NATIONAL ACADEMY OF SCIENCES

HERSCHEL L. ROMAN

1914—1989

A Biographical Memoir by

MICHAEL S. ESPOSITO

Any opinions expressed in this memoir are those of the author(s) and do not necessarily reflect the views of the National Academy of Sciences.

Biographical Memoir

COPYRIGHT 1996

NATIONAL ACADEMIES PRESS
WASHINGTON D.C.

Courtesy of Caryl Roman

Herschel C. Roman

HERSCHEL L. ROMAN

September 29, 1914–July 2, 1989

BY MICHAEL S. ESPOSITO

HERSCHEL L. ROMAN, PROFESSOR emeritus and founding chairperson of the Department of Genetics at the University of Washington, made fundamental contributions to studies of the nature of the gene and chromosome behavior in maize during the early phase of his career. Later he led the emergence of *Saccharomyces cerevisiae,* budding yeast, as a premier unicellular organism for study of the basic genetics of eukaryotes. Hersch, as he preferred to be called, was a brilliant researcher, an inspired teacher, and a stalwart colleague of those who shared his love for genetic experimentation and his commitment to the welfare of genetic biology.

An innovator of pace-setting tools for genetic analysis, Hersch was the recipient of numerous distinguished national and international honors in addition to his election to the National Academy of Sciences: Guggenheim fellow, Paris; Fulbright research scholar, Paris; president, Genetics Society of America; American Academy of Arts and Sciences; Gold Medal, Christian Hansen Foundation, Copenhagen; Thomas Hunt Morgan Medal, Genetics Society of America; honorary doctorate, University of Paris; Doctor of Science, honoris causa, University of Missouri-Columbia; and presi-

dent of the International Congress of Yeast Genetics and Molecular Biology. In this latter role Hersch encouraged international research cooperation and collegiality among yeast geneticists for two decades.

As chair of genetics at Seattle, founding editor of the *Annual Review of Genetics*, chair of the NIH Genetics Training Committee, chair of the NIH Research Career Award Committee, member of the NSF Genetic Biology Panel, and consultant to the Biology Division of Oak Ridge National Laboratory, Hersch fostered the growth and dissemination of genetic research for over a quarter century.

Born in the village of Szumsk on the Polish-Russian border on September 29, 1914, Hersch came to the United States with his family in 1921. He spent his youth in the small towns of northern Minnesota and Wisconsin, and received his undergraduate and graduate training at the University of Missouri at Columbia, Missouri. Hersch maintained a special affection for his alma mater which had nourished his interest in science and facilitated his entry into the field of genetics.

Hersch majored in chemistry and received his undergraduate degree in 1936. In his senior year he was employed as an undergraduate assistant by Lewis J. Stadler. Stadler, an eminent maize geneticist, was professor of field crops and senior geneticist for the U.S. Department of Agriculture. Stadler required assistance in making physical measurements and calibrating the large quartz monochrometer used for mutant induction. Hersch's undergraduate training in chemistry and physics suited him to the task. This was the golden era of genetics at Missouri. Stadler and a team of premier researchers that included Daniel Mazia, Barbara McClintock, Joseph O'Mara, Ernest Sears, Luther Smith, and Fred Uber were fruitfully engaged in a variety of genetic studies. McClintock was awarded the Nobel Prize in 1983; the oth-

ers were of similar stature. Hersch was drawn into the excitement surrounding the group effort to determine the action spectrum of induced mutation in maize and became a graduate student under the tutelage of Stadler. His fellow graduate students included Seymour Fogel and John Laughnan.

Stadler's chief goal was to define the nature of the gene. Hersch participated in the continual refinement of the conceptual and technical tools required. In collaboration with Stadler, he documented the fact that the chromosomal rearrangements and losses of genetic material induced by X rays imposed a serious limitation on the usefulness of X rays for study of point mutations. Few X-ray induced changes could possibly be due to such gene mutations and even these few were suspect. However, ultraviolet light induced changes more closely resembled spontaneous gene mutations. This fundamental observation suggested that one might obtain information about the chemical composition of the gene by determining the action spectrum of ultraviolet light mutagenesis. Stadler's group later showed that ultraviolet light of the wavelength absorbed by nucleic acid induced gene mutations most efficiently.

