BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
W. James Nelson	Professor of Biology, and of Molecular & Cellular Physiology, and the Ruby J. and Daphne Donohue Munzer Professor
eRA COMMONS USER NAME (credential, e.g., agency login) NELSON.WILLIAM	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Manchester University, U.K.	B.Sc.	1975	Genetics/Cell Biology
Chester Beatty Institute for Cancer Research	Ph.D.	1978	Rad. Biology/Genetics
Max-Planck Institute for Cell Biol., Heidelberg	Postdoc	1978-1982	Cell Biology
California Institute of Technology, Pasadena, CA	Sr Res Fellow	1982-1984	Cell/Develop. Biology

A. PERSONAL STATEMENT

My major scientific interests in mechanisms that regulate compartmentalization of the plasma membrane into different domains in polarized cells span the life-time of this Award, now in year 26 and which has funded all our work in this area. Initially, my laboratory contributed to understanding the role of the membrane-cytoskeleton (spectrin, ankyrin) in the polarized distribution of membrane proteins such as the Na-pump (*Cell* **39**, 309-320, 1984; *Nature* **328**, 533-536, 1987), mechanisms involving in vesicle trafficking to different membrane domains (*Cell* **93**, 731-740,1998; *J. Cell Biol*. **155**, 593-604, 2001; *ibid,* **178**, 323-335, 2007), and particularly the role of cell-cell interactions as a spatial cue for the development of epithelial polarity (*Cell* **62**, 309-316, 1990; *ibid* **123**, 889-901, 2005; *J. Cell Biol.,* **178**, 323-335, 2007; *Science*, **331**, 1336-1339, 2011). We have also been interested in the organization and function of septin proteins, a poorly understood but important cytoskeleton in animal cells: my laboratory provided the first evidence that septins interact with sub-populations of microtubules to regulate post-Golgi vesicle trafficking (*J. Cell Biol.* **180**, 295-303, 2008), and form a diffusion barrier at the base of the primary cilium (*Science*. **329**, 436-439, 2010) [this project is being successfully continued by a former postdoc, Elias Spiliotis]. A major focus of our current work is to understand the regulation of cell-cell adhesion. We provided the first live cell analysis of the distributions of E-cadherin (*J. Cell Biol*. **142**, 1105-1119, 1998), actin and Rho family GTPase activities (*J. Cell Biol.* **178,** 517-527, 2007) during initial cell-cell adhesion, reconstituted protein-protein interactions in the cadherin-catenin-actin complex with surprising results (*Cell* **123**, 889-90, 2005; *ibid*, **123**, 903-915, 2005), and extended these studies to *Dictyostelium* (*Science*, **331**, 1336-1339, 2011), *C. elegans* (*Proc. Natl. Acad. Sci. (U S A).* **107**, 14591-14596, 2010) and zebrafish (*Development* **139**, 537-546, 2012). The results have provided novel insights into the regulation of cell-cell adhesion, and some surprising evidence of evolutionary conservation of epithelial organization. During the course of these studies we have acquired a broad range of techniques including: biochemical techniques to detect, measure and manipulate multi-protein complexes in cells, in cell extracts and by expression in *E. coli* and insect cells (*Cell* **123**, 889-901, 2005; *J. Cell Biol.* **178,** 517-527, 2007; *J. Cell Biol.* **189**, 339-352**,** 2010), high resolution fixed and live cell imaging (*J. Cell Biol*. **135**, 1899-1911, 1996; *Proc. Natl. Acad. Sci. (USA).* **107**, 13324-13329, 2010), the manufacture of micro-patterned surfaces (*FEBS Lett.* 581**,** 4539-4543, 2007**;** *Proc. Natl. Acad. Sci. (USA).* **107**, 13324-13329, 2010), and biophysical approaches (FRAP, FRET) to examine protein dynamics in live cells (*Cell* **123**, 889-90, 2005; *J. Cell Biol.* **178**, 517-527, 2007).

B. POSITIONS AND HONORS

Academic Positions: Associate Member (1985-1989), and Member (1989-1990) Institute for Cancer Research, Philadelphia, PA; Associate Professor (1990-1994), Professor (1994-), and Chairman (1994-2001), Department of Molecular & Cellular Physiology, Stanford University; Rudy J. and Daphne Donohue Munzer Endowed Professor (2001-); Senior Associate Dean for Research, and Graduate and Postdoctoral Education, Stanford University (2001-2003); Professor, Department of Biology, Stanford University (2005-).

Teaching/Mentoring Awards (selected): Award for Outstanding Service to Graduate Students, Stanford University (2000, 2004, 2009); Award for Graduate Teaching, Stanford University (2001, 2004); Graduate Student Service Award, Stanford University (2004); Excellence in Teaching (Medical Students), Stanford University (2005, 2008); Dean's Award for Distinguished Achievements in Teaching, Stanford University (2009); Outstanding BioAIMS (Minority & Diversity) Advocate Award (2012).

