Vita

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Universities Attended:

University of New Brunswick (2022)
Bachelors of Science

University of New Brunswick (2025)
Masters of Science
Biology

Conference Presentations:

Piezo1-mediated detection of mechanical force regulates post-translational activation of matrix metalloproteinase-2 (Mmp2) through Mmp14 in growing zebrafish embryos. Developmental Biology Symposium, Halifax, Canada 2024

Piezo1-mediated detection of mechanical force regulates post-translational activation of matrix metalloproteinase-2 (Mmp2) in growing zebrafish embryos. Conference of the Biological Sciences, Fredericton, Canada 2024

Piezo1-mediated detection of mechanical force regulates post-translational activation of matrix metalloproteinase-2 (Mmp2) in growing zebrafish embryos. Canadian Society of Zoologists 63rd Annual Meeting, Moncton, Canada 2024

Post-Translational Activation of Mmp2 by Mmp14 is Triggered by Mechanical Signalling Through Piezo1 and Erk During Embryonic Growth in Zebrafish

UNIVERSITY OF NEW BRUNSWICK

THESIS DEFENCE AND EXAMINATION

in Partial Fulfillment

of the Requirement for the Degree of
Master of Science

by

Jillian E. Hickey

in the Department of Biology

U.N.B., Fredericton, N.B.

Wednesday, April 23rd, 2025
11:30 a.m.

Bailey Hall, Room 102

Examining Committee

Dr. Bryan Crawford	Supervisor
Dr. Alla Gagarinova	Internal Examiner
Dr. Yang Qu	External Examiner
Dr. Jason Addison	Chair of Oral Examination

Abstract

To grow and change shape during development, wound healing and regeneration, multicellular tissues must remodel their extracellular matrix (ECM). The matrix metalloproteinases (MMPs) are the primary effectors of ECM remodeling, making their proper regulation central to normal development, and their mis-regulation central to many diseases. All MMPs are synthesized as inactive pro-enzymes that are activated post-translationally by the proteolytic removal of an auto-inhibitory N-terminal domain. Using a novel transgenic zebrafish, we can visualize and quantify the proteolytic activation of matrix metalloproteinase 2 (Mmp2) in intact embryos. Interestingly, in the epidermis of growing embryos, Mmp2 is activated in a patchwork-like pattern, suggesting that the stretching of this tissue as the embryo grows may stimulate ECM remodeling. Piezo1 is a stretch-sensitive calcium channel that is abundant in the epidermis of zebrafish embryos; I hypothesized that mechanical activation of Piezo1 by stretching of the epidermis due to growth of the underlying tissue triggers expression of membrane type 1 MMP (Mmp14) via calcium dependent Erk signalling, resulting in patches of Mmp2 activation in the epidermis. Consistent with this hypothesis, I observed increased *mmp14b* expression in the epidermis using hybridization chain reaction after treatment with the Piezo1 agonist Yoda1, and decreased *mmp14b* expression after treatment with either the Piezo1 inhibitor GsMTx4 or the MEK/ERK pathway inhibitor PD0325901. I also found increased Mmp2 activation patches following treatment with Yoda1, and reduction of Mmp2 activation following treatment with GsMTx4 or PD0325901. These findings suggest a new link between mechanical stretching of epithelial tissues and the biochemical mechanisms of ECM remodeling *in vivo*, shedding light on the feedback mechanisms regulating tissue morphogenesis in vertebrates.