

# Curriculum Vitae

## Andrea Page-McCaw, PhD

**Professional Address:** Department of Cell and Developmental Biology  
Vanderbilt University Medical Center  
U-4200 Learned Lab/MRBIII  
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**Home address:** 3733 Central Ave.  
Nashville 37205  
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**Personal Data:** Née Andrea Page, Boston, 1966  
Married to Patrick S. Page-McCaw  
Children Rebecca (b. 2000), Sarah (b. 2005)

### I. Education

Harvard University (Cambridge, Massachusetts), AB *Magna Cum Laude*. 1989.

Massachusetts Institute of Technology (Cambridge, Massachusetts), PhD in Biology.  
Thesis: The Meiotic Cell Cycle and Sister-Chromatid Cohesion in  
*Drosophila* Oocytes. Advisor: Terry L. Orr-Weaver, PhD. 1998.

University of California (Berkeley, California), Postdoctoral training in the laboratory of  
Gerald M. Rubin, PhD, Dept. of Molecular and Cell Biology. 1998-2004.

### II. Awards and Fellowships

High honors on undergraduate thesis, Harvard University. 1989.

National Science Foundation Predoctoral Fellowship. 1992-1995.

Jane Coffin Childs Postdoctoral Fellowship. 1998-2001.

Short Talk Award, Matrix Metalloproteinases Gordon Research Conference. 2003.

Basil O'Connor Starter Scholar Research Award, March of Dimes. 2007-2009.

Inaugural Chancellor Faculty Fellowship, Vanderbilt University, 2015-2017.

Elected Fellow, American Association for the Advancement of Science, 2018

### III. Academic Appointments

Assistant Professor, Department of Biology, Rensselaer Polytechnic Institute (Troy, New York). 2004- 2010.

Associate Professor with Tenure, Department of Biology, Rensselaer Polytechnic Institute (Troy, New York). 2010.

Associate Professor, Department of Cell and Developmental Biology 2010-present  
Department of Cancer Biology (now defunct) 2010-2017  
Tenure awarded 2013  
Vanderbilt University School of Medicine (Nashville, Tennessee)

Professor, Department of Cell and Developmental Biology, 2019-present

Director of Graduates Studies, Cell and Developmental Biology, 2019-present

### Center and Program Affiliations

Member, Center for Biotechnology and Interdisciplinary Studies, Rensselaer Polytechnic Institute, 2004-2010.

Member, Program in Developmental Biology, Vanderbilt University, 2010-present.

Member, Vanderbilt-Ingram Cancer Center Host-Tumor Interactions Program, Vanderbilt University Medical Center, 2010-present.

Member, Center for Matrix Biology, Vanderbilt University Medical Center, 2014-present.

Member, Program in Cancer Biology, Vanderbilt University, 2017-present.

## **IV. Other Employment**

Paralegal/junior lobbyist at the law firm of Garvey, Shubert, and Barer (Washington DC). 1989-1990.

Research Assistant in the laboratory of Timothy Bestor, Ph.D., Dept. of Anatomy, Harvard Medical School (Boston, Massachusetts). 1990-1991.

## **V. Professional Organizations**

1. Member, Genetics Society of America (2004-present)
2. Member, American Association for the Advancement of Science (2006-present)
3. Member, Society for Developmental Biology (2006-present)
4. Member, American Society for Cell Biology (2012-present)
5. Member, American Society for Matrix Biology (2018-present), Elected Councilor, 2019-2022

## **VI. Professional Activities**

### **Intramural (Rensselaer Polytechnic Institute)**

1. Member, Faculty Search Committee, 2004-2005.
2. Organizer, Biology Department weekly seminar series. 2006-2010.
3. Member, Graduate Curriculum Committee. 2006-2010.
4. Member, Institute Library Task Force, 2006.
5. Member, Search committee for Associate Director for the Center for Biotechnology and Interdisciplinary Studies. 2006.
6. Academic advisor to 15-20 biology undergraduates annually. 2006-2010.
7. Member, Rotation Ad Hoc Committee, 2006.
8. Member, Search Committee for Department Head, 2005-2006.
9. Member, Search Committee for Department Head, 2006-2007.
10. Chair, Graduate Student Orientation Committee, 2007.
11. Member, Faculty Search Committee, 2007-2008.
12. Member, Website and Marketing Committee. 2007-2010.
13. Chair, Faculty Search committee. 2009-2010.

### **Intramural (Vanderbilt)**

#### **Departmental Service**

14. Co-organizer, Research Exchange (REx), Cell and Developmental Biology trainee seminar series. 2011-2019.
15. Chair, Cell and Developmental Biology Awards Committee. 2012-present.
16. Member, Faculty Search Committee, Dept. of Cell and Developmental Biology. 2012-13.
17. Member, Curriculum committee, Dept. of Cell and Developmental Biology. 2015-present.
18. CDB Faculty Mentoring Committee for Vivian Gama. 2016-present.

19. Member, Faculty Search Committee, Dept. of Cell and Developmental Biology. 2016-17.
- School of Medicine and University Service
20. Initiator and organizer of “Superfly”, a monthly group meeting of insect laboratories at VU. 2010-2012.
21. Member, Biomedical Graduate Awards and Honors Committee. 2011-2016
22. Organizer, VU Mini-Symposium on Matrix Metalloproteinases, with presentations by 11 laboratories, April 18, 2011.
23. Co-organizer, Program in Developmental Biology Annual Retreat. 2012.
24. Member, Medical Scientist Training Program (MSTP) Admissions Committee. 2014-2018.
25. Member, Steering Committee for Training Program in Stem Cell & Regenerative Developmental Biology (T32). 2014-present.
26. Member, Honor Fellowship Committee, Vanderbilt University. 2015.
27. Member, University Committee on Laboratory Science Immersion. 2015-2016.
28. Member, Trans-Institutional Programs (TIPs) Review Panel, Vanderbilt University, 2016-2018.
29. Member, Graduate Faculty Council, Vanderbilt University, 2017-2018.
30. Member, Provost's Sexual Misconduct Prevention Committee, Vanderbilt University 2017-2018.
31. Member, Committee on the Status of Women in Vanderbilt Basic Sciences, 2018-2019.
32. Vanderbilt Delegate to the Action Collaborative on Preventing Sexual Harassment in Higher Education, the National Academies, Washington DC.

