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We are using the nematode Caenorhabditis elegans to investigate aspects of nerve cell development and function. The wealth of developmental, anatomical, genetic, and molecular information available for C. elegans provides a powerful and multifaceted approach to these studies. Our work has focused on the study of a set of six neurons that are the sensory receptors for gentle touch (the touch cells), to address two questions: 1) How is neuronal cell fate determined? and 2) What is the molecular basis of mechanosensation, a sensory modality that underlies a variety of senses(e.g., touch, hearing, and balance)? We also work on neuronal degeneration, microtubule structure and function, and channel structure and function. Facilitating these studies is the development of new experimental methods, such as Green Fluorescent Protein and reconstituted GFP as gene and protein markers, a two component system (recCaspase) to selectively kill particular cells, and method to generate temperature-sensitive strains for virtually any C. elegans gene.

We initially approached touch cell development by mutational analysis, obtaining more than 450 mutations (in 17 genes) that produce a touch insensitive phenotype. These touch genes are needed for the generation, specification, and function of the cells. The first two groups contain genes that regulate touch cell development, and the last group (function) contains genes that are developmental targets of this regulation. Many of the genes that regulate touch cell differentiation are transcription factors. In addition we have identified seven other genes that in combination with these genes specify the number and differentiation of the touch cells. Twelve touch genes are needed for touch cell function. Using genetics, molecular biology, and electrophysiology, we have identified a transduction channel complex with proteins encoded by four of these genes that underlies the touch response in these cells. Two of the proteins, MEC-4 and MEC-10, form the pore of the channel; the other two proteins, MEC-2 and MEC-6 are associated with the pore-forming proteins and are essential for channel activity. MEC-2 is of particular current interest because it is part of a large family of cholesterol-binding proteins. The channel complex is localized as puncta along the touch receptor neuron process. This localization requires components in the extracellular matrix. Two of these components, MEC-1 and MEC-9 are made the touch cells; a third, the collagen MEC-5, is not.

We are currently studying how these and other genes expressed in these cells act to transduce touch. Our current model is that the channel complex is associated with the extracellular matrix. This tethering can lead to movement of the complex in the membrane leading to its opening.

MedLine Listing of Dr. Chalfie's Publications

Representative Recent Publications

Huber, T. B., et al. (2006) Podocin and MEC-2 Bind Cholesterol to Regulate the Activity of Associated Ion Channels Proc. Natl. Acad. Sci. USA 103: 17079-17086.
Chelur, D., and Chalfie, M. (2007) Targeted cell killing by reconstituted caspases Proc. Natl. Acad. Sci. USA 2283-2288.
R. O'Hagan, M. Chalfie, and M. B. Goodman (2005) The MEC-4 DEG/ENaC channel of C. elegans touch receptor neurons transduces mechanical signals. Nature Neuroscience 8: 43-50. Article
S. Zhang, C. Ma, and M. Chalfie. (2004) Combinatorial marking of cells and organelles with reconstituted fluorescent proteins. Cell 119: 137-144. Article
S. Zhang, J. Arnadottir, C. Keller, G. A. Caldwell, C. A. Yao, and M. Chalfie. (2004) MEC-2 is recruited to the putative mechanosensory complex in C. elegans touch receptor neurons through its stomatin-like domain. Curr. Biol. 14: 1888-1896. Article
L. Emtage, G. Gu, E. Hartwieg and M. Chalfie (2004) Extracellular proteins organize the mechanosensory channel complex in C. elegans touch receptor neurons. Neuron 44: 795-807. Article
Chelur DS, Ernstrom GG, Goodman MB, Yao CA, Chen L, O' Hagan R, Chalfie M (2002) The mechanosensory protein MEC-6 is a subunit of the C. elegans touch-cell degenerin channel Nature 420: 669-73. Article
Ernstrom GG, Chalfie M. (2002) Genetics of sensory mechanotransduction. Annu Rev Genet. 36: 411-53. Article
Goodman MB, Ernstrom GG, Chelur DS, O'Hagan R, Yao CA, Chalfie M. (2002) MEC-2 regulates C. elegans DEG/ENaC channels needed for mechanosensation Nature 415(6875): 1039-42. Article