OMICS Group Conferences
Accelerating Scientific Discovery

International Conference and Exhibition on
Neurology & Therapeutics

May 14-16, 2012 Embassy Suites Las Vegas, USA

Coupling energy metabolism and intracellular calcium homeostasis

W.D. Watson, J.T. Cole, W. S. Kean, H.B. Pollard and A. Verma

Uniformed Services University of the Health Sciences, USA

Brain cells expend large amounts of energy sequestering calcium (Ca^{2+}), while loss of Ca^{2+} compartmentalization leads to cell damage or death. Upon cell entry, glucose is converted to glucose-6-phosphate (G6P), a parent substrate to several metabolic major pathways, including glycolysis. Recently, this laboratory discovered G6P significantly reduced Ca^{2+} accumulation in rat brain endoplasmic reticulum (ER) microsomes. Since G6P diffusely reduces radiotracer 45Ca2+ accumulation in a pattern similar to thapsigargin in fresh frozen rat brain sections, we hypothesized that G6P regulates Ca^{2+} accumulation by acting as an endogenous ligand for sarco-endoplasmic reticulum calcium ATPase (SERCA). Whole brain ER microsomes were pooled from adult male Sprague-Dawley rats. Using radio-isotopic assays, $^{45}Ca^{2+}$ accumulation was quantified following incubation with increasing amounts of G6P, in the presence or absence of thapsigargin, a potent SERCA inhibitor. To qualitatively assess SERCA activity, the simultaneous release of inorganic phosphate (Pi) coupled with Ca^{2+} accumulation was quantified. Addition of G6P significantly and decreased Ca^{2+} accumulation in a dose-dependent fashion (1-10 mM). The reduction in Ca^{2+} accumulation was not significantly different that seen with addition of thapsigargin. Addition of glucose-1-phosphate or fructose-6-phosphate, or other glucose metabolic pathway intermediates, had no effect on Ca^{2+} accumulation. Further, the release of Pi was markedly decreased, indicating G6P-mediated SERCA inhibition as the responsible mechanism for reduced Ca^{2+} uptake. Simultaneous addition of thapsigargin and G6P did decrease inorganic phosphate in comparison to either treatment alone, which suggests that the two treatments have different mechanisms of action. Therefore, G6P may be a novel, endogenous regulator of SERCA activity. Additionally, pathological conditions observed during disease states that disrupt glucose homeostasis, may be attributable to Ca^{2+} dystasis caused by altered G6P regulation of SERCA activity.

Biography

CAPT William D. Watson, US Navy,graduated from Annapolis in 1984, completed his M.D. in 1997 and Ph.D.in 2000 at The Uniformed Services University of the Health Sciences in Bethesda, MD, where he is currently the Vice Chair of the Department of Neurology after serving various assignments, including Chair of Neurology at Bethesda Naval Hospital. He also is the currently appointed Neurology Specialty Leader, advising the Navy Surgeon General on all matters relating to Navy Neurology. He has published 14 papers in reputed journals and serves as an editorial board member of repute.

wwatson@usuhs.mil