### Extramural

1. Co-chair of session “Morphogenesis and Organogenesis,” Northeast Regional Developmental Biology Conference, Woods Hole, MA. 2006.
2. *Ad hoc* manuscript reviewer for *The American Journal of Pathology*, *Biochemical Journal*, *Biophysical Journal*, *Cell Reports*, *Developmental Biology*, *Developmental Cell*, *Genetics*, *Insect Biochemistry and Molecular Biology*, *International Journal of Cell Biology*, *The International Journal of Developmental Biology*, *The Journal of Cell Biology*, *The Journal of Cell Science*, *PLoS Genetics*, *Scientific Reports*, *Stem Cell Reports*, *Trends in Endocrinology and Metabolism*, *Wound Repair and Regeneration*. 2005-present.
3. *Ad hoc* grant reviewer for
  - a. the Wellcome Trust (UK). 2005.
  - b. National Science Foundation. 2008, 2011, 2014.
  - c. Congressionally Directed Medical Research Programs, Pathobiology-2, Breast Cancer Research Program. 2009.
  - d. the Medical Research Council (UK), Population and Systems Medicine Board. 2011.
  - e. Intracellular Interactions Study Section (ICI), Center for Scientific Review, NIH. June and October, 2012
  - f. the Biotechnology and Biological Sciences Research Council (UK Research Council), 2013
  - g. National Centre for the Replacement and Refinement & Reduction of Animals in Research (UK private funding agency), 2014.
  - h. Villum Foundation, 2015.
4. Permanent Member, Intracellular Interactions Study Section (ICI), Center for Scientific Review, NIH, 2013-2019. Co-chair 2016-2018.
5. Elected southeastern US representative to the *Drosophila* Board, 2014-2017.
6. Chair, *Drosophila* Communications Committee of the *Drosophila* Board, 2015-16.
7. Co-chair of session, “Model Organisms and Development,” Gordon Research Conference on Matrix Metalloproteinases, Newry ME, 2015.

8. Co-chair of workshop, “Advocacy, Training/Education, and Community”, *Drosophila* Research Ecosystem Meeting, HHMI Janelia Research Campus, 2016.
9. Session Co-Chair, Signal Transduction and Cell Biology, 59<sup>th</sup> Annual *Drosophila* Research Conference, Philadelphia PA, 2018.
10. Editorial Board Member, *Matrix Biology*, 2018- present.
11. Councilor, American Society for Matrix Biology, 2019-2022.

## VII. Teaching Activities

### Graduate and undergraduate teaching at Rensselaer Polytechnic Institute

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|-----------|---|
| Spr 2005  | • Graduate Biology Core (BIOL-6961). 2h discussing papers.  |
| Fall 2005 | • Genetic Engineering (undergrad. BCBP-4310). 2h.   |
| Spr 2006  | • Graduate Biology Core (BIOL-6963). 2h discussing papers.  |
| Spr 2007  | • Graduate Biology Core (BIOL-6963). 6h discussing papers.<br>• Embryology (undergrad. BIOL-2410). <b>Designed new course</b> under old course name, later changed to BIOL-4961 Developmental Biology. 56h.   |
| Fall 2007 | • Graduate Biology Core (BIOL-6961). 4h on scientific writing.  |
| Spr 2008  | • Graduate Biology Core (BIOL-6963). 7h on genetic analysis and developmental biology.<br>• Developmental Biology (undergrad. BIOL-4961). 56h.  |
| Fall 2008 | • Graduate Biology Core (BIOL-6961). 4h on scientific writing.  |
| Spr 2009  | • Graduate Biology Core (BIOL-6963). 7h on genetic analysis and developmental biology.  |
| Fall 2009 | • Cell and Developmental Biology Lab (undergrad. BIOL-4740). <b>Designed semester curriculum</b> based on <i>Drosophila</i> embryos and S2 cells; taught 2h lecture and discussion.<br>• Genetics (undergrad. BIOL-2500). 2h.<br>• Graduate Biology Core (BIOL-6961). 4h on scientific writing. |
| Spr 2010  | • Graduate Biology Core (BIOL-6963). 8h on genetic analysis and developmental biology.<br>• Developmental Biology (undergrad. BIOL-4250). 56h.  |

### Graduate teaching at Vanderbilt University

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|-----------|---|
| Spr 2011  | • Genetics of Model Organisms (CBio/HGen349). 3h lecture on <i>Drosophila</i> genetics.<br>• Cancer and Embryonic Development (CBio/CanB320). 2h lecture on extracellular matrix.<br>• Pathobiology of the Extracellular Matrix (Path335). 1h lecture on matrix metalloproteinases. |
| Sum 2011  | • Introduction to Developmental Biology (CBio312). <b>Designed two 1h lab classes</b> and taught 4h.  |
| Fall 2011 | • Cell Biology (CBio310). 3h lecture on matrix metalloproteinases.  |
| Spr 2012  | • Molecular Developmental Biology (CBio341). Co-leader of second module and taught 8h seminar.<br>• Nobel Laureates (CBio338). 1h lecture.  |
| Sum 2012  | • Introduction to Developmental Biology (CBio312). 2h lab, 2h lecture.  |
| Fall 2012 | • Bioregulation FOCUS (IGP300), graduate seminar analyzing research literature. 30 h.<br>• Cell Biology (CBio310). 3h lecture on extracellular matrix.  |
| Spr 2013  | • Cancer and Embryonic Development (CBio/CanB320), co-organizer. 46h.   |
| Fall 2013 | • Bioregulation FOCUS (IGP300), graduate seminar analyzing research literature. 30 h.   |
| Fall 2013 | • Cell Biology (CBio310). 3h lecture on extracellular matrix.   |

