The oxidative stress and diabetic complications

Lu CAI
Kosair Children’s Hospital Research Institute, the Department of Pediatrics of the University of Louisville, USA

Oxidative stress derived from various etiologies including environmental exposure, life-style changes, and systemic inflammation, can damage pancreatic β-cells, leading to the deficiency of insulin as type 1 diabetes, and also induce peripheral tissues as insulin resistance, leading to type 2 diabetes. Metabolic abnormalities in the body of individuals with diabetes cause mitochondrial superoxide overproduction that in turn activates multiple pathways: polyol pathway flux, increased formation of AGEs (advanced glycation end products), increased expression of the receptor for AGEs and its activating ligands, activation of protein kinase C isoforms, and overactivity of the hexosamine pathway, to generate excessive reactive oxygen or nitrogen species (ROSs or RNSs), which damages multiple organs, resulting in diabetic complications. Diabetic cardiomyopathy can occur independent of vascular disease, although the mechanisms are largely unknown. Current consensus is that the oxidative stress derived from metabolic syndrome causes cardiomyocyte abnormal gene expression, altered signal transduction, and the activation of pathways leading to programmed myocardial cell deaths. The resulting myocardial cell loss thus plays a critical role in the development of cardiac structural remodeling and dysfunction, “cardiomyopathy”. To support the above notion, our studies with in vitro and in vivo animal modes showed the prevention of diabetes and diabetic complications in the cardiomyocytes or transgenic mice with overexpression of antioxidant genes or supplementation of exogenous antioxidants. Among these clinical-translational antioxidants, metallothionein and its upstream nuclear transcriptional factor Nrf2 as well as their potent inducers have been received attention with greatly potential to be applied in clinics for patients with diabetes.