For his doctoral dissertation Hersch undertook an analysis of the inheritance and segregational behavior of the supernumerary heterochromatic B-type chromosomes that occur in many strains of maize. Unlike the standard A-type complement of chromosomes that comprise the maize genome, B-type chromosomes, consistent with their total heterochromatization, are dispensable. Maize strains devoid of B-type chromosomes are indistinguishable from those containing as many as ten. Within maize strains that contain B-type chromosomes, the number of B-type chromosomes varied widely. Cytogenetic studies of the meiotic behavior of B-type chromosomes revealed that they are fragile

and frequently degraded during meiosis. This did not explain the great variability in the number of B-type chromosomes from plant to plant. Moreover, there was no evidence of meiotic nondisjunction of B-type chromosomes that might explain the numerical variation in the number of B-type chromosomes per plant.

Controlled breeding experiments between strains that contain no B-type chromosomes and strains containing one or two B-type chromosomes suggested that mitotic nondisjunction of B-type chromosomes occurs at high frequency during one or both of the postmeiotic mitotic divisions that comprise pollen grain formation in maize. Hersch set out to answer three questions: (1) Does mitotic nondisjunction of B-type chromosomes occur during pollen grain formation? (2) Does nondisjunction occur during one or both mitoses? (3) What portion of a B-type chromosome is responsible for the putative mitotic nondisjunction? To answer these questions he devised a critical experiment that came to be regarded as a classic exemplar of maize cytogenetics.

In a particularly aesthetic example of the manner in which a corn kernel serves as a Petri plate for a gifted maize geneticist, Hersch identified the principal features of B-type chromosome biology. Since B-type chromosomes are devoid of marker genes, Hersch constructed eight interchanges (translocations) between A-type and B-type chromosomes that incorporated appropriate dominant genetic markers on the A-type component of the interchange. The translocations were used to determine whether a specific region of a B-type chromosome is responsible for its unusual transmission properties and to monitor the behavior of B-type chromosomes during the two postmeiotic mitotic divisions involved in pollen grain formation. A-B translocations in which an A-type chromosome contributed the cen-

tromere behaved like normal A-type chromosomes; however, A-B translocations in which a B-type chromosome contributed the centromere behaved like B-type chromosomes. These results indicated that the centromere region of a B-type chromosome is responsible for its peculiar behavior.

The genetic markers incorporated into the A-type components of A-B translocations that contained a B-type centromere affected the color of the kernel and adult plant as well as the texture of the kernel. The markers could therefore be used to detect postmeiotic mitotic nondisjunction and the fate of the resultant nuclei.

Hersch observed that B-type chromosomes undergo mitotic nondisjunction at very high frequency during the second division of the microspore. Consequently, the two gametes of the pollen grain contain two different chromosomal complements. For example, a pollen parent of genotype 0 B/1B, where B is an A-B interchange in which the centromeric component is of the B-type, frequently gives rise to pollen grains in which one of the gametes contains 0 B chromosomes while the other contains 2B chromosomes, due to mitotic nondisjunction during division of the generative nucleus. The 0 B gamete of such pollen grains preferentially unites with the two polar haploid nuclei (seed parent) of the developing kernel to yield the triploid endosperm of the kernel, while the 2B gamete preferentially unites with the egg nucleus of the kernel to yield the plant zygote containing two B-type chromosomes.

Mitotic nondisjunction of B-type chromosomes during pollen grain development coupled with directed fertilization of the seed parent egg nucleus by the hyperhaploid 2B gametic nucleus maintains B-type chromosomes in maize populations. B-type chromosomes, having acquired survival properties that compensate for their meiotic fragility and

apparent lack of relevance to the life of their host, were harbingers of the modern concept of selfish DNA.

Life as a graduate student in Stadler's group demanded a total commitment of mental and physical energy to the maize genetics program. While Hersch and his colleagues benefited from Stadler's powers of analysis, warmth, and encouragement, they were also expected to be responsive to Stadler's affirmative and demanding leadership. Hersch was more than equal to the task. Moreover, he enjoyed a close relationship with the Stadler family and forged lifetime friendships during his Columbia days. While a graduate student, he met and married his wife Caryl Kahn. Their first daughter, Linda, was born while Hersch was a graduate student.

