OBITUARY

George Emil Palade (1912–2008)

A founding father of modern cell biology.

George Emil Palade died on 7 October at the age of 95. He was among the greatest scientists of the twentieth century, whose momentous discoveries in cell biology are still actively pursued by many laboratories worldwide.

The son of a philosophy professor and a teacher, Palade was born in Jassi (Iași), the former capital of Moldavia, the eastern province of Romania. He studied medicine at the University of Bucharest. Having spent the Second World War in the medical corps of the Romanian army, he moved to Istanbul shortly before moving on to New York City in 1946 for postdoctoral studies at New York University.

Following a short stint there, in a life-changing event Palade was invited by Albert Claude to join his laboratory at the Rockefeller Institute for Medical Research — now Rockefeller University. The previous year, Claude and his colleagues Keith Porter and Ernest Fullam had published the first electron micrograph of an animal cell grown in culture, describing a “lace-like cytoplasmic network”, later named the endoplasmic reticulum. Furthermore, Claude and his collaborators George Hogeboom and Walter Schneider had recently developed procedures involving differential centrifugation to break up tissues and to separate cellular components into three main fractions — nuclei, mitochondria and ‘microsomes’. So Palade joined an already famous laboratory that was on the cusp of even greater discoveries.

He soon became a key member of the lab, contributing vigorously to optimizing methods for both cell fractionation (such as introducing sucrose solutions for better preservation of cellular organelles) and electron microscopy (using osmium tetroxide to get better contrast). These technical advances facilitated many pivotal discoveries by Palade and his colleagues throughout the 1950s and 1960s, among them a detailed description of the membranes of mitochondria and chloroplasts. His other achievements included the discovery in 1955 of “a small particulate component of the cytoplasm” — often referred to as the ‘Palade granule’ until it morphed into the ‘ribosome’ in 1958 — and the description in 1963 with Marilyn Farquhar of “junctional complexes in various epithelia”, which connect epithelial cells together.

With Claude moving back to Belgium in 1949, the partial disassembly of

‘the Rockefeller group’ began, ending with Porter’s departure to Harvard in 1961. In fond memory of Porter’s contributions, a picture of him, with the title “Our father who art at Harvard”, decorated the Palade lab at Rockefeller for many years.

In parallel with his discoveries using electron microscopy, Palade sought to understand the function of these newly defined cellular structures. Biochemical

studies with Philip Siekevitz in his lab on the microsome fraction were published in classic papers in which microsomes were identified as broken and sealed bits of the endoplasmic reticulum. Subsequently, through *in vivo* labelling with ^{14}C -leucine and isolation of labelled chymotrypsin protein from cell fractions, Palade and Siekevitz showed that this protein was primarily synthesized in microsomes. These results led to the proposal that the endoplasmic reticulum is the synthesis site for secretory proteins, an idea further supported by experiments carried out by David Sabatini and Colvin Redman, who demonstrated that the initial event in the protein secretion pathway was directional release of nascent polypeptide chains into the microsomal lumen.

With another colleague, Jim Jamieson, Palade developed the technique of pulse-chase labelling in tissue slices, which allowed the pathway of secreted proteins to be tracked in time and traced within cells. One important, but initially controversial, postulate was that secretory proteins are transported in quanta — in vesicular carriers that bud from a donor membrane and deliver their contents by fusion to a target membrane.

Palade ran his laboratory very informally. There were no regular lab meetings. Instead, there were bimonthly seminars, at which lab members were introduced to ideas by speakers from other labs. Often Palade summarized the essence of a presentation, particularly if the speaker had failed to do so. He had the ability to link the most disparate observations into a coherent and testable working hypothesis. He effortlessly passed this trait on to many of his students and postdocs, who chose their research topics with very little interference from him. He did, however, reserve the right to challenge research plans. While I was an assistant professor in his lab, he suggested I set up a cell-free system to study the initial step in

the secretory pathway — a task much easier said than done. But after two years of trying, I succeeded and it certainly made a big difference to my career.

He took considerable interest in the papers that were published by his lab. Even when he was not listed as an author, he meticulously edited and corrected each paper with his immaculate handwriting at the edge or on the opposite empty page of the typewritten manuscripts. I treasure the corrections he made on all my manuscripts during that time.

Palade moved to Yale in 1973, where he stayed until he joined the University of California, San Diego (UCSD) in 1990. At both universities, he continued to make many crucial discoveries and, as at Rockefeller, built thriving departments of cell biology. At UCSD, he served as the first dean of scientific affairs until his retirement at the age of 87.

Many of Palade’s students and their second-, third- and fourth-generation ‘descendants’ are still major contributors to the field of cell biology. Among the prizes he was awarded are the Lasker prize, the Gairdner award and the Louisa Gross Horwitz Prize. He was also a joint recipient of the 1974 Nobel Prize in Physiology or Medicine.

Palade was deeply interested in music, the fine arts and history. He was an eloquent speaker, and his lectures are legendary examples of his lucidity and passion for his subject. He worked productively until his late eighties, when Parkinson’s disease forced him to reduce his activities. It must have been hard for him to cope with these physical constraints, although his intellectual curiosity and passion remained intact for much longer. He is survived by his wife, Marilyn Farquhar, two children from his first marriage and two grandchildren.

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