Introducing Samuel M. Wu, the 2009 Recipient of the Friedenwald Award

It is a great pleasure to introduce Dr. Samuel M. Wu, the 2009 recipient of the Jonas Friedenwald award. Over the past 30 years, Sam's research has pioneered investigations on rod and cone photoreceptor interactions and parallel information-processing pathways in the retina. His studies have focused largely on the detailed molecular, cellular, and synaptic mechanisms underlying light-evoked signal processing in the retina, as well as the synaptic mechanisms underlying eye diseases. He has made discoveries on how individual ion channels, neurotransmitters, and gene products mediate synaptic function and retinal dysfunction and has developed several mouse models for retinal diseases such as retinitis pigmentosa, glaucoma, and macular degeneration.

At one level, his laboratory has performed meticulous cell-by-cell and synapse-by-synapse analyses of individual functional pathways throughout the retina. At the same time, however, he has also been able to transform his individual findings into a broader conceptual framework by integrating results from many species to derive general, cross-species principles of retinal synaptic operations, as you will hear in his presentation.

Sam received a bachelor's degree in physics and biophysics from the University of California, Berkeley, in 1973 and later did his doctoral training with John Dowling, receiving a PhD in biophysics from Harvard University in 1979. He then trained for 3 years as a postdoctoral fellow in neurobiology at my laboratory at UC Berkeley. After that training, he joined the faculty of Baylor College of Medicine in Houston 1982, where he is currently a professor of ophthalmology, neuroscience, and molecular physiology and biophysics, and holds the Camille and Raymond Hanks Chair in Ophthalmology. He is also the recipient of many awards, but if I were to list them, I wouldn't have time to tell you more about his achievements in retinal research.

Sam's work falls into three main categories: photoreceptor network and signaling, stratum-by-stratum organization of the inner retina, and retinal disease models.

**Photoreceptor Network and Signaling**

Sam's laboratory has discovered that rod-cone coupling was modulated by light, so that rods and cones can process signals independently under dark-adapted conditions and they mix signals at higher background levels. Sam characterized an intrinsic current in rods and cones that shapes the response mediated by specific HCN1 channels. These are the channels responsible for the complex dynamics of the rod network. Finally, he and his coworkers discovered a rod→HC→cone sign-inverting synaptic pathway, possibly representing one mode of the HC-to-cone feedback synaptic transmission.

Sam and his group have upset what we thought was a simple dichotomy between amphibian and mammalian vertebrates. We had thought that bipolar cells in amphibians receive mixed rod/cone inputs but that those in mammalians receive segregated inputs from rods and cones. But Sam’s laboratory has shown that bipolar cells in dark-adapted salamander retinas can be rod- or cone-dominated and that in the mouse retina, some cone-bipolar cells receive direct rod inputs and some rod bipolar cells receive direct cone inputs.

**Stratum-By-Stratum Organization of the Inner Retina**

His group identified stratum-by-stratum rules for correlating salamander BC light response characteristics with the patterns of axon terminal ramification in the IPL. Remarkably, they also found that such stratum-by-stratum rules are applicable, not only in amphibians, but also to bipolar cells in the mouse retina.

Recently, Sam’s laboratory also found that the antagonistic receptive fields of rod-dominated, cone-dominated, and mixed bipolar cells are mediated by different synaptic circuitry, thereby allowing for flexibility in function-specific modulation of bipolar cell receptive fields and contrast sensitivity under different lighting conditions.

**Retinal Disease Models**

Sam has now performed functional and anatomic analyses of several mutant and disease mouse models and has unraveled mechanisms and time courses of how gene mutations and diseases alter retinal function and synaptic organization. These include mouse models for cone-rod and rod-cone dystrophies and congenital stationary night blindness.

His group used a laser-induced acute glaucoma model to identify early signs of glaucomatous damage in the retina. They recently found that the earliest sign of human glaucoma (loss of general sensitivity) may be mediated by defects at the rod bipolar cell-AII amacrine cell synaptic level.

Overall, Sam has been a constant and highly visible contributor to ARVO. His work is known and admired for its outstanding contributions in characterizing synaptic interactions at the inner and outer retina and for setting the highest standards within our vision research community for retinal systems analysis.

So, fasten your seatbelts for a roller coaster ride through the retina, following many of Sam’s important discoveries.

Frank Werblin