Ph.D. Candidate

Rachael Anne Wyatt

Graduate Academic Unit

Biology

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August 19, 2020

1:00 p.m. (Atlantic)

Virtual Defence

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Examining Board:
Dr. Shawn MacLellan (Biology)
Dr. Cheryl Patten (Biology)
Dr. Sara Eisler (Chemistry)
Dr. Bryan Crawford (Biology) Supervisor
Dr. Thomas Pulinilkunnil, Adjunct Prof. (Biological Sciences, UNBSJ) Supervisor

External Examiner: Dr. Scott Holley
Professor of Molecular, Cellular & Developmental Biology
Yale University

The Oral Examination will be chaired by:
Dr. Kevin Englehart, Associate Dean of Graduate Studies

BIOGRAPHY

Universities attended (with dates & degrees obtained):

2014 – present PhD candidate, University of New Brunswick
2013 M.A. in English, Concordia University, Montreal, QC
2011 B.A. in English (Honours), University of New Brunswick, Fredericton, NB.
2011 B.Sc. in Biology-Chemistry (Honours) UNB, Fredericton, NB.

Publications:

2019 Fallata, A.M., **Wyatt, R.A**., Levesque, J.M., Dufour, A., Overall, C.M., Crawford, B.D., 2019. "Intracellular Localization in Zebrafish Muscle and Conserved Sequence Features Suggest Roles for Gelatinase A Moonlighting in Sarcomere Maintenance." Biomedicines 7, 93.

2017 **Wyatt, R. A**.; Trieu, N. P. V.; Crawford, B. D. Zebrafish Xenograft: An Evolutionary Experiment in Tumour Biology. Genes 8 (2017): 220.

Colpitts, C., Ektesabi, A.M., **Wyatt, R.A.**, Crawford, B.D., Kiani, A., 2017. Mammalian fibroblast cells avoid residual stress zone caused by nanosecond laser pulses. Journal of the Mechanical Behavior of Biomedical Materials 74, 214–220.

Colpitts, C., Ektesabi, A.M., **Wyatt, R.A.**, Crawford, B.D., Kiani, A., 2017. Mammalian Fibroblast Cells Show Strong Preference for Laser-Generated Hybrid Amorphous Silicon-SiO2 Textures. Journal of Applied Biomaterials & Functional Materials 15, 84–92.

2016 Radmanesh, M., Ektesabi, A.M., **Wyatt, R.A.**, Crawford, B.D., Kiani, A., 2016. Mouse embryonic fibroblasts accumulate differentially on titanium surfaces treated with nanosecond laser pulses. Biointerphases 11:3, 031009.

2014 **Wyatt, R. A.**. "The Limits of Energy: Richard Norman's *Zero Kelvin*" (2014).

2013 **Wyatt, R. A.**. "Adam Dickinson's The Polymers." *Lemon Hound*, vol. 5 (2013).

2009 **Wyatt, R. A.**, Jonathan Y. Keow, Natalie D. Harris, Charles A. Haché, Daniel H. Li, Bryan D. Crawford. "The Zebrafish Embryo: A Powerful Model System for Investigating Matrix Remodeling." Zebrafish 6.4 (2009): 347-354.

Selected Conference Presentations:

2020 **Wyatt, R.A.**, E. J. Jeffrey, M. A. Mabey, B. D. Crawford. "Zebrafish notochord elongation requires the activation of matrix metalloproteinase-2 mediated by serine proteases." Society for Developmental Biology 79th Annual Meeting. 14 July 2020. Poster presentation.

2019 **Wyatt, R.A.**, University of New Brunswick. "Mmp2 Activation During Notochord Elongation in Zebrafish Embryos." 12th Annual Atlantic Regional Comparative Physiology Workshop. 19 Oct 2019. Oral presentation.

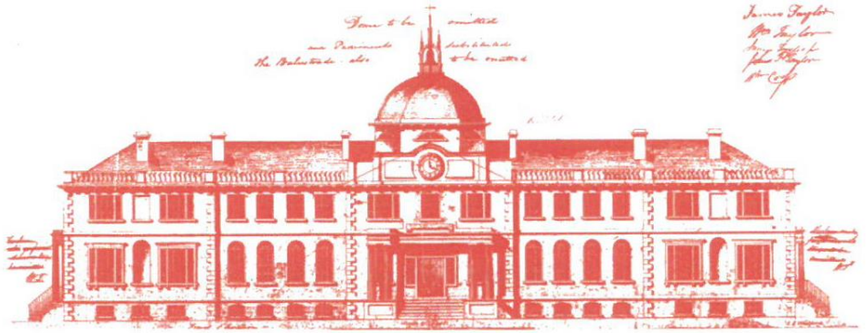
2018 Trieu N.P.V., **Wyatt, R.A.**, Pugh, E., University of New Brunswick. "Investigating the Regulation and Roles of Matrix Metalloproteinases In Vivo." 6th Annual Atlantic Developmental Biology Symposium. 8 Jun 2018. Oral presentation.
(Several Other Conference Presentations)

Patterns and Mechanisms of Post-Translational Regulation of Mmp2 *in vivo* During Zebrafish Development

Abstract

In addition to cells, multicellular tissues are made up of context-specific complexes of secreted proteins that are assembled dynamically outside cells to produce the physical characteristics of the vertebrate body and organs. The resistive strength of tendons, the elasticity and impermeability of skin and the support structure of the skeleton are functional largely because of the extracellular matrix (ECM). The development and maintenance of these tissues requires careful orchestration between assembly and degradation of components. Matrix metalloproteinases (MMPs) are one of the enzyme families known to degrade ECM. Matrix metalloproteinase-2 (MMP-2), my enzyme of interest, is known to have roles in pathologies such as arthritis, where its function is protective, and cancer metastasis, where it is activated as part of the migration and invasion of metastatic cells. It is an enzyme that requires post-translational activation by proteolytic cleavage, and therefore its role cannot be fully described by either mmp2 transcript patterns or Mmp2 protein accumulation. Using a transgenic zebrafish line with the epitope-mediated MMP activation (EMMA) assay construct, for the first time we can localize activation of Mmp2 *in vivo*, and here I describe its presence and activation during embryonic development.

Though endogenous Mmp2 is expressed ubiquitously during the development of a zebrafish embryo, I show here that it is proteolytically active in a much smaller set of structures. It is most strongly activated in the notochord, epithelium, fin folds and neural tube. Active Mmp2 has a role during the morphogenesis of the notochord, a driving structure in vertebrate development, and in the fin folds where actinotrichia are collagen-based ECM structures that form the basis for fin rays. Further, I show that the activation mechanisms of Mmp2 are tissue- and stage-dependent: mechanisms that require metalloproteases are required for the activation of Mmp2 during fin fold development, but mechanisms dependent upon serine proteases are involved in the activation of Mmp2 in the notochord during notochord elongation and straightening. This is the first description of activation patterns *in vivo* and offers a starting point from which to examine the requirement of metalloproteases during development and to interrogate their mechanisms of activation.



Home of the School of Graduate Studies, Sir Howard Douglas Hall was designed by J.E. Woolford in 1825 and is the oldest university building in Canada still in use.

The University of New Brunswick recognizes that the university sits on traditional Wolastoqey territory. The river that runs right by our university – the St. John River – is also known as Wolastoq, along which live the Wolastoqiyik -- the people of the beautiful and bountiful river.

UNIVERSITY OF NEW BRUNSWICK

SCHOOL OF GRADUATE STUDIES

ORAL EXAMINATION

Rachael Anne Wyatt

IN PARTIAL FULFILMENT
OF THE REQUIREMENTS FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY