

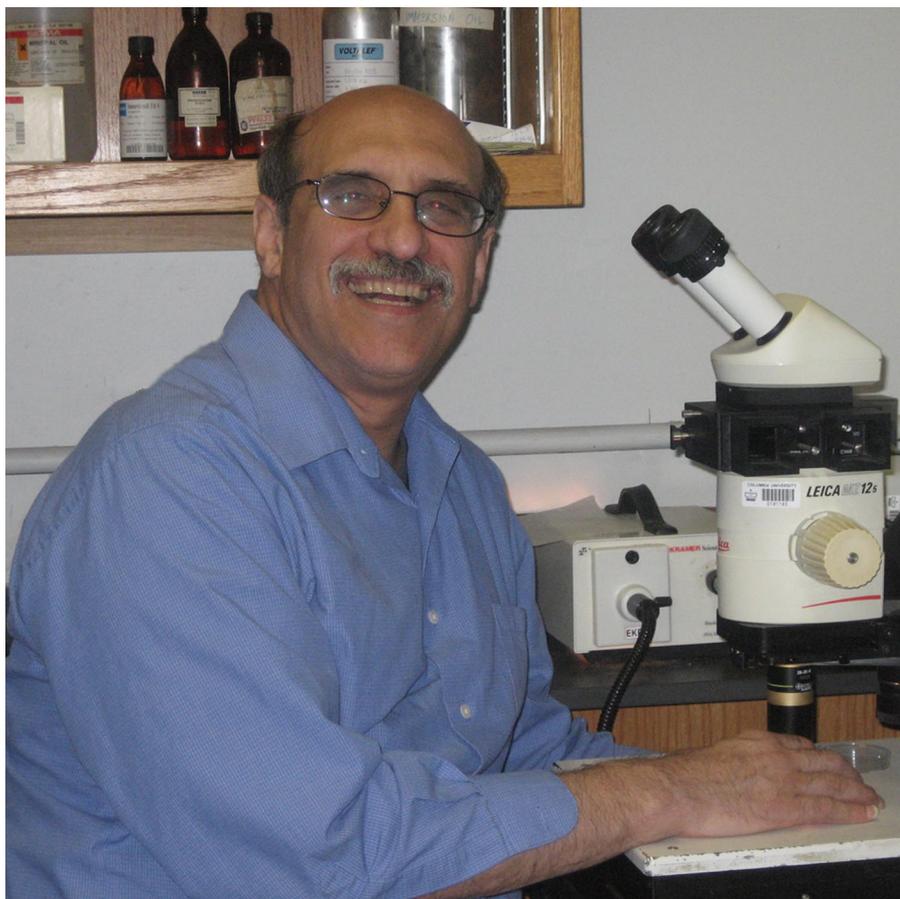
## Profile of Martin Chalfie

Despite having a bad reputation, cholesterol is an essential component of the plasma membranes of animal cells, where it is thought to modulate the properties of the lipid bilayer. Cholesterol can also bind directly to proteins in the membrane. In his Inaugural Article published in 2006, Martin Chalfie, the William R. Kenan, Jr., Professor of Biological Sciences at Columbia University (New York), in collaboration with Thomas Benzing (University of Cologne, Germany), identified a new class of cholesterol-binding proteins among the prohibitin (PHB)-domain protein family (1). PHB-domain proteins appear to regulate a variety of membrane functions, from cell signaling to mechanosensation. Studying two members of the family, MEC-2 and Podocin, Chalfie, Benzing, and their colleagues found that cholesterol is crucial for the activity of two different classes of channel proteins to which the PHB-domain proteins bind. They suggest that the binding of cholesterol by the PHB-proteins alters the local lipid environment of associated membrane proteins and changes their activity.

### Questioning Research

Chalfie, born in 1947 and elected to the National Academy of Sciences in 2004, grew up in Chicago. As a child, all elements of science interested him, but he feels his early activities were somewhat mundane. “Unfortunately, I did not have that real indicator of a career in science that many of my friends have. I did not make explosives and almost destroy my home,” he says. As a child, he cut out newspaper comics about nature for a scrapbook and, in high school, participated in a weekly science club after school. “I was fairly good at science in school,” he recalls. “That was the positive reinforcement to keep me going.” Chalfie entered Harvard University (Cambridge, MA) in 1965 and thought that he would major in math. He soon switched gears. “I was attracted to biochemistry because I could do a little bit of everything: chemistry, math, and biology,” he explains. “The subject also seemed new and exciting.”

During his junior year, Chalfie took a cell physiology class with Woody Hastings, but Chalfie could not register for the laboratory portion and wrote a paper instead. The subject, the role of cyclic AMP (cAMP) in sodium transport in the toad bladder, would later spark an idea that led to Chalfie’s first published research article. In the meantime,



Martin Chalfie

Hastings provided Chalfie with one of his fondest memories of Harvard. “I never seemed to be able to get to the biology library when it was open, so I asked Woody for permission to get a library key for late night reading,” he recalls. “Most of my professors seemed very distant, so I was amazed when he got up from his desk, walked down four flights of stairs to the library office, and said, ‘Give this boy a key.’ I’ve since learned that this kindness was characteristic of him.”

Chalfie spent the summer after his junior year working in the laboratory of Klaus Weber at Harvard. Chalfie set out to study the active site of aspartate transcarbamylase, but “although I kept trying to do the experiments, I failed miserably all summer,” Chalfie says. “I decided I shouldn’t be in science.” So for his senior year, Chalfie took the last required course for the biochemistry major and then other courses that interested him, including law, theater, and Russian literature.

After graduating in 1969 and still unconvinced about a career in research,

Chalfie took a series of short-term jobs, including a stint selling dresses for his parents’ dress manufacturing business in Chicago. In 1970 he began teaching high school at Hamden Hall Country Day School (Hamden, CT).

Chalfie took the advice of a fellow teacher and applied to work in the laboratory of Jose Zadunaisky at Yale University (New Haven, CT) during the summer of 1971. During the initial interview, Zadunaisky told Chalfie about his work measuring chloride transport in the frog cornea by using an Ussing chamber. “I thought about the paper I had written for Woody Hastings, and forgetting that that research involved sodium, not chloride, transport, toad and not frog, and bladder and not cornea—although it did measure transport with a Ussing chamber—I tried to impress Jose by asking if cAMP was involved,” Chalfie recalls. “He liked the

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