



BIOGRAPHICAL MEMOIRS

DAN LESLIE LINDSLEY JR.

October 13, 1925–June 22, 2018

Elected to the NAS, 1974

A Biographical Memoir by James A. Kennison

DAN LESLIE LINDSLEY, Jr. had a long and productive research career in genetics, primarily in the genetics of *Drosophila melanogaster*. His publications span seventy years, from 1946 to 2016. His fame derived not only from his wide-ranging genetic studies, but also from his major contributions to the community of *Drosophila* researchers and to the Genetics Society of America.

Dan Lindsley's contributions to the community of *Drosophila* researchers began very early in his career. He helped to organize an informal meeting in Madison, Wisconsin, in 1958. That meeting became the first Annual *Drosophila* Research Conference, which continues to this day. He organized the conferences in 1961 in Oak Ridge, Tennessee, and in 1977 in La Jolla, California. When the organizers decided to add a historical talk to the opening nights of the conferences, Dan was asked to give the inaugural talk at the San Diego conference in 1996. Dan attended almost every conference until 2017 in San Diego (just a year before his death), where he was presented with a special award in appreciation of his contributions to the conferences.

In addition to his strong support of the annual *Drosophila* conferences, Dan also made two other extremely important contributions to the *Drosophila* community. In 1944, Calvin Bridges and Katherine Brehme published descriptions of all the known mutants and chromosome aberrations in *Drosophila melanogaster*. This publication had long been out of print (and out of date) when Dan and Ed Grell, one of Dan's colleagues at the Oak Ridge National Laboratory, published an update in 1968 entitled *Genetic Variations of Drosophila*

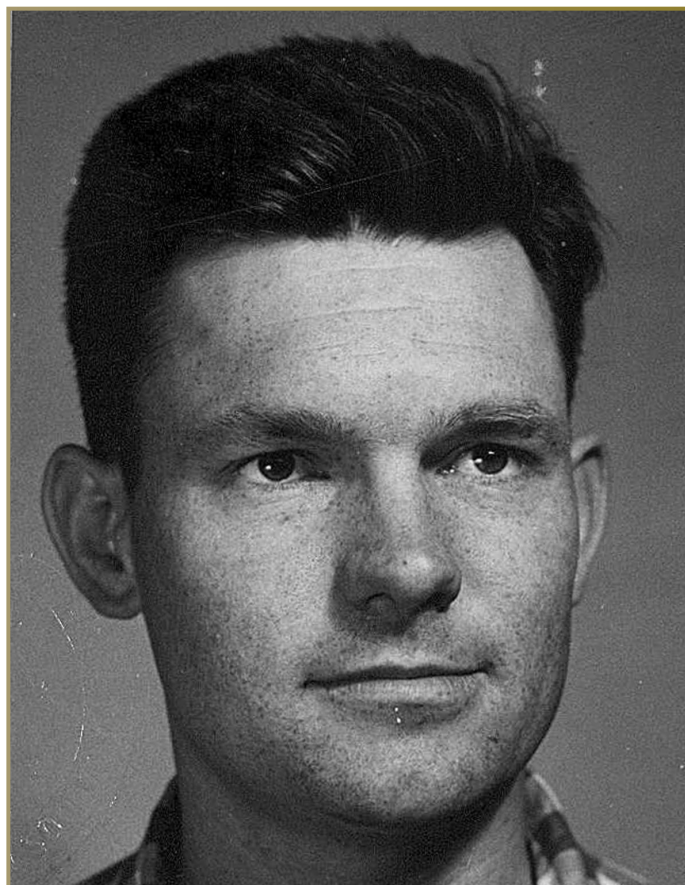


Figure 1 Portrait of Dan Lindsley in 1960 from his official Brazilian government visa for temporary residence.

melanogaster. Known as the “red book” because of the color of its binding, it was essential for *Drosophila* researchers in the decades before the Internet. Less than ten years after its publication, Dan had already begun an update with Georgianna Zimm that was published as *The Genome of Drosophila melanogaster* in 1992. Dan had retired from the University of California at San Diego the prior year and declared that the next revision needed to be done online and by someone else. He had already initiated discussions with a group at the annual *Drosophila* meeting in New Orleans in 1989 to use



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the information in his book with Georgie Zimm as the basis for Flybase (flybase.org), an online database dedicated to the known genetic, molecular, and developmental information on the model organism *Drosophila melanogaster*.

In addition to his support of the *Drosophila* research community, Dan also was a strong supporter of the Genetics Society of America, serving as treasurer (1975–77), vice president (1985), and president (1986). Dan received the Thomas Hunt Morgan Medal from the Genetics Society in 1989 for his lifetime achievements in the field of genetics. Dan was elected to the National Academy of Sciences in 1974 and the American Academy of Arts and Sciences in 1975. In 2000, he received the Distinguished Alumni Award from the California Institute of Technology (Caltech).

RESEARCH CAREER OVERVIEW

Dan's research career began (and continued for more than seven decades) with investigations on chromosome organization and behavior. His first major contribution was the synthesis in 1950 of the first compound-XY chromosome, a single chromosome that combined all the genes essential for viability and fertility from both the *X* and the *Y* chromosomes in *Drosophila*. Because males with two *Y* chromosomes are viable and fertile, the availability of this compound-XY chromosomes greatly facilitated the recovery and analysis of mutations of the heterochromatic *Y* chromosome. Dan also published important investigations detailing the effects of chromosome structure on recombination and chromosome behavior in meiosis. He also did genetic screens for mutations that disrupted meiosis, first by isolating mutations segregating in wild populations of *Drosophila melanogaster* on the streets of Rome, and later by using chemical mutagenesis to induce and characterize new mutations in the lab. These studies were one of the first attempts to genetically dissect a developmental process in a multicellular eukaryote.

Dan also helped plan and perform an experiment that has been described as the first large-scale genomics experiment in *Drosophila*. Dan and seventeen others isolated and characterized a large collection of *Y*-autosome translocations. Crosses between selected *Y*-autosome translocations generated flies with duplications and deletions spanning almost the entire autosomal genome to study the effects of gene dosage on the survival and phenotype of adult *Drosophila*. These segmental aneuploids also proved to be very useful in mapping the structural genes for enzymes. Many genes in *Drosophila* are dosage sensitive. The levels of gene products are roughly proportional to the number of wild-type copies of the gene. With just biochemical assays for the levels of enzymatic activities, *Drosophila* researchers were able to map the structural genes for many enzymes using this collection of *Y*-autosome translocations. For two decades, Dan maintained hundreds

of the mutant strains that carried these translocations and provided them to anyone who requested them. Many *Drosophila* researchers, including myself, found these stocks essential for the early stages of a research project.

Dan first realized the importance of genome organization to spermatogenesis through his investigations of radiation-induced chromosome aberrations at Oak Ridge. While recovering and studying *X*-chromosome aberrations in the late 1950s and early 1960s, Dan discovered that differential regulation of the sex chromosomes and the autosomes in spermatogenesis was essential for normal male fertility. In 1965, Dan called this control at the level of entire chromosomes, decades before the role of epigenetics in gene regulation became popular. He was also the first to realize that this differential regulation appeared to be conserved between *Drosophila* and mammalian spermatogenesis. The majority of chromosomal translocations between the *X* chromosome and the autosomes cause male sterility. This sterility could not be explained by DNA damage at the sites of chromosomal interchange, but appears to result from disrupting differential regulation of the *X* chromosome and the autosomes. Regulation at the level of whole chromosomes in spermatogenesis was a major focus of research in his lab at UCSD. Dan and his postdoctoral fellow Eliezer Lifschytz published a model to account for this differential chromosomal regulation. More than fifty years later, this is still the most widely accepted model. Dan continued to be fascinated by this problem for the rest of his life.

Investigations of the effects of chromosome aberrations on male fertility led Dan to spend years trying to collect data to answer two different, but related questions. The first question was the number of genes in *Drosophila* that are essential for normal spermatogenesis. The second related question was how many of those genes are essential solely for male fertility, with no essential function for viability or female fertility. Dan found that not only were significant numbers of essential genes also required for normal spermatogenesis, but that as much as 20 percent of the *Drosophila* genome might function exclusively during spermatogenesis.

FAMILY, EDUCATION, AND ACADEMIC CAREER

Dan was born October 13, 1925, in Evanston, Illinois. His parents, Dan Leslie Lindsley and Ruth Christine Hubbard Lindsley, moved the family to Seattle a few months later. In the early 1930s, the family moved to southern California, where Dan and his younger brother, George Edward Lindsley, spent most of their childhood. In the seventh grade, Dan met Lois Jean Whistler. The pair began dating in the eleventh grade and both graduated from South Pasadena High School in 1943. Dan and Jean were married in 1947 and would have four children, Kathy Salak, Dale Lindsley, Peggy



Figure 2 Dan working on his butterfly collection. Photo from his 2011 holiday card sent to his many friends.

