BIOGRAPHICAL SKETCH

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NAME: Conway, Daniel E.

eRA COMMONS USER NAME (credential, e.g., agency login): danielconway

POSITION TITLE: Assistant Professor of Biomedical Engineering

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Rice University, Houston, Texas	B.S.	05/2003	Bioengineering
Georgia Institute of Technology and Emory University, Atlanta, Georgia	Ph.D.	05/2009	Biomedical Engineering
University of Virginia, Charlottesville, Virginia	Postdoc	06/2013	Mechanobiology

A. Personal Statement

Mechanical forces on cells regulate development, homeostasis, and disease. Mechanotransduction, or the conversion of mechanical forces into intracellular chemical signaling events, occurs in nearly every type of cell, suggesting that cells are intrinsically mechanosensitive. My laboratory focuses on developing and utilizing techniques that measure changes in cellular tension with protein specificity. My background makes me uniquely qualified for this research. My undergraduate and graduate degrees are in Bio/Biomedical Engineering, providing me with a strong background in cell biology and engineering design to model the physiological forces of the vasculature. In my post-doctoral studies I worked under the guidance of Martin Schwartz, where I developed novel FRET-based tension sensors capable of resolving forces across mechanosensitive proteins in endothelial cells. A major finding of my post-doctoral work was that application of shear stress to endothelial cells elicits rapid and opposite changes in the forces across VE-cadherin and PECAM-1, a finding which challenged existing theories of mechanotransduction. This finding was not predicted by experimental models and therefore would not have been observed without techniques capable of resolving force with protein-specificity.

As a new independent investigator, I have started my lab with two Ph.D. students, a Master's student, and several undergraduate researchers who have all become well-versed using this force-measurement technique. Since arriving at VCU (August 2013), my lab is currently focused on using this force measurement technique to resolve the mechanical forces across tight junctions, adherens junctions, and desmosomes to understand the role of forces at epithelial cell-cell junctions. My lab is also using this technique to measure the mechanical forces applied across the nuclear LINC complex. My approach to directly measure mechanical forces across multiple load-bearing structures in the cell will enhance the fundamental understanding of cellular biomechanics and mechanobiology, with wider application to the advancement of human health and disease.

B. Positions and Honors

Positions and Employment

2003-2009 PhD student; Graduate Research Assistant, Department of Biomedical Engineering, Georgia Institute of Technology and Emory University, Atlanta, Georgia

2009-2013 Postdoctoral Fellow, Cardiovascular Research Center, University of Virginia, Charlottesville, Virginia

2013- Assistant Professor (tenure track), Department of Biomedical Engineering, Virginia Commonwealth University, Richmond, Virginia

Other Experience and Professional Memberships

2006- Member, Biomedical Engineering Society

2013- Member, American Heart Association

2014, 2017 Reviewer, Vascular Biology Basic Science Committee, American Heart Association

Honors

2003-2006 National Science Foundation Graduate Research Fellowship

2003-2007 President's Fellowship, Georgia Institute of Technology

2008 Tidman Travel Award, Dept. Biomedical Engineering, Georgia Tech/Emory

2009-2011 NHLBI Cardiovascular Research Training Grant, University of Virginia

2011-2013 American Heart Association Postdoctoral Fellowship

2015 Faculty Mentor Award, Undergraduate Research Opportunities Program, VCU

2016 Best Faculty Member in Biomedical Engineering, VCU Undergraduate Student-selected Award

C. Contributions to Science

1. My work during graduate school focused on identifying differential responses of endothelial cells to pro- and anti-atherogenic fluid shear stress. I designed a novel shear stress system that could accurately reproduce the complex physiological shear stress observed at the wall of the carotid sinus, a commonly observed site for atherosclerosis. Microarray results from my work allowed me to identify new genes and signaling pathways differentially regulated by these two forms of shear stress, including cytochrome p450 enzymes and zinc-binding and -transporting proteins.
    a. **Conway DE**, Williams RW, Eskin SG, McIntire LV. Endothelial cell responses to atheroprone flow are driven by two separate flow components, low time-average shear stress and fluid flow reversal. *Am J Physiol Heart Circ Physiol*. 2010;298(2):H367-74 PMCID: PMC2822569
    b. **Conway DE**, Sakurai Y, Weiss D, Vega JD, Taylor WR, Jo H, Eskin SG, Marcus CB, McIntire LV. Expression of CYP1A1 and CYP1B1 in human endothelial cells is regulated by fluid shear stress. *Cardiovascular Research*, 2009;81(4):669-677. PMCID: PMC2642602
    c. **Conway DE**, Lee S, Eskin SG, Shah AK, Jo H, McIntire LV. Endothelial metallothionein expression and intracellular free zinc levels are regulated by shear stress. *Am J Physiol Cell Physiol*. 2010;299(6):C1461-7. PMCID: PMC3006326
    d. Yee A, Bosworth KA, **Conway DE**, Eskin SG, McIntire LV. Gene Expression of Endothelial Cells under Pulsatile Non-reversing vs. Steady Shear Stress; Comparison of Nitric Oxide Production. *Annals of Biomedical Engineering*, 2008;36(4):571-9. PMID: 18256937

