Heme oxygenase is an important switch-box that ameliorates cardio-renal complications in diabetes

Impaired insulin signaling, and deregulated glucose metabolism are associated with the progressive alterations in structure and function of vital organs like the heart and kidneys in diabetic patients. Our recent studies indicate that upregulating the heme oxygenase (HO) system with HO-inducers like hemin and heme-arginate potentiates insulin signaling and improve glucose metabolism in different animal models of type-1 and type-2 diabetes including (i) streptozotocin-induced diabetic rats, (ii) Zucker diabetic fatty rats (ZDF), (iii) obese Zucker rats, (iv) Goto-Kakizaki rats (lean type-2 diabetic model) as well as other models that display glucose intolerance like spontaneously hypertensive rats and uninephrectomized DOCA-salt hypertensive rats, suggesting a universal role of the HO-system in regulating insulin signaling and glucose metabolism. The administration of HO-inducers (i) attenuated inflammatory mediators including cytokines like TNF-α, IL-6, IL-1β that in turn stimulate chemokines such as MCP-1 and MIP-1α to promote macrophage-M1 infiltration, (ii) uppressed oxidative stress including NF-κB, activating-protein (AP)-1, AP-2, and c-Jun-N-terminal-kinase and 8-isoprostane, (iii) enhanced fundamental proteins implicated in the insulin signal transduction pathway like IRS-1, PI3K and PKB, (iv) reduced insulin/glucose intolerance (IPITT), (v) increased insulin sensitivity and the inability of insulin to enhance GLUT4 was overturned. These were associated with improved cardiac hemodynamics and the attenuation of cardiac hypertrophy, collagen deposition in cardiomyocytes and the reduction of left ventricular longitudinal muscle fiber thickness, a pathophysiological feature of cardiomyocyte hypertrophy. Similarly, HO reduced renal histological lesions such as glomerulosclerosis, tubular necrosis, tubular vacuolization, interstitial macrophage infiltration and abated pro-fibrotic/extracellular-matrix proteins like collagen and fibronectin that deplete nephrin, an important transmembrane protein which forms the scaffolding of the podocyte slit-diaphragm allowing ions to filter but not massive excretion of proteins, hence proteinuria. Thus, diabetic complications such as cardiomyopathy and nephropathy were markedly improved. Taken together, these studies suggest that the HO-system could be considered and important switch box that when potentiated adequately can rescue organ damage in diabetes.

Biography

Joseph Fomusi Ndisang is an Associate Professor in the University of Saskatchewan College of Medicine, Department of Physiology. He received postdoctoral training in Physiology at the University of Saskatchewan College of Medicine from 2000-2005. He obtained a PhD in Pharmacology & Toxicology from the University of Florence, Italy, 2000. He obtained a Doctor of Pharmacy degree from University of Florence, Italy in 1995. He has received several distinguished awards and distinctions including: (i) Fellow of the Canadian Cardiovascular Society (FCCS) in 2016, (ii) Fellow of the American Heart Association (FAHA) in 2011; (iii) Fellow of the International College of Angiology (FICA) in 2007; (iv) Young Investigator Award by International College of Angiology (2007); (v) Young Investigator Award by the American Society of Pharmacology & Experimental Therapeutics-Division for Drug Discovery, Development & Regulatory Affairs (2005); (vi) Young Investigator Award by the Society of Experimental Biology and Medicine (2005); (vii) Caroline turn Suden/Frances A Hellebrandt Professional Opportunity Award for Meritorious Research by the American Physiological Society (2005); and (viii) Recognition Award for Meritorious Research by a Young Investigator by the American Physiological Society (2004). Top 5% of cited authors in journals of Biology and Biochemistry in 2011, by Thomson-Reuters. Currently, Dr. Ndisang is an Editor for Frontiers in Bioscience (impact factor 3.8) and Executive Guest Editor for Current Medicinal Chemistry (impact factor 3.7). He has published more than 64-full length manuscripts in peer-reviewed journals and more than 80 abstracts. Dr. Ndisang has served as external PhD examiner for several universities in Canada, has given more than 30-invited talks, and has also served as peer-reviewer for several reputed journals and granting agencies in United States, United Kingdom, Canada, New Zealand and Poland. Research Interest: His research is mainly focused on investigating the role of the heme oxygenase system in hypertension, diabetes (types-1 and -2), and obesity.