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## 1999

### Daniel Goodenough

Dan Goodenough was a "faculty brat" at Yale, where his father was a prominent historian. When he was 14, he left New Haven to attend the Groton School in Massachusetts, determined to become an architect.

Goodenough went to Harvard in 1962, where he pursued his love of drawing and buildings and majored in architecture. But by his junior year he found to his dismay that he "had no talent at all" for architecture. At this time, his sister, Ursula Goodenough, was a grad student in Keith Porter's lab at Harvard, and her example influenced him to switch majors to biology. Besides, he reflects, "academic life was bred in the bone and [he] couldn't get away from it."

Ursula Goodenough remembers that while she hadn't taken much science in high school, her brother had, so there was "an interesting synergy when he moved from humanistic subjects to the sciences." As an undergraduate, he joined a research project studying olfactory ciliary regeneration with Sergei Sorokin in the Anatomy Department chaired by Don Fawcett, the ASCB's first president. There, Goodenough gravitated to electron microscopy and enjoyed interaction with other members of the then small anatomy department. Having only recently started studying biology in earnest, Goodenough admits that he "wasn't a very attractive Ph.D. candidate," and was declined admission to every graduate program where he applied except Harvard. The admission gained him not just an advanced education but also a student draft deferment, allowing him to avoid Vietnam. Goodenough insists that had school not protected him, he would have followed friends to a commune in Canada to keep from going to war.

Happily for him, in the mid-60's, most anatomy departments, including Harvard's, were deeply engaged in cell biology research. "The great excitement at that time was the opening offered into the subcellular world by the electron microscope and by following in the steps of DeDeuve, Claude and Palade to combine biochemistry with the ultracentrifuge to fractionate cells and figure out what the organelles were doing," Goodenough recalls. He worked for Jean-Paul Revel, who had just described the gap junction as intercellular interaction distinct from the tight junction. Goodenough recalls that Revel was a "magical" teacher after whom Goodenough modeled himself. With Revel, Goodenough sought to isolate the gap junction, work he continues to pursue today. His thesis work was on liver cell subcellular fractionation. At the time, he explains, "there was no assay for the gap junction other than its structure. The only way to isolate the junction was to use standard methods of rate sedimentation and sucrose density fractionation and to assay the resulting fractions by electron microscopy: a tedious process." His key insight at that time was that gap junctions were insoluble in certain detergents that would solubilize most other membrane structures. This led to the conclusion that it would be possible to purify the junctions and study their protein composition and structure.

In 1970, Goodenough was awarded a National Science Foundation post-doctoral fellowship to study at the Cardiovascular Research Institute at UCSF. There he worked in Walther Stoeckenius' lab. Stoeckenius was engaged in pioneering studies on the purple membrane from *Halobacterium halobium*, but he allowed Goodenough to continue his work on the gap junction. During the year with Stoeckenius, Goodenough "developed a method to purify the junctions from mouse liver, and was able to demonstrate (for the first time) that the junction was formed of one principle protein, dubbed connexin." He was also the first to "obtain x-ray diffraction patterns of isolated junctions, and demonstrate the feasibility of studying the molecular structure of the junction's integral membrane protein using crystallographic techniques." Some 100 mice or 36 rats had to be used for each experiment, since the gap junctions were a relatively small proportion of the cell surface area.

When Revel left Harvard for Cal Tech, Fawcett recruited Goodenough to fill Revel's position at Harvard. Aside from familiarity, a particular attraction to returning to Boston was a collaboration with Don Caspar, who was then at the Dana Farber Cancer Institute. As it turned out, the two ended up neighbors in Brookline. Goodenough would bicycle samples home, which Caspar would put in his refrigerator and take to his lab the next day. Caspar says of their collaboration that it was "a tremendously wonderful experience. Dan is a marvelous person and it was very rewarding to work with him." He continues to admire not only Goodenough's scientific work, but what he has done for medical education at Harvard Medical School. The collaboration led to a low-resolution three-dimensional model of the intercellular channel.

Goodenough continued his study of gap junctions, trying to determine "what complex functions emerge due to the interactions of groups of cells which single cells cannot do." Today, his lab focuses on targeted gene knockouts of members of the connexin gene family in mice. These studies have revealed roles for gap junctional communication in the development of the ovarian follicle, in electrical conduction through the bundle of His, and on homeostasis and growth of the eye lens. Currently, he is interested in a knockout of a new neuron-specific connexin which is expressed in the retina. "This may lead to discoveries in... visual acuity or dark adaptation," Goodenough explains hopefully.

Goodenough also continues his work with the tight junction. This project was difficult to get started because the tight junction resisted many attempts at biochemical purification. Together with Bruce Stevenson, Janet Siliciano and Mark Mooseker, he finally "got his foot in the door" by using a monoclonal antibody approach, allowing him to identify one of the proteins that is part of the tight junction.

Goodenough is widely recognized for his excellence as a teacher. Since 1976, he has won eleven teaching awards, including the Harvard Medical School Faculty Prize for Excellence in Teaching and several appreciation awards by medical school classes. Goodenough's devotion to teaching requires that he "basically work two jobs," but he believes that the level of effort is incumbent on someone who has been given "an enormous amount of privilege." Goodenough carries the forbidding title of the Master of the Oliver Wendell Holmes Society at Harvard, which gives him a central role in the overall medical curriculum planning as well. Of her brother's involvement with students, Ursula Goodenough reflects affectionately that he has "an unbelievable depth of kindness."

Goodenough has sought to reach beyond the typical science classes in medical education. He helped develop and teaches a course on Human Health and Global Environmental Change and he is also developing a new course on Cultural Competence in Medicine, in which students are encouraged to think about their own ethnicity and race and the cultural rules and biases that they bring to the practice of medicine. The third unconventional class he teaches is called Living with Life-Threatening Illness. In this course, students are assigned to a patient who has a terminal diagnosis. The students engage in a relationship with "their" patient and learn from them about the experience of their illness and their medical care. The patients thus teach about their experience of living with a life-threatening illness.

Jennifer Ehlin, a student of Goodenough says, "[he] is one of the best instructors I have ever had the privilege of learning from. He has an exceptional knack for explaining things so they instantly make a tremendous amount of sense... He also showed extreme amounts of patience. We could not start off our medical school journey with a better teacher."

Goodenough joined the ASCB as soon as he entered graduate school in 1968. At his first ASCB meeting, he remembers being star-struck by those present. He gave his first talk the following year, and still recalls the sense of terror he felt about giving the presentation. Some years later, Goodenough served on the ASCB Council. Later, when his sister was President, she asked him to serve as Chair of the Nominations Committee. He currently serves on the Editorial Board of the *Molecular Biology of the Cell*.

Goodenough and his wife Carol have been married for 31 years. Carol is a social worker at the Brookline Community Mental Health Center, where she specializes in family therapy. The Goodenoughs have two daughters, Sophie, 27, and Abigail, 24, who, like their mother, work in human services – Sophie with disabled toddlers in St. Petersburg, Florida, and Abigail at the Covenant House in New York, with homeless teenagers. The Goodenoughs often retreat to their cabin in the mountains of New Hampshire. It is on an old blueberry farm with no water or electricity. There, Goodenough reads, cuts wood, hikes and swims in the river. Although he claims he is not an outdoorsman, in the winter they hike in on snowshoes when the roads are closed, to stay the weekend.