THE FACULTY OF MEDICINE
Harvard University

Eva Julia Neer

Eva Neer, M.D., Professor of Medicine died from breast cancer on February 20, 2000. A petite woman, with an effervescent smile and twinkling eyes, she illuminated the campuses of Harvard College, Medical School and Brigham and Women's Hospital (BWH) for nearly 25 years with enthusiasm for science and art, research and teaching.

Eva's family fled Nazi occupied Warsaw in 1939, immigrating first to Brazil and then settling in New York. Although unable to continue their academic professions in the US, her parents instilled in Eva a fierce love of scholarly endeavors. She entered Radcliffe College and at this time she met and married Robert Neer (now Associate Professor of Medicine, Massachusetts General Hospital). She attended medical school at Columbia, but ultimately left clinical medicine to pursue post-graduate research in Dr. Guido Guidotti's biochemistry laboratories at Harvard College. In Guidotti's laboratory she purified adenylyl and guanylyl cyclase from adrenal medulla, working to better understand the enzyme that generates the universal second messenger cAMP. During this time she had two children, Richard and Robert. In the days before strict laboratory regulations, the Neer boys could be found playing around the laboratory in the midst of centrifuges while Eva carried out her experiments. These years also initiated her long-standing relationship with undergraduates in Department of Biochemistry and Molecular Biology at Harvard College, relationships that were sustained even after she moved to the Medical School Campus. Although Eva's early work on the biological chemistry of signaling proteins had no obvious relationship to cardiac disease, Thomas Smith, M.D., the newly-appointed Chief of the Cardiovascular Division at BWH, had the good sense to hire her in 1976 as the sole basic scientist on his staff.

At BWH Eva's work began in earnest on the identification of proteins that modulate signals between cell surface receptors and adenylate cyclase (and other effector proteins). These modulator proteins (known

In tribute to their dedicated efforts to science and medicine, deceased members of the Harvard Faculty of Medicine (those at the rank of full or emeritus professor) receive a review of their life and contributions with a complete reflection, ***a Memorial Minute****.*

as G proteins because of their regulation by GTP) became the focus and passion of the remainder of her scientific career. Her rigorous biochemical approach led to the discovery of a new class of G proteins (termed G_o), one of the most abundant signaling proteins in brain, and established the existence of a large and complex family of G proteins. In 1985 a collaboration between Eva and David Clapham M.D., Ph.D. on the identification of the coupling of muscarinic receptors in heart to an ion channel, IKACh, defined the mechanism for activation of this channel, and in the process confronted the dogma of G protein signal transduction. Prior to their work, signal transduction through G proteins was assumed to always take place via release of an activated G protein alpha subunit (Gα). At that time the G protein signal transduction field assumed that G protein-coupled receptors catalyzed release of the Gα subunit from its Gβγ anchor and that Gα subunits were the messengers that activated a particular effector molecule. Gβγ subunits were thought to be mundane membrane bound proteins that simply buffered the active Gα subunit. However studies by Neer, Clapham and colleagues (published in 1987) showed that contrary to expectation, Gβγ, not Gα, directly gated IKACh. This finding evoked a lively and well-known controversy in the signal transduction field that was finally settled in favor of Neer and Clapham's Gβγ hypothesis. During years of sometimes-bitter controversy, Eva Neer always took the high road, relying on data rather than acrimony to make her point. She was honest and forthright, and inspired those around her to be the same.

Eva continued to pursue the structure and function of Gβγ. After the crystal structure of the complex was revealed independently by the Sprang and Sigler laboratories, she characterized the sites of interaction of the protein with Gα and phospholipase Cβ, and, in collaboration with Temple Smith, provided insights about the structures of proteins like Gβγ. She also worked on G proteins in cardiac cells by identifying Gα genes, producing transgenic mice with modified G protein function, and posing interesting questions about the mechanisms of heart failure. At the time of her death six manuscripts were ready for submission.

Eva's scientific creativity and energy were appropriately rewarded with the highest of praise. She was propelled through academic ranks to full-time Professor of Medicine in 14 short years at Harvard Medical School. Indeed she was the second woman to have ever achieve this rank in a Department of Medicine at the Medical school. Throughout her research tenure Eva consistently and successfully competed for federal grants and was recognized by a coveted Merit Award from the National Institutes of Health. She received many other awards and honors, notably the American Heart Association's Basic Research Prize, the Excellence in Science Award from Federation of American Societies for Experimental Biology, and election into the American Academy of Arts and Sciences and the National Academy of Science.

In addition to her impressive scientific accomplishments, Eva's legacy reaches beyond the bench. Over the years, Eva developed a broad reputation as a superb teacher and thoughtful mentor for Harvard College undergraduates, Harvard medical students, and her own research fellows. She served as Chairman of the Board of Tutors in Biochemical Sciences at the College, and was the Associate Master

of the Walter Bradford Cannon Society at the Medical School. Eva brought her passion for discovery and high standards of scientific proof to students at both campuses, always maintaining that it was impossible to truly understand one's own research unless one could explain it lucidly to others. This axiom was put into action in a seminar series Eva initiated at the Cannon Society, where medical students presented their research projects to one another and Eva's incisive comments provoked both scientific clarity and personal inspiration.

A natural communicator, Eva had no trouble interesting students in the complexities of molecular three-dimensional structures of G proteins, oftentimes by interweaving examples of literature and art. During a remarkable Soma Weiss lecture given one year before her death, Eva likened the intensity of G-proteins signaling to a classical Florentine painting of a soldier coyly reaching for the breasts of a scantily clad maiden. Smiling at her audience she discussed, with equal passion and with a knowing twinkle in her eye, classical art and the biochemistry of G-protein activation. The moment was quintessential Eva - scholarly, scientific and witty. She was the arbiter of knowledge and taste, scientific, cultural, and literary. Whether one needed to know the correct approach for determinant a protein's buoyant density, the name of Hector's wife in the Iliad, or the low-down on the latest Bars Lurhman film, Eva could be counted on for answers.

Eva served as a tutor to undergraduates concentrating in Biochemical Sciences, nurturing both their professional careers and personal lives. Conferences were often held in her office – a small space with a comfortable sofa, table and desk filled with books and red-lined manuscripts, and walls equally cluttered by favorite works of art and photos of her sons Robert and Richard set in far away places. An ornately decorated gothic letter "G" held a prominent position and from above sculpted gargoyles stood guard. Students entering that room also entered Eva's life; she contemplated their questions, encouraged their skepticism and provided good counsel to a myriad of inquiries about how to balance research with life. An important mentor for both women and men, Eva demonstrated what achievements were possible by pursuing science passionately, regardless of gender issues. While sensitive to issues facing women, Eva never allowed herself to be distracted by them, feeling that she could best inspire simply by being the very best scientist she could be. Eva also served as a critical member of the Senior Advisory Committee on Women at Partners Health Care System, which attempted to define problems impeding the advancement of women in academic medicine and to construct mechanisms for change. She worked hard for consensus, but never with compromise of her high scholarly standards.

Renowned for her intellect, tough and probing questions and poignant retorts in scientific discussions, Eva's face always shone with warmth in her smile and sparkle in her eyes. She taught her student and colleagues so much: to work hard, to care passionately about science and each other, and always to see the world with joy. Her passion, wit, and intellectual achievements live on to inspire all those colleagues and friends fortunate to have been touched by her.

Respectfully submitted,

Christine Seidman, *Chairperson*
David Clapham
Thomas Michel