WEIHONG HE
Sichuan University, Chengdu,
China

Inhibition of runx1 reduces infarct size and decreases cathepsin levels in rats after acute myocardial infarction

Abstract:

Myocardial infarction (MI) is a leading cause of death worldwide. Acute MI leads to prolonged ischemia and subsequent cell death. The loss of cardiomyocytes after MI leads to cardiac remodelling, the progression of which leads to heart failure which is linked to increased deaths or hospitalizations. New therapeutic targets are urgently needed to reduce infarct size and prevent cardiac remodelling among patients with MI. Recent evidence shown that Runt-related transcription factor-1 (RUNX1), a member of the core-binding factor family of transcription factors, has a critical role in the heart after MI and increased RUNX1 expression under pathological conditions leads to decreased cardiac function. The previous study performed with a cardiomyocyte-specific Runx1-deficient mouse reveals that reducing RUNX1 function prevents adverse cardiac remodeling after MI and identifies RUNX1 as a new target for preventing adverse cardiac remodeling. The present work sought to investigate the effects of RUNX1 inhibitors on infarct size in a rat model of acute MI. In this study MI was surgically induced in rats by performing coronary artery ligation and the infarct size was determined through 2,3,5-triphenyltetrazolium chloride (TTC) staining. We found that rats treated with a small molecule inhibitor of Runx1 (Ro5-3335) demonstrated a reduced infarct size at 24 hours after MI. Data-independent acquisition proteomics revealed that Runx1 inhibition led to decreased cathepsin levels in rat hearts treated with Ro5-3335 relative to control hearts. Interestingly, Dr. He's previous study has shown that inhibition of a specific type of cathepsin (cathepsin-L) can reduce infarct size in isolated hearts following ischemia reperfusion injury. This study suggests that Runx1 inhibition reduces infarct size after acute MI and the beneficial effects may be associated with decreased cathepsin levels.

Biography

Weihong He is a principal investigator and associate professor at the Department of Physiology, West China School of Basic Medical Sciences and Forensic Medicine, Sichuan University. Weihong obtained an MD (2012) at West China School of Medicine & West China Hospital, Sichuan University, and completed a PhD (2017) at the BHF Glasgow Cardiovascular Research Centre, University of Glasgow. Weihong was associate professor at Jining Medical University (2018-2020). Since 2020, Weihong has led a research group to study the pathophysiology of cardiovascular diseases and to investigate novel therapeutic drugs for the treatment of myocardial infarction and cerebral infarction at Sichuan University. He also teaches physiology and mentors both national and international students. Weihong has expertise in a number of methodologies which span the level of biochemistry, cell biology, isolated heart, and whole animal in vivo disease models.