

GRADUATE AND POSTDOCTORAL STUDIES

MCGILL UNIVERSITY



FINAL ORAL EXAMINATION
FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

OF

KRITTIKA MITTAL
DEPARTMENT OF NATURAL RESOURCE SCIENCES

THE USE OF TRADITIONAL AND ALTERNATIVE
METHODS TO STUDY ENDOCRINE DISRUPTION IN
MODEL AVIAN SPECIES

13th June 2018
9:15 AM

Macdonald Stewart Building, Room MS2-022
McGill University, Macdonald Campus

COMMITTEE:

Dr. A. Watson (Pro-Dean) (Plant Science)
Dr. L. Whyte (Chair) (Natural Resource Sciences)
Dr. N. Basu (Supervisor) (Natural Resource Sciences)
Dr. S. George (Internal Examiner) (Food Science and Agricultural Chemistry)
Dr. S. Faucher (Internal Member) (Natural Resource Sciences)
Dr. R. Duggavathi (External Member) (Animal Science)

Dr. Josephine Nalbantoglu, Dean of Graduate and Postdoctoral Studies
Members of the Faculty and Graduate Students
are invited to attend

ABSTRACT

Chemical contamination is a global threat with over 100,000 chemicals currently lacking toxicity data. Toxicity testing of chemicals is integral to hazard determination and risk assessment. Traditional whole animal (*in vivo*) testing, which has been the mainstay for several decades, often tend not to account for sex, developmental stage, and duration of exposure. They are also resource-intensive and raise significant ethical concerns pertaining to animal use. This has led to a surge in the development of alternative methods (cells and tissues) to screen and prioritize chemicals. Despite the promise shown by such methods, little is known about how they perform against whole animal tests. Overall, this thesis aimed to advance knowledge on A) traditional and alternative toxicity testing methods, and B) the effects of 17 α -Trenbolone (17 α -T- a model endocrine disrupting chemical commonly used in livestock as a growth promoter) in model avian species. The specific aims of this thesis were to Aim 1) use *in vivo* exposures and next-generation RNA-

analysis covering a larger biological space may be needed to identify genomic biomarkers that could be linked to apical outcomes. In Aim 3, hierarchical clustering analysis of gene expression results across three alternative methods showed similarities between liver slice culture and *in ovo* liver, while hepatocytes were more different from the *in ovo* liver. In Aim 4, bibliometric searches of resource-related costs from various data-streams showed that the status quo in toxicity testing will likely be unable to provide toxicity data for all existing and emerging chemicals. For example, median cost of *in vivo* studies is \$118,000, they tend to use 130 animals and take around 4.5 months, while median cost of *in vitro* studies is \$2,500, they tend to use 20-40 animals and take around 2 weeks. In summary, this work demonstrated that liver slices showed similarities to the *in ovo* liver and indicated potential for the use of alternatives in toxicity testing; further, this work showed that even using traditional methods results may vary depending on factors such as sex, developmental stage, and exposure duration. This thesis advances knowledge on two fronts: A) differences among alternative testing methods to aid in their future implementation in toxicity testing of chemicals, and the reduction of traditional methods, and B) the importance of including aforementioned factors while examining molecular and biochemical endpoints in toxicity studies.

CURRICULUM VITAE

UNIVERSITY EDUCATION

- 2014 – present **PhD Renewable Resources, McGill University, Montreal.** Thesis: The use of traditional and novel methods to study endocrine disruption in model avian species. Supervisor: Dr. Nil Basu.
- 2009 – 2011 **M.S. (Non-thesis) Biomedical Engineering, University of Michigan, Ann Arbor.**
Concentration: Biotechnology
- 2005 - 2009 **B.E. Biotechnology, People's Education Society Institute of Technology, Visvesvaraya Technological University, Bangalore.**

EMPLOYMENT

- 2011-2013 Research Associate, University of Michigan, Ann Arbor, 20550 Tn -0 0 9.48 113.76 561.24 Tm [(I)-4(T)0

PUBLICATIONS

IN PREP

1. **Mittal K.**, Crump D., Basu N. A Comparative Study of Alternative Toxicity Testing Methods: Effects on Hepatic Gene Expression in the Chicken Embryo. In prep, expected submission June 2018. *Environmental Toxicology and Chemistry*.
2. **Mittal K.**, Crump D., Head J., Hecker M., Hogan N., Xia J., Hickey G., Maguire S., Basu N. Can Alternative Toxicity Testing Methods be more Efficient than Traditional Methods? In prep, expected submission July 2018. *Environmental Science and Technology*.
3. **Mittal K.**, Henry P.F.P., Cornman R.S., Sprague D.T., Basu N., Karouna-Renier N.K. Sex- and Developmental Stage-related Differences in the Hepatic Transcriptome of Japanese quail (*Coturnix japonica*) Exposed to 17 β -Trenbolone. In prep, expected submission July 2018. *Environmental Toxicology and Chemistry*.
4. **Mittal K.**, Henry P.F.P., Armstrong B., Murphy C., Basu N., Karouna-Renier N.K. Assessing Short-Term Effects of 17 β -Trenbolone on the Japanese Quail Hypothalamic-Pituitary-Gonadal-Liver Axis. In prep, expected submission July 2018.

4. Head, J. A., **Mittal, K.**, & Basu, N. (2014). Application of the Luminometric Methylation Assay to ecological systems: a review.