

International Conference on

DIABETES AND ITS COMPLICATIONS

May 28-29, 2018 Osaka, Japan

Heme oxygenase ameliorates cardio-renal complications in diabetic animals

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Impaired glucose metabolism and dysfunctional insulin signaling are forerunners of cardio-renal complications. Upregulating heme oxygenase (HO) with HO-inducers potentiates insulin signaling and improved glucose metabolism in type-1 and type-2 diabetic models. Particularly, pro-inflammatory/oxidative mediators including: Cytokines (TNF- α , IL-6, IL-1 β); chemokines (MCP-1, MIP-1 α); macrophage-M1 infiltration; NF- κ B; AP-1; AP-2; cJNk and 8-isoprostane were suppressed by the HO-inducer, hemin whereas components of insulin-signaling such as IRS-1, GLUT4, PI3K and PKB were robustly enhanced. Furthermore, hemin reduced insulin/glucose intolerance. These were associated with the amelioration of cardiac lesions (hypertrophy, collagen deposition in cardiomyocytes and left ventricular longitudinal muscle-fiber thickness) and the improvement of renal lesions (glomerulosclerosis, tubular necrosis, tubular vacuolization and interstitial macrophage infiltration). In addition, the HO-inducer, hemin and abrogated pro-fibrotic/extracellular-matrix proteins like collagen and fibronectin that deplete nephrin, a protein which forms the scaffolding of the podocyte slit-diaphragm for filtration. Correspondingly, improved cardiac hemodynamics and reduced albuminuria/proteinuria and enhanced creatinine clearance was observed suggesting improved cardiac and renal functions. Collectively, these data suggest that, HO-inducers may be explored in the search for novel and effective remedies against cardio-renal complications.

Biography

Joseph Fomusi Ndisang is an Associate Professor in the University of Saskatchewan, College of Medicine, Department of Physiology. He has received his Postdoctoral training in Physiology at the University of Saskatchewan College of Medicine from 2000-2005. He has obtained his PhD in Pharmacology and Toxicology from the University of Florence, Italy (2000) and Doctor of Pharmacy degree from University of Florence, Italy (1995). He has received several distinguished awards and distinctions including Fellow of the Canadian Cardiovascular Society in 2016; Fellow of the American Heart Association in 2011; Fellow of the International College of Angiology in 2007; Young Investigator Award by International College of Angiology in 2007; Young Investigator Award by the American Society of Pharmacology and Experimental Therapeutics-Division for Drug Discovery, Development and Regulatory Affairs in 2005, etc. Currently, he is an Editor for *Frontiers in Bioscience* and Executive Guest Editor for *Current Medicinal Chemistry*. He has published more than 64-full length manuscripts in peer-reviewed journals and more than 80 abstracts. His research focuses on the role of the heme oxygenase system in hypertension, diabetes (types-1 and -2) and obesity.

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