Awards and Honors (selected): MRC Pre-Doctoral Research Fellowship (1975-1978); International Union Against Cancer International Postdoctoral Fellowship (1982-1983); Senior Investigator Award, American Heart Association (1983-1985); National Eye Institute Research Award (1984); Young Investigator's Prize in Basic Sciences, American Heart Assoc.-Los Angeles Affiliate (1984); Established Investigator Award, American Heart Association (1988-1993); Max-Planck Research Prize (with Rolf Kemler), Max-Planck Gessellschaft, Germany (1992); Visiting Professor, Alexander von Humboldt Stiftung (1992); Henry Pickering Bowditch Lectureship Award from the American Physiological Society (1994); Burroughs-Wellcome Visiting Professorship in the Basic Medical Sciences (1999); NIH (NIGMS) M.E.R.I.T. Award (2003); Elected, Vice-Chair (2006)/Chair (2008), Gordon Research Conference "Signaling by Adhesion Receptors"; Elected, Fellow of the American Academy of Arts and Sciences (2009); Visiting Scholar, l'Universite Paris Diderot (2012).

Major Lectures (selected): Keynote Speaker, XXXIInd Int. Congress of Physiological Sciences, Glasgow, UK (1993); Kroc Foundation Distinguished Lecturer, Western Association of Physicians (1996); The Burton L. Baker Memorial Lecturer, University of Michigan Sch. Med. (1996); Honors Program Lecturer, New York University Medical Center (1998); Lundberg Lecture, University of Gothenberg, Sweden (1999); Distinguished Lecturer 2000, Univ. Southern California School of Pharmacy (2000); The Louis Avioli Lecture, Washington University School of Medicine (2003); Keynote Speaker, Research Day, University of North Carolina (2005); Raymond Fong Memorial Lecture, University of Iowa (2005); Rudin-Kase Dean's Lecture, Mt. Sinai Sch. Med., New York (2006); 1st Szent-Gyorgyi Lecture, The Mayo Clinic, Rochester NY (2007); European Molecular Biology Laboratory Distinguished Visitor Lectures (2008); Alma Howard Memorial Lecture, McGill University, Montreal, Canada (2009); The Malvin and Eleanor Mayer Lecture in the Life Sciences, Biology Colloquium, MIT (2010); The Irvin Isenberg Endowed Lecture, Marine Biology Laboratory, Woods Hole (2011); 11th Daniel Mazia Memorial Lecture, Hopkins Marine Station, Stanford University (2012).

Professional Societies: American Society for Cell Biology (1982-)

Editorial/Review Boards (current): Board of Reviewing Editors, *Science (*2001-); Editorial Board, *Journal of Cell Science (*2003-); Scientific Review Board, Howard Hughes Medical Institute (2003-); Senior Editor, *Molecular Biology of the Cell (*2010-)*;* Board of Reviewing Editors, *eLife (*2012-).

Government Service (selected): Member, NSF Cell Biology Panel (1990-1994); Member, NIH CDF-2 (Molecular Cytology) Study Section (1999-2003); Committee of Visitors, Molecular & Cellular Biosciences Program, NSF (2002); Appointed to Council, National Institutes of General Medical Sciences, NIH (20072011).

C. SELECTED (PEER-REVIEWED) PUBLICATIONS RELEVANT TO THIS PROJECT (from 87 published during the funding period (2002 – 2012), and 259 total publications; **bold**, personnel supported by this Award)

Polarity, Membrane Domains and Protein Trafficking

• Müsch, A., Cohen, D., **Yeaman, C., Nelson, W. J.**, Rodriguez-Boulan, E. and Brennwald, P. J. (2002). A mammalian homologue of the Drosophila tumor suppressor *lethal (2) giant larvae* interacts with basolateral exocytic machinery in MDCK cells. *Mol. Biol. Cell*. **13**, 158-168. *PMCID: PMC65098*

• Pokutta, S., **Drees, F.**, Takai, Y., **Nelson, W. J.** and Weis, W. I. (2002). Biochemical and structural definition of the L-afadin and actin binding domains of alpha-catenin. *J. Biol. Chem*. **277**, 18868-18874. *PMCID: PMC3368618*

• **Yeaman, C., Grindstaff, K. K.** and **Nelson, W. J.** (2004). Mechanism of Sec6/8 (exocyst) complex localization to the apical junctional complex during polarization of epithelial cells. *J. Cell Science*, **117**, 559-570. *PMCID: PMC3368615*

• **Yeaman, C.,** Ayala, M. I., Wright, J. R., Bossard, C., Bard, F., Ang, A., Maeda, Y, Seufferlein, T., Mellman, I., **Nelson, W. J.** and Malhotra, V. (2004). Protein kinase D (PKD) regulates basolateral protein exit from the *trans*-Golgi Network. *Nature Cell Biol*. **6**, 106-112. *PMC in progress*

