

## BIOGRAPHICAL SKETCH

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|                                                                                                                                                   |                                                            |           |                       |
|---------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|-----------|-----------------------|
| NAME<br>Cheney, Richard E.                                                                                                                        | POSITION TITLE<br>Professor of Cell Biology and Physiology |           |                       |
| eRA COMMONS USER NAME<br>RICHARD_CHENEY                                                                                                           |                                                            |           |                       |
| EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i> |                                                            |           |                       |
| INSTITUTION AND LOCATION                                                                                                                          | DEGREE<br><i>(if applicable)</i>                           | YEAR(s)   | FIELD OF STUDY        |
| Oregon State University, Corvallis, OR                                                                                                            | BS                                                         | 1976-1980 | Biochem. & Biophysics |
| Washington University, St. Louis, MO                                                                                                              | PhD                                                        | 1981-1989 | Neurobiology          |
| Yale University, New Haven, CT                                                                                                                    | Postdoc                                                    | 1990-1995 | Cell Biology          |

### A. Personal Statement

My research focuses on unconventional myosins and the actin cytoskeleton, an area of central importance in deafness as well as the fundamental cell biology underlying neural development and dendritic spine formation, cancer metastasis, and angiogenesis. Several forms of human deafness are caused by mutations in unconventional myosins, and unconventional myosins, along with the actin cytoskeleton, are required for the proper formation and function of stereocilia, the mechanosensors for hearing. My research has led to the discovery and characterization of several unconventional myosins, including Myo5a (brain myosin-V), Myo5c, Myo10, and Myo19. Much of our current research focuses on Myo10 (myosin-X), and we have shown that this MyTH-FERM myosin localizes to the tips of filopodia and has potent filopodia inducing activity. Filopodia, like stereocilia and microvilli, contain a core of bundled actin filaments, and our work with Myo10 has led to the discovery of a novel form of motility within filopodia that has important implications for all these cellular protrusions. Since we have previously shown that Myo10 binds to integrins, we hypothesize that Myo10 is a component of a filopodial tip complex that constitutes a specialized site of polymerization, adhesion, and mechanotransduction. Because the tips of filopodia and related protrusions such as microvilli and stereocilia have critical roles in the formation and functions of these structures, we propose to determine the fundamental properties of the filopodial tip complex in terms of its composition, dynamics, and roles in cell signaling. Myo10's functions as a key component of invadopodia and as cytoskeletal effector of PI3 kinase also make it important to investigate Myo10's roles in cancer biology. My background in unconventional myosins, cytoskeletal cell biology, and imaging is thus ideal for research in these areas. The additional expertise provided by my UNC colleagues Drs. Rich Superfine and Klaus Hahn in imaging, biosensors, photo-activation, biological forces, and mechanotransduction also provides us with novel and highly innovative approaches to define the fundamental properties and functions of the filopodial tip complex.

### B. Positions and Honors

#### Positions:

|             |                                                                                                                                                                                                                                                                                                              |
|-------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1981-89     | Graduate student. Thesis research on brain spectrin and the microvillar cytoskeleton with Drs. Mark Willard and Nobutaka Hirokawa in the Department of Anatomy and Neurobiology, Washington University School of Medicine.                                                                                   |
| 1990-95     | Postdoctoral fellow. Research with Dr. Mark Mooseker at Yale University Dept. of Biology. Cloned, purified and characterized brain myosin-V, designed PCR screen that identified numerous unconventional myosins, performed phylogenetic analysis of myosins, and identified and characterized the IQ motif. |
| 1994-95, 97 | Instructor. Cellular and Molecular Physiology Course, molecular motors section, Marine Biological Laboratory, Woods Hole, MA.                                                                                                                                                                                |
| 1995-02     | Assist. Professor. Dept. of Cell & Molecular Physiology, School of Medicine, UNC Chapel Hill                                                                                                                                                                                                                 |
| 2002-07     | Assoc. Professor. Dept. of Cell & Molecular Physiology, School of Medicine, UNC Chapel Hill<br>Director of Graduate Studies for the Physiology PhD Program (2004-07)                                                                                                                                         |
| 2008-2012   | Professor. Dept. of Cell and Molecular Physiology, School of Medicine, UNC Chapel Hill                                                                                                                                                                                                                       |
| 2012-       | Professor. Dept. of Cell Biology and Physiology, School of Medicine, UNC Chapel Hill                                                                                                                                                                                                                         |