- Cell Migration in Normal and Diseased States (CanB341/BSci341). 3h lecture on wound healing.
- Spr 2014 • Nobel Laureates (CBio338). 1h lecture.
- Sum 2014 • Introduction to Developmental Biology (CBio312). 2h lab, 2h lecture.
- Fall 2014 • Bioregulation FOCUS (IGP300), graduate seminar analyzing research literature. 30 h.
- Spr 2015 • Cancer and Embryonic Development (CBio320). 2h lab, 2h lecture.
- Fall 2015 • Bioregulation FOCUS (IGP8001), graduate seminar analyzing research literature. 30 h.
- Cell Biology (CBio8310). 3h on scientific writing.
- Spr 2016 • Nobel Laureates (CBio8338). 1h lecture.
- Fall 2016 • Bioregulation FOCUS (IGP8001), graduate seminar analyzing research literature. 30 h.
- Cell Biology (CBio8310). 3h on scientific writing.
- Spr 2017 • Nobel Laureates (CBio8338). 1h lecture.
- Cancer and Embryonic Development (CBio8320). 1h lecture.
- Sum 2017 • Introduction to Developmental Biology (CBio8312). 2h lab, 2h lecture.
- Fall 2017 • Bioregulation FOCUS (IGP8001), graduate seminar analyzing research literature. 30 h.
- Cell Biology (CBio8310). 3h on scientific writing.
- Spr 2018 • Nobel Laureates (CBio8338). 1h lecture.
- Sum 2018 • Introduction to Developmental Biology (CBio8312). 2h lab, 2h lecture.
- Fall 2018 • Bioregulation (IGP8001). **Designed new lectures** on genetic analysis of cell autonomy (2h).
- Bioregulation FOCUS (IGP8001), graduate seminar analyzing research literature. 30 h.
- Spr 2019 • Nobel Laureates (CBio8338). 1h lecture.

### Laboratory Trainees at Rensselaer Polytechnic Institute

#### *Graduate student-RPI*

1. Shuning Zhang                      Biology graduate student, PhD 2007

#### *Rotation students-RPI*

2. Mianzhi Gu                          Rotation student, spring 2005
3. Seemanti Ramanath                Rotation student, fall 2006
4. Rick Chen                            Rotation student, summer 2007
5. Cuiping Zhao                        Rotation student, fall 2008
6. Sagarika Nag                        Rotation student (BS/PhD program), spring 2009
7. Vimla Singh                         Rotation student, fall 2009
8. Payel Datta                         Rotation student, fall 2009
9. David Drew                         Rotation student, spring 2010

#### *Staff-RPI*

10. Gyna Sroga                         Staff Research Specialist, 2004-2005
11. Bernadette Glasheen             Staff Senior Research Specialist, 2005-2010
12. Barbara Zaffo                      Staff Research Assistant II, 2008-2010

#### *Undergraduates-RPI*

13. Caitlin Piette                      Undergraduate, spring 2005-spring 2007  
*Caitlin won First Prize in RPI Undergraduate Research Poster Competition – Theoretical Division, Spring 2006.*
14. Nicholas Simms                    Undergraduate, spring 2005-spring 2007
15. Jessica McGovern                 Undergraduate, summer 2005-spring 2006
16. Aashish Kabra                     Undergraduate, fall 2005-fall 2006

- 17. Joel Warner Undergraduate, fall 2005- spring 2006
- 18. Natalie Fuster Solivan Undergraduate (University of Puerto Rico-Mayague)  
HHMI summer program for minority students, 2007
- 19. Margaret Bray Undergraduate, summer 2007
- 20. Kaleena Shirley Undergraduate, fall 2006-spring 2010
- 21. Elizabeth Rose Undergraduate, fall 2007-spring 2008
- 22. Elizabeth Muscatiello Undergraduate, spring 2008-spring 2010
- 23. Richard Rodriguez Undergraduate, fall 2008-spring 2010
- 24. Shaina Feldman Undergraduate, fall 2009-spring 2010

*High school students-RPI*

- 25. Megan Bedell High School Student, Emma Willard School, summer 2007
- 26. Cordelia Lee High School Student, Emma Willard School, fall 2008.

Past Laboratory Trainees at Vanderbilt

*Postdoctoral trainees-Vanderbilt*

- 27. Xiaoxi Wang, PhD Postdoctoral fellow, 2011-2017
- 28. Joshua Clanton, PhD Postdoctoral fellow, 2013-14

*Graduate students-Vanderbilt*

- 29. Laura Stevens CDB graduate student, PhD 2012
- 30. Sarah Broderick CDB graduate student, PhD 2013
- 31. A. Scott McCall MD/PhD student, Dept. of Pharmacology, 2013-2014  
(PhD student with Billy Hudson working on a collaborative project in my lab under my supervision)
- 32. Erica Shannon CDB graduate student, PhD 2017
- 33. Angela Howard CDB graduate student, PhD 2019

*Rotation students-Vanderbilt*

- 34. Rubin Baskir IGP rotation student, fall 2011
- 35. Stacey Lee IGP rotation student, spring 2011
- 36. Alison Wright Pre-candidacy graduate student, 2011-2012
- 37. Diana Cha IGP rotation student, fall 2011
- 38. Daniel LePage IGP rotation student, fall 2011
- 39. Stephanie Moore IGP rotation student, fall 2013
- 40. Karrie Dudek IGP rotation student, spring 2015
- 41. Mabel Seto IGP rotation student, winter 2016
- 42. Lauryn Luderman IGP rotation student, spring 2016
- 43. Justin Avila IGP pre-matriculation student, summer 2016
- 44. Bryan Cawthon Pre-candidacy graduate student, 2016-2018
- 45. Trevor Hann IGP rotation student, spring 2018
- 46. Gillian Fitz IGP rotation student, fall 2018
- 47. James White IGP rotation student, fall 2018

