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| BIOGRAPHICAL SKETCH Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person.  **DO NOT EXCEED FOUR PAGES.** | | | | |
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| NAME  Jody Rosenblatt | | POSITION TITLE  Associate Professor | | |
| eRA COMMONS USER NAME  JSRosenblatt | |
| EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)* | | | | |
| INSTITUTION AND LOCATION | DEGREE  *(if applicable)* | | YEAR(s) | FIELD OF STUDY |
| University of California, Berkeley | BA | | 1988 | Molecular Biology |
| University of California, San Francisco | PhD | | 1998 | Biochem. & Biophysics |
| University College London | Postdoc | | 2005 | Cell Biology |

**A. Personal Statement**

The goal of my research program is to investigate the signaling and mechanisms that control cell extrusion, and what governs the direction a cell extrudes from an epithelium. I previously discovered a process that epithelia use to remove dying cells while maintaining a functional barrier, termed ‘extrusion’. We have recently identified that cells destined to extrude produce a lipid, Sphingosine 1-Phosphate, which binds a G-protein coupled receptor (S1P2) in neighboring epithelial cells to extrude them. Inducing cell death triggers cell extrusion to ensure that no gaps form in the epithelial barrier. However, more importantly, we have recently found that normally epithelial cells die by extrusion—crowding induces lives cells to die, which die from detachment of the underlying matrix and its survival signaling. Extrusion is critical for preventing tumor formation, as disrupting the signaling pathway driving extrusion causes cells to lose contact inhibition and form epithelial masses. Although cells normally die following extrusion, aggressive tumor cells that typically upregulate survival signaling could use extrusion to escape their primary sites within epithelia. Their eventual fate depends on the direction that they extrude, as apical extrusion could still suppress tumor formation by eliminating cells through the lumen, whereas basal extrusion beneath the epithelium could enable cells to invade. Importantly, oncogenic mutations in APC, KRas, or AKT drive cells to extrude basally, suggesting that basal extrusion could be key for aggressive tumors harboring these mutations to become invasive and metastatic. To test if basal extrusion can initiate invasion in a model system where we can also manipulate gene function using transgenics, morpholinos, mutants, or inhibitors, we have developed an *in vivo* model for simple epithelia using zebrafish epidermis. The optical clarity of zebrafish epidermis allows visualization of single cell movements, divisions, and cell extrusion/death critical to testing the fate of cells that have invaded from the epidermis without causing a wound healing response intrinsic to intravital filming non-transparent organisms. Further, we have made lines to drive gene expression specifically in the basal or surface epidermal layer, or in specialized epidermal cells. Additionally, my lab has been investigating the role of failed extrusion in promoting epithelial and endothelial barrier function diseases such asthma and cerebral cavernous malformations.

**B. Positions and Honors**

**Positions and Employment**

1. Research Assistant, University of Utah, Salt Lake City, UT
   1. Undergraduate Research Assistant, University of California, Berkeley, CA
   2. Research Assistant, Chiron Corporation, Emeryville, CA
   3. Research Assistant, University of California, San Francisco, CA
   4. Graduate Student, University of California, San Francisco, CA
   5. Postdoctoral Fellow, University College London, London UK

2005-2011 Assistant Professor, Oncological Sciences, University of Utah, Salt Lake City, UT

2005-present Investigator, Huntsman Cancer Institute

2011-present Associate Professor, Oncological Sciences, University of Utah, Salt Lake City, UT

**Other Experience and Professional Memberships**

1992-present Member of The American Society for Cell Biology

2001-present Member of The British Society for Cell Biology

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| |  |  | | --- | --- | | 2002-present | Referee for Current Biology | | | | |
| 2002-present | | Referee for Nature | |
| 2002-present   |  |  | | --- | --- | | 2003-present | Referee for Journal of Cell Biology | | | Referee for Nature Cell Biology  Referee for The Journal of Cell Biology | |
| 2010-present  2008-present | Referee for Molecular Biology of the Cell  Referee for PLOS Biology |
| 2006 - Present | Review Wellcome Trust Senior Fellowship Applications |
| 2010 | Reviewed a Cancer Research UK Career Development Award Application |

**Awards and Selected Presentations**

1988 Genetics Society of America Grant for summer research

1992-1995 National Science Foundation Fellowship

1999-2001 Human Frontiers Research Postdoctoral Fellowship (declined for EMBO use)

1999-2000 EMBO postdoctoral Fellowship

2000-2003 American Cancer Society Postdoctoral Fellowship

2005-2010 Wellcome Trust Senior Research Fellow (for group leader position at Cambridge University, declined)

2007-2012 NIH Director’s New Innovator Award (1 of 29 awarded)

