David J. L. Luck

1929–1998

BIOGRAPHICAL *Memoirs*

A Biographical Memoir by James E. Darnell, Jr.

NATIONAL ACADEMY OF SCIENCES

DAVID J. L. **LUCK**

January 7, 1929–May 23, 1998

Elected to the NAS, 1984

Photo courtesy Rockefeller Archives Center.

David Luck was a scientist whose research at the Rockefeller University on the genetics of the organelles inside cells advanced the field of cell biology. To accomplish his work Luck built on not only the basic skills of microscopy, cell fractionation and biochemistry, but also added the power of genetics through the use of single-celled eukaryotes, both *Neurospora* and *Chlamydomonas*. He was a greatly admired scientist throughout the world.

By James E. Darnell, Jr.

Early life

David Luck was born on January 7, 1929 in Milwaukee, Wisconsin. Along with his sister Merriam, he grew up there attending public schools. As a youngster his scientific bent was evident. An early interest in chemistry was due perhaps to the influence of an aunt who was a chemist and an uncle who was a physician. Because of the family influence, plus the effects of a very good biology teacher, he had early thoughts about medical subjects, especially biochemistry.

On attending the University of Chicago as an undergraduate, where the medical school and its biochemistry department are on the same campus as the undergraduate school, he saw at first hand the union of chemistry with medicine. He chose to go to Harvard Medical School in 1949 with the idea of ultimately becoming a medical scientist, with the emphasis on scientist. Formalized MD-PhD programs did not exist until the mid-1960's, so upon graduation David became a medical intern in 1953 at the Massachusetts General Hospital, notable then as now for having a strong research division. He was set to finish clinical training there, but the post-Korean war draft was still active, and one month before finishing his assistant residency he was drafted into the Army Medical Corps. In 1957 David returned to clinical training at Massachusetts General Hospital, but he decided that medical research was too primitive scientifically.

(Photo courtesy Rockefeller Archive Center.)

The Rockefeller University

David Luck arrived in 1958 at the newly christened Rockefeller University, which before 1953 had been The Rockefeller Institute for Medical Research, as a trained physician. His aim was to obtain a PhD and become what he really wanted to be, a scientist. The foundations of the discipline of cell biology had been established at Rockefeller by a formidable array of minds: first Albert Claude, and later Keith Porter, George Palade and finally Christian de Duve. Naturally, David gravitated to cell biology.

He spoke to George Palade, who did not at first eagerly embrace him as a prospective student but did not reject him either. Palade's style was non-directive; he expected a student to soak in the atmosphere and invent his own project. After casting around for some months, David settled on a project that joined biochemistry and cell structure. Porter had found that glycogen synthase activity might be membrane associated, perhaps in vesicles that in liver cells had been visualized by electron microscopy in close vicinity with glycogen particles. By cell fractionation, David separated glycogen particles from membrane-enclosed vesicles and showed that the enzyme synthesizing glycogen from uridine diphosphoglucose was associated with the glycogen particles themselves. (1). After defending his thesis in 1961 he had a number of months remaining before his June 1962 graduation. He was given the independence in the Palade-Porter groups to work on other problems of his choosing. This was a freedom that greatly benefited the cell biology field.

During his training at Rockefeller, David had taken a course taught by the legendary C. B. van Niel, the transplanted Dutch microbiologist. This course, taught at the Hopkins Marine Station in Pacific Grove, California, influenced a whole generation of scientists. Van Niel emphasized the flexibility of choice offered by the variety of single cell eukaryotic organisms with which cell biology could be coupled with genetics to greatly enhance the depth of information that could be extracted, a staple notion used by David the rest of his career.