Hersch received his Ph.D. degree in 1942 and accepted an academic appointment in botany at the University of Washington. To his dismay, there were neither greenhouse facilities nor acreage on which to grow experimental crops. Moreover, Seattle's maritime climate prevented the proper maturation of maize ears. Hersch's professional activities, like those of so many of his contemporaries, were soon interrupted by World War II. Hersch joined the Army Air Corps and served until 1946. After his military discharge Hersch resumed his maize studies. He was awarded a Gosney Fellowship for three successive summers to participate in the robust maize genetics program headed by Edgar G. Anderson at the California Institute of Technology in Pasadena.

Thereafter, Hersch brought his crops to maturity on distant rented acreage in the hot climate of eastern Washington state. This solution proved impractical; thus, in 1950 Hersch decided to switch to an organism that could be grown in the laboratory. To take advantage of the growing power of microbial genetics he chose the budding yeast *Saccharomyces cerevisiae* because of its unicellular character,

availability of both haploid and diploid strains, and ability to undergo both mitosis and meiosis in the unicellular state.

The choice was made with trepidation. The genetics of budding yeast was in its infancy and there was concern that it did not routinely follow normal Mendelian inheritance. This concern was unfounded. Hersch, together with his U.S. and foreign colleagues, provided unambiguous genetic data that showed budding yeast is a unicellular eukaryote whose chromosomes exhibit the expected mitotic and meiotic behavior. Hersch, Howard C. Douglas, and Donald C. Hawthorne comprised the initial yeast genetics team at Seattle.

While Hersch's principal research interests were in the areas of gene mutation, chromosome behavior and recombination, he made insightful contributions to many aspects of yeast genetics throughout his long and distinguished career. He chose research topics with extreme care and only after he was convinced that there was enough information available to design critical and informative experiments. His early studies went to the heart of the concern that budding yeast might not exhibit normal Mendelian inheritance. This concern arose from reports from the Lindegren laboratory of numerous exceptions to normal 2+:2m segregations in tetrads from yeast +/m diploids. Hersch demonstrated that the abnormal meiotic segregation patterns (4+:0m, 3+:1m, 1+:3m, and 0+:4m) reflected, at least in part, the contribution of mitotic recombination before meiosis and the failure to detect the accumulation of polyploid cells in populations of parental strains.

In the early 1950s geneticists were still struggling with the fundamental question, What is a gene? In order to answer this question it was essential to establish experimental tests that could distinguish non-complementing mutant alleles of the same gene (heteroalleles) from mutant alleles

of closely linked discrete genes that confer the same phenotype, but fail to complement one another when tested in diploid cells (pseudoalleles). Investigators approached this issue by collecting and characterizing the properties of large collections of independently isolated but phenotypically similar mutants. A view of the gene as a linear array of mutational sites separable by recombination began to emerge, but remained vulnerable to the uncertainties imposed by the concern over pseudoalleles.

Hersch explored the possibility that heteroalleles might be distinguished from pseudoalleles by differences in the way in which they recombine with one another during mitosis and meiosis. In order to carry out experiments he sought a convenient method to obtain large numbers of spontaneous mutations that confer the same phenotype. The difficulty of obtaining sufficient numbers of spontaneous mutations had imposed limitations on related studies in maize. He found that haploid yeast strains that incorporate either an *ade1* or an *ade2* mutation provide a rich source of spontaneous mutations at other genetic loci that control adenine biosynthesis.

Both *ade1* and *ade2* mutants accumulate a red pigment due to the block in adenine biosynthesis and form red colonies on nutrient medium, in contrast to all other yeast strains which form white colonies. Hersch observed that spontaneous mutations of genes that control steps in adenine biosynthesis that precede those controlled by *ade1* and *ade2* block the accumulation of red pigment. When such mutations arise within a population of *ade1* or *ade2* haploids they are readily detected by their restored ability to form white colonies and persistent adenine auxotrophy. (Revertants of *ade1* or *ade2* strains also form white colonies; however, revertants are adenine prototrophs and easily identified as such.) White *adex ade1* and *adex ade2* double mutants have a

selective growth advantage over *ade1* and *ade2* red strains and, with time, emerge as white papilla on the surface of red *ade1* or *ade2* haploid colonies.

Hersch was well aware of the value of a color shift system in genetic experiments from his previous studies with maize. He subsequently exploited the red-white system for studies of both gene mutation and recombination. The red-white system remains a valuable tool in modern recombinant DNA yeast research.

