Paul F. Cranefield Award to Tsung-Yu Chen

The late Paul F. Cranefield, M.D., Ph.D. was the Editor of the Journal of General Physiology for 30 yr, 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 in order to obtain insights into fundamental mechanisms that underlie biological function at all levels.

When Dr. Cranefield 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, MA. 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 many outstanding candidates. One stood out, namely Tsung-Yu Chen from the Center for Neuroscience at University of California, Davis, who has made many important contributions toward understanding the function of the ClC family of anion permeable channels. Dr. Chen accepted the Award at the September, 2004, meeting of the Society.

Dr. Chen received his M.D. and M.S. from National Yang-Ming Medical College, Taiwan. He then came to the US, where he received his Ph.D. from Johns Hopkins University, where he worked in the laboratory of King-Wai Yau and studied the Ca^{2+}-calmodulin modulation of cyclic nucleotide-gated cation channels. He received his post-doctoral training with Chris Miller at Brandeis University, where he began his studies on the ClC family of anion channels. Dr. Chen initially focused on the nonequilibrium, permeant ion-dependent gating of the ur-ClC, ClC0 isolated from *Torpedo* electroplax. The gating of ClC channels differs fundamentally from the gating of voltage-dependent cation channels, as the channels are double-barreled pores that can gate in two different modes: a slow mode, involving a common gate that controls both barrels; and a fast mode, involving the individual barrels, in which the major source of the voltage-dependent gating is Cl^- movement through the pore, as demonstrated by Dr. Chen.

Since this seminal work, Dr. Chen has strived to understand the basis for this tantalizing gating mechanism. Last year he (with M.-F. Chen, and C.-W. Lin) published three landmark articles in *The Journal of General Physiology*, in which he used the x-ray structure {Dutzler MacKinnon 2002} of CLC-ec1, a bacterial ClC homologue from *Escherichia coli* as the starting point for an unusually comprehensive study of the ion permeation and gating properties of ClC0. We now know that the bacterial homologue is not an ion channel but an H^+/Cl^- exchanger, but ClC-ec1 turned out to be a most valuable tool for deciphering the intricacies of ClC0 permeation and gating. Most importantly, the ClC-ec1 structure provided the framework that allowed Dr. Chen and his collaborators to conclude that the ion selectivity is controlled relatively simply by electrostatic interactions between the permeant ions and key pore-lining residues. Moreover, a systematic cysteine mutagenesis study allowed Dr. Chen and colleagues to provide important limits on where the gate controlling ion permeation through the pore should be localized, namely extracellular to the selectivity filter.

These conclusions were obtained through a dedicated effort that involved a rigorous experimental design in which the permeant ion concentration was altered by two orders of magnitude (a technical feat) and an unusually rigorous approach to the data analysis and interpretation. We were most pleased to publish these articles, which firmly establish Dr. Chen as a leader in anion channel research.

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