## Honors and memberships:

|            |                                                                                           |
|------------|-------------------------------------------------------------------------------------------|
| 1981-84    | National Science Foundation Predoctoral Fellowship                                        |
| 1990       | Muscular Dystrophy Society Postdoctoral Fellowship                                        |
| 1991-93    | American Cancer Society Postdoctoral Fellowship                                           |
| 1994-95    | NIH Training Fellowship with the Liver Center at the Yale University School of Medicine   |
| 2002       | Hettleman Prize for Scholarly and Artistic Achievement by Junior Faculty                  |
| 1998       | NIH NINDS Special Emphasis Panel for Program Project Grants                               |
| 2000       | NIH NINDS Special Emphasis Panel, Neurobiology of Diabetic Complications                  |
| 2005       | NIH NIDCD Special Emphasis Panel, Protein Interactions in Auditory and Vestibular Biology |
| 2005-2010  | NIH NIDCD Board of Scientific Counselors, Chair 2009-2010                                 |
| 2010       | NIH NHLBI Board of Counselors, ad hoc reviewer                                            |
| 2011, 2012 | NIH NIDCD Communication Disorders Review Committee, ad hoc reviewer                       |

ad hoc reviewer for NSF

editor for Cytoarchitecture, 2011-present; guest editor for PNAS, 2011, 2012

reviewer for Biophys J, Cell, Curr Biol, J Biol Chem, J Cell Biol, J Cell Sci, Mol Biol Cell, Nature, Nature Cell Biology, and PNAS

American Society for Cell Biology

Biophysical Society

UNC Neuroscience Center

UNC Neurobiology Curriculum and Otolaryngology Training Program

UNC Lineberger Comprehensive Cancer Center

UNC Center for Computational and Systems Biology

## C. Selected peer-reviewed publications (in chronological order)

### Most relevant to the current application:

1. Berg, J.S., and Cheney, R.E. (2002) Myosin-X is an Unconventional Myosin that Undergoes Intrafilopodial Motility. **Nature Cell Biology** 4:246-250. (*Recommended by Faculty of 1000*)
2. Zhang, H., Berg, J.S., Li, Z., Sousa, A., Bhaskar(Bohil), A., Lennartsson, P., Cheney, R.E., and Strömblad, S. (2004) Myosin-X is a Novel Link Between Actin and Integrins. **Nature Cell Biology**, 6:523-531. (*featured on cover and rated "Must Read" by Faculty of 1000*)
3. Bohil, A.B., Robertson, B.W., and Cheney, R.E. (2006) Myosin-X is a molecular motor that functions in filopodia formation. **Proc. Natl. Acad. Sci. USA**, 103:12411-12416. PMC1567893
4. Kerber, M.L., Jacobs, D.T., Campagnola, L., Dunn, B.D., Yin, T., Sousa, A.D., Quintero, O.A., and Cheney, R.E. (2009) A novel form of motility in filopodia revealed by imaging myosin-X at the single-molecule level. **Curr. Biol.** 19:967-973. PMC2817954. (*selected for ASCB minisymposium*)
5. Kerber, M.L., and Cheney, R.E. (2011) Myosin-X: a MyTH-FERM myosin at the tips of filopodia. **J. Cell Sci.** 124:3733-3741. PMC3225264