Using the red-white system, Hersch initially described five loci controlling adenine biosynthesis, *ADE3*, *ADE4*, *ADE5*, *ADE6*, and *ADE7*. The remaining *ADE* genes (*ADE8-ADE13*) were identified in later investigations. The initial working material consisted of eighty-three mutations at the *ADE3-ADE7* loci and eight mutations at the *ADE1* and *ADE2* loci. Novel *ade* mutants were assigned to the same *ADE* gene by their failure to complement one another's adenine auxotrophy and their ability to complement the adenine auxotrophy of mutants of the other *ADE* genes.

Comparisons of the frequencies with which diploids homozygous for an identical pair of alleles (homoallelic diploids, e.g., *ade3-1/ade3-1*) and diploids heterozygous for mutant alleles of independent origin (heteroallelic diploids, e.g., *ade3-1/ade3-3*) yield adenine prototrophic revertants during mitotic cell division and following meiosis provided indisputable evidence that intragenic recombination occurs principally by non-reciprocal recombination. Homoallelic diploids yielded Ade+ revertants due to gene mutation during mitosis and after meiosis at low frequencies that were essentially indistinguishable from those observed in mitotic cultures of a haploid carrying the same *ade* mutant.

Heteroallelic diploids exhibited two types of behavior. The vast majority (e.g., *ade3-1/ade3-3*) yielded Ade+ revertants following mitosis at frequencies that were at least ten

times higher than the frequencies of Ade+ revertants found in control mitotic populations of the two homoallelic diploids incorporating the pertinent *ade* alleles (e.g. *ade3-1/ade3-1* and *ade3-3/ade3-3*). Hersch correctly concluded that the enhanced yield of Ade+ revertants represented the contribution of mitotic intragenic recombination to the yield of Ade+ revertants. Since chromosome pairing and recombination at high levels occur during meiosis, Hersch also determined the meiotic yield of Ade+ prototrophs of heteroallelic and homoallelic diploids. Following meiosis, heteroallelic diploids typically yielded Ade+ prototrophs at frequencies ten to a thousand times greater than their corresponding mitotic values. In contrast, meiosis did not enhance the yield of Ade+ prototrophs from homoallelic diploids. This result was consistent with the view that intragenic recombination is the principal source of the Ade+ revertants of heteroallelic diploids.

A minority of heteroallelic diploids (e.g., *ade3-1/ade3-2*) yielded Ade+ revertants during mitosis and after meiosis at frequencies that were indistinguishable from those of the pertinent homoallelic diploids (i.e., *ade3-1/ade3-1* and *ade3-2/ade3-2*). Such experimental data provided an operational definition of mutants occupying the same mutational site (i.e., heteroalleles inseparable by recombination). Hersch noted that the dimension of a mutational site is limited by the resolving power of intragenic recombination; thus, mutants of independent origin that are inseparable by recombination might represent identical mutations or different mutational changes of the same region of a gene.

The frequency of spontaneous gene mutation and the proportion of apparent spontaneous point mutations inseparable by recombination varied coordinately by a factor of ten among *ADE* genes. Hersch suspected that the differences reflected the physical sizes of the *ADE* genes. Eliza-

beth W. Jones, a fellow graduate student, and I with Hersch's guidance constructed genetic fine structure maps of *ADE3*, *ADE6*, and *ADE8* that supported this interpretation. Recent DNA sequencing studies of the yeast genome confirm these early findings.

Budding yeast provided an opportunity to compare the properties of mitotic and meiotic heteroallelic recombination. Hersch's initial studies showed that heteroallelic recombination in both mitosis and meiosis results principally from non-reciprocal recombination (i.e., gene conversion). Reciprocal intragenic recombination occurred rarely in both mitotic and meiotic cell populations.

During meiosis of yeast non-reciprocal recombination between heteroalleles occurs in frequent non-random association with orthodox reciprocal recombination of heterozygous markers flanking the heteroallelic locus. During mitosis non-reciprocal recombination between heteroalleles also occurs in non-random association with orthodox reciprocal recombination of heterozygous markers flanking the heteroallelic locus; however, in mitotic cells the extent of non-random association is typically less than in meiosis. This difference led Herschel to suspect that non-reciprocal and reciprocal recombination might be separate consequences of chromosomal pairing and genetic exchange. He saw an analogy between gene conversion in yeast and DNA transformation in bacteria (namely, localized uptake of a small segment of donor DNA by a recipient chromosome).

