University of Prince Edward Island

Faculty of Veterinary Medicine
Summary of Dissertation

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of the Requirements for the

DEGREE OF DOCTOR OF PHILOSOPHY

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Mitochondrial Responses to Metals and Nutritional Stress in Rainbow Trout: Linking Bioenergetic Disruption to Redox Imbalance

Aquatic ecosystems face mounting threats from pollution and environmental change, yet our understanding of how multiple stressors interact within biological systems remains limited. This thesis investigates how metals exposure and nutritional stress converge on mitochondrion, the central hub of cellular energy conversion and redox regulation, in rainbow trout (*Oncorhynchus mykiss*). Using isolated mitochondria, permeabilized cardiac fibers, and in vivo nutritional manipulations, this work links bioenergetic disruption to redox imbalance. I show that mitochondrial responses to copper, cadmium, and zinc, both individually and in binary mixtures, are highly context dependent, varying with respiratory substrate, metabolic state, redox site, tissue type, and nutritional status. Effects of metal mixtures frequently deviated from additivity, with antagonistic and synergistic interactions predominating, challenging the assumption that metals act independently. Notably, zinc emerged as the most potent inhibitor of cardiac mitochondrial oxidative phosphorylation, revealing an unexpected sensitivity of the trout heart to this essential trace metal. Metals exposure disrupted reactive oxygen species (ROS, measured as hydrogen peroxide) homeodynamics by altering both production and scavenging pathways. Critically, metals exposure weakened the canonical relationship between mitochondrial NAD(P)H redox state and ROS production, undermining a foundational paradigm in mitochondrial physiology. Nutritional stress (starvation) further modulated these responses, impairing mitochondrial function in both heart and liver, with refeeding fully restoring liver mitochondrial performance but only partially rescuing cardiac function, highlighting tissue-specific vulnerability. Together, these findings demonstrate that metal mixtures and energy limitation interact in complex, non-additive ways to disrupt mitochondrial bioenergetics and redox balance with direct consequences for cardiac performance and organismal fitness, underscoring the need for integrative approaches when assessing impacts of environmental stressors in aquatic organisms.

Publications

1. Tetteh, P. A., Kalvani, Z., Stevens, D., Sappal, R., Kamunde, C. (2025). Nutritional Status Modulates Mitochondrial Bioenergetic and Redox Responses to Zinc Exposure in Rainbow Trout. Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology, 110417.

2. Tetteh, P. A., Kalvani, Z., Stevens, D., Sappal, R., Kamunde, C. (2025). Copper, Cadmium, and Zinc Trigger Multifaceted Effects and Interactions on Cardiac Mitochondrial Bioenergetics and Reactive Oxygen Species Production in Rainbow Trout. Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology, 110286.

3. Tetteh, P. A., Kalvani, Z., Stevens, D., Sappal, R., Kamunde, C. (2024). Interactions of Binary Mixtures of Metals on Rainbow Trout (*Oncorhynchus Mykiss*) Heart Mitochondrial H_2O_2 Homeodynamics. Aquatic Toxicology, 106986.

4. Kalvani, Z., Tetteh, P., Kamunde, C., Stevens, D., van den Heuvel, M. R. (2025). Naphthenic Acid-Induced ROS Emissions by Rainbow Trout Mitochondria. Toxics, 13(12), 1015.

5. Ontita, N. C., Amanze, C., Anaman, R., Shanshan, X., Kwofie, F., Tetteh, P. A., Zeng, W. (2025). Mechanistic Insights into Biphasic Effects of Ce (III) on Anode Biofilms in Bioelectrochemical Systems during Industrial Wastewater Treatment. Water, Air, & Soil Pollution, 236(8), 1–25.

6. Kamunde, C., Wijayakulathilake, Y., Okoye, C., Chinnappareddy, N., Kalvani, Z., Tetteh, P., van den Heuvel, M., Sappal, R., Stevens, D. (2024). Effect of Skeletal Muscle Mitochondrial Phenotype on H_2O_2 Emission. Comparative Biochemistry and Physiology Part B: Biochemistry and Molecular Biology, 271, 110940.

Submitted

7. Tetteh, P. A., Kalvani, Z., Stevens, D., Sappal, R., Kamunde, C. (2025). Metals Exposure Dissociates Mitochondrial NAD(P)H Redox State from H_2O_2 Emission. Comparative Biochemistry and Physiology, Part C: Manuscript number CBPC-D-25-01307.

Presentations

1. 50th Annual conference of Canadian Ecotoxicity Workshop (CEW), (October 2024), Kitchener-Waterloo, Ontario, Canada "Modulation of Mitochondrial Bioenergetics and Reactive Oxygen Species Production by Binary Mixtures of Copper, Cadmium, and Zinc in Permeabilized Fish Cardiac Fibers".

2. 40th Annual conference of Aquaculture Canada Conference (ACC), (June 2024), Charlottetown, PEI, Canada "Interaction of Feed Restriction and Zn Exposure on Liver and Heart Mitochondrial Bioenergetics in Rainbow Trout, *Oncorhynchus mykiss*".

3. 63rd Annual conference of Canadian Society of Zoologist (CSZ), (May 2024), Moncton, New Brunswick, Canada "Interactive Effects of Hypoxia-Reoxygenation and Trace Metals Mixtures on Heart Mitochondrial Bioenergetics During Fatty Acid and Pyruvate Oxidation".

4. 63rd Annual conference of Canadian Society of Zoologist (CSZ), (May 2024) Moncton, New Brunswick, Canada (Poster Presentation), "Effect of Nutritional Status and Zn on Liver Mitochondrial Respiration and H_2O_2 Metabolism in Rainbow Trout, *Oncorhynchus mykiss*".

5. 49th Annual conference of Canadian Ecotoxicity Workshop (CEW), (October 2023) Ottawa, Ontario, Canada "Interactions of Trace Metals on Heart Mitochondrial Reactive Oxygen Species Metabolism".

Biographical Data – Born in Samreboi, Ghana.

Awards

1. 2023, Canadian Ecotoxicity Workshop (CEW) Travel Award, Ottawa, Canada.

2. 2022, 2023, Annual Graduate Students Scholarship Award, University of Prince Edward Island.