2. During my postdoctoral studies I focused on developing techniques to measure the mechanical forces across proteins that were putative mechanotransducers. I developed novel FRET-based force sensors for cell-cell junction proteins VE-cadherin and PECAM-1, and used these sensors to examine how force across these two proteins regulates endothelial function. A major finding was that that application of fluid shear stress reduced cellular contractility, changing the paradigm that mechanical forces are passively applied across the cellular cytoskeleton.
    a. **Conway DE**, Breckenridge MT, Hinde E, Graton E, Chen CS, Schwartz MA. Fluid shear stress modulates mechanical tension across VE-cadherin and PECAM-1 in endothelial cells. Current Biology, 2013 23(11): 1024-30. PMCID: PMC3676707
    b. **Conway DE**, Schwartz MA. Mechanotransduction of shear stress occurs through changes in VE-cadherin and PECAM-1 tension: Implications for cell migration. Cell Adhesion and Migration. Cell Adhesion & Migration, 2014; 8(4). PMID: 25482618

c. Tornavaca O, Chia M, Dufton N, Almagro LO, **Conway DE**, Randi AM, Schwartz MA, Matter K, Balda MS. ZO-1 controls endothelial adherens junctions, cell-cell tension, angiogenesis and barrier formation. Journal of Cell Biology, 2015 208(6): 821-38. PMCID: PMC4362456
d. Daneshjou N, Sieracki N, van Nieuw Amerongen GP, **Conway DE**, Schwartz MA, Komarova YA, Malik AB. Rac1 functions as a reversible tension modulator to stabilize VE-cadherin trans-interaction. Journal of Cell Biology, 2015 208(1): 23-32. PMCID: PMC4395484

3. My current laboratory at VCU is focused on developing new tools to measure forces at cell-cell junctions, resolving forces across adherens, tight, and desmosomal junctions. We are especially interested in determining how forces across cell-cell junctions serve as a communication mechanism regulating proliferation and collective cell migration. Additionally, we have developed a nesprin tension sensor and have determined the nucleus is subject to constitutive, actomyosin-based tension. Our ultimate goal is to understand how forces are transmitted across the structures of a cell.
    a. Arsenovic PT,* Ramachandran I,* Bathula K, Zhu R, Narang JD, Noll NA, Lemmon CA, Gundersen GG, **Conway DE**. Nesprin-2G, a Component of the Nuclear LINC Complex, Is Subject to Myosin-Dependent Tension. Biophys J. 2016 Jan 5;110(1):34-43. PMCID: PMC4805861
    b. Brenner MD, Zhou R, **Conway DE**, Lanzano L, Gratton E, Schwartz MA, Ha T. Spider Silk Peptide Is a Compact, Linear Nanospring Ideal for Intracellular Tension Sensing. Nano Lett. 2016 Mar 9;16(3):2096-102. PMCID: PMC4851340
    c. Arsenovic PT, Bathula K, **Conway DE**. A Protocol for Using Förster Resonance Energy Transfer (FRET)-force Biosensors to Measure Mechanical Forces across the Nuclear LINC Complex. J Vis Exp. 2017 Apr 11;(122).
    d. Vellala PS, Bathula K, Arminger TJ, **Conway DE***, Dahl KN*. Progerin expression in cells under confinement and force reveal the physical mechanism of lamina defects. Integrative Biology. *Revised manuscript under review* .

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1pUoA2sFnqx/bibliograpahy/47319016/public/?sort=date&direction=ascending

D. Research Support
Ongoing Research Support

NIH NIGMS R35GM119617 Conway (PI) 09/01/16-05/31/21
Cell junction and nuclear forces as mediators of epithelial cell homeostasis
Maximizing Investigators' Research Award to provide research support for the Conway laboratory to study the role of cell-cell and nuclear mechanical forces in fundamental cellular processes.

NSF CAREER Award CMMI1653299 Conway (PI) 03/01/17-02/28/22
CAREER: Mechanical forces on the nuclear LINC complex
NSF CAREER award provides support for the study of how cytoskeletal forces are applied across the LINC complex and onto the nuclear lamina.

NIH NIAMS R03AR068096 Conway (PI) 02/01/16-11/30/18
Measurement of Mechanical Tension Across Desmosomes
Small project grant to identify how mechanical forces across desmosomes regulate skin biology.

American Heart Association 16SDG27370007 Conway (PI) 01/01/16-12/31/19
Role of VE-cadherin and PECAM-1 tension in endothelial cell barrier function, mechanotransduction, and wound repair
Seed grant to investigate how endothelial cell-cell junction forces regulate barrier, mechanotransduction, and angiogenesis.

Jeffress Trust Awards Program in Interdisciplinary Research Conway (PI) 08/31/15-05/31/17
Measurement of Mechanical Tension on the Nuclear Membrane
Seed grant to provide initial project support for investigating the mechanical forces applied to the nucleus of a cell

Completed Research Support

VCU Presidential Research Quest Fund Conway (PI) 07/01/14-12/31/15
Measurement of mechanical tension across desmosome cadherins
Seed grant to provide initial project support to generate preliminary data for external grant applications. The goal of this study is to develop new biosensors to determine if desmosomes in skin are subject to mechanical tension.

American Cancer Society Institutional Research Grant Conway (PI) 12/01/14-11/30/15
Measurement of E-cadherin mechanical tension during EMT-induced junction disassembly
Seed grant to provide initial project support investigating the mechanical changes across E-cadherin during EMT-induced junction disassembly.