Hersch wished to determine whether mitotic gene conversion and intergenic recombination could be dissociated. Drawing upon his previous experience in the Stadler group, Hersch initiated a series of experiments aimed at determining whether there might be physical or chemical agents that could preferentially induce mitotic non-reciprocal recombination (gene conversion) or reciprocal intergenic re-

combination of heterozygous markers. Taking advantage of the red-white colony color system, he examined the inductive effects of ultraviolet light, X rays, nitrosoguanidine, and ethylmethane sulfonate upon mitotic gene conversion and reciprocal recombination. Early studies of the effects of ultraviolet light upon mitotic recombination in yeast diploids, performed in collaboration with Francois Jacob at the Institut Pasteur and Satya Kakar, showed that gene conversion and reciprocal recombination of heterozygous markers flanking the site of gene conversion are separable events. Later analyses of the recombinagenic effects of X rays, ethylmethane sulfonate, and nitrosoguanidine led to the same conclusion.

The separation of gene conversion and reciprocal mitotic recombination was not limited to mitotic recombination induced by physical or chemical agents. Hersch, William Boram, John Golin, and I later reported that certain hyper-recombination mutants enhance mitotic gene conversion but have little effect upon reciprocal recombination.

During the early stages of these studies all of the mitotic recombination data could be interpreted on the assumption that mitotic gene conversion and reciprocal recombination occur in G2 (after chromosomal replication), as they do during prophase of meiosis. There was no need to think otherwise; however, the mitotic data demonstrating the separation of gene conversion from reciprocal recombination of heterozygous markers flanking the site of gene conversion could not be easily accommodated by meiotic molecular models of gene conversion and crossing-over. These models had been designed to explain the very frequent association of meiotic gene conversion and reciprocal exchange of heterozygous markers flanking the site of gene conversion. According to the models, formation of regions

of heteroduplex DNA involving a donor and a recipient pair of non-sister chromatids united by one crossing DNA strand (a Meselson-Radding structure) or a pair of crossing strands (a Holliday structure) is the chromosomal DNA substrate that yields both gene conversion (by mismatch repair of heteroduplexes) and the associated reciprocal exchange of flanking heterozygous markers (by appropriate endonucleolytic scission of the cross-strand DNA connection).

Hersch focused on providing an explanation for the contrasting properties of mitotic and meiotic recombination in yeast. In the late 1970s the puzzle began to unfold. Hersch, Francis Fabre, John Golin, Judy Wildenberg, and I obtained proof that spontaneous and induced gene conversion occurred almost exclusively during the G1 phase of the mitotic cycle. Spontaneous G2 gene conversion occurred rarely, although it could be induced in G2 cells by ultraviolet light or X-ray radiation. At this juncture the classical model of G2 mitotic gene conversion needed to be abandoned. It was possible to account for the simultaneous occurrences of G1 mitotic gene conversion and reciprocal recombination of flanking heterozygous markers by replicational resolution of Holliday structures, as occurs in some bacteriophages. An additional model could also be envisaged; one in which gene conversion that occurs in G1 induces nearby crossing-over in G2 of the same cell.

In order to evaluate these models Hersch devised diploid genotypes that would allow him to question whether recombinant mitotic colonies contain genotypes diagnostic of recombination events in G1 and G2. This series of experiments was the crowning achievement of his stellar studies of recombination in yeast. They are all the more remarkable because they were initiated as Hersch, with Caryl's devoted assistance, courageously fought to recover from the severe stroke he suffered in 1976. Hersch confirmed that

about 80% of gene conversion events occur in G1, while about 20% occur in G2. Moreover, he obtained evidence that resolution of Holliday junctions occurs by endonucleolytic scission in both G1 and G2 cells. Hersch and Mary M. Ruzinski also presented evidence of G1 gene conversion followed by G2 reciprocal intergenic recombination and occasional G2 gene conversion in red-white sectored colonies. Hersch summarized these findings in his final paper published posthumously in *Genetics*.

Earlier in his career Hersch and Fred Sherman observed that diploid cells exposed to sporulation medium, in which they will eventually undergo meiosis, commit to heteroallelic recombination before they commit to completion of the meiotic nuclear divisions. Rochelle Easton Esposito, Dianne Plotkin, and I confirmed this finding and also demonstrated that such cells commit to intergenic recombination before they commit to meiosis. Hersch opined that this early commitment to recombination might reflect the capacity of diploid cells to undergo G1 recombination, although the vast majority of meiotic gene conversions and reciprocal recombination occur later during the prophase stage of meiotic G2 cells; thus, the different properties of mitotic and meiotic recombination could be explained if G1 events play a major role in mitosis and a minor role in meiosis, while G2 events play a minor role in mitosis and a major role in meiosis.

