

## Paul F. Cranefield Award to Tzyh-Chang Hwang



Paul F. Cranefield, M.D., Ph.D., was the Editor of *The Journal of General Physiology* for 30 years, from 1966 to 1995. During this time, he worked incessantly to further the mission of the journal: to promote and publish studies at the interface between biology, chemistry, and physics to obtain insights

into fundamental mechanisms that underlie biological function at all levels.

When Paul stepped down as Editor, the Council of the Society of General Physiologists discussed how best to acknowledge his numerous contributions to *The Journal* and thus to the Society. In the end it was decided to institute a Paul F. Cranefield Award, which should go to a young investigator who in the preceding year had published an article of exceptional quality in *The Journal*. The award would be given at the Annual Meeting and Symposium of the Society, which takes place in Woods Hole, Massachusetts. It also was decided that the criteria for selecting the awardee should be so stringent that the award might not be given every year.

I am pleased to say that despite these high standards, there were several outstanding candidates. One of these stood out, namely Tzyh-Chang Hwang from the Department of Physiology and Biophysics at the University of Missouri-Columbia. He accepted the Award at the September 2000 meeting of the Society.

Dr. Hwang received his Ph.D. from Johns Hopkins University, where his thesis research was on the properties of epithelial anion channels and the cystic fibrosis transmembrane conductance regulator (CFTR) in particular. His postdoctoral training was at The Rockefeller University, where he focused on the regulation

of CFTR function, which turns out to be much more complicated than is the case for the channels involved in cellular electrophysiology. CFTR possesses two nucleotide-binding domains as well as a regulatory domain with multiple phosphorylation sites. These domains are important for normal channel function because not only is phosphorylation of the CFTR required for channel activation, but also normal channel opening itself depends on the hydrolysis of ATP. However, the relationships that exist between ATP hydrolysis and channel gating have been extraordinarily difficult to define. First, because the pattern of channel gating varies with the protein's phosphorylation state, which means that it becomes a challenge to examine the gating properties of a homogeneous channel population. Second, because ATP binding and hydrolysis at either of the two nucleotide binding domains, in principle, can control channel gating. The puzzle has yet to be solved; but, Dr. Hwang and his colleagues have provided important information about the gating mechanisms of CFTR based on quantitative analyses of the ATP dependence of openings and closings in native channels as well as channels with mutated nucleotide domains.

In an article published in the April 1999 issue of *The Journal*, Dr. Hwang and his colleagues (S. Zeltwanger, F. Wang, G.-T. Wang, and K.-D. Gillis) provided the first direct evidence (in the form of a maximum in the closed-time probability density function) for the presence of irreversible steps in the gating of CFTR channels, which is consistent with gating being controlled by cycles of ATP hydrolysis. In addition, the article provided novel evidence supporting the existence of two kinetically distinct open states of a CFTR channel: one involving ATP binding and hydrolysis at only one of the nucleotide binding domains; and one involving ATP binding and hydrolysis at both nucleotide binding domains. The gating is indeed complicated and, together, these results serve as benchmarks for further studies of CFTR gating. We were most pleased to publish this work.