

A Perspective on Glutathione Redox Metabolism of Elderly Zucker Diabetic Fatty Rat Heart

Abstract

The Zucker diabetic fatty (ZDF) rat is a genetic model in which the homozygous (FA/FA) male animals develop obesity and type 2 diabetes. Morbidity and mortality from cardiovascular complications, due to increased oxidative stress and inflammatory signals, are the hallmarks of type 2 diabetes. The precise molecular mechanism of contractile dysfunction and disease progression remains to be clarified. Therefore, we have investigated molecular and metabolic targets in male ZDF (30–34 weeks old) rat heart compared to age matched Zucker lean (ZL) controls. Hyperglycemia was confirmed by a 4-fold elevation in non-fasting blood glucose (478.43 ± 29.22 mg/dL in ZDF vs. 108.22 ± 2.52 mg/dL in ZL rats).

Our results have suggested that mitochondrial dysfunction and increased oxidative stress in ZDF rats might be associated, at least in part, with altered NF- κ B/JNK dependent redox cell signaling. These results might have implications in the elucidation of the mechanism of disease progression and designing strategies for diabetes prevention.

Keywords: Zucker rats • diabetes • obesity • oxidative stress • cardiomyocytes • mitochondria

Introduction

Cardiomyopathy and alternative vas complications related to redoubled inflammatory and aerophilic stress responses area unit the foremost causes of accelerated arterial sclerosis, fleshiness and polygenic disease . Persistent symptom and lipidaemia area unit believed to be the most causes of redoubled aerophilic stress, mitochondrial dysfunctions, pathology and cell death of cardiomyocytes in diabetes and associated complications .

The male Zucker diabetic fatty (ZDF) rat could be a genetic model during which homozygous (FA/FA) animals ad libitum develop kind a pair of polygenic disease and fleshiness, whereas feminine rats become diabetic solely when feeding high fat diet . the most reason for this resistance in feminine Zucker rats seems to be the presence of high concentration of inhibitor glutathione (GSH) and low aerophilic stress . ZDF rats additionally exhibit redoubled internal secretion resistance, aerophilic stress, lipidaemia, redoubled inflammatory responses and abnormal energy metabolism that area unit the key options of diabetes.

Discription

An increase in aerophilic stress in diabetic heart myocytes was determined. a rise in ROS production was amid a moderate however important increase in LPO and a rise in aerophilic macromolecule carbonylation as determined by DNPH coupling of oxidised proteins. enzyme activity was found to be considerably activated . These results counsel that enzyme seems to be the most protein concerned in H₂ O₂ clearance as we tend to

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determined no marked alteration in GSH-Px activity in ZDF rats.

Cytochrome P450 2E1 (CYP 2E1) protein activity was additionally redoubled considerably in ZDF rat heart compared to ZL rat heart myocytes (Figure 3). CYP 2E1 isoenzyme has been reported to be concerned in aerophilic stress and a rise in protein activity has additionally been reported in polygenic disease and fleshiness a major decrease within the activities of mitochondrial inner membrane metabolic process complexes has been determined in ZDF rat hearts (Figure 4). NADH-dependent benzoquinone enzyme (Complex I) activity was markedly reduced (42%) in ZDF rat heartn myocytes compared to ZL rat hearts nIncreased NF-κB activity and reduce within the within the expression additionally counsel a rise in unhealthy sign in fleshiness . redoubled redoubled activity as seen in fleshiness and alternative inflammatory conditions is additionally concerned in uncoupling internal secretion resistance from supermolecule metabolism . A study by Aragno et al. has additionally shown reduced heart ventricle cardiac muscle ability and redoubled heart condition, following the impairment of NF-κB signalling in ZDF rats.

Our results might also counsel a vital role of those sign proteins in cardiomyocyte survival from aerophilic stress connected unhealthy responses.

Acknowledgement

None

Conflict of Interest

No conflict of interest

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