Hersch's philosophy of research was to ask good questions and to design critical experiments that provide answers showing the way to a deeper understanding. He eschewed inductive leaps in favor of solid data. His scientific legacy to the general scientific community is surely his major role in the growth and development of yeast molecular genetics, but those of us intrigued by mechanisms of recombination have received a special gift and envoi—a uni-

fied view of mitotic and meiotic recombination as variations upon the theme of G1 and G2.

I was privileged to perform my doctoral research under Hersch's guidance from 1962 to 1967. Hersch's standard of performance was excellence. He was an exacting mentor and used his incisive mastery of the Socratic approach to uncover the merits and defects of proposed work. He was personally supportive, but most of all he wanted us to experience the self-assurance and enjoyment that comes from knowing that one has done a well designed experiment.

The welfare of the genetics graduate students at Seattle was Herschel's prime concern; we were his academic family. On social occasions Hersch, his wife Caryl, and their daughters Linda and Ann treated us to festive dining, conversational repartee and welcome respite from the pressures of graduate student life. In 1980 Hersch stepped down as chair of the genetics department. On that occasion, former graduate students, postdoctoral fellows, professional colleagues, and friends returned to Seattle from all over the world to attend a research conference convened to celebrate Hersch's stewardship of the department and to honor his concern and affection for students. Hersch's dedication to students has been memorialized at the University of Washington, Seattle, by the Herschel and Caryl Roman Undergraduate Science Scholarship awarded to outstanding science majors in their junior year.

Hersch loved the arts, literature, and rhododendrons. I fondly recall accompanying him on walks in his garden and listening to him describe the special attributes and parentage of members of his floral collection. The memorial rhododendron garden established by the Roman family in the University of Washington Arboretum bears an apt inscription: "This display was funded by the Roman family in memory of Herschel L. Roman, founder of the University of Wash-

ington Genetics Department, who loved both the beauty and the genetic principles so vividly exhibited by rhododendron hybrids."

Hersch completed the manuscript of his last paper a few days before his death on July 2, 1989. He is survived by his wife Caryl, his daughters Linda Roman and Ann Roman Weiner, his brother Arnold, his sister Ruth Levin, and his grandson Aaron Weiner.

HONORS AND DISTINCTIONS

Gosney Fellow, California Institute of Technology, host: Edgar G. Anderson, 1946-48
Guggenheim Fellow, University of Paris, host: Boris Ephrussi, 1952
Fulbright Research Scholar, University of Paris, host: Boris Ephrussi, 1956
President, International Congress of Yeast Genetics and Molecular Biology, 1961-84
President, Genetics Society of America, 1968
Elected to the American Academy of Arts and Sciences, 1969
Elected to the National Academy of Sciences, 1970
Citation of Merit, University of Missouri-Columbia, 1973
Gold Medal, Emil Christian Hansen Foundation, Copenhagen, 1980
Thomas Hunt Morgan Medal, Genetics Society of America, 1985
Honorary doctorate, Université Pierre et Marie Curie, Paris, 1986
Doctor of Science, Honoris causa, University of Missouri-Columbia, 1989

SELECTED BIBLIOGRAPHY

1947

Mitotic nondisjunction in the case of interchanges involving the B-type chromosome in maize. *Genetics* 32:391-409.

1948

With L. J. Stadler. The effect of X-rays upon mutation of the gene A in maize. *Genetics* 33:273-303.

Directed fertilization in maize. *Proc. Natl. Acad. Sci. U.S.A.* 34:36-42.

1950

Factors affecting mitotic nondisjunction in maize. *Genetics* 35: 132.

1951

With A. J. Ullstrup. The use of A-B translocations to locate genes in maize. *Agron. J.* 43:450-54.

With D. C. Hawthorne and H. C. Douglas. Polyploidy in yeast and its bearing on the occurrence of irregular genetic ratios. *Proc. Natl. Acad. Sci. U.S.A.* 37:79-84.

1953

With S. M. Sands. Heterogeneity of clones of Saccharomyces derived from haploid ascospores. *Proc. Natl. Acad. Sci. U.S.A.* 39:171-79.

1955

With B. Ephrussi and H. Hottinguer. Suