## BIOGRAPHICAL SKETCH

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NAME: Celeste M. Nelson, Ph.D.

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

POSITION TITLE: Professor

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 |
|---|---|---|---|
| Massachusetts Institute of Technology | S.B. | 1994-1998 | Biology |
| Massachusetts Institute of Technology | S.B. | 1994-1998 | Chemical Engineering |
| Johns Hopkins University School of Medicine | Ph.D. | 1998-2003 | Biomedical Engineering |
| Lawrence Berkeley National Laboratory | | 2003-2007 | Mammary Gland Biology |
| Woods Hole Marine Biological Laboratory | | 2007 | Embryology |

### A. Personal Statement

At the departments of Chemical & Biological Engineering and Molecular Biology at Princeton University, I have built and directed a multidisciplinary research team that combines microscale tissue engineering, molecular cell biology, and finite element method-based approaches to investigate the mechanical control mechanisms underlying development and disease progression. As a PI on several past and present competitive grants, my directing and collaborating with other researchers has been fruitful, leading to more than 100 peer-reviewed publications. I have a passion for teaching and mentoring, and many of my previous trainees are now highly successful young leaders in tenure-track positions.

### B. Positions and Honors

**Positions (all at Princeton University):**

2007-2012 Assistant Professor, Chemical & Biological Engineering
2008- Associated Faculty, Molecular Biology
Member, Cancer Institute of New Jersey
2012-2016 Associate Professor, Chemical & Biological Engineering
2014-2017 Director of Graduate Studies, Chemical & Biological Engineering
2016- Professor, Chemical & Biological Engineering

**Honors:**

1995-1998 Edward Abdun-Nur Memorial Fellowship
1997-1998 Biotechnology Process Engineering Center Research Fellowship
1997-1998 Amoco Foundation Fellowship
1997-1998 Cunningham Memorial Fellowship
1997 Elected to Tau Beta Pi National Engineering Honor Society
1998 Elected to Phi Beta Kappa
1999 National Science Foundation Graduate Fellowship (declined)
1999-2003 Whitaker Foundation Graduate Fellowship
2004 Ruth L. Kirschstein National Research Service Award Postdoctoral Fellowship (declined)

| | |
|---|---|
| 2004-2007 | DOD Breast Cancer Research Program Postdoctoral Fellowship |
| 2007 | LBNL Outstanding Performance Award |
| 2007- | Burroughs Wellcome Fund Career Award at the Scientific Interface |
| 2008- | David & Lucile Packard Foundation Fellowship |
| 2009 | E. Lawrence Keyes, Jr./Emerson Electric Co. Faculty Advancement Award |
| 2009, 2010 | Princeton Engineering Commendation for Outstanding Teaching |
| 2010- | Alfred P. Sloan Fellowship in Molecular Biology |
| 2010 | MIT Technology Review TR35 (Young Innovators under 35) |
| 2011 | Allan P. Colburn Award, American Institute of Chemical Engineers (AIChE) |
| 2012 | Camille Dreyfus Teacher-Scholar Award |
| 2013 | E. Llewellyn-Thomas Distinguished Lecture, University of Toronto |
| 2014 | Princeton School of Engineering and Applied Science (SEAS) Distinguished Teacher Award |
| 2014 | Thiele Lectureship, University of Notre Dame |
| 2016 | American Institute of Medical & Biological Engineering (AIMBE) College of Fellows |
| 2016 | President's Award for Distinguished Teaching (Princeton University) |
| 2016 | HHMI Faculty Scholar |
| 2017, 2018 | Blavatnik National Award Finalist for Young Scientists in Life Sciences |
| 2018 | Princeton Engineering Commendation for Outstanding Teaching |

**C. Contribution to Science (selected from 118 peer-reviewed publications)**
[total ISI citations = 8819; average citations per paper = 56; H-index = 41]