### Additional publications of importance to the field:

1. Cheney, R.E., O'Shea, M., Heuser, J., Coelho, M.V., Espreafico, E.M., Wolenski, J.W., Forscher, P., Larson, R.E., and Mooseker, M.S. (1993) Brain Myosin-V Is a Two-Headed Unconventional Myosin with Motor Activity. **Cell** 75:13-23. (*featured in accompanying Review article*)
2. Wang, F.S., Wolenski, J.W., Cheney, R.E., Mooseker, M.S., and Jay, D. (1996) Function of Myosin-V in Filopodial Extension of Growth Cones. **Science** 273:660-663.
3. Mehta, A.D., Rock, R.S., Rief, M., Spudich, J.A., Mooseker, M.S., and Cheney, R.E. (1999) Myosin-V is a Processive Actin-Based Motor, **Nature** 400:590-593.
4. Berg, J.S., Derfler, B.H., Pennisi, C.P., Corey, D.P., and Cheney, R.E. (2000) Myosin-X: A Novel Myosin with Pleckstrin Homology Domains, Associates with Regions of Dynamic Actin. **J. Cell Sci.** 113:3439-51.

5. Weber, K.L., Sokac, A.M., Berg, J.S., Cheney, R.E., and Bement, W.M. (2004) A microtubule-binding myosin required for nuclear anchoring and spindle assembly. **Nature**, 431:325-329. (*rated Must Read by Faculty of 1000 and featured in an accompanying News and Views article*)
6. Sousa, A.D., Berg, J.S., Robertson, B.W., Meeker, R., and Cheney, R.E. (2006) Myo10 in brain: developmental regulation, identification of a headless isoform, and dynamics in neurons. **J. Cell Sci.** 119:184-94. (*featured on journal cover*)
7. Jacobs, D.T., Weigert, R., Grode, K.D., Donaldson, J.G., and Cheney, R.E. (2009) Myosin Vc is a molecular motor that functions in secretory granule trafficking. **Mol. Biol. Cell** 20:4471-4488. PMC2770936
8. Quintero, O.A., DiVito, M.M., Adikes, R.C., Kortan, M.B., Case, L.B., Lier, A.J., Panaretos, N.S., Slater, S.Q., Rengarajan, M., Feliu, M., and Cheney, R.E. (2009) Human Myo19 is a novel myosin that associates with mitochondria. **Curr. Biol.** 19:2008-2013 PMC2817954 (*selected for an ASCB minisymposium and featured in an accompanying Dispatches article*)
9. Raines, A.N., Nagdas, S., Kerber, M.L., and Cheney, R.E. (2012) Headless Myo10 is a Negative Regulator of Full-length Myo10 and Inhibits Axon Outgrowth in Cortical Neurons. **J Biol Chem** 287:24873-24883. PMC3408153
10. Liu, K.C., Jacobs, D.T., Dunn, B.D., Fanning, A.S., and Cheney, R.E. (2012) Myosin-X functions in polarized epithelial cells. **Mol Biol Cell** 23:1675-1687. PMC3338435 (*selected for an ASCB minisymposium*)

## D. Research Support

### Ongoing research support

R01-DC03299-15 Cheney (PI)

NIH/NIDCD

"Myosin-X and the Molecular Basis of Filopodia Function"

This grant supports our research on the fundamental properties of myosin-X and its functions in cells such as neurons and epithelial cells.

Role: PI

7/01/2007-6/30/2012

(currently in a no cost extension)

### Completed research support

PO1-HL080166-05 Burrridge (PI)

NIH/NHLBI

"Adhesion and Migration in Inflammation"

This PPG with two other investigators (Drs. Keith Burrridge and Susan Smyth) and an Imaging Core focused on investigating mechanisms of adhesion and migration in processes such as transendothelial migration.

Role: PI of Project 3

8/1/2006-7/31/2011

### Pending research support

National Innovative Research Grant Proposal 13-0157 Cheney (PI)

American Heart Association

"Filopodia and the Filopodial Tip Complex in Endothelial Cells"

This 2 year proposal focuses on investigating the composition and dynamics of the filopodial tip complex in endothelial cells, with the goal of defining the molecular mechanisms of filopodial function in angiogenesis.

Role: PI

1/01/2012-12/31/2014

(proposed)