- **Reilein, A.** and **Nelson, W. J.** (2005). Adenomatous polyposis coli protein is a component of an organizing template for cortical microtubule networks. *Nature Cell Biol.* **5**, 463-473. *PMCID: PMC3368611*
- **Nejsum, L.** and **Nelson, W. J.** (2007). A molecular mechanism directly linking E-cadherin adhesion to development of epithlelial cell surface polarity. *J. Cell Biol.* **178**, 323-335. *PMCID: PMC2064450*
- **Halbleib, J. M.,** Sääf, A. M., Brown, P. O. and **Nelson, W. J**. (2007). A switch in global gene expression programs during development of a polarized epithelium *in vitro. Mol. Biol. Cell.* **18**, 4261-4278**.** *PMCID: PMC2043570*
- **Hunt, V. S.** and **Nelson, W. J.** (2007). Fabrication of a dual substrate display to test roles of cell adhesion proteins in vesicle targeting to plasma membrane domains. *FEBS Lett.* 581, 4539-4543. *PMCID: PMC2682434*
- **Spiliotis, E., Hunt, V. S.,** Hsu, Q., Kinoshita, M. and **Nelson, W. J**. (2008). Epithelial polarity requires septin coupling of vesicle transport to polyglutamylated microtubules. *J. Cell Biol.* **180**, 295-303. *PMCID: PMC2213583*
- **Hu, Q.,** Milenkovic, L., Jin, H., Scott, M. P., Nachury, M., **Spiliotis, E.** and **Nelson, W. J.** (2010). A septin diffusion barrier at the base of the primary cilium maintains ciliary protein distributions. *Science*. **329**, 436-439. *PMCID: PMC3092790*
- **Dickinson, D., Nelson, W. J***. and Weis, W. I*. (2011). A polarized epithelium organized by α- and b-catenin predates metazoan origins. *Science*, **331**, 1336-1339. *PMCID: PMC3152298* *joint corresponding/senior authors
- **Dickinson, D.,** Robinson, D., **Nelson, W. J*.** and Weis, W. I*. (2012). α-Catenin and IQGAP regulate myosin localization to control epithelial tube morphogenesis in *Dictyostelium*. *Developmental Cell*, **in press.** *joint corresponding/senior authors. *PMCID: in progress*

Cell-Cell Adhesion

- **Ehrlich, J. S., Hansen, M. D. H.** and **Nelson. W. J.** (2002). Spatio-temporal regulation of Rac1 localization and lamellipodia dynamics during epithelial cell-cell adhesion. *Developmental Cell*, **3**, 259-270. *PMCID: PMC3369831*
- Pokutta, S., **Drees, F.**, Takai, Y., **Nelson, W. J.** and Weis, W. I. (2002). Biochemical and structural definition of the L-afadin and actin binding domains of alpha-catenin. *J. Biol. Chem*. **277**, 18868-18874. *PMCID: PMC3368618*
- Amieva, M., **Vogelmann, R.,** Covacci, A., Tomkins, L. C., **Nelson, W. J.** and Falkow, S. (2003). *Helicobacter pylori* CagA targets and disrupts the epithelial apical junctional complex. *Science,* **300**, 1430-1434. *PMCID: PMC3369828*
- **Yamada, S., Drees, F**., Pokutta, S., Weis, W. I*., and **Nelson, W. J*.** (2005). Deconstructing the cadherin-catenin-actin complex. *Cell* **123**, 889-901. *PMCID: PMC3368712* *joint corresponding/senior authors
- **Drees, F.,** Pokutta, S., **Yamada, S., Nelson, W. J*.**, and Weis, W. I*. (2005). Alpha-catenin is a molecular switch that binds E-cadherin/β-catenin and regulates actin filament assembly. *Cell* **123**, 903-915. *PMCID: PMC3369825* *joint corresponding/senior authors
- **Yamada, S.** and **Nelson, W. J**. (2007). Localized Rho activation regulates actomyosin contraction and compaction of epithelial cell-cell adhesion. *J. Cell Biol.* **178**, 517-527**.** *PMCID: PMC2064836*
- **Perez, T.,** Tamada, M., Sheetz, M. P. and **Nelson W. J.** (2008). Hierarchical organization of immediate-early signaling events regulating E-cadherin cell-cell adhesion. *J. Biol. Chem.* 282, 5014-5022*. PMCID: PMC3372897*
- Zhang, Y., Sivisankar, S., **Nelson, W. J**., Chu, S (2009). Resolving cadherin interactions and binding cooperativity at the single molecule level. *Proc. Natl. Acad. Sci (USA).* **106,** 109-114. *PMCID: PMC2629205*
- **Benjamin, J., Kwiatkowski, A.,** Yang, C., Korobova, F., Pokutta, S., Svitkina, S., Weis, W. I. and **Nelson, J.** (2010). αE-catenin regulates actin dynamics independently of cadherin-mediated cell-cell adhesion. *J. Cell Biol.* **189**, 339-352**.** *PMCID: PMC2856910*
- **Borghi, N., Lowndes, M.** Maruthamuthu, L., Gardel, M. L. and **Nelson, W. J.** (2010). Regulation of cell motile behavior by crosstalk between cadherin- and integrin-mediated adhesions. *Proc. Natl. Acad. Sci. (USA).* **107**, 13324-13329. *PMCID: PMC2922157*
- **Kwiatkowski, A. V.,** Maiden, S. L., Pokutta, S., Choi, H. J., **Benjamin, J. M.,** Lynch, A. M., **Nelson, W. J*.,** Weis, W. I*. and Hardin, J*. **(**2010). In vitro and in vivo reconstitution of the cadherin-catenin-actin complex from Caenorhabditis elegans. *Proc Natl Acad Sci (U S A).* **107**, 14591-14596. *PMCID: PMC2930443* *joint corresponding/senior authors

• **Harris, E.** and **Nelson, W. J.** (2010). APC regulates endothelial cell migration independent of roles in β-catenin signaling and cell-cell adhesion. *Mol. Biol. Cell.* **21**, 2611-23. *PMCID: PMC2912348*
• **Kitt, K. N.** and **Nelson, W. J.** (2011). Rapid suppression of activated Rac1 by cadherins and nectins during de novo cell-cell adhesion. *PLoS One*. **6**, e17841. *PMCID: PMC3055898*
• **Schepis, A.,** Sepich, D. and **Nelson, W. J.** (2012). αE-Catenin regulates cell-cell adhesion and membrane blebbing during Zebrafish gastrulation. *Development* **139**, 537-546*. PMCID: PMC3252354*
• **Hartsock, A.** and **Nelson, W. J.** (2012). Competitive regulation of E-cadherin juxtamembrane domain degradation by p120-catenin binding and Hakai-mediated ubiquitination. *PLoS One.* **7**, e37476. *PMCID: PMC3365061*
• **Borghi, N., Sorokina, M.,** Shcherbakova, O. G., Weis, W. I., Pruitt, B. L., **Nelson, W. J.** and Dunn, A. (2012). E-cadherin is under constitutive actomyosin-generated tension that is increased at cell-cell contacts upon externally applied stretch. *Proc. Natl. Acad. Sci. USA.* **in press.** *PMCID: in progress*

D. CURRENT SUPPORT

NIH GM35527-26 (P.I. Nelson) 04/01/03-03/31/13 (MERIT AWARD)
35% effort
Topogenesis of Na/K-ATPase in Polarized Epithelial Cells
The goals of the work were to define mechanisms involved in protein trafficking to nascent basolateral membrane domains, to examine early stages in the organization of cadherin cell adhesion complexes and vesicle trafficking machinery during cell-cell adhesion.
This is application is a renewal of this Award

NIH 1U01GM094663-02 (Co-PIs. Liddington, Nelson) 7/1/10-6/30/15
15% effort
Assembly, dynamics and evolution of cell-cell and cell-matrix adhesions
The goals of the Nelson project are to examine the evolution of α-catenin from Dictyostelium to mammals, to define similarities and differences in the interactions of evolutionarily diverse α-catenin with the cadherin/β¬catenin complex and the actin cytoskeleton, and to obtain structures of α-catenin for making chimeric proteins to test protein domains in different organisms.
No scientific or budgetary overlap

NSF EFRI-MIKS (Co-PIs Pruitt, Nelson, Dunn, Weis) 07/01/11-06/30/14
10% effort
Force Sensing and Remodeling by Cell-Cell Junctions in Multicellular Tissues
The goals of the Nelson project are to use force sensors to determine how mechanical forces at cell-cell contacts are transmitted from the outside to the inside of the cell.
No scientific or budgetary overlap

PENDING SUPPORT

NIH PO1 GM102089-01 (Co-PIs Beachy, Nachury, Nelson) 4/01/13-09/30/18
10% effort
Mechanisms of cilium-based signaling
The goals of the Nelson Project are to analysis septin localization and dynamics, to define protein interactions with septins at the diffusion barrier, and test the role of septin and associated proteins as a diffusion barrier.
No scientific or budgetary overlap

COMPLETED SUPPORT NIH GM 78270-04 (P.I. Nelson) 11/01/06-10/30/10
20% effort
Regulation of Cell Migration by the APC-Microtubule Complex
The goal of the work was to understand the mechanism(s) by which adenomatous polyposis coli (APC) regulate microtubules and cell polarization during directional cell migration in response to extracellular signals