1. Role of physical forces in morphogenesis of the lung. My group has been studying the effects of mechanical forces on airway development using birds, mammals, and reptiles as model systems. We have uncovered several surprising roles for physical forces in airway morphogenesis, including the need for apical constriction during branching in the avian lung and a previously unrecognized role for airway smooth muscle during bifurcation events in the mammalian lung. Our results suggest that airway complexity is highly regulated by mechanical forces and cannot be explained solely by genetic controls.
   a. **Nelson CM**, Gleghorn JP, Pang MF, Jaslove J, Goodwin K, Varner VD, Miller E, Radisky DC, Stone HA. Microfluidic chest cavities reveal that transmural pressure controls the rate of lung development. *Development,* 144: 4328-4335 (2017).
   b. Kim HY, Pang MF, Varner VD, Kojima L, Miller E, Radisky DC, **Nelson CM**. Localized smooth muscle differentiation is essential for bifurcation during branching morphogenesis of the mammalian lung. *Dev. Cell,* 34: 719-726 (2015).
   c. Varner VD, Gleghorn JP, Miller E, Radisky DC, **Nelson CM**. Mechanically patterning the embryonic airway epithelium. *Proc. Natl. Acad. Sci. USA,* 112: 9230-9235 (2015).
   d. Kim HY, Varner VD, **Nelson CM**. Apical constriction initiates new bud formation during monopodial branching of the embryonic chicken lung. *Development,* 140: 3146-3155 (2013).

2. Engineered tissue models of branching morphogenesis. My group has created tissue engineering approaches to build 3D epithelial tissues that can be used to study the physical forces and biochemical signaling that drives branching morphogenesis. We have shown that branches emerge at specific sites because of gradients of autocrine inhibitory morphogens and mechanical stresses, and have identified the gene expression changes that drive branching from these regions.
   a. Gjorevski N, Piotrowski AS, Varner VD, **Nelson CM**. Dynamic tensile forces drive collective migration through three-dimensional extracellular matrices. *Sci. Rep.,* 5: 11458 (2015).
   b. Lee K, Gjorevski N, Boghaert E, Radisky DC, **Nelson CM**. Snail1, Snail2, and E47 promote mammary epithelial branching morphogenesis. *EMBO J.,* 30: 2662-2674 (2011).
   c. Gjorevski N, **Nelson CM**. Endogenous patterns of mechanical stress are required for branching morphogenesis. *Integr. Biol.,* 2: 424-434 (2010).
   d. **Nelson CM**, VanDuijn MM, Inman JL, Fletcher DA, Bissell MJ. Tissue geometry determines sites of branching morphogenesis in organotypic cultures. *Science,* 314: 298-300 (2006).

3. Mechanical forces and epithelial-mesenchymal transition (EMT). My group has worked to define the role of physical forces in tissue dysmorphogenesis, and has specifically uncovered the role of tissue

stiffness and intercellular contractility in regulating EMT. We have found that mechanical stresses regulate EMT both by altering the nuclear localization of MRTF-A, as well as by altering the membrane localization of Rac1b.

a. Pang MF, Siedlik MJ, Han S, Stallings-Mann M, Radisky DC, **Nelson CM**. Tissue stiffness and hypoxia modulate the integrin-linked kinase ILK to control breast cancer stem-like cells, *Cancer Res.,* 76: 1-11 (2016).
b. Lee K, Chen QK, Lui C, Cichon MA, Radisky DC, **Nelson CM**. Matrix compliance regulates Rac1b membrane localization, NADPH oxidase assembly, and epithelial-mesenchymal transition. *Mol. Biol. Cell,* 23: 4097-4108 (2012).
c. Gomez EW, Chen QK, Gjorevski N, **Nelson CM**. Tissue geometry patterns epithelial-mesenchymal transition via intercellular mechanotransduction. *J. Cell. Biochem.,* 110: 44-51 (2010).
d. Radisky DC, Levy DD, Littlepage LE, Liu H, **Nelson CM**, Fata JE, Leake D, Godden EL, Albertson DG, Nieto MA, Werb Z, Bissell MJ. Rac1b and reactive oxygen species mediate MMP3-induced EMT and genomic instability, *Nature,* 436: 123-127 (2005).

4. Mechanical forces and stem cell differentiation. My group has led efforts to uncover the relative roles of mechanical forces in regulating stem and progenitor cell phenotype. Our efforts have unveiled the critical roles of cell shape and mechanics in the fates of mesenchymal stem cells, mammary progenitor cells, and breast cancer-like stem cells.
   a. Pang MF, Siedlik MJ, Han S, Stallings-Mann M, Radisky DC, **Nelson CM**. Tissue stiffness and hypoxia modulate the integrin-linked kinase ILK to control breast cancer stem-like cells. *Cancer Res.,* 76: 1-11 (2016).
   b. Lui C, Lee K, **Nelson CM**. Matrix compliance and RhoA direct the differentiation of mammary progenitor cells. *Biomech. Modeling Mechanobiol.,* 11: 1241-1249 (2012).
   c. McBeath R, Pirone DM, **Nelson CM**, Bhadriraju K, Chen CS. Cell shape, cytoskeletal tension, and RhoA regulate stem cell lineage commitment. *Dev. Cell,* 6: 483-495 (2004).

Full publication record can be found at
http://www.ncbi.nlm.nih.gov/myncbi/collections/bibliography/41156728/

## D. Ongoing Research Support (past three years)

**Active**

Dreyfus — Nelson (PI) — 7/1/2012 – 5/30/2019
Camille & Henry Dreyfus Foundation
"The chemistry of morphogenesis: Quantitative analysis of transcription factor kinetics during tissue development"
This award investigates the regulation of transcription factor localization during branching morphogenesis.

CMMI-1435853 — Nelson (PI) — 9/1/2014 – 8/31/2018
NSF
"The mechanics of lung development in three different species"
This proposal compares physical mechanisms of branching in a model bird, mammal, and reptile.

R01 HL120142 — Nelson (PI) — 8/15/2014 – 6/30/2019
NIH/NHLBI
"Mechanical regulation of mesenchyme and mammalian lung development"
This proposal investigates how smooth muscle contraction and differentiation affect airway epithelial morphogenesis during development of the lung.

R01 CA187692 — Nelson (PI; MPI = Radisky) — 6/1/2015 – 5/31/2020
NIH/NCI
"Biochemical and biophysical effects of the ECM on breast epithelial cells"
This multi-PI proposal investigates the role of the microenvironment in signaling downstream of Rac1b.

HHMI 55108548 Nelson (PI) 11/1/2016 – 10/31/2021
HHMI
This Faculty Scholars Award supports the Nelson group's work on lung development.

NJHF Nelson (PI) 3/1/2017 – 12/31/2018
New Jersey Health Foundation
"Airway remodeling and redox signaling in asthma"
This award establishes a model system to investigate the role of redox signaling in asthma.

U01 CA214292 Tien (PI; MPI = Nelson) 4/1/2017 – 3/31/2022
NIH/NCI
"Engineered invasive human breast tumors with integrated capillaries and lymphatics"
This contract proposal builds engineered breast tumors to investigate tissue-tumor interactions.

**Completed**

R01 GM083997 Nelson (PI) 5/1/2008 – 4/30/2014
NIH/NIGMS
"Spatial patterning of branching morphogenesis"
This proposal investigates the relationship between inhibitory morphogen gradients and patterned gene expression during branching morphogenesis of mammary epithelial cells.

R21 HL110335 Nelson (PI) 7/1/2011 – 6/30/2014
NIH/NHLBI
"Mechanical regulation of branching morphogenesis"
This proposal investigates the role of cytoskeletal contractility during branching of 3D engineered culture models and organ explants.

Sloan BR-5117 Nelson (PI) 9/16/2010 – 9/15/2014
Alfred P. Sloan Foundation
Sloan Fellowship in Molecular Biology
This fellowship investigates the mechanical regulation of tissue morphodynamics.

1006489 Nelson (PI) 1/1/2007 – 12/31/2015
Burroughs Wellcome Fund
"Biophysical dynamics in the regulation of tissue morphogenesis"
This Career Award investigates the relative roles of mechanics and biochemical signals during branching morphogenesis in mammary epithelial culture models.

R01 HL120872 Nelson (co-I; PI = Kahn) 9/1/2014 – 6/30/2016
NIH/NHLBI
Genetic investigation of pulmonary lymphatic development and function
In this subcontract, the Nelson group measures compliance of embryonic lungs.

Packard 2008-33018 Nelson (PI) 11/15/2008 – 11/14/2017
David & Lucile Packard Foundation
Packard Fellowship for Science and Engineering
This fellowship dissects the spatiotemporal regulation of multicellular dynamics during branching morphogenesis.

R21 HL118532 Nelson (PI) 2/18/2014 – 1/31/2017
NIH/NHLBI
"Exogenous fluid forces and branching morphogenesis of the mammalian lung"
This proposal investigates the role of transmural pressure on expression and signaling downstream of FGF10 in the mouse embryonic lung.