University of Prince Edward Island

Faculty of Veterinary Medicine
Summary of Dissertation

Submitted in Partial Fulfilment
of the Requirements for the

DEGREE OF DOCTOR OF PHILOSOPHY

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Interactions of copper with temperature and oxygen depletion stress on reactive oxygen species (ROS) homeostasis in heart mitochondria

Mitochondria are a common target of abiotic stressors that alter reactive oxygen species (ROS) metabolism. Thus, assessing the effects of stressors on mitochondrial ROS metabolism can be used to integrate effects of stressors in aquatic ectotherms. The overarching aim of this thesis was to probe the interactions of copper (Cu) with temperature rise and anoxic stress on ROS homeostasis in rainbow trout (*Oncorhynchus mykiss*) heart mitochondria. First, the interactions of Cu and temperature on mitochondrial ROS (as H_2O_2) emission were examined and it was found that Cu modulated H_2O_2 emission differently depending on temperature and substrate type. Specifically, the magnitude of the stimulatory and inhibitory effects of Cu on the rate of H_2O_2 emission varied with temperature during succinate oxidation while H_2O_2 emission in mitochondria oxidizing glutamate-malate was not altered by temperature rise. Second, effects of thermal stress and Cu on H_2O_2 scavenging systems and mitochondrial ROS consumption capacity were investigated. Results indicated that the glutathione (GSH)-dependent peroxidase pathway is the predominant H_2O_2 scavenging system in heart mitochondria. The effect of thermal stress depended on substrate wherein temperature rise suppressed the rate of H_2O_2 consumption during oxidation of glutamate-malate or succinate but not palmitoylcarnitine. Notably, Cu intensified the temperature-induced suppression of H_2O_2 consumption. Third, assessment of how anoxia-reoxygenation and Cu influence mitochondrial H_2O_2 emission showed that anoxia-reoxygenation suppressed H_2O_2 emission regardless of the duration of anoxia and substrate type by increasing activities of antioxidant enzymes and suppressing ROS production from QH_2/Q isopotential sites. Moreover, anoxia-reoxygenation attenuated or intensified the effect of Cu depending on the redox site and duration of anoxia exposure. Altogether, this thesis improves our knowledge about the interactions of Cu with thermal stress and anoxia in fish heart and established that changes in mitochondrial ROS metabolism can integrate effects of multiple stressors in aquatic organisms.

Publications

Isei, M.O., Chinnappareddy, N., Stevens, D., Kamunde, C. (2021). Anoxia-reoxygenation alters H_2O_2 efflux and sensitivity of redox centers to copper in heart mitochondria. Comp Biochem Physiol C Toxicol Pharmacol. 248: 109111.

Isei, M.O., Stevens, D., Kamunde, C. (2021). Temperature rise and copper exposure reduce heart mitochondrial reactive oxygen species scavenging capacity. Comp Biochem Physiol C Toxicol Pharmacol. 243: 108999.

Isei, M.O., Kamunde, C. (2020). Effect of copper and temperature on heart mitochondrial hydrogen peroxide production. Free Radic Biol Med. 147: 114-128.

Manuscript Submitted to CBPC

Isei, M.O., Stevens, D., Kamunde, C. (2021). Copper modulates heart mitochondrial H_2O_2 emission during oxidation of palmitoylcarnitine and pyruvate. CBPC (submitted).

Presentations

27th Annual conference of the Society for Redox Biology and Medicine (SfRBM) (Nov., 2020) Virtual online conference"Temperature rise and copper exposure reduce heart mitochondrial H_2O_2 consumption"

26th Annual conference of the Society for Redox Biology and Medicine (SfRBM), (Nov., 2019) Planet Hollywood Resort, Las Vegas, Nevada, USA "Copper acts at multiple sites in the mETS to stimulate or inhibit heart mitochondrial ROS production"

Annual Graduate Students Conference (May, 2019) University of Prince Edward Island, PEI, Canada "Effect of assay conditions on H_2O_2 emission in heart mitochondria"

Awards

Annual Graduate Students scholarship award, (CAD 5000)
University of Prince Edward Island