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Biophysicist in Profile

Clara Franzini-Armstrong

"It has been said that anyone can be replaced, and in most instances this is true. However, this is not the case with Clara," says Paul Allen about collaborator Clara Franzini-Armstrong, Professor Emerita in the Department of Cell and Developmental Biology at the University of Pennsylvania's School of Medicine. Allen, Professor of Anesthesia at Brigham and Women's Hospital in Boston, continues, "My colleagues and I dread the day that Clara will eschew her microscope and lab to spend full time enjoying life and her grandchildren."

The "irreplaceable" Franzini-Armstrong's long and accomplished career in science was birthed in the "Cradle of the Renaissance," Firenze, Italy. Born a year before the start of World War II, she vaguely remembers spending the worst of the wartime in a hill village. Her idyllic postwar childhood included "long leisure periods in beautiful settings like the Dolomites, competing with my brothers on strenuous mountain hikes, my twin brother's protection and affection, and roller skating in Piazzale Michelangelo, overlooking the whole majestic city."

Life wasn't all play; Franzini-Armstrong also studied hard. Her parents were first-generation scientists, but for her and her three brothers, a career in science seemed a natural choice. Their father, an atomic physicist, loved teaching - including his children. Their mother, one of few women then with a physics degree, did not pursue a science career but encouraged her daughter to do so. "She gave me total equality with my brothers in all academic questions," says Franzini-Armstrong. Her brother Paolo became a particle physicist, Carlo a medical doctor who assembled the first interference microscope in Pisa, and Marco an accomplished mineralogist.

Franzini-Armstrong enrolled in the biological sciences program at the University of Pisa in 1956. At Pisa, she gained three life-changing opportunities. First, the Ministry of Education gave the first electron microscope to the University. Pathology Department Chair Puccinelli "handed me a book, sent me to Rome for a few days to visit an EM lab, and gave me the charge of learning electron microscopy," she says. She wrote the first EM thesis in Pisa.

Later, Pellegrino urged Franzini-Armstrong to observe changes induced by denervation on skeletal muscle-and she has done electron microscopy of skeletal and cardiac muscle since, for 50 years. The third event was Keith R. Porter's offer of post doctoral training in his laboratory at Harvard University. "A whole new world of cell biology and advanced electron microscopy opened up," she says. "Porter was a charismatic teacher, a dynamic person who organized cell biology in the US, and a friend." Her first milestone discovery occurred just two weeks before she was to leave his lab. "I still remember the excitement of being able to demonstrate that transverse tubules open at the cell surface, a key finding in understanding how muscle is activated to contract," she recalls.

Franzini-Armstrong credits a dozen other scientists who heavily influenced her work. Among them, Richard Podolsky improved her foundation on the physiology of muscle activation as she worked as his research assistant at National Institutes of Health, 1963-64. In Sir Andrew Huxley's lab 1964-66, she came to understand contractile machinery, appreciate optics, and better deal with "the early difficulties of trying to raise a family while doing science." Paul Horowicz helped her transition from trainee to faculty member at the University of Rochester, 1967-1975, giving her the freedom to pursue science without heavy teaching and committee work while her children were young.

Of her career, Franzini-Armstrong says, "My main field of interest has been the disposition of membranes and macromolecular complexes that are responsible for excitation-contraction (e-c) coupling in skeletal and cardiac muscles." She sees four phases to the structural work in her career. Her early work defined the nature and distribution of the two membrane systems involved in calcium cycling. The second phase revealed the location of the channels through which calcium is released during muscle activation and showed that a limiting factor in the design of muscles capable of high activity rates is not the density of calcium release channels, but that of the pump protein. The third phase established the specific relationship between the L type calcium channels of plasmalemma and T tubules-CaV channels or dihydropyridine receptors (DHPRs) and the Ca release channels of the sarcoplasmic reticulum (RyRs)—in skeletal and cardiac muscles. Her current interest is "the supramolecular complex that allows interaction between a number of molecules in the sarcoplasmic reticulum that control calcium release, again using structural approaches to understand molecular interactions."

Franzini-Armstrong inspires her students and colleagues. "Clara is a scientist with strong determination and humanity at the same time,"

says Simona Boncompagni, a researcher at the University G. d'Annunzio of Chieti in Italy. "Her career is characterized by high scientific achievements and immense productivity, but she is always open to new collaborations." Paul Allen agrees. "On a bench at a Biophysical Society meeting 13 years ago, she single handedly saved my career as a scientist and helped create one of the most successful multi-center group collaborations that ever existed. I knew who Clara was from her extraordinary reputation as the world's premier expert in muscle histology and ultra-structure. What I could not imagine was that she would want to collaborate with me!"

Franzini-Armstrong is married to Clay Armstrong, renowned channel electrophysiologist, professor of physiology at the University of Pennsylvania, and recipient of numerous prizes. They have one son and three daughters. John pursued a career in audio engineering and business. Katie is a biochemist currently



at home with children and pursuing science teaching. Sandra, with physics and music degrees, is principle viola in a symphony and quartet. Cecilia is a neuroscientist now at home with three children.

Francini-Armstrong claims of her nine grandchildren that "each, of course, is the best that was ever produced." In addition to enjoying the children, she and her husband like mountain trekking, sometimes in remote regions of the world, and downhill skiing.