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Joseph Fomusi Ndisang

University of Saskatchewan College of Medicine, Canada

Role of heme oxygenase in cardio-renal organ damage in diabetes

Cardiac and renal damage are common complications in diabetes. Here, we report that upregulating Heme-Oxygenase (HO) alleviate cardiac and renal dysfunction in type-1 and -2 diabetes by suppressing pro-inflammatory cytokines such as TNF-α, IL-6, IL-1β and chemokines like MCP-1 and MIP-1α as well as abating mediators of oxidative stress (NF-κB, activating-protein (AP)-1, AP-2, cJNK and 8-isoprostane. In contrast, important proteins implicated in the insulin signalling like IRS-1, PI3K and PKB were potentiated whereas insulin/glucose intolerance was reduced. Furthermore, insulin sensitivity was enhanced while the inability of insulin to enhance GLUT4 was overturned. Interestingly, the potentiation of insulin signaling by HO was associated with significant reduction of renal histological lesions such as glomerulosclerosis, tubular necrosis, tubular vacuolization, interstitial macrophage-M1 infiltration as well as pro-fibrotic/extracellular-matrix proteins like collagen and fibronectin that deplete nephrin, an important scaffolding protein of the podocyte slit-diaphragm that regulate selective permeability and thus prevent proteinuria. Consistently, in HO-treated animals, we observed reduced proteinuria/albuminuria, whereas creatinine clearance increased suggesting improved renal function. Interestingly, HO also reduced cardiac hypertrophy, attenuated collagen deposition in cardiomyocytes, abated left ventricular longitudinal muscle fiber thickness and improved cardiac hemodynamics. Collectively, these results suggest an important role of HO in alleviating cardio-renal damage in diabetes.

Biography

Joseph Fomusi Ndisang is currently working as an Associate Professor in the University of Saskatchewan College of Medicine, Department of Physiology. He has completed 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 in 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 (2007), Young Investigator Award by the American Society of Pharmacology and Experimental Therapeutics-Division for Drug Discovery, Development and Regulatory Affairs (2005), Young Investigator Award by the Society of Experimental Biology and Medicine (2005), Caroline tum Suden/Frances A Hellebrandt Professional Opportunity Award for Meritorious Research by the American Physiological Society (2005) and Recognition Award for Meritorious Research by a Young Investigator by the American Physiological Society (2004). He is currently an Editor for Frontiers in Bioscience and Executive Guest Editor for Current Medicinal Chemistry. He has published more than 65-full length manuscripts in peer-reviewed journals and more than 80 abstracts. His research is mainly focused on hypertension, diabetes (types-1 and -2) and obesity.

joseph.ndisang@usask.ca