Role of heme oxygenase in insulin signaling and glucose metabolism

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Impaired insulin signaling and deregulated glucose metabolism are amongst the hallmarks in diabetes. Here, we report the effects of the cytoprotective enzyme, heme-oxygenase, (HO) on insulin signaling and glucose metabolism. The administration of the HO-inducer, hemin, to streptozotocin-induced diabetic animals normalized hyperglycemia and the potentiated important proteins implicated in the insulin-signal transduction pathway such as IRS-1, PI3K and GLUT4. Interestingly, the anti-diabetic effects of hemin was accompanied by enhanced levels of adiponectin, improved insulin sensitivity and reduced glucose intolerance. These were associated with the reduction of oxidative/inflammatory mediators like 8-isoprostone, nuclear-factor-kappaB, activating-protein (AP-1), AP-2 and c-Jun-NH2-terminal-kinase. Furthermore, hemin suppressed the pro-inflammatory macrophage-M1-phenotype alongside several pro-inflammatory agents, chemokines and cytokines including macrophage-inflammatory-protein-1-alpha (MIP-1α), macrophage-chemoattractant-protein-1 (MCP-1), TNF-α, IL-1β and IL-6. Conversely, hemin significantly enhanced the anti-inflammatory macrophage-M2-phenotype and IL-10.

We conclude that upregulating the HO system abates hyperglycemia in diabetic animals by nullifying inflammation and oxidative stress, while concomitantly potentiating insulin signalling and glucose metabolism. Thus HO-inducers may be explored in the search for novel remedied against type-1 diabetes.

Biography

Joseph Fomusi Ndisang is an Associate Professor in the Department of Physiology of University of Saskatchewan, College of Medicine. He has completed his Postdoctoral training in Physiology at the University Of Saskatchewan, College of Medicine. He has received his PhD in Pharmacology & Toxicology from the University of Florence, Italy and received a Doctor of Pharmacy degree from University of Florence, Italy. He has got several distinguished awards and distinctions including: Associate Fellow of the Scientific Council of the International College of Angiology (2007).

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