University of Prince Edward Island

Faculty of Veterinary Medicine
Summary of Dissertation

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DEGREE OF DOCTOR OF PHILOSOPHY

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Effect of environmental stress on reactive oxygen species metabolism and oxidative stress response in rainbow trout (*Oncorhynchus mykiss*)

Aquatic organisms are exposed to different environmental stressors including temperature variations, low dissolved oxygen and metals pollution that may cause physiological perturbation attributed to altered mitochondrial function and dysregulation of reactive oxygen species (ROS) metabolism. Therefore, it is important to understand how these stressors act and interact to disrupt ROS homeostasis leading to oxidative stress. The study investigated the effects of temperature, anoxia-reoxygenation and cadmium on rainbow trout (*O. mykiss*) liver mitochondrial ROS (as hydrogen peroxide, H_2O_2) production and consumption under different bioenergetic states. The overall hypothesis was that temperature, anoxia-reoxygenation and Cd will stimulate ROS emission and that the combined effect of cadmium and temperature or anoxia-reoxygenation will heighten the individual stressor effects. Temperature and cadmium acted cooperatively to increase the rate of H_2O_2 emission. Cadmium evoked a graded H_2O_2 emission response that plateaued at 5 μM for mitochondria oxidizing malate-glutamate governed by site I_F, but a biphasic concentration-response with a spike in H_2O_2 emission at 1 μM cadmium followed by gradual diminution at higher cadmium concentration dictated by site II_F during succinate oxidation. Anoxia-reoxygenation attenuated H_2O_2 emission while cadmium evoked monotonic responses for glutamate-malate and palmitoylcarnitine-malate but evoked a biphasic response for succinate or glycerol 3-phosphate oxidizing mitochondria. Anoxia-reoxygenation severely inhibited mitochondrial respiration with palmitoylcarnitine-malate compared with succinate and glutamate-malate, while glycerol 3-phosphate supported respiration was very low compared. The effect of anoxia-reoxygenation and cadmium on site-specific H_2O_2 emission depended on the concentration, substrate and site. Contrary to the expectation, anoxia-reoxygenation blunted the effect of cadmium on mitochondria site-specific H_2O_2 emission. However, cadmium did not alter the kinetics of mitochondrial H_2O_2 consumption or the activities/concentration of components of mitochondrial antioxidant systems. Overall, the study unveiled the mechanisms by which temperature, anoxia-reoxygenation and Cd disrupt mitochondrial ROS metabolism, and increased the understanding of how these stressors cause oxidative stress.

Publications

Published

1.Chidozie N. Okoye, Don Stevens, Collins Kamunde (2021). Modulation of mitochondrial site-specific hydrogen peroxide efflux by exogenous stressors. Free Rad Biol Med., 164: 439 – 456.

2.Okoye C. N., MacDonld-Jay N., Kamunde C. (2019). Effects of bioenergetics, temperature and cadmium on liver mitochondria reactive oxygen species production and consumption. *Aquatic Toxicology*, 214: 105264.

Under Revision

1.Okoye, C.N., Stevens, D. and Kamunde C., 2021. Factors affecting liver mitochondrial hydrogen peroxide emission. Comp. Biochem. Physiol. B. Manuscript number: CBPB-D-21-00198

Submitted

1.Okoye, C.N., Chinnappareddy, N., Stevens, D. and Kamunde, C., 2021. Anoxia-reoxygenation modulates cadmium-induced liver mitochondrial reactive oxygen species emission during oxidation of glycerol 3-phosphate. Comp. Biochem. Physiol., C Manuscript number: CBPC-D-21-00429

Awards Received

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