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PIONEERS IN NEUROLOGY

George D. Pappas (1926–2015)

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George D. Pappas (Fig. 1), a pioneer researcher whose interests traversed anatomy, cell biology and neuroscience, was born on November 26, 1926, in Portland, Maine, to Demetrios Papatheodorou and his wife Anna (née Dracopoulou), a couple of Greek ancestry. Pappas earned his B.A. degree (1947) from Bowdoin College, Maine, and M.Sc. (1948) and Ph.D. (1952) degrees from Ohio State University with a thesis on the structure and cytochemistry of *Amoebidae* [1].

Pappas became associated with legendary researchers in the heyday of the great discoveries concerning the cell's organelles. In 1952–1954, he trained in electron microscopy as a visiting investigator at the Rockefeller Institute for Medical Research (Rockefeller University since 1965) under Keith Porter (1912–1997), an apprentice himself of Albert Claude (1899–1983) and founding father of the field of "cell biology" [2]. Pappas continued in 1954–1956 as a postdoctoral fellow in anatomy in New York University College of Medicine. He next joined the College of Physicians and Surgeons of Columbia University as assistant and associate professor of anatomy (1956–1966), moved to Albert Einstein College of Medicine of Yeshiva University as professor of anatomy and neuroscience (1967–1977), and finally settled in Chicago as professor and chairman of anatomy and cell biology at University of Illinois College of Medicine (1977–1996), and professor of psychiatry afterward, reaching emeritus status in 2008. He was a long-time visiting investigator, member of the neurobiology faculty, and trustee (1975–1981) of the Marine Biological Laboratory in Woods Hole, Massachusetts [1, 3, 4].

In six decades between 1955 and 2013, Pappas contributed over 200 articles to professional journals, and served on the editorial board of *Anatomical Record*, *Biological Bulletin*, *Brain Research*, *Journal of Neurocytology*, *Microstructure*, and *Neurological Research*. He made seminal discoveries, being the first to describe the double limiting nuclear membrane and the ordered array of nuclear pores [3], the collagen morphogenesis in fibroblasts [2], and the ultrastructure of electrotonic synapses [5]. He provided a morphological basis for understanding the EEG, and showed that there is no correlation between the amount of secreted neurotransmitter and the number of presynaptic vesicles present in identified synapses [3].

In 1972, he jointly edited a neuroscience classic on the synapses [6] with Dominick Purpura (1927–2019), under the auspices of the New York Society of Electron Microscopy, and introduced the term "synaptology." This interdisciplinary endeavor covered morphological, developmental, molecular and physiological correlates of electrotonic and chemical transmission in the mammalian and invertebrate nervous systems, and included an account of synaptosomes.

His other research comprised comparative morphofunctional studies on the ultrastructure of mitochondria, endoplasmic reticulum, and nuclear envelope; endocytosis, micropinocytosis, morphology of the blood–brain barrier, synaptosomal protein phosphorylation, and growth cones in relation to synaptogenesis; neuromuscular junctions, lumbosacral cord, pinealocytes, neurohypophysis, red nucleus, septohippocampal pathway, anterior ventral cochlear nucleus, oculomotor nuclei, raphé nuclei, habenula, caudate, neocortical neuropil and capillaries, cornea, choroid plexus, ependymal cells, and intermediate filament cytoskeleton of astrocytes; and animal models of gangliosidosis, schizophrenia, and depression (Medline). In 2001, he described "porocytosis," a transient pore array fusion that secretes the neurotransmitter packet without membrane fusion [7].

In translational neuroscience, Pappas pioneered the use of intraspinal subarachnoid grafts of adrenal chromaffin cells and genetically engineered human mesenchymal stem cells for the alleviation of intractable pain in laboratory rodents, primates, and in cancer patients, through the release of endogenous opioid peptides into pain modulatory regions [8, 9]. He co-authored more than 30 papers on that topic between 1986 and 2013.

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Fig. 1 George D. Pappas at the Schmitt Neurological Sciences Symposium on *Transplantation into the Mammalian CNS*, held from June 30 to July 3, 1987, at the University of Rochester, New York. Unpublished photograph by the author

Pappas served as secretary (1967–1973) and president (1974–1975) of the American Society for Cell Biology, where he was succeeded by Nobel laureate George Palade [4]. As chairman of the Public Affairs Committee of the American Association of Anatomists, Pappas became a strong voice for biomedical research by setting up a cascading network for the dissemination of information related to legislative bills in the United States Congress, the use of laboratory animals, and fetal research. His input was influential regarding NIH appropriations and the drive by the Association of American Medical Colleges to increase Federal funding by $647,000,000 for fiscal year 1985 to cover 6200 new or competitive renewal grants.

Further, he was an active member of the Society for Neuroscience, the Harvey Society, and the Cajal Club. Since 1994, Pappas regularly attended the annual meetings of the newly founded American Society for Neural Transplantation (now, American Society for Neural Therapy and Repair). He was elected fellow of the American Association for the Advancement of Science, the New York Academy of Sciences, and the Chicago Institute of Medicine. Pappas received a doctorate *honoris causa* from the National University of Athens in 1988, and the Henry Gray Award from the American Association of Anatomists in 2003 for discoveries concerning the nuclear membrane, nuclear pores, electrical synapses, and the dynamic nature of extracellular brain pathways [3]. In 2010, he was honored by the Microscopy Society of America with its Distinguished Scientist Award in the biological sciences.

On January 23, 1952, Pappas married Bernice Levine (1928–2014), a graduate of Brooklyn College and Ohio State University. They parented two daughters. George and Bernice Pappas were outspoken activists of profound integrity and kindness. In 1952, the president of Ohio State University, Howard Landis Bevis (1885–1968), suspended George, then a junior staff member in zoology, for declining 64 times to answer questions before the Ohio Un-American Activities Commission; Bernice resigned her position as a laboratory technician in bacteriology a week before she was called to appear before the Commission [10]. In 1969, Pappas dissuaded several distinguished scientists, including Jacques Monod, François Jacob, Étienne Wolff, André Lwoff, Francis Crick and Sydney Brenner, from participating in academic activities promoted by the military dictatorship of the Colonels in Greece, as evidenced in documents in the Original Repository of the Wellcome Library for the History and Understanding of Medicine (http://archives.wellcome.ac.uk).

Pappas died peacefully on August 12, 2015, in Bronx, New York, in his 89th year. The Marine Biological Laboratory lowered its flag to half-staff in memory of its former trustee and society member emeritus [4].

Declarations

Conflicts of interest The author declares no conflict of interest.

Ethical standards This study was performed in accordance with ethical standards.

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