





## Lucy Erin O'Brien

Associate Professor of Molecular and Cellular Physiology

Molecular & Cellular Physiology

 NIH Biosketch available Online

 Curriculum Vitae available Online

### CONTACT INFORMATION

#### • Administrative Contact

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### Bio

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### ACADEMIC APPOINTMENTS

- Associate Professor, Molecular & Cellular Physiology
- Member, Bio-X
- Member, Institute for Stem Cell Biology and Regenerative Medicine
- Member, Stanford Cancer Institute

### ADMINISTRATIVE APPOINTMENTS

- Member, Stanford Diabetes Research Center, (2017- present)
- Member, Stanford Cancer Institute, (2016- present)
- Associate Member, Institute for Stem Cell Biology and Regenerative Medicine, (2013- present)

### HONORS AND AWARDS

- Predoctoral Fellowship for Science and Engineering, Department of Defense (1993-1996)
- Predoctoral Fellowship, American Heart Association (1998-2001)
- Postdoctoral Fellowship, American Heart Association (2006)
- Genentech Foundation Fellow, Life Sciences Research Foundation (2007-2009)
- Mentored Research Scientist Development Award (K01), NIH/NIDDK (2010-2015)
- Gabilan Faculty Fellow, Stanford (2013)

### PROFESSIONAL EDUCATION

- Postdoctoral Scholar, UC Berkeley , Stem Cell Biology
- Ph.D., UCSF , Biomedical Sciences / Cell Biology (2001)
- B.A., Harvard University , Biochemistry (1992)

### LINKS

- O'Brien Lab Website: <http://www.stemdynamics.org>

## Research & Scholarship

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### CURRENT RESEARCH AND SCHOLARLY INTERESTS

Animals live in dynamic environments where external conditions vary at cyclic or irregular intervals. When faced with environmental change, an individual's physiological fitness requires that its organ systems functionally adapt. One type of organ adaptation occurs through tissue growth and shrinkage, tuning an organ's functional capacity to meet variable levels of physiologic demand. An "economy of nature", adaptive remodeling breaks the allometry of the body plan that was established during development. Unlike embryonic growth, adult organ remodeling is reversible and repeatable, suggesting that it occurs through different mechanisms. Stem cells are key players in at least some of these mechanisms. But, basic questions remain largely unanswered: How do stem cells sense different levels of functional demand? How do they help translate this information into appropriate changes in organ size?

We have developed the *Drosophila* midgut as a simple invertebrate model to uncover the rules that govern adaptive remodeling. In adult flies, the midgut is a stem cell-based organ analogous to the vertebrate small intestine. We have found that when dietary load increases, midgut stem cells activate a reversible growth program that increases total intestinal cell number and digestive capacity. The midgut is a uniquely tractable model to study adaptive growth; not only can gene expression be manipulated and lineages traced at single-cell and whole-tissue levels, but complete population counts of all cell types are possible. Our goal is to understand how this nutrient-driven mechanism regulates stem cell behavior for lifelong optimization of organ form and function.

## Teaching

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### COURSES

#### 2022-23

- Foundations in Experimental Biology: BIOS 200 (Aut)
- MCP Bootcamp: MCP 207 (Aut)

#### 2021-22

- Foundations in Experimental Biology: BIOS 200 (Aut)
- MCP Bootcamp: MCP 207 (Aut)

#### 2020-21

- Foundations in Experimental Biology: BIOS 200 (Aut)
- MCP Bootcamp: MCP 207 (Aut)

#### 2019-20

- MCP Bootcamp: MCP 207 (Aut)

### STANFORD ADVISEES

#### Doctoral Dissertation Reader (AC)

Yuhang Fan, Alex Lessenger, Tessa Logan

#### Postdoctoral Faculty Sponsor

Anthony Galenza, Takao Ito, Charlie Lang, Jason Millington, Aparna Sherlekar Banerjee

#### Doctoral Dissertation Advisor (AC)

Miriam Sun

### GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Molecular and Cellular Physiology (Phd Program)

## Publications

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### PUBLICATIONS

- **Bellymount enables longitudinal, intravital imaging of abdominal organs and the gut microbiota in adult *Drosophila*.** *PLoS biology*  
Koyama, L. A., Aranda-Díaz, A. n., Su, Y. H., Balachandra, S. n., Martin, J. L., Ludington, W. B., Huang, K. C., O'Brien, L. E.  
2020; 18 (1): e3000567
- **Disruption of EGF Feedback by Intestinal Tumors and Neighboring Cells in *Drosophila*.** *Current biology : CB*  
Ngo, S. n., Liang, J. n., Su, Y. H., O'Brien, L. E.  
2020
- **Long-term live imaging of the *Drosophila* adult midgut reveals real-time dynamics of division, differentiation, and loss.** *eLife*  
Martin, J. L., Sanders, E. N., Moreno-Roman, P., Jaramillo Koyama, L. A., Balachandra, S., Du, X., O'Brien, L. E.  
2018; 7
- **Feedback regulation of steady-state epithelial turnover and organ size** *NATURE*  
Liang, J., Balachandra, S., Ngo, S., O'Brien, L.  
2017; 548 (7669): 588+
- **Beyond the niche: tissue-level coordination of stem cell dynamics.** *Annual review of cell and developmental biology*  
O'Brien, L. E., Bilder, D.  
2013; 29: 107-136
- **Fly Cell Atlas: A single-nucleus transcriptomic atlas of the adult fruit fly.** *Science (New York, N.Y.)*  
Li, H., Janssens, J., De Waegeneer, M., Kolluru, S. S., Davie, K., Gardeux, V., Saelens, W., David, F. P., Brbic, M., Spanier, K., Leskovec, J., McLaughlin, C. N., Xie, et al  
2022; 375 (6584): eabk2432
- **The nature of cell division forces in epithelial monolayers.** *The Journal of cell biology*  
Gupta, V. K., Nam, S., Yim, D., Camuglia, J., Martin, J. L., Sanders, E. N., O'Brien, L. E., Martin, A. C., Kim, T., Chaudhuri, O.  
2021; 220 (8)
- **Microfluidics for mechanobiology of model organisms.** *Methods in cell biology*  
Kim, A. A., Nekimken, A. L., Fechner, S., O'Brien, L. E., Pruitt, B. L.  
2018; 146: 217-59
- **A Model for Adult Organ Resizing Demonstrates Stem Cell Scaling through a Tunable Commitment Rate.** *Biophysical journal*  
Du, X. n., O'Brien, L. E., Riedel-Kruse, I. H.  
2017; 113 (1): 174-84
- **Regional specificity in the *Drosophila* midgut: setting boundaries with stem cells.** *Cell stem cell*  
O'Brien, L. E.  
2013; 13 (4): 375-376
- **Altered Modes of Stem Cell Division Drive Adaptive Intestinal Growth** *CELL*  
O'Brien, L. E., Soliman, S. S., Li, X., Bilder, D.  
2011; 147 (3): 603-614
- **STAT1 Is Required for Redifferentiation during Madin-Darby Canine Kidney Tubulogenesis** *MOLECULAR BIOLOGY OF THE CELL*  
Kim, M., O'Brien, L. E., Kwon, S., Mostov, K. E.  
2010; 21 (22): 3926-3933
- **Morphological and biochemical analysis of Rac1 in three-dimensional epithelial cell cultures** *METHODS IN ENZYMOLOGY, VOL 406, REGULATORS AND EFFECTORS OF SMALL GTPASES: RHO FAMILY*  
O'Brien, L. E., Yu, W., Tang, K., Jou, T. S., Zegers, M. M., MOSTOV, K. E.  
2006; 406: 676-691
- **beta 1-integrin orients epithelial polarity via Rac1 and laminin** *MOLECULAR BIOLOGY OF THE CELL*  
Yu, W., Datta, A., Leroy, P., O'Brien, L. E., Mak, G., Jou, T. S., Matlin, K. S., MOSTOV, K. E., Zegers, M. M.

2005; 16 (2): 433-445

- **Formation of multicellular epithelial structures.** *Novartis Foundation symposium*  
Mostov, K., Brakeman, P., Datta, A., Gassama, A., Katz, L., Kim, M., Leroy, P., Levin, M., Liu, K., Martin, F., O'Brien, L. E., Verges, M., Su, et al  
2005; 269: 193-200
- **ERK and MMPs sequentially regulate distinct stages of epithelial tubule development** *DEVELOPMENTAL CELL*  
O'Brien, L. E., Tang, K., Kats, E. S., Schutz-Geschwender, A., Lipschutz, J. H., Mostov, K. E.  
2004; 7 (1): 21-32
- **Epithelial polarity and tubulogenesis in vitro** *TRENDS IN CELL BIOLOGY*  
Zegers, M. M., O'Brien, L. E., Yu, W., Datta, A., MOSTOV, K. E.  
2003; 13 (4): 169-176
- **Hepatocyte growth factor switches orientation of polarity and mode of movement during morphogenesis of multicellular epithelial structures** *MOLECULAR BIOLOGY OF THE CELL*  
Yu, W., O'Brien, L. E., Wang, F., Bourne, H., MOSTOV, K. E., Zegers, M. M.  
2003; 14 (2): 748-763
- **Opinion - Building epithelial architecture: insights from three-dimensional culture models** *NATURE REVIEWS MOLECULAR CELL BIOLOGY*  
O'Brien, L. E., Zegers, M. M., Mostov, K. E.  
2002; 3 (7): 531-537
- **Analysis of membrane traffic in polarized epithelial cells.** *Current protocols in cell biology / editorial board, Juan S. Bonifacino ... [et al.]*  
Lipschutz, J. H., O'Brien, L. E., Altschuler, Y., Avrahami, D., Nguyen, Y., Tang, K., MOSTOV, K. E.  
2001; Chapter 15: Unit 15 5-?
- **Rac1 orientates epithelial apical polarity through effects on basolateral laminin assembly** *NATURE CELL BIOLOGY*  
O'Brien, L. E., Jou, T. S., Pollack, A. L., Zhang, Q. H., Hansen, S. H., Yurchenco, P., Mostov, K. E.  
2001; 3 (9): 831-838
- **Exocyst is involved in cystogenesis and tubulogenesis and acts by modulating synthesis and delivery of basolateral plasma membrane and secretory proteins** *MOLECULAR BIOLOGY OF THE CELL*  
Lipschutz, J. H., Guo, W., O'Brien, L. E., Nguyen, Y. H., Novick, P., Mostov, K. E.  
2000; 11 (12): 4259-4275