Remembered

GUIDOTTI, Guido

Pioneer in Membrane Protein Biochemistry

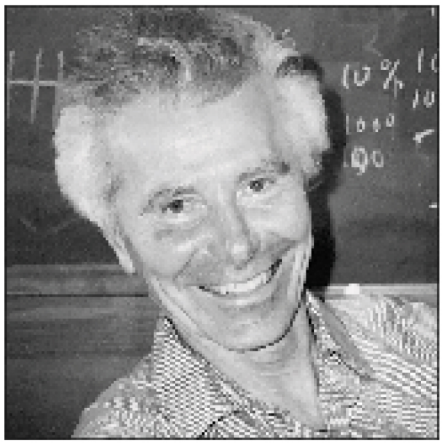
Guido Guidotti, Higgins Professor of Biochemistry at Harvard University, passed away on April 5, 2021 from prostate cancer. Guido trained as a physician and then devoted 50+ years of curiosity-driven pioneering scientific research to understanding how proteins embedded in biological membranes perform their physiological functions in transport and signal processing. He was a giant in this field. He was also renowned as an inspiring teacher and as a gentle and truly remarkable human being whose smile could light up a room.

Guido was born in Firenze, Italy in 1933 and grew up in Siena and then in his beloved Napoli. He came to the United States at the end of World War II for a year, as an American Field Service student in Decatur, Illinois. His host family then supported his return, originally to pursue a medical career. He completed pre-medical studies at Millikin University in Decatur, obtained an M.D. from Washington University School of Medicine in St. Louis and was an intern and resident in internal medicine at Barnes Hospital. He then obtained a PhD from Rockefeller University and never looked back. Guido came to Harvard University in 1963, remaining there until his death.

The trajectory of Guido's discoveries is the wandering, yet mysteriously coherent, path of a scientist, and a person, who was not afraid of anything. After early seminal studies on hemoglobin, whose sequence and biochemical properties he famously determined using his own blood, Guido initiated his membrane protein research. At that time, almost nothing was known. A colleague relates that: "I saw Guido give a plenary lecture at a meeting. He started by drawing two parallel lines on the chalkboard, [corresponding to the two sides of the membrane], and wrote 'inside' to the far left and 'outside' to the far right, [denoting the inside and outside of the cell]. He commented that this summarized, to his knowledge, the state of understanding of how membrane proteins were structured in the membrane and how they functioned." Guido's ensuing research filled in his chalkboard drawing.

By 1976, Guido could write, largely on the basis of work from his own laboratory, that: "Solutes are carried across eukaryotic plasma membranes by oligomeric glycoproteins which span the cell membrane and conduct transport by undergoing conformational changes." He identified the structures and topologies of the protein responsible for the red blood cell ion transport that enables removal of carbon dioxide from tissues into the lungs, of the enzyme that maintains the electrical properties of neurons by sodium and potassium ion transport, and many others. He also carried out pioneering studies into hormone regulation of membrane protein activity. Finally, Guido's intuition over decades of research culminated in his discovery that a protein called CD39 sits in the cell membrane and hydrolyzes extracellular adenosine triphosphate (ATP), as a so-called "ecto-ATPase", thereby ensuring that this extracellular ATP is present at an appropriate concentration. When CD39 activity is aberrant or missing, neurons in the brain do not recover after they fire; blood does not know when to clot (and when not); inflammatory responses in cancer, infection and disease are compromised; veins and arteries calcify; and pain responses are perturbed. Guido's discovery lit up the research community, and his findings in this area set the stage for currently exploding therapeutic efforts which target CD39 as a way to ameliorate the above pathologies. Guido's later research also revealed a remarkable mechanism in which CD39 activity is governed by mechanical effects within the membrane. Finally, both CD39 and ATP have been implicated in COVID-19 infection, in part by work to which Guido recently contributed.

Guido was not only a world-renowned scientist but was off-scale as both a laboratory mentor and a teacher. Many of the thousands of undergraduates to whom he taught biochemistry went on to be doctors. He could never go into a hospital setting in Boston without someone saying "I took your biochemistry course." In the last year of his life, he taught three popular courses, in biochemistry, in membrane proteins, and a freshman seminar entitled "What is Life."



Guido was known by everyone with whom he came in contact as a very special person. Above all, he was kind, generous, and enabling of everyone in his sphere, beginning with the members of his research group. Additionally, scientific fame and credit were never the point. Most famously, Guido would not put his name on his students' or post-doctoral fellows' publications unless he had contributed to the experiments with his own hands, until ultimately forced to do so by funding organizations. He was also an accomplished soccer player and bicyclist and had extensive knowledge of, and interest in, art, music and books. He was unusually insightful, wise and foresighted, not only in his scientific work but in life in general.

Guido's spirit and influence live on in the beloved members of his family, who always came first in his life: his brother Mario and Mario's wife Ludi Borello; their daughter Alice and her two children Gaia and Fabio; Guido's son Guido, Jr., his wife Anna Yoo and their son Nicholas Yoo Guidotti, who was the sunshine of Guido's later life; and Nancy Kleckner, his soul mate, wife and Harvard colleague for more than 40 years. Guido also remains an important presence in the lives and research of the many trainees and visiting scientists who passed through his laboratory. The community of Guido will always cherish his spirit and his love, which will help in the difficult times ahead when everyone he touched must somehow now manage without him.

A detailed summary of Guido's research and documentation of other aspects of his life, plus comments from many of his students and colleagues, can be found at https://nrs.harvard.edu/URN-3:HUL.INSTREPOS:37368811 Donations in Guido's memory can be sent to "Death with Dignity" https://deathwithdignity.org/