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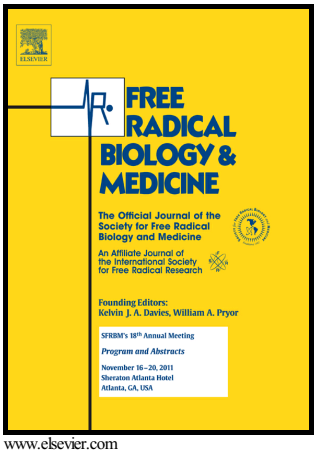

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Modulation of Signaling Mechanisms in the Heart by Thioredoxin 1

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Abstract
Myocardial ischemia/reperfusion and heart failure are the major cardiac conditions in which an imbalance between oxidative stress and anti-oxidant mechanisms is observed. The myocardium has endogenous reducing mechanisms, including the thioredoxin (Trx) and glutathione systems, that act to scavenge reactive oxygen species (ROS) and reduce oxidized proteins. The Trx system consists of Trx, Trx reductase (TrxR), and an electron donor, NADPH, where Trx is maintained in a reduced state in the presence of TrxR and NADPH. Trx1, a major isoform of Trx, is abundantly expressed in the heart and exerts its oxidoreductase activity through conserved Cys32 and Cys35, reducing oxidized proteins through thiol disulfide exchange reactions. In this review, we will focus on molecular targets of Trx1 in the heart, including transcription factors, microRNAs, histone deactylases, and protein kinases. We will then discuss how Trx1 regulates the functions of its targets, thereby affecting the extent of myocardial injury caused by myocardial ischemia/reperfusion and the progression of heart failure.

Keywords
Thioredoxin, disulfide, anti-oxidant, ischemia/reperfusion

Abbreviations

Akt	protein kinase B
AMPK	Adenosine Monophosphate-activated Protein Kinase
Ang-II	Angiotensin-II
AP1	Activator protein 1 (AP-1)
ASK1	Apoptosis Signal-regulating kinase
Atg4	Autophagy related-4
ATP	Adenosine Triphosphate
CDDP	cis-diammine-dichloroplatinum