

In addition to analyzing electrical responses to external force *in vivo*, we have taken the first steps toward reconstructing this ion channel complex in *Xenopus* oocytes. So far, we have bypassed the need for mechanical gating by studying a constitutively active mutant channel (the “d” form). Coexpression of MEC-4d and MEC-10d produces a constitutively active current that, like native MRCs (7), is carried by Na⁺ and blocked by amiloride (12). By contrast with native MRCs, however, neither MEC-2 nor MEC-6 was required to produce detectable channel activity in oocytes (12, 13). Both accessory proteins increased activity of expressed MEC-4d/10d channels at least tenfold without inducing a detectable increase in surface expression of either MEC-4 or MEC-10 (12, 13), which suggests that MEC-2 and MEC-6 increase single-channel conductance or open probability. Preliminary studies of single MEC-4d/10d channels suggest that neither MEC-2 nor MEC-6 significantly increases single-channel conductance, however (14). Additional studies of both expressed and native channels are needed to clarify the function of these accessory proteins in mechanotransduction.

By demonstrating that native MRCs require intact copies of *mec-4*, *mec-10*, *mec-2*, and *mec-6*, we show that each of these four genes is required for the first step in mechanotransduction—namely, activation of sensory mechanotransduction channels. Such channels may be directly gated by mechanical energy, because MRCs can be detected within 1 ms of stimulation. Because both *C. elegans* touch receptor neurons and mammalian Pacinian corpuscles respond preferentially to changes in force (7, 8), we speculate that DEG/ENaC channels could be sensory mechanotransduction channels in nonciliated mechanoreceptor neurons in nematodes and mammals alike. These initial studies raise new questions, such as: How do touch receptor neurons detect changes in force while remaining insensitive to continuous force application? How is force transferred from the worm’s cuticle to transduction channels? What determines sensitivity? A better understanding of the answer to this last question could lead to improved diagnosis and treatment of sensory neuropathy.

References

1. Centers for Disease Control and Prevention, “National diabetes fact sheet: General information and national estimates on diabetes in the United States” (U.S. Department of Health and Human Services, Centers

for Disease Control and Prevention, 2004).
 2. E. D. Adrian, *J. Physiol.* **61**, 49 (1926).
 3. E. D. Adrian, Y. Zotterman, *J. Physiol.* **61**, 151 (1926).
 4. M. Chalfie *et al.*, *J. Neurosci.* **5**, 956 (1985).
 5. G. G. Ernmstrom, M. Chalfie, *Annu. Rev. Genet.* **36**, 411 (2002).
 6. M. B. Goodman, D. H. Hall, L. Avery, S. R. Lockery, *Neuron* **20**, 763 (1998).
 7. R. O’Hagan, M. Chalfie, M. B. Goodman, submitted.
 8. M. Mendelson, W. Loewenstein, *Science* **144**, 554 (1964).
 9. H. Suzuki *et al.*, *Neuron* **39**, 1005 (2003).

10. R. C. Hardie, *J. Exp. Biol.* **204**, 3403 (2001).
 11. M. Huang, M. Chalfie, *Nature* **367**, 467 (1994).
 12. M. B. Goodman *et al.*, *Nature* **415**, 1039 (2002).
 13. D. S. Chelur *et al.*, *Nature* **420**, 669 (2002).
 14. A. L. Brown, M. B. Goodman, unpublished data.
 15. The research described here is the happy result of excellent collaborations with scientists at the University of Oregon, Columbia University, and Stanford University. It would not have been possible except by working jointly. I thank all of you. Research in my lab is supported by fellowships from the Alfred P. Sloan Foundation, the Donald B. and Delia E. Baxter Foundation, and a grant from the National Institute of Neurological Disorders and Stroke.

2004 Grand Prize Winner

Dr. Miriam B. Goodman grew up in Lexington, Massachusetts, and Bethesda, Maryland. As a high school student, she worked in research labs at the National Institutes of Health where she wrote scientific software. She earned a bachelor’s degree in Biochemistry from Brown University in 1986. As a graduate student in neurobiology at the University of Chicago, she analyzed voltage-dependent ion channels that tune vertebrate hair cells. After being awarded her Ph.D. in 1995, she pursued postdoctoral work in *C. elegans* neurophysiology and genetics at the University of Oregon and Columbia University. Currently, Dr. Goodman is an Assistant Professor of Molecular and Cellular Physiology at Stanford University. Work in her laboratory focuses on delineating the molecular events that give rise to the sense of touch. Outside the laboratory, Dr. Goodman enjoys cooking with friends, hiking, rock-climbing, and going to the movies. Though currently sidelined, Dr. Goodman has also played soccer since age 8.



Finalists



Kang Shen, for his essay “Synaptic Matchmakers: Molecular Mechanisms of Synaptic Specificity.” Dr. Shen was born and raised in Wuhan, China. He studied clinical medicine at Tongji Medical University of China. After graduating in 1994, he joined the graduate program at Duke University, where he studied the spatial and temporal control of CaMKII localization in hippocampal neurons in the laboratory of Dr. Tobias Meyer. After receiving his Ph.D. in 1999, he pursued postdoctoral work in Dr. Cornelia Bargmann’s lab at the University of California, San Francisco, where he addressed the question of synaptic specificity, using *C. elegans* as a model system. Dr. Shen started his own lab at Stanford University in 2003, focusing on understanding molecular mechanisms of synaptic target specificity. Outside of the laboratory, Dr. Shen enjoys a variety of sports and outdoor activities.

Qin Shen, for her essay “Preventing Aging in Neural Stem Cells: Regulating Asymmetric Versus Symmetric Cell Divisions.” Dr. Shen was born and grew up in China. She earned her Bachelor’s degree in Pharmacology from Shanghai Medical University in 1991. In 1996, she entered the graduate program in Neuroscience at Albany Medical College, New York, under the guidance of Dr. Sally Temple, who specializes in neural stem cell development. Her Ph.D. project, completed in 2001, focused on asymmetric cell division and the generation of cell diversity in the embryonic murine cerebral cortex. She is now a postdoctoral fellow in Dr. Temple’s laboratory working on mechanisms regulating neural stem cell self-renewal and cell fate choices, including interactions between neural stem cells and endothelial niche cells. The mother of a toddler, Dr. Shen also carves out a little time for gardening and reading.



For the full text of essays by the finalists and for information about applying for next year’s awards, see *Science Online* at <http://www.sciencemag.org/feature/data/prizes/ependorff/eppenprize.shtml>