

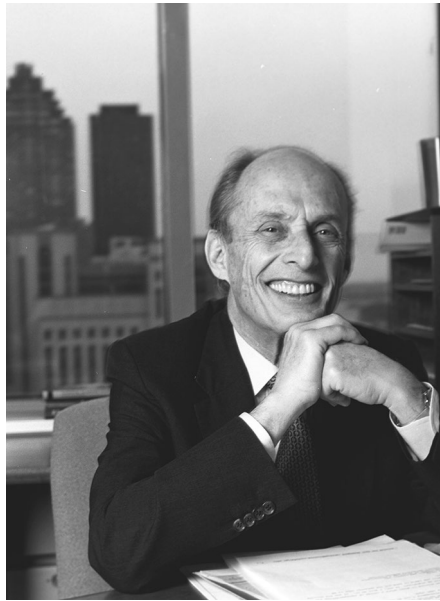
## “For Paul”

On April 13, the neuroscience community lost a remarkable scientist and true humanitarian. Paul Greengard, co-recipient of the Nobel Prize in Physiology or Medicine in 2000, Vincent Astor Professor and head of the Laboratory of Molecular and Cellular Neuroscience at the Rockefeller University in New York City, died of an apparent heart attack at age 93. Paul will be remembered for his seminal contributions to neuroscience, for pioneering the field of neuronal signal transduction and for training hundreds of neuroscientists. For anyone who knew Paul it will come as no surprise that up until a few hours before his death, Paul was doing what he liked the best: working on a scientific manuscript.

Paul lived life at a scale and complexity that truly matched his favorite study object—the brain. Paul was born in New York City on 11 December 1925. His mother, Pearl Meister Greengard, died giving birth to the man who would become a world-renowned scientist and a champion of advocating for the advancement of women in science. His father remarried soon thereafter, and the existence of his birth mother was kept a secret from Paul until he was in college. The lack of any memories or physical evidence of the existence of his mother deeply affected Paul throughout his life. In honor of his late mother, he and his wife, the sculptor Ursula von Rydingsvard, donated his Nobel Prize winnings to establish the Pearl Meister Greengard prize, which recognizes the work of accomplished women scientists.

Paul’s career was by no means traditional. The whirlwinds of Paul’s young scientific years moved him from the military to academia to industry and back to academia. During World War II, Paul spent 3 years in the United States Naval Reserve, which included work at the Massachusetts Institute of Technology to develop an early radar aircraft-detection system against Japanese kamikaze airplanes. Paul subsequently obtained an A.B. in mathematics and physics from Hamilton College and a Ph.D. in biophysics from the Johns Hopkins University, studying the properties of frog peripheral nerves as they degenerate. After postdoctoral training in neuropharmacology in England, which in addition to allowing him to study the impact of drugs on neurotransmitter release, must have left an imprint on Paul’s legendary sense of humor, he briefly entered the pharmaceutical industry with the idea of applying his knowledge of basic science for therapeutic drug development. Met with strong resistance, he decided to move back to academia, and in 1968 Paul joined the faculty of Yale University.

It was at Yale where Paul performed his pioneering research on neuronal signal



Credit: Photo taken by Barry Swimar and provided by Greengard Lab/Rockefeller University

transduction. At this time, neuroscience was dominated by electrophysiologists, who were making great strides in understanding of the electrical properties of neurons. However, inspired by the work of Earl Sutherland and Edwin Krebs, who first elucidated the role of cyclic AMP (cAMP) and cAMP-dependent protein kinase (PKA) in glycogen metabolism, Paul proposed that neurons are not just simple electrical conduits but could be tuned by signaling molecules. His devotion to sophisticated poetry (he was able to cite entire pages of Shakespeare from memory) did not preclude his fascination with the odd-sounding acronyms of second messengers. Paul showed that cAMP was produced in response to the neurotransmitter dopamine in brain extracts and could mimic its effects. His subsequent findings revealed a true symphony of complex interplays between kinases and phosphatases that had not previously been appreciated. These neuromodulatory

signaling cascades (or “slow synaptic transmission” as Paul referred to it in his Nobel essay in *Science*) are now a major research area in neuroscience, recognized as centrally important to many nervous system disorders. His discoveries were among the first to characterize neuronal cell types based on their molecular and biochemical differences, paving the way for current studies of neuronal cell type diversity.

Paul moved to the Rockefeller University in 1983, where he continued to conduct the highest level of science until his very last day. Although Paul was a reductionist at heart and spent much of his career addressing basic science questions, he recognized the clinical and translational applications of his work. His approach to science was mesmerizing, as it carried a mix of dry attachment to detail with a fervid venturing into new territories where Alzheimer’s disease, Parkinson’s disease, depression, and schizophrenia could become understood and cured. Paul’s commitment was infectious and his approach relentless; he maintained an active lab of more than 60 people until the day of his death.

Paul loved to be surrounded by creative people, and his research group consisted of an eclectic group of scientists from many races and nationalities. He admired the people in his lab and sought to understand and help provide what would allow each of them to succeed in science and life. His enthusiasm about science and the people working with him was his major driving force to come to the lab, every day of the week, despite any obstacle that life put in his way. As representatives of his last generation of female trainees, we particularly wish to emphasize his truly remarkable support for women scientists, as it came from a deeply felt and natural appreciation that there is no limit for women and their accomplishments. He was a true humanitarian and he held his belief in human dignity and equality above everything. Paul led us by example, with the help of humor and a secretly acquired, never-ending supply of chocolate

(as officially documented in a 2013 *Nature* article titled “Chocolate habits of Nobel prizewinners”<sup>2</sup>). He was always available, both to share our excitement and to keep us on our toes. He inspired us to be creative and humble, to overcome obstacles and push ourselves further, and to never stop wondering. He instilled in us a deep appreciation of rigorous and discovery-based science that has the power to elevate.

Paul was not interested in superficial advances but rather preferred to delve deep into the details of a particular question or problem, frequently over extended sushi dinners or at his favorite table at Felidia. The topics would range from science to art to politics and Paul was never fully satisfied with the answers currently available in any field. Paul’s trainees and collaborators all know the dedication with which he wrote and edited manuscripts, paying attention to every detail and trimming it to the essentials. Paul would not rest until each word precisely conveyed its intended meaning. Paul was unapologetically true to his scientific ideals and expected the best from those who worked with him.

On a personal level, Paul’s charm and soft voice belied a famously dry wit and often wry sense of humor. At a moment’s notice

he could switch from a serious scientific discussion to a witty joke and back again, leaving his conversation partner pondering about what just happened. A native New Yorker, Paul developed a passionate love for dogs (particularly very large ones), lobster rolls, and art, which was fostered by strong connections to the art world through his wife, Ursula von Rydingsvard. Her large sculpture crafted from beams of cedar wood and simply titled “For Paul” is part of the permanent collection at Storm King Art Center in New Windsor, NY.

Paul was like a father to us and many others. He deeply cared about those around him and had a unique gift to make people feel recognized and appreciated. He knew our relatives and friends and warmly welcomed them to the extended Greengard family. He went out of his way to help each of us with issues outside the lab ranging from health concerns to family, career, and life advice. His mentorship did not end after leaving the lab. Paul remained highly interested in our well-being and it was not unusual to receive a “Happy Birthday” message from him or a call just to see how we were doing. He always had time to catch up on life and science and would generously and graciously offer his advice and guidance

to all of us. Because he believed so firmly in our success, he instilled in us the confidence to try anything.

Paul was a man of remarkable intelligence and mental integrity. He never stopped caring about humanity and its destiny. He never stopped fighting against any form of discrimination. He never ceased to be Paul, a man of incredible wit, sharp humor, and endless curiosity. For many of us, his death has left a void that is impossible to fill. We miss him every day. □

Helen S. Bateup<sup>1</sup> , Myriam Heiman<sup>2</sup> and Anne Schaefer<sup>3\*</sup> 

<sup>1</sup>Chan Zuckerberg Biohub, San Francisco, CA, USA.

<sup>2</sup>The Picower Institute for Learning and Memory, The Broad Institute of MIT and Harvard, Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, MA, USA. <sup>3</sup>Nash Family Department of Neuroscience, Department of Psychiatry, Friedman Brain Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA.

\*e-mail: [anne.schaefer@mssm.edu](mailto:anne.schaefer@mssm.edu)

Published online: 1 July 2019

<https://doi.org/10.1038/s41593-019-0450-z>

#### References

1. Greengard, P. *Science* **294**, 1024–1030 (2001).
2. Golomb, B. A. et al. *Nature* **499**, 409 (2013).