2008 Laura and Arthur Colwin Endowed Summer Research Fellowship, Marine Biological Labs

2008 British Society for cell Biology Autumn Meeting, Selected Speaker and Session Chair

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| 2011 Gordon Research Conference on Cell Contact and Adhesion, Selected Speaker  2011 American Society for Cell Biology, Invited speaker  2012 Gordon Research Conference on Glycolipids and Sphingolipids, Invited Speaker  2012 Society for Developmental Biology Meeting, Invited Speaker  2012 EMBO Conference on Morphogenesis & Dynamics of Multicellular Systems, Invited speaker  2013 British Society for Cell Biology, Invited speaker  2013 Gordon Research Conference on Apoptotic Cell Recognition & Clearance, Invited speaker  2013 Seminar at MD Anderson, Houston, Texas  2013 Seminar at the Keck Center, University of Southern California |

2013 American Society for Cell Biology, Session Chair

2014 Workshop on Mechanics and Growth of Tissues: From Development to Cancer

2014 Seminar at University of Colorado, Denver

2014 Seminar at the Skirball Institute, New York University

**B. Selected peer-reviewed publications** (selected from 29 peer-reviewed publications)

**Most relevant to the current application**

**1. Rosenblatt J**, Raff MC, Cramer LP. (2001). An epithelial cell destined for apoptosis signals its neighbors to extrude it by an actin- and myosin-dependent mechanism. Curr Biol,  11(23),  1847-57. (**cover**) PMID: 11728307

>Highlighted in: *Science*, *The Journal of Cell Biology, Current Biology, Current Opinion in Cell Biology*, *American Society for Cell Biology Press Book* and noted as a ‘must read’ in *Faculty of 1000*

**2.** Slattum G, McGee KM, **Rosenblatt J**. (2009). P115 RhoGEF and microtubules decide the direction apoptotic cells extrude from an epithelium. J Cell Biol, 186(5), 693-702. (**cover**) PMID: 19720875

>Highlighted in *Science, The Journal of Cell Biology*, and *Faculty of 1000*

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| **3**. Andrade D, **Rosenblatt J**. (2011). Apoptotic regulation of epithelial cellular extrusion. Apoptosis,16(5),  491-501. PMID: 21399977  **4**. Gu Y, Forostyan T, Sabbadini R, **Rosenblatt J**. (2011). Epithelial cell extrusion requires the sphingosine-1-phosphate receptor 2 pathway. J Cell Biol, 193(4), 667-76. (**cover**) PMID: 21555463  >Highlighted in: *The Journal of Cell Biology, Nature Cell Biology, and Faculty of 1000*  **5.** Eisenhoffer GT and **Rosenblatt J**. (2011) Live imaging of cell extrusion from the epidermis of developing zebrafish. Journal of Visualized Experiments. Jun 27;(52). pii: 2689. doi: 10.3791/2689. PMID: 21730948  **6**. Marshall T, Lloyd IE, Delalande JM, Nathke I, and **Rosenblatt J**. The tumor suppressor adenomatous polyposis coli controls the direction a cell extrudes from an epithelium.*Mol Biol Cell*, (21): 3962-70 (2011).PMID:21900494  >Highlighted in Science Signaling, and the American Society for Cell Biology Newsletter, and won the Molecular Biology of the Cell Paper of the Year. |
| **7**. Eisenhoffer GT\*, Loftus PD\**,* YoshigiM, Otsuna H, Chien CB,Morcos PA, and **RosenblattJ**. Overcrowding induces extrusion of live cells to control epithelial cell numbers. *Nature*, 484(7395):546-9. (2012). PMID:22504183  >Highlighted in *Cell*, and reviewed in *Cell, Nature Reviews Molecular and Cell Biology, Current Biology*, and *medecine-sciences*  **8.** Gu Y and **Rosenblatt J** (2012)New emerging roles for epithelial cell extrusion. *Current Opinion in Cell Biology,* 24(6):865-70.  **9.Rosenblatt J** (2012) Programmed cell death: a new way worms get rid of unwanted cells. *Current Biology*, [Volume 22, Issue 19](http://www.cell.com/current-biology/issue?pii=S0960-9822(12)X0019-8), R844-R846  **10.** Eisenhoffer GT and **Rosenblatt J (**2013**)** Bringing balance by force: live cell extrusion controls epithelial cell numbers**.** *Trends in Cell Biology* (4):185-92.  **11.**Slattum GM, Gu Y, and **Rosenblatt J**. Oncogenic K-Ras promotes basal extrusion of epithelial cells by degrading S1P through autophagy. *Current Biology,* Jan 6;24(1):19-28  >Highlighted in Science Stke.  **12. Rosenblatt J** and Gartner Z. (2014) Cells: shaping tissues and organs, Molecular Biology of the Cell, *in press.*  **13.**Slattum GM and **Rosenblatt J** Tumour cell invasion: an emerging role for basal epithelial cell extrusion. *Nature Reviews Cancer, under revision.* (invited review).  **Additional recent publications of importance to the field (in chronological order)**  **1. Rosenblatt J**; Peluso P; Mitchison TJ. The bulk of unpolymerized actin in *Xenopus* Egg extracts is ATP-bound. *Molecular Biology of the Cell* 1995: 227-236.PMID: 7787248  **2**. Welch MD, Mallavarapu *A,* **Rosenblatt J**, and Mitchison TJ*. Actin Dynamics in vivo.* Current Opinion in Cell Biology, 1997 9: 54-61. PMID: 9013669  **3. Rosenblatt J** Agnew BJ, Abe H, Bamburg JR, and Mitchison TJ. Xenopus actin-depolymerizing factor/cofilin (XAC) is responsible for the turnover of actin filaments in *Listeria monocytogenes* tail. *The Journal of Cell Biology*, 1997, 136: 1323-1332. PMID: 9087446  **4. Rosenblatt J** and Mitchison TJ. Signal transduction: Actin, cofilin, and cognition. Nature, 1998 393:739-740. PMID: 9655388  **5.** Welch MD, **Rosenblatt J**, Skoble J, Portnoy DA, Mitchison TJ Interaction of human Arp2/3 complex and the *Listeria monocytogenes* ActA protein in actin filament nucleation. Science. 1998 3:281(5373):105-8. PMID: 9651243  **6. Rosenblatt J**, Cramer LP, Baum B, McGee KM. (2004). Myosin II-dependent cortical movement is required for centrosome separation and positioning during mitotic spindle assembly. Cell, 117(3), 361-72. (**cover**) PMID: 15109496  >Highlighted in: *Cell, The Journal of Cell Biology, Nature Cell Biology, and Faculty of 1000*  **7. Rosenblatt J**. (2005). Spindle assembly: asters part their separate ways. [Review]. Nat Cell Biol, 7((3)), 219-22. PMID: 15738974  **8. Rosenblatt J.** (2008). Mitosis: moesin and the importance of being round. *Curr Biol, 18(7),* R292-3. PMID: 18397735 |