Researching organelles

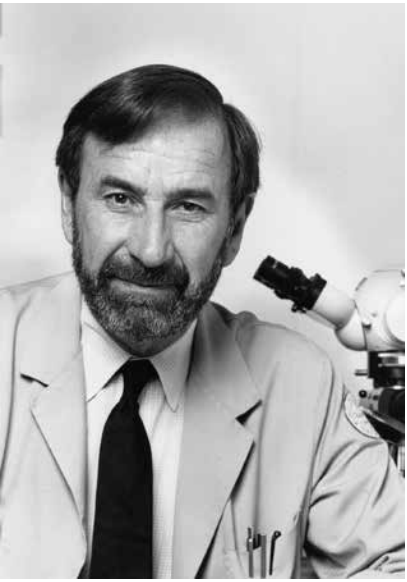
Getting an assist from Ed Tatum, who had moved from Yale to Rockefeller, David learned about culturing *Neurospora*. He was attracted to the study of the biogenesis and function of organelles in that organism. Tatum was not particularly interested in the biochemistry of organelles, and no one in the cell biology group was working on single cell organisms. Thus, David was on his own. During the next several years he made substantial progress studying *Neurospora* mitochondria, which by that time were suspected of having some aspects of inheritance of their own, separate from nuclear genes. His earliest radiochemical labeling experiments supported the idea that independent new synthesis and mitochondrial division accounted for the constant number of mitochondria in growing *Neurospora crassa* cells (2, 3).

David turned to characterizing the nucleic acids in mitochondria. Joined by Ed Reich, an MD working with Tatum toward his PhD, David accomplished for the first time the clear isolation of mitochondrial DNA, which had a different buoyant density from nuclear DNA (4). Genetic traits attributable to mutant mitochondria had been shown to be transmitted in *Neurospora crassa* only from the maternal partner. Using a different *Neurospora* strain selected because its mitochondrial DNA had a different buoyant density from that of *Neurospora crassa*, David and Reich (5) showed, based on which density of DNA was transferred in crosses, that the maternally inherited information was encoded in mitochondrial DNA.

David and postdoctoral fellows who later joined his laboratory also demonstrated by RNA/DNA hybridization that the ribosomal RNAs in mitochondrial ribosomes were synthesized in the mitochondrion by the endogenous RNA polymerase found in the organelle (6, 7). Finally, they showed that both the large and small rRNA molecules in mitochondrial ribosomes are derived from a precursor RNA, or pre-rRNA, as had been discovered by that time to be true for cytoplasmic ribosomal RNAs first in cultured mammalian cells and later in bacteria.

All of this was accomplished in the first eight years after David's graduation. During this time he also rose through the ranks, becoming an assistant professor, first associate professor, and then full professor.

In 1972 a student, Paul Lizardi, and David demonstrated with specific antibodies that in contrast to the ribosomal RNA, the ribosomal proteins found in mitochondrial ribosomes were definitely made on cytoplasmic ribosomes outside mitochondria and



(Photo courtesy Rockefeller Archive Center.)

transported into the organelle to form mitochondrial ribosomes (8). This discovery shed light on two important problems: genes most likely arising from the mitochondrial genome (originally derived from a bacterial symbiont) were now nuclear, and the cytoplasmic protein products of these genes were specifically targeted to enter the mitochondrion.

In the mid 1970's a second single cell eukaryote, *Chlamydomonas reinhardtii*, became the focus of David's research life, and remained so for the rest of his career. Microscopists had been fascinated for decades by cell organelles that themselves had to be replicated once each cell division cycle. David was attracted to two such structures, centrioles, whose ultimate fate is to participate in the mitotic separation of new chromosomes, and basal bodies, found at the base of cilia and flagella, cellular projections into the extracellular space that, when waved in a controlled motion, allow cells possessing them to swim. Both centrioles and basal bodies are sites for the assembly of microtubules that compose the mitotic spindle or the axonema of cilia and flagella and themselves consist of tubulin subunits. Because of the controlled duplication and partitioning of centrioles and basal bodies into mother and daughter cells, it had been conjectured that some mechanism separate from nuclear control governed centriolar and basal body formation in the cell cytoplasm.

