis. She listed changes of these microRNAs in metabolic syndrome and its component pathologies, and discussed challenges impeding clinical application of microRNAs in cardiovascular therapy [9]. In the fourth article, Ma and coworkers discussed the therapeutic potential of targeting novel transient receptor potential channels in the treatment of cardiometabolic diseases and I/R injury [10]. In the fifth review, Han and colleagues suggested that activation of SIRT1 participates in metabolic and physiologic processes such as metabolism, stress, apoptosis and energy balance in ischemia injury and cardiometabolic disease [11]. In the next article by Li and associates from Remin Hospital Wuhan University, current knowledge of biological functions of interferon regulatory factors in innate immune responses and immune cell development was discussed where the contemporary molecular mechanisms of interferon regulatory factors are discussed in metabolic diseases, cardiac remodeling, vascular remodeling, and stroke [12]. In the seventh article, the cholinergic anti-inflammatory pathway modulated through α7 nicotinic acetylcholine receptor (α7nAChR) was scrutinized by Fu and colleagues with a focus in the pathological processes in myocardial infarction, atherosclerosis, hypertension and stroke [13]. The eighth article by Guo *et al.* reviewed the apelinergic pathway as an attractive target to treat conditions associated with cardiometabolic syndrome. They have highlighted the important regulatory roles of apelin in energy metabolism and cardiovascular function, and potential risks that could jeopardize the therapeutic benefit [14]. In the ninth article, Sun and colleagues discussed insulin resistance, endothelial dysfunction and life style changes in the development of cardiovascular disease in diabetic patients. They also tackled the potential strategies and challenges in targeting cardiovascular risks in diabetic individuals [15]. In the next article, Tian and coworkers discussed human cellular repressor of E1A-stimulated genes (CREG) and its role as a secreted glycoprotein in maintaining cellular homeostasis, and withstanding cell and tissue pathological challenges [16]. In the eleventh article, Ren and colleagues described the nature, pathology and differential diagnosis of cardiac tumors based on imaging techniques including transthoracic and transesophageal echocardiograms, computed tomography (CT) scans and magnetic resonance imaging (MRIs) [17]. A plethora of clinical and experimental evidence has depicted a cardioprotective role for the mitochondrial chaperon aldehyde dehydrogenase (ALDH2), an enzyme metabolizing acetaldehyde to innocuous acetic acid, in cardiovascular diseases [18]. In the 12th article, Zhang and colleagues discussed the implications of ALDH2 genotype and ALDH2 regulators in various cardiovascular anomalies, highlighting their clinical importance in cardiovascular therapy [19]. In the last article by Liu and Sun, the biology and pathobiology roles of ALDH2 in the ischemic cardiovascular disease were reviewed focusing on the genetic evidence associated with the East Asian population with the ALDH2*2 mutant allele. Clinical implications to restore ALDH2 function in this population has been examined in cardiovascular disease settings [20].

Although this special issue has shed some insights towards the better understanding of in the regulation of ischemia-reperfusion injury and cardiometabolic diseases, it is noteworthy that the topics covered here probably raise more questions than answers. First, it is rather challenging for individuals with ischemic heart or cardiometabolic diseases to come up with a unified therapeutic regimen. Second, similar to all animal models, experimental animal or cell models for ischemia-reperfusion and cardiometabolic diseases suffer from limitations to mimic the authentic pathological changes under clinical settings. Therefore, special caution is needed when applying knowledge from bench-side to the bed-side practice. Third, given the complexity

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in the onset and development of cardiovascular diseases, it is rather difficult to pinpoint exactly which intervention targeting ischemia-reperfusion injury or cardiometabolic disease is better than the others, let alone the options of life style modification which is not included in our special issue. We certainly hope that this special series will help physicians and scientists to identify novel therapeutic targets or concepts in an effort to better engage management against ischemia-reperfusion injury and cardiometabolic diseases.

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Dr. Jun Ren
(*Guest Editor*)
Department of Cardiology, Fudan University Zhongshan Hospital
Shanghai, 210032
China
Tel: (307) 766-6131; Fax: (307) 766-2953
E-mail: jren@uwyo.edu

Dr. Yingmei Zhang
(*Guest Editor*)
University of Wyoming College of Health Sciences
Laramie, WY 82071
USA
Tel: (307) 766-6131; Fax: (307) 766-2953
E-mail: zhangym197951@126.com