**C. Research Support**

ACTIVE

1R01GM102169-02 (Rosenblatt) 08/01/2012 – 04/30/2016 3.0 calendar

NIH/NIGMS $193,500

The role of extrusion in controlling epithelial homeostasis

The major goals of this project are to answer the following:

1. Does S1P-mediated extrusion promote cell death in mammalian cultured monolayers?
2. Does S1P-mediated extrusion drive cell death and compensatory proliferation in zebrafish epidermis?
3. How does the stretch-activated channel Piezo 1 activate S1P-mediated extrusion?
4. What regulates susceptibility to extrusion?

Role: PI

3R01GM102169-02S1 (Rosenblatt) 8/01/2013 – 4/30/2016 .96 calendar

NIH/NIGMS $53,333

The role of extrusion in controlling epithelial homeostasis

The major goals of this project are to answer the following:

1) Does stretching activate epithelial cells to proliferate directly at the G2 phase of the cell cycle?

2) What molecular pathway translates physical stretch into activation of cell division?

Role: PI

120464 (Eisenhoffer) 07/01/2011 – 06/30/2014 0 calendar

American Cancer Society Postdoctoral Fellowship $52,000

Role Of Cell Extrusion in Epithelial Homeostasis and Carcinogenesis

Role: Mentor

None (Rosenblatt) 01/01/2012 – 06/30/2014 0 calendar

Cell Response and Regulation Cancer Center Support Grant$40,000

Developing new chemotherapeutic treatments of K-Ras-driven tumors with aberrant extrusion

The major goals of this grant are:

1) Test if inhibiting FAK eliminates epidermal masses in zebrafish S1P2 mutants.

2) Test if S1P2 expression is reduced in a NSCLC mouse model.

3) Test if LSL-KrasG12D/+ tumor cells are defective in extrusion and if blocking FAK increases cell death response of cisplatin treatment.

4) Test if FAK inhibitors could improve treatment of NSCLC mice.

Role: PI

PENDING

1R01GM103921-01 (Rosenblatt) 10/01/2012 – 9/30/2017 3.0 calendar

NIH/NIGMS $250,000

Mechanisms controlling the direction a cell extrudes from an epithelium

The major goals of this project are to answer the following:

1. Investigate the role of S1P and dynamic microtubules in controlling the direction a cell extrudes.
2. How does oncogenic KRas promote basal extrusion of epithelial cells?
3. Is basal extrusion of oncogenic KRas cells sufficient to induce their invasion from a zebrafish epidermis?

Role: PI

OVERLAP

None

COMPLETED

1DP2OD002056-01 (Rosenblatt) 09/30/2007 – 08/31/2012 6.0 calendar

NIH/NIGMS - NIH Director’s New Innovator Award $300,000

Identification of Signals that Extrude an Apoptotic Cell from an Epithelium

The major goals of this project are to identify the signaling pathway that initiates extrusion, identify the lipid extruding ring signal (EXR), and test disruption of extrusion signaling in zebrafish embryos.

KG101297 (Marshall) 09/01/2010 – 08/31/2013 0 calendar

Susan G. Komen Breast Cancer Foundation $60,000

Postdoctoral Fellowship

Cell Extrusion In 3-D Models

Role: Mentor