Lindsley, and Dart (Dan Arthur) Lindsley. Jean Lindsley earned a bachelor's degree in biology and was an assistant to Mel Green at the University of Missouri while Dan was working on his master's degree. Jean left science to raise their four children, but in 1977 she began teaching life science to seventh-grade students at The Bishop's School in La Jolla until her retirement in 1990. Whenever I spoke with Dan over the last thirty years of his life, he began every conversation with the recent exploits and accomplishments of his family. Both Dan and Jean treasured their children, grandchildren, and great-grandchildren. They were devoted to each other until Jean Lindsley's death from breast cancer in 2005.

After entertaining me with the latest news about his family, Dan always followed with accounts of his latest expeditions to collect butterflies. Dan became an avid collector early in childhood. As a teenager in Pasadena, Dan would make occasional evening visits to the home of George Rudkin, a physicist and faculty member at Caltech, for information and advice. Rudkin was also an enthusiastic collector and more than willing to encourage Dan. Later in his career, Dan's sabbaticals were in foreign locations that provided not only stimulating scientific interactions, but also the ability to collect butterflies in exotic locations, including Brazil, Italy, Australia, and Spain. Dan would usually show interested visitors his large and brilliantly-colored butterflies from Brazil, but he once told me his greatest interest was in the Lepidopteran family HesperIIDae, mostly smaller and dull-colored butterflies commonly known as "skippers." After Dan and Jean both retired, they would often join trips

to isolated foreign locations with other avid collectors. Dan only stopped going on foreign collecting trips when he was in his late eighties. He told me it was no longer enjoyable when he was no longer able to chase the butterflies fast enough to catch them. By then, Dan had become involved in a biodiversity survey of the undeveloped canyon that led from his backyard down to the shore of the Pacific Ocean. This biodiversity survey was part of an undergraduate course. Dan hung a white bedsheet on his back patio with a light directed at it at night. Dan would go out at 2 a.m. and shake the insects on the bedsheet into collecting jars and give them to the students for DNA barcode identification. Dan donated his large collection of butterfly specimens from six continents to the Florida Museum's McGuire Center for Lepidoptera and Biodiversity at the University of Florida in Gainesville.

After Dan graduated from high school in 1943, he enlisted in the U.S. Navy and joined the V-12 Navy College Training Program to become a physician. Dan was sent to the University of Texas for two years to take undergraduate courses. He then moved to the University of Arkansas College of Medicine to continue his training. One of Dan's professors at the University of Texas, Allen B. Griffen, was very impressed with Dan. When Griffen moved to the University of Missouri, he offered Dan a position in his lab if Dan wanted to transfer to the University of Missouri School of Medicine to finish his medical training. At the end of his first year in Arkansas, Dan's request to transfer to medical school in Columbia, Missouri, was approved by the Navy. Dan arrived in Columbia to discover that he would not be admitted owing to his lack of credits in certain required courses. Dan decided to give up training to be a physician and remain at the University of Missouri to continue his academic studies in Griffen's lab. Because World War II had ended the year before, Dan's request for a discharge from the Navy was granted.

Dan earned his bachelor's degree from the University of Missouri in 1947 and began his graduate studies. At the same time, Ed Novitski arrived at the University of Missouri to spend a year as a research associate. This was the first time that Dan and Ed worked at the same institution. Between 1947 and 1958, Dan and Ed would work at the same institutions four different times, and Ed would be a major influence in Dan's early career. Ed Novitski had completed his doctoral studies with Alfred Sturtevant at Caltech in 1942. He would return to Sturtevant's lab in 1948 as a postdoctoral fellow. At Novitski's suggestion, Dan wrote to Sturtevant inquiring about the possibility of transferring to Caltech to finish his own graduate studies. After Sturtevant offered Dan a position in his laboratory, Dan received his master's degree from the University of Missouri and moved to Sturtevant's lab in Pasadena in 1949. I asked Dan what it was like to learn genetics from Sturtevant. Dan told me that

he actually learned most of his *Drosophila* genetics from Ed Novitski. Dan's thesis research topic in Sturtevant's lab was the consequences of spontaneous spermatogonial exchange in long inversions of the *X* chromosome. These exchanges were rare and often occurred between the *X* and *Y* chromosomes. The products of these exchanges between the *X* and *Y* chromosomes were chromosomes that contained only part of the genetic material from the *X* chromosome and part of the genetic material from the *Y* chromosome. After discussions with Novitski, Dan designed an elegant experiment that used these products of spermatogonial exchanges to synthesize a single chromosome that contained all the genetic material from both the *X* and *Y* chromosomes (the first compound *XY* chromosome).

Novitski left Sturtevant's lab in 1951 to return to the University of Missouri as a professor of zoology. Dan received his Ph.D. from Caltech in 1952 and moved to Princeton for postdoctoral studies with Ken Cooper. Soon after Dan arrived, Ken Cooper moved to the University of Rochester. After a year in Princeton, Dan moved to Novitski's lab in Missouri for his second year of postdoctoral studies. Larry Sandler was a graduate student with Novitski when Dan arrived. Dan and Larry quickly became lifelong friends and collaborators. Their collaborations resulted in ten joint publications between 1958 and 1977. Dan told me that he and Larry spoke on the phone almost every week until Larry's sudden death in 1987 at the age of fifty-six.

Dan accepted a position in the biology division of Oak Ridge National Laboratory in 1954. Larry Sandler received his Ph.D. from the University of Missouri in 1956 and moved to Oak Ridge to spend two years as a postdoctoral fellow before moving to the University of Wisconsin. Dan and Larry collaborated on synthesizing compound sex chromosomes of different constitutions and examining their consequences on meiosis. The collaborations between Dan and Larry in Missouri and Tennessee gave them such great scientific and personal satisfaction that they arranged to go to Rome in 1965 to spend another year working together. Their families rented adjoining apartments near the lab, and Dan and Larry collected wild *Drosophila* on the streets of Rome. In the lab, they screened the progeny of these flies to isolate mutations that were segregating in the wild populations and had effects on fertility or meiosis. The most interesting meiotic mutants from this screen provided thesis projects for several of Larry's graduate students when he returned to his lab at the University of Washington.

The satisfaction that Dan and Larry received from the Rome experience led them to undertake another joint experiment in 1970, three years after Dan had left Oak Ridge to join the faculty of the University of California, San Diego (UCSD). With the help of a large group of graduate students, postdoctoral fellows, and visiting scientists, hundreds

of new translocations between the *Y* chromosome and the autosomes were induced and characterized. Crosses were made between translocations with different autosomal break-points to generate aneuploid flies with small duplications and deletions for adjacent regions that spanned the entire lengths of both large autosomes. The publication in 1972 describing this experiment is unusual for that period with respect to the authorship. There are eighteen coauthors, with Dan and Larry considering themselves co-first authors. Although large numbers of authors and co-first authors are both now commonplace, they were novel in the *Drosophila* research community in 1972.

When Dan moved to La Jolla in 1967 to join the faculty of UCSD, he was among the early members of the Department of Biology. By the time of his retirement in 1991, Dan had taught introductory genetics for almost twenty-five years. He also taught an undergraduate laboratory course in cytogenetics, as well as upper-level courses in advanced genetics and chromosome behavior. In addition to teaching, Dan also served on many departmental committees. He chaired the departmental committee overseeing the graduate program for many years. He also served as the department chair from 1977 to 1979. As department chair, he initiated annual departmental retreats.

Because few of the graduate students enrolling in the Department of Biology at UCSD were interested in *Drosophila* genetics, most of the students in Dan's lab were undergraduates. I consider myself very fortunate to have been one of the four graduate students at UCSD to choose Dan's lab for my thesis research. In my four and half years in Dan's lab, it was always crowded with at least a half-dozen undergraduates, an occasional first-year graduate student doing a six-week research rotation, and numerous visiting faculty members on sabbaticals from universities around the world. In the summers there were no classes, so Dan would hire eager undergraduates to assist in research projects. For most of them, it was their first experience doing full-time research. Each fall, Dan would ask some of the best students from his previous year's introductory genetics course to be teaching assistants for that year's course. As both a teaching assistant for his cytogenetics and introductory genetics courses and as a student in his advanced genetics and chromosome behavior courses, I reaped the benefits of Dan's excellent teaching style. His students learned not only the fundamentals of genetics, but also the experiments that led to their discovery. Dan believed that students would remember the principles of genetics far longer if they understood the questions that led to their discovery. His love of *Drosophila* and genetics were infectious. He had an encyclopedic knowledge of *Drosophila* and loved to share it.

Dan Lindsley was a kind and generous person. He had a wry sense of humor and loved practical jokes. He is remembered with great respect, gratitude, and affection by those of us privileged to have known him. Dan died of natural causes in his home in La Jolla on June 22, 2018, at the age of ninety-two.

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