*Undergraduate students-Vanderbilt*

- 48. Zhongyang (John) Cao Vanderbilt Undergraduate, 2011-2013
- 49. Andrea Cuentas Condori Undergraduate Intern (Cayetano Heredia Univ, Peru), 2013
- 50. Joshua Stark Vanderbilt Undergraduate, 2015-2017
- 51. Dhiraj Peddu Vanderbilt Undergraduate, 2015-2017
- 52. Bushra Akbar University of Chicago undergrad, summer 2018

*High school students-Vanderbilt*

- 53. Calisa Henry Aspinaut high school student, summer 2018

Current Trainees

54. Kimberly LaFever	Lab Manager, 2010-present
55. William Ramos-Lewis	CDB graduate student, 2014-2018 (on leave)
56. James O'Connor	CDB graduate student, 2017-present
57. Indrayani Waghmare	Postdoctoral fellow, 2016-present

Thesis Committees

<u>Name</u>	<u>Mentor</u>	<u>Department</u>	<u>Years</u>
1. Ying Wang	Julie Stenken	Chem. & Chem. Biol./RPI	2006-08
2. Iwen Fu	Fern Finger	Biology/RPI	2006-07
3. Amanda Lund	George Plopper	Biology/RPI	2007-09
4. Crystal Miller	Heather Broihier	Neurosci./Case Western.	2009
5. Cong Yao	Patrick Page-McCaw	Biology/RPI	2009
6. Dominick Papandrea	Russell Ferland	Biology/RPI	2010
7. Julie Merkle	Laura Lee	Cell&Dev Bio/VUSOM	2010-11
8. Teagan Walter	Stacey Huppert	Cell&Dev Bio/VUSOM	2011-13
9. Kimberly Gooding	Maureen Gannon	Cell&Dev Bio/VUSOM	2012-15
10. Lehanna Sanders	Antonis Hatzopoulos	Cell&Dev Bio/VUSOM	2012-16
11. Jonathan Fleming	Chin Chiang	Cell&Dev Bio/VUSOM	2012-14
12. Kenyi Saito-Diaz	Ethan Lee	Cell&Dev Bio/VUSOM	2012-17
13. Jing Liu	Guoqiang Gu	Cell&Dev Bio/VUSOM	2012-2015
14. Nicole Diggins	Donna Webb	Biological Sci/VUA&S	2013-2018
15. Daniel LePage	Seth Bordenstein	Biological Sci/VUA&S	2013-16
16. Garrett League	Julian Hillyer	Biological Sci/VUA&S	2013-2017
17. Laura Armstrong	Kevin Ess	Cell&Dev Bio/VUSOM	2013-2017
18. Richard Guyer	Ian Macara	Cell&Dev Bio/VUSOM	2013-14
19. Sarah Hainline	Laura Lee	Cell&Dev Bio/VUSOM	2013-14
20. Monica Lacy	M. Shane Hutson	Physics/VUA&S	2013-17
21. Winston Ty McCleery	M. Shane Hutson	Physics/VUA&S	2014-2015
22. Leif Neitzel (Chair)	Ethan Lee	Cell&Dev Bio/VUSOM	2015-present
23. Casey Neilson (Chair)	Jason MacGurn	Cell&Dev Bio/VUSOM	2015-present
24. Andrea Cuentas Condori	David Miller	Cell&Dev Bio/VUSOM	2016-present
25. Cherie' Scurrah	Ken Lau	Cell&Dev Bio/VUSOM	2016-present
26. Aaron Stevens	M. Shane Hutson	Physics/VUA&S	2017-present
27. Michael Yarboro (Chair)	Jeff Reese	Cell&Dev Bio/VUSOM	2017-present
28. Xiaodun Yang	Guoqiang Gu	Cell&Dev Bio/VUSOM	2017-present
29. Tessa Popay (Chair)	William Tansey	Cell&Dev Bio/VUSOM	2017-present
30. Yan Yan	Julián Hillyer	Biological Sci/VUA&S	2018-present
31. Shannon Townsend	Maureen Gannon	Physiology/VUSOM	2018-present
32. Logan Richards	Jared Nordman	Biological Sci/VUA&S	2019-present

Qualifying Exam (only) Committees

<u>Name</u>	<u>Mentor</u>	<u>Department</u>	<u>Year</u>
1. Uma Challa	Jamie Rusconi	Bio. Sci./SUNY Albany	2006
2. Erica Hutchins	Jamie Rusconi	Bio. Sci./SUNY Albany	2008
3. Maria Apostolopoulou	Lee Ligon	Biology/RPI	2008
4. Kevin Bridges	Kevin Ess	Cell&Dev Bio/VUSOM	2011
5. Michelle Krakoiak	Richard Peek	Cancer Biology/VUSOM	2012
6. Kate Venmar	Barbara Fingleton	Cancer Biology/VUSOM	2012
7. Patrick Mulcrone	Florent Elefteriou	Cancer Biology/VUSOM	2013
8. Kalen Petersen (Chair)	David Miller	Cell&Dev Bio/VUSOM	2016

## VIII. Research Support

### Active

1R01GM117899 (A. Page-McCaw, PI) 2/1/2016-12/31/2019  
 NIH/NIGMS \$205,000/yr direct  
*Wnt/Wg Extracellular Ligand Distribution and Regulation.* The major goals of this project are to understand how Wnt ligands are distributed and their levels are regulated to promote proper stem cell maintenance and differentiation.

1R21AR072510 (A. Page-McCaw, PI) 7/1/2017 – 6/30/2019  
 NIH/NIAMS \$275,000 direct (2 yr)  
*A new model for analyzing basement membrane repair.* This exploratory/developmental grant will develop a model of basement membrane damage and analyze the role of collagen IV crosslinking in repair. Impact score: 11, priority score 1.0%.

1R01GM130130 (A. Page-McCaw, PI, and M.S. Hutson, MPI) 8/15/2018-4/30/22  
 NIH/NIGMS \$215,000/yr direct  
*Cellular Integration of Information in the Detection and Response to Epithelial Damage.* The major goals of this interdisciplinary project are to identify the upstream information that triggers the release of calcium around wounds and the downstream consequences of this calcium release.

### Student Fellowship

AHA Predoctoral Award (James O'Connor, PI) 7/1/2019-6/30/2021  
 American Heart Association \$26,844/yr  
*Calcium signaling dynamics in the early response to wounds.*

### Completed

2R01GM073883 (A. Page-McCaw, PI) 8/1/2006-7/31/2017  
 NIH/NIGMS \$200,000/yr direct  
*Matrix metalloproteinases in Drosophila wound healing.* The major goals in the last funding period are to determine the molecular interactions among Mmp1 and two proteins required for its localization; determine how MMPs maintain and promote expansion of basement membranes; and determine how MMPs modify signaling pathways in the wound environment.

5-FY07-99 (A. Page-McCaw, PI) 2/1/2007-1/31/2009  
 March of Dimes Basil O'Connor Starter Scholar Research Award \$67,500/yr direct  
*Elucidating How an MMP Regulates Cell Adhesion in Drosophila.*  
 The goals of this project were to determine how Ninjurin A and Mmp1 promote a loss of cellular adhesion, both *in vivo* and in cell culture.

Vanderbilt Univ. Central Discovery Grant (Shane Hutson, PI) 6/01/2012-5/31/2014  
 Role on grant: co-PI  
*Optogenetic and pharmacological investigations of epithelial wound detection.* The major goal of this project is to initiate collaborative research between physicist Shane Hutson and developmental biologist Andrea Page-McCaw with a focus on wound detection and healing. Specifically, the goal is to perform single-input/multiple-output experiments to mathematically model a mechanosensor circuit that functions during cell-shape oscillations and the initial response to laser-generated wounds.

1R03HD074834-01(A. Page-McCaw, PI) 6/3/2013-5/31/2015  
 NIH/NICHHD \$50,000/yr direct



*MMP regulation of stem cell proliferation in the Drosophila ovary.* This small project identifies a mechanism for how *Mmp2* regulates Wingless signaling to control follicle cell proliferation in the *Drosophila* ovary.

1R21AR068933-01 (A. Page-McCaw, PI)  
NIH/NIAMS

5/1/2015 – 4/30/2017  
\$245,000 direct (2 yr)

*FlpOn: an optogenetic circuit for user-designed mosaics and its application to wound healing.* This exploratory/developmental grant will develop a novel genetic tool and apply it to epithelial wounding studies.

## IX. Publications and Presentations

\* indicates equal contribution by indicated authors

### Primary Research Bibliography

1. A. Czank, R. Hauselmann, A. W. Page, H. Leonhardt, T. H. Bestor, W. Schaffner, and M. Hergersberg. Expression in mammalian cells of a cloned gene encoding murine DNA methyltransferase. *Gene* 109, 259-263. (1991)
2. L. L. Carlson, A. W. Page, and T. H. Bestor. Properties and localization of DNA methyltransferase in preimplantation mouse embryos: implications for genomic imprinting. *Genes and Development* 6, 2536-2541. (1992) Cover article.
3. H. Leonhardt\*, A. W. Page\*, H.-U. Weier, and T. H. Bestor. A targeting sequence directs DNA methyltransferase to sites of DNA replication in mammalian nuclei. *Cell* 71, 865-873. (1992)  
*Cover article, cited over 1000 times.*
4. A. W. Page and T. L. Orr-Weaver. The *Drosophila* genes *grauzone* and *cortex* are necessary for proper female meiosis. *Journal of Cell Science* 109, 1707-1715. (1996)
5. L. Frostesjo, I. Holm, B. Grahn, A. W. Page, T. H. Bestor, and O. Heby. Interference with DNA methyltransferase activity and genome methylation during F9 teratocarcinoma stem cell differentiation induced by polyamine depletion. *Journal of Biological Chemistry* 272, 4359-66. (1997)
6. L. K. Elfring, J. M. Axton, D. D. Fenger, A. W. Page, J. L. Carminati, and T. L. Orr-Weaver. The *Drosophila* PLUTONIUM protein is a specialized cell cycle regulator required at the onset of embryogenesis. *Molecular Biology of the Cell* 8, 583-593. (1997)
7. A.W. Page and T. L. Orr-Weaver. Activation of the meiotic divisions in *Drosophila* oocytes. *Developmental Biology* 183, 195-207. (1997) Cover article.
8. D. P. Moore\*, A. W. Page\*, T. T. Tang, A. W. Kerrebrock, and T. L. Orr-Weaver. The cohesion protein MEI-S332 localizes to condensed meiotic and mitotic centromeres until sister chromatids separate. *Journal of Cell Biology* 140, 1003-1012. (1998)
9. A. Page-McCaw, J. Serano, J. M. Sante, and G.M. Rubin. *Drosophila* matrix metalloproteinases are required for developmental tissue remodeling but not embryonic development. *Developmental Cell* 4, 95-106. (2003)

*This foundational study from my postdoctoral fellowship reports the generation and analysis of the Drosophila MMP mutants. Since publication, the APM lab has responded to hundreds of requests for these stocks from labs in ~20 countries.*

10. L. Myllykangas, J. Tyynela, A. Page-McCaw, G.M. Rubin, M.J. Haltia, and M.B. Feany. Cathepsin D-deficient Drosophila recapitulate the key features of neuronal ceroid lipofuscinoses. *Neurobiology of Disease* 19, 194-199. (2005)  
*APM generated and contributed the cathepsin D mutant fly on which this study is founded.*
11. S. Zhang, G.M. Dailey, E. Kwan, B.M. Glasheen, G.E. Sroga, and A. Page-McCaw. An MMP liberates the Ninjurin A ectodomain to signal a loss of cell adhesion. *Genes & Development* 20, 1899-1910. (2006)  
*This study finds that a conserved Ninjurin membrane-spanning protein associates with an MMP and is functionally dependent on an MMP. The first description and analysis of a Ninjurin family member in Drosophila, this study was featured in Science STKE on 5 July 2006.*
12. M. Beaucher, E. Hersperger, A. Page-McCaw, and A. Shearn. Metastatic ability of Drosophila tumors depends on MMP activity. *Developmental Biology* 303, 625-634. (2007).  
*Using a Drosophila tumor transplantation model developed by the Shearn lab, we found that Drosophila MMPs, like mammalian MMPs, promote tumor progression and metastasis. This project was conceived jointly by Allen Shearn and APM, and APM provided critical Drosophila reagents and continuing intellectual contributions.*
13. C.M. Miller, A. Page-McCaw, and H. T. Broihier. Matrix metalloproteinases promote motor axon fasciculation in the Drosophila embryo. *Development* 135, 95-109. (2008)  
*It was previously suspected that MMPs were important for axon outgrowth, but there was no genetic data supporting this model. This study reports the surprising discovery that, rather than promoting outgrowth, Dm Mmp2 inhibits outgrowth and promotes fasciculation. APM provided key intellectual input and the MMP mutants that were the basis for the study.*
14. B.M. Glasheen, A. Kabra, and A. Page-McCaw. Distinct functions for the catalytic and hemopexin domains of a Drosophila matrix metalloproteinase. *Proceedings of the National Academy of Sciences USA* 106, 2659-64. (2009)  
*Showcasing the flexibility of the Drosophila model for analyzing MMP function, this is the first in vivo MMP structure-function study in any organism. Utilizing numerous Drosophila MMP alleles and transgenic animals, we discovered that the highly conserved hemopexin domain is required for only some MMP functions, those that seem to involve tissue invasion, and thus the hemopexin domain modulates the function of the holoenzyme.*
15. B.M. Glasheen, R.M. Robbins, C.E. Piette, G.J. Beitel, and A. Page-McCaw. A matrix metalloproteinase mediates airway remodeling in Drosophila. *Developmental Biology* 44, 772-783. (2010)  
*This study investigated how Mmp1 promotes tracheal tube elongation. In collaboration with tubulogenesis expert Greg Beitel (Northwestern), the APM lab characterized how tubes elongate normally at a cellular level, and we determined that Mmp1 is required for the expansion of the extracellular matrix lining the tubes and for the coordination of the cellular and ECM components. The model of an MMP requirement for expanding ECM is novel and influences our current thinking about MMP function in basement membrane expansion.*
16. C. M. Miller, N. Liu, A. Page-McCaw, and H. T. Broihier. DmMmp2 regulates the matrix molecule Faulty attraction (Frac) to promote motor axon targeting. *J. Neurosci.* 31, 5335-47. (2011)  
*In one of the few MMP candidate-substrate identification studies in Drosophila, we identified and analyzed Frac, the MMP substrate required for axon fasciculation (ref. 3 above). APM contributed the two-hybrid screen identifying the substrate and provided important intellectual guidance. This article was highlighted in "This Week in the Journal" section of the same issue.*

17. R.L. Schmidt, F.M. Rinaldo, S.E. Hesse, M. Hamada, Z. Ortiz, D.T., Belefond, A. Page-McCaw, J.L. Platt, and A.H. Tang. Cleavage of PGRP-LC receptor in the *Drosophila* IMD pathway in response to live bacterial infection in S2 cells. *Self Nonself* 2, 125-141. (2012)  
*The APM lab provided Drosophila reagents for this study.*
18. L. J. Stevens and A. Page-McCaw. A secreted MMP is required for re-epithelialization during wound healing. *Molecular Biology of the Cell* 23, 1068-1079. (2012)  
*We report that both Drosophila MMPs are required for healing epidermal wounds, for coordinating cell movements at wound sites, and for basement membrane remodeling. This foundational study was the basis for the R01 renewal proposal.*
19. S. Broderick, X., Wang, N. Simms, and A. Page-McCaw. *Drosophila* Ninjurin A induces nonapoptotic cell death. *PLoS One* 7(9), e44567. (2012)  
*In the first genetic characterization of Ninjurin in any system, we report that Ninjurin A is not required for viability, and its overexpression in vivo triggers non-apoptotic cell death. These findings suggest a new function for this conserved family of stress-induced proteins.*
20. A.S. McCall, C.F. Cummings, G. Bhave, R. Vanacore, A. Page-McCaw, and B.G. Hudson. Bromine is an essential trace element for assembly of collagen IV scaffolds in tissue development and architecture. *Cell* 157, 1380-1392 (2014).  
*This paper finds that bromine is a required cofactor required for collagen IV basement-membrane crosslinking, mediated by the enzyme peroxidase. This requirement raised the possibility that bromine is a previously unrecognized essential element. To test this hypothesis, the APM lab raised Drosophila without bromine and found that bromine is required in vivo for basement membrane integrity and organism viability. Importantly, bromine-deprived flies phenocopy peroxidase mutants, and chemico-genetic interactions demonstrate that bromine and peroxidase function together to promote basement membrane integrity. The journal's monitoring editor told us the Drosophila work makes this story interesting to readers of Cell.*
21. X. Wang and A. Page-McCaw. A matrix metalloproteinase mediates long-distance attenuation of stem-cell proliferation. *The Journal of Cell Biology* 7, 923-936 (2014).  
*We report a new mechanism that shapes long-range signaling gradients. In the Drosophila ovary, Wg spreads 50  $\mu$ m from its source to signal the proliferation of somatic stem cells. We found that Wg spreading is facilitated by the glypican Dlp, which in turn is cleaved by the matrix metalloproteinase Mmp2. Thus, Mmp2 antagonizes glypican function, Wingless signaling, and stem cell proliferation, each of which may have significant implications in other systems. An accompanying commentary for our article, written by Norbert Perimon and colleagues, opens the issue of JCB.*
22. K.S. LaFever, X. Wang, P. Page-McCaw, G. Bhave, and A. Page-McCaw. Both *Drosophila* matrix metalloproteinases have released and membrane-tethered forms but have different substrates. *Scientific Reports* 7, 44560-16 (2017).  
*This study represents the first biochemical analysis of the two Drosophila MMPs. Drosophila offers the simplest system for MMP genetic analysis, but before this work there were no biochemical studies to complement the genetics.*
23. E.K. Shannon, A.S. Stevens, W. Edrington, Y. Zhao, A.K. Jayasinghe, A. Page-McCaw, and M.S. Hutson. Multiple Mechanisms Drive Calcium Signal Dynamics around Laser-Induced Epithelial Wounds. *Biophysical Journal* 113, 1623-1635 (2017).  
*In collaboration with Shane Hutson's lab (Vanderbilt Physics), we analyze the earliest known epithelial wound response, an influx of cytosolic calcium in a field of cells surrounding a wound. The Hutson lab's equipment allowed high temporal resolution, and we found this response initiated within an impressively short period, ~10 ms after wounding, triggered by*

wound-induced cellular damage. We dissected this calcium response into three distinct and overlapping mechanisms, using a combination of quantitative modeling and genetic analysis. The APM lab performed all the experimental manipulations and shared in the analysis; APM and MSH shared the role of corresponding author, with an APM student as first author. This article was featured on the National Science Foundation's Science360 news webpage, "Discovering the complexity of cellular wound healing."  
<https://news.science360.gov/archives/20171005/>

24. X. Wang and A. Page-McCaw. Wnt6 maintains anterior escort cells as an integral component of the germline stem cell niche. *Development* 145, dev158527-20 (2018).

*This paper reports a second critical cell type in the Drosophila germline stem cell niche, the anterior escort cells. These cells are maintained by a Wnt6 signal from the other, previously known niche cell type, the cap cells. This work is important in elucidating the requirements and complexities of stem cell niches in vivo. These studies follow from our 2014 JCB paper on Wnt signaling in the fly ovary.*

25. L. Neitzel, M. Broadus, N. Zhang, L. Sawyer, H. Wallace, J. Merkle, J. Jodoin, P. Sitaram, E. Crispi, W. Rock, L. Lee, D.J. Pan, K. Gould, A. Page-McCaw, and E. Lee. *Drosophila Cdc14* plays a conserved role in cilia function. *Biology Open* 7, bio035394 (2018). Corrected August 2018.

*APM supervised the design and analysis of some Drosophila experiments and serves as co-corresponding author.*

26. W. Ramos-Lewis, K.S. LaFever, and A. Page-McCaw. A scar-like lesion is apparent in basement membrane after wound repair *in vivo*. *Matrix Biology* 74, 101-120 (2018).

*Basement membranes are damaged along with cells during many types of wounds, and their damage contributes to many human diseases, yet virtually nothing was known about how they repair. This study represents the first mechanistic analysis of basement membrane repair after wounding. Unexpectedly, we find that epidermal basement membranes repair with a thickened and irregular scar, that the matrix components needed for repair do not come from the apposed epidermis but from distant organs, and that the hierarchy of assembly for repair is subtly different than for basement membrane assembly de novo in embryos.*

27. A. M. Howard, K. S. LaFever, A. M. Fenix, C. R. Scurrah, K. S. Lau, D. T. Burnette, G. Bhave, N. Ferrell, and A. Page-McCaw. DSS-induced damage to basement membranes is repaired by matrix replacement and crosslinking. *Journal of Cell Science*, in press. (2019)

*Although it has been suggested that the intestinal irritant DSS damages the basement membranes around the fly gut, the nature of the damage has not been identified and no mechanism has been proposed. In this manuscript, we demonstrate that DSS accumulates within the gut basement membrane, and we perform mechanical testing to show that the basement membrane becomes weaker after DSS exposure. We use electron microscopy and morphological characteristics of the damaged tissue to show that the basement membrane is repaired within 48 hours after DSS removal and that repair requires a replacement of damaged matrix components and crosslinking. This paper establishes a new model of basement membrane damage and demonstrates its utility for genetic analysis of repair.*

28. X. Wang, K. S. LaFever, and A. Page-McCaw. Extracellular spreading of Wg is required for Drosophila oogenesis. In revision.

*The secreted Wingless protein (founding member of the Wnt family) has long been considered a morphogen that spreads from its source to signal at a distance. Recently, however, a high-profile study found that when Wingless was tethered the plasma membrane, flies were viable and normally patterned, presenting a significant challenge to the model that Wingless spreads from its source. Our work with Dlp and Mmp2 (ref. 21) was premised on a model that Wingless spreads across the germarium. To resolve this challenge to our model, we analyzed the tethered-*

*Wingless flies. We find that long-distance Wingless spreading is required for oogenesis, consistent with our earlier work.*

### **Invited Reviews and Book Chapter (Peer reviewed)**

29. A. W. Page and T. L. Orr-Weaver. Stopping and starting the meiotic cell cycle. *Current Opinion in Genes and Development* 7, 23-31. (1997)
30. A. Page-McCaw\*, A.J. Ewald\*, and Z. Werb. Matrix metalloproteinases and the genetic regulation of tissue remodeling. *Nature Reviews Molecular Cell Biology* 8, 221-233. (2007) Cover article.  
*This influential review has been cited more than 2000 times. APM proposed the topic and wrote most of the text.*
31. A. Page-McCaw. Remodeling the Model Organism: Matrix Metalloproteinase Functions in Invertebrates. *Seminars in Cell and Developmental Biology* 19, 14-23. (2008)
32. K. Brew and A. Page-McCaw. Dm1 and Dm2 Matrix Metalloproteinases. In Neil D. Rawlings and Guy Salvesen (Eds.) *Handbook of Proteolytic Enzymes, 3<sup>rd</sup> Edition*, 850-854. Waltham: Academic Press (2013).
33. K. Saito-Diaz, T.W. Chen, X. Wang, C.A. Thorne, H.A. Wallace, A. Page-McCaw, and E. Lee. The Way Wnt Works: Components and Mechanism. *Growth Factors* 31, 1-31 (2013).
34. I. Waghmare and A. Page-McCaw. Wnt Signaling in Stem Cell Maintenance and Differentiation in the Drosophila Germarium. *Genes* 9, E127 (2018).
35. W. Ramos-Lewis and A. Page-McCaw. Basement membrane mechanics shape development: Lessons from the fly. *Matrix Biology* 75-76, 72-81 (2019).

### **Invited Seminars and Conference Presentations**

1. Selected speaker, EMBO Workshop on Meiotic Maturation: Signal Transduction Pathways and Checkpoint Controls, Cuenca, Spain. 1997.
2. Selected speaker, 43<sup>rd</sup> Annual Drosophila Research Conference, San Diego, CA. 2002.
3. Invited speaker, Department of Biology, Rensselaer Polytechnic Institute, Troy, NY. 2003.
4. Invited speaker, Department of Molecular Medicine and Genetics, University of Michigan Medical School, Ann Arbor, MI. 2003.
5. Invited speaker, Brookdale Department of Molecular, Cell, and Developmental Biology, Mount Sinai School of Medicine, New York, NY. 2003.
6. Invited speaker, Cancer Center, Massachusetts General Hospital, Harvard Medical School, Boston, MA. 2003.
7. Invited speaker, Department of Biology, Vanderbilt University, Nashville, TN. 2003.
8. Selected speaker, Gordon Research Conference on Matrix Metalloproteinases, Big Sky, MT. 2003.
9. Invited speaker, Extracellular Matrix workshop, 45<sup>th</sup> Annual Drosophila Research Conference, Washington DC. 2004.
10. Invited speaker, Gordon Research Conference on Proteases and Their Inhibitors, Colby-Sawyer College, NH. 2004.

11. Invited speaker, Matrix Metalloproteinase Inhibitors (MMPi)s: Expanding the Horizon (conference), New York, NY. 2004.
12. Invited speaker, Gordon Research Conference on Matrix Metalloproteinases, Big Sky, MT. 2005.
13. Invited speaker, Institute for Cell Engineering seminar series, Johns Hopkins Medical School, Baltimore, MD. 2006.
14. Selected speaker, 48<sup>th</sup> Annual Drosophila Research Conference, Philadelphia, PA. 2007.
15. Invited speaker, NanoBiotech 2007 (conference), Rensselaer Polytechnic Institute, Troy NY. 2007.
16. Invited speaker, Department of Biological Sciences seminar series, University at Albany, NY. 2007.
17. Invited speaker, Extracellular Matrix Workshop, 49<sup>th</sup> Annual Drosophila Research Conference, San Diego CA. 2008.
18. Invited speaker, Center for Cell Biology and Cancer Research seminar series, Albany Medical College, Albany, NY. 2009.
19. Invited speaker, Dept. of Genetics, Case Western Reserve Medical School, Cleveland, OH. 2009.
20. Invited speaker, Dept. of Cell and Developmental Biology, Vanderbilt Medical Center, Nashville, TN. 2009.
21. Invited speaker, Cell Biology Dept. (jointly hosted by Genetics Dept.), Yale University Medical School, New Haven, CT. 2009.
22. Selected speaker, Gordon Research Conference on Matrix Metalloproteinases, Les Diablerets, Switzerland. 2009.
23. Invited speaker, Department of Pathology, Vanderbilt Medical Center, Nashville, TN. 2011.
24. Organizer and speaker, VUMC Mini-Symposium on Matrix Metalloproteinases. 2011.
25. Selected speaker, Gordon Research Conference on Tissue Repair and Regeneration, New London, NH. 2011.
26. Invited speaker, Center for Matrix Biology, Vanderbilt Medical Center, Nashville, TN. 2012.
27. Invited speaker, Dept. of Biology, Western Kentucky University. 2014.
28. Invited speaker and co-chair of session, Model Organisms and Development, Gordon Research Conference on Matrix Metalloproteinases, Newry, ME. 2015.
29. Invited speaker, Cell & Molecular Biology Seminar Series, St. Jude's Research Hospital, Memphis TN. 2016.
30. Invited speaker, Wound Healing Workshop, 58<sup>th</sup> Annual Drosophila Research Conference, San Diego, CA. 2017.
31. Invited speaker, Collagen Gordon Research Conference, New London, NH. 2017.
32. Invited speaker, Symposium on Comparative Biology of Tissue Repair, Regeneration, and Aging. MDI Biological Laboratory. 2017.
33. Invited speaker, Duke University Development and Stem Cell Biology Colloquium. 2018
34. Invited speaker, Fox Chase Cancer Center, Philadelphia PA. 2018
35. Invited speaker, Washington University Dept. of Genetics, Saint Louis MO. 2018
36. Invited speaker, Developmental Mechanics Workshop, 59<sup>th</sup> Annual Drosophila Research Conference, Philadelphia, PA. 2018. (I transferred this presentation to my graduate student, James O'Connor.)
37. Organizer and speaker, Terry Orr-Weaver Celebration Symposium, Whitehead Institute, September 2018.
38. Invited speaker, University of Vermont Pharmacology Seminar Series, June 2019.