

## Editorial

### New Therapeutic Approaches in the Management of Cardiometabolic Diseases: Bringing the Concepts Together

Cardiometabolic syndrome refers to a group of cardiometabolic risk factors that greatly increase the risk for cardiovascular diseases and other health problems. As per the consensus of the National Heart, Lung and Blood Institute (NHLBI) and American Heart Association (AHA), cardiometabolic syndrome is a constellation of 3 or more of the following risk factors: abdominal obesity, high triglycerides, dyslipidemia (low- and high-density lipoprotein cholesterol), hypertension, and elevated fasting blood glucose [1]. At this time, the therapeutic strategies are mainly aimed at the management of individual risk factors including dyslipidemia, hypertension and diabetes [2]. With the ever-rising prevalence of cardiovascular anomalies including cardiac hypertrophy, hypertension, arrhythmias, and heart failure in cardiometabolic diseases [3], it is pertinent to identify and develop novel diagnostic and therapeutic techniques to better manage the cardiovascular risk in cardiometabolic diseases. For example, the recent application of the new class of anti-diabetic drugs sodium glucose co-transporter 2 (SGLT2) inhibitors has greatly improved the cardiovascular benefits for drugs targeting cardiometabolic syndrome [4]. Here we will present this special issue of "Current Drug Target" on "Drug discovery and development in the management cardiometabolic diseases" to discuss a number of new therapeutic options in the field. Our enthusiasm for this topic came from the profound opportunities for novel therapeutic concepts in cardiometabolic diseases. It is essential to broaden our understanding for the precise mechanisms behind these therapeutic modalities in the management of cardiometabolic diseases.

In the first review article of this series, Li and colleagues discussed the pivotal role of ubiquitin (Ub) and ubiquitin-like proteins (UBLs)-associated post-translational modification in the regulation of protein function in cardiac cells. Conjugation of Ub or UBLs to target proteins may modulate both physical and physiological properties of protein substrates, thus governing a number of disease processes including cardiac diseases [5]. In the second article, Zhu and Zhang reviewed how the interplay between apoptosis and autophagy controls cell death or proliferation in vascular smooth muscle cells, neointimal hyperplasia and restenosis pathogenesis [6]. In the third article of this series, the authors also shed light on the conservative autophagy process to provide some valuable insights into the potential mechanism of autophagy in the onset and development of rheumatic autoimmune diseases [7]. In the fourth article, the authors discussed the forefront of pancreatic cancer treatment, and the potential role of parargeting autophagy in therapeutics against pancreatic cancer [8]. Autophagy has recently drawn some attention as a novel drug target in the management of cardiovascular and metabolic diseases [9], although the potential of autophagy in drug development may be a daunting process for cardiometabolic and other human disorders. In the fifth review, Janardhanan reported that endocrine disrupting chemicals impair physiological homeostasis, leading to developmental and reproductive abnormalities. Ample evidence has validated the significance of exposure to endocrine disrupting chemicals in cardiometabolic disorders [10]. In the next article, Chen and associates discussed the promises of ApoE4 as a potential target for the management of coronary heart disease and Alzheimer's disease. Carriers of the ApoE4 allele seem to display hypercholesterolemia, which would accelerate the progression of coronary atherosclerosis and Alzheimer's disease. They have discussed the interconnection between coronary heart disease and the devastating neurodegenerative diseases [11]. In the seventh article, Ceylan and colleagues discussed the SGLT2 inhibitors as the new class of antidiabetic agents, and possible advantages of the new SGLT2 inhibitors over the traditional hypoglycemic agents in the control of body weight, blood pressure and hyperuricemia [12]. In the eighth article, the authors revisited the recent clinical trials on SGLT2 inhibitors including empagliflozin and canagliflozin and highlighted the cardiovascular benefits of these SGLT2 inhibitors in type 2 diabetic patients. They dissected the regulatory roles of SGLT2 inhibitors in energy metabolism and cardiovascular function, and factors that may compromise the therapeutic benefit [13]. In the ninth article, Obradovic and colleagues discussed the potential role of proprotein convertase subtilisin/kexin type 9 (PCSK9) in the treatment of hypercholesterolemia. They also highlighted the potential opportunities and challenges in targeting PCSK9 in the clinical settings [14]. In the next article, Kobayashi and colleagues discussed the role of iron as a risk factor for coronary artery disease, in particularly whether iron is toxic or not in patients with coronary heart diseases [15]. In the last article of this series, Feng and colleagues from Fuwai Hospital reviewed the recent concept and knowledge of non-cardiomyocytes in the regulation of cardiomyocyte proliferation and differentiation during postnatal cardiac regeneration, in an effort to identify potential targets for the treatment of heart failure [16].

Although our special issue has updated some of the recent hot topics in the understanding of cardiometabolic diseases, it leaves behind much more unanswered questions that remain to be explored with intense research effort in future. First, cardiometabolic syndrome is not a disease entity, thus making it rather challenging to formulate a unified therapeutic regimen for a given individual with cardiometabolic diseases. Second, experimental animal or cell culture models for cardiometabolic diseases may not be able to recapitulate the true pathological changes under clinical settings. Therefore, the translation of knowledge from bench-side to the bed-side practice remains a long journey. Third, given the complexity and multiple independent risk factors in the etiology of cardiometabolic diseases, it is almost impossible to rule a particular intervention to be superior than others, letting alone the option of life style modification as a key element in the management of cardiometabolic syndrome (not included in our special issue considering the central theme). We would hope that this special series will help the scientific society to identify novel therapeutic targets or concepts in the management of cardiometabolic diseases.

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