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Heme oxygenase is an important molecular switchbox that can be potentiated to ameliorate cardiorenal complications in diabetes

mpaired insulin signalling 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 hemeoxygenase (HO) with HO-inducers like hemin and hemearginate 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 signalling and glucose metabolism. The administration of HO-inducers (i) attenuated inflammatory mediators including cytokines like TNF- α , IL-6, IL-1 β that in turn stimulate chemokines such as MCP-1 and MIP-1 α to promote macrophage-M1 infiltration, (ii) suppressed oxidative stress including NF-kB, activating-protein (AP)-1, AP-2, and c-Jun-Nterminal-kinaseand 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. Collectively, these studies indicate that diabetic complications such as cardiomyopathy and nephropathy were markedly improved, and suggest that the HO-system could be considered an important switch box that when potentiated adequately can rescue organ damage in diabetes. Thus, HO may be explored in the search for novel and effective remedies capable of reducing both patient and healthcare-cost burden associated with diabetes and related cardio-renal complications.

Biography

Joseph Fomusi Ndisang is the Associate Professor in the University of Saskatchewan College of Medicine, Department of Physiology. He received Postdoctoral training in Physiology from the University of Saskatchewan College of Medicine in 2000-2005. He obtained a PhD in Pharmacology & Toxicology from the University of Florence, Italy in 2000. He obtained a Doctor of Pharmacy degree from University of Florence, Italy in 1995. He has received several distinguished awards and Distinctions including: Fellow of the Canadian Cardiovascular Society (FCCS), Fellow of the American Heart Association (FAHA), Fellow of the International College of Angiology (FICA), Young Investigator Award by International College of Angiology, Young Investigator Award by the American Society of Pharmacology & Experimental Therapeutics-Division for Drug Discovery, Development & Regulatory Affairs, Young Investigator Award by the Society of Experimental Biology and Medicine, Caroline tum Suden/Frances A Hellebrandt Professional Opportunity Award for Meritorious Research by the American Physiological Society and Recognition Award for Meritorious Research by a Young Investigator by the American Physiological Society. 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.

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