Chlamydomonas has two flagella, which are utilized to wave in directed fashion so as to move the cell toward light. In 1976, David was joined by Gianni Piperno with whom he began a study of the proteins in the flagellar apparatus (9-13). This pioneering work led to the first characterization of a number of the functional flagellar-associated proteins that are widely conserved in eukaryotes. David's group subsequently identified a number of mutants affecting flagellar structure and/or movement and others that failed to duplicate the flagellae upon cell division (14-20). One of the mutations resulted in cells with a single flagellum rather than two. By the early 1980's, through a combination of protein and genetic analysis, David's laboratory had enumerated approximately a dozen different flagellar proteins for which mutations existed. In succeeding years these flagellar mutations were shown to segregate in a Mendelian fashion as if encoded by nuclear

genes, although their location on already established chromosomes could not be clarified until *in situ hybridization* procedures were improved.

Recombination analysis showed that the flagellar mutations mapped as one unusual linkage group nicknamed the Uni Chromosome, because of the mutant that had one flagellum. David reported these results in 1986, together with a remarkable technical assistant, Zenta Ramanis. With John Hall and Ramanis (21) he pursued the appealing hypothesis that in growing cells a functional centriolar DNA exists in basal bodies, as had been suspected for some years. Continuation of this research however did not support the hypothesis. In his last major paper (22) with John Hall, using a probe for Uni-Chromosome DNA they established by *in situ hybridization* that in metaphase cells the "basal body/centriolar DNA" is present on a single condensed chromosome with no particular orientation. In the same paper in interphase cells they located the DNA within the nucleus close to its periphery and near the site where cytoplasmic basal bodies are normally associated with the nuclear envelope. These findings were a forerunner of many more recent reports suggesting that the location of chromosomes within the nucleus is not random but, in an as yet unknown manner, facilitates the transfer of useful genetic information to specific cytoplasmic sites.

Academic affairs

Aside from his major discoveries in eukaryotic cell biology, David played a major role in faculty affairs at Rockefeller. From its inception as The Rockefeller Institute for Medical Research in 1901 through its transformation into a graduate university chartered in 1953 as The Rockefeller University, the structure of the institution was that of independent research laboratories, each headed by an established scientist (or in a few cases two such scientists).

The laboratory leaders were designated members. Young people who joined the research groups most often worked in the same scientific field and could become associate members. In a relatively few instances associate members were elevated to full member status, and then established independent laboratories. Only after the institute became a university were academic titles used, along with the usual academic aspirations for independence. Some of the laboratories, notably including that of George Palade, encouraged the development of scientific independence in young associates with ultimate elevation to professorship. David personally, and science in general, profited from Palade's wisdom in this regard.

By the mid 1980's a number of professors recruited from other academic institutions had joined Rockefeller University (including myself in 1974). By this time the need for a different system of bringing young scientists, typically post-doctoral fellows of demonstrated talent, to Rockefeller as independent investigators, both for diversification and modernization of subject matter, seemed necessary. Fortunately, Joshua Lederberg, who became President of Rockefeller University in 1978, agreed. When funds from the Lucille P. Markey Charitable Trust were secured to underwrite this plan in the mid 1980s, David and a small committee of others sought young candidates for independent positions equivalent to assistant professorships (at first called University Fellows). Beginning in 1985 Gunter Blobel and George Cross joined David and myself to recommend specific candidates who were then appointed by Lederberg. Of the 26 scientists to become Rockefeller University full professors since 1985, 18 came from this source of initial tenure track appointments as assistant professor.

Much of the 1994-1998 years David served as Rockefeller University's Vice President for Academic Affairs. On the Rockefeller campus not only was he appreciated for his science, but viewed by students and faculty alike as a bastion of quiet strength and gentlemanly wisdom.

The author is indebted to the Rockefeller Archives, especially a detailed interview with David Luck conducted by Judith Schwartz, for many of the precise dates and details of Luck's career.

SELECTED BIBLIOGRAPHY

Numbers in parentheses refer to text callouts.

1961 (1) Glycon synthesis form uridine diphosphate glucose. The distribution of the enzyme in liver cell fractions. *J. Biophys. Biochem. Cytol.* 10:195-209.

1963 (2) Genesis of mitochondria in *neurospora crassa*. *Proc. Natl. Acad. Sci. U.S.A.* 49:233-240.

(3) Formation of mitochondria in *Neurospora crassa*. A quantitative radioautographic study. *J. Cell Biol.* 16:483-499.

1964 (4) With E. Reich. DNA in mitochondria of *Neurospora crassa*. *Proc. Natl. Acad. Sci. U.S.A.* 52:931-938.

1966 (5) With E. Reich. Replication and inheritance of mitochondrial DNA. *Proc. Natl. Acad. Sci. U.S.A.* 55:1600-1608.

1967 (6) With M. R. Rifkin and D. D. Wood. Ribosomal RNA and ribosomes from mitochondria of *Neurospora crassa*. *Proc. Natl. Acad. Sci.U.S.A.* 58:1025-1032.

1969 (7) With D. D. Wood. Hybridization of mitochondrial ribosomal RNA. *J. Mol. Biol.* 41:211-224.

1972 (8) With P. M. Lizardi. The intracellular site of synthesis of mitochondrial ribosomal proteins in *Neurospora crassa. J. Cell Biol*. 54:56-74.

1976 (9) With G. Piperno. Phosphorylation of axonemal proteins in *Chlamydomonas reinhardtii*. *J. Biol. Chem.* 251:2161-2167.

1977 (10) With G. Piperno. Microtubular proteins of *Chlamydomonas reinhardtii*. An immunochemical study based on the use of an antibody specific for the beta-tubulin subunit. *J. Biol. Chem.* 252:383-391.

(13) With G. Piperno and B. Huang. Two-dimensional analysis of flagellar proteins from wild-type and paralyzed mutants of *Chlamydomonas reinhardtii*. *Proc. Natl. Acad. Sci. U.S.A.* 74:1600-1604.

1979 (11) With G. Piperno. An actin-like protein is a component of axonemes from *Chlamydomonas flagella*. *J. Biol. Chem.* 254:2187-2190.

(12) With G. Piperno. Axonemal adenosine triphosphatases from flagella of *Chlamydomonas reinhardtii*. Purification of two dyneins. *J. Biol. Chem.* 254:3084-3090.

(14) With B. Huang and G. Piperno. Paralyzed flagella mutants of *Chlamydomonas reinhardtii*. Defective for anonemal doublet microtubule arms. *J. Biol. Chem.* 254:3091-3099.

1981 (16) With B. Huang, G. Piperno and Z. Ramanis. Radial spokes of *Chlamydomonas flagella*: genetic analysis of assembly and function. *J. Cell Biol.* 88:80-88.

1982 (15) With B. Huang and C. J. Brokaw. A regulatory mechanism for flagellar function is revealed by suppressor analysis in *Chlamydomonas*. *Prog. Clin. Biol. Res.* 80:159-164.

(17) With B. Huang and Z. Ramanis. Suppressor mutations in *Chlamydomonas* reveal a regulatory mechanism for flagellar function. *Cell* 28:115-124.

(18) With C. J. Brokaw and B. Huang. Analysis of the movement of *Chlamydomonas flagella*: the function of the radial-spoke system is revealed by comparison of wild-type and mutant flagella. *J. Cell Biol.* 92:722-732.

(19) With B. Huang, Z. Ramanis and S. K. Dutcher. Uniflagellar mutants of *Chlamydomonas*: evidence for the role of basal bodies in transmission of positional information. *Cell* 29:745-753.

1984 (20) With S. K. Dutcher and B. Huang. Genetic dissection of the central pair microtubules of the flagella of *Chlamydomonas reinhardtii*. *J. Cell Biol.* 98:229-236.

1989 (21) With J. L. Hall and Z. Ramanis. Basal body/centriolar DNA: molecular genetic studies in *Chlamydomonas. Cell* 59:212-132.

1995 (22) With J. L. Hall. Basal body-associated DNA: *in situ* studies in *Chlamydomonas reinhardtii*. *Proc. Natl. Acad. Sci. U.S.A.* 92:5129-5133.

Published since 1877, *Biographical Memoirs* are brief biographies of deceased National Academy of Sciences members, written by those who knew them or their work. These biographies provide personal and scholarly views of America's most distinguished researchers and a biographical history of U.S. science. *Biographical Memoirs* are freely available online at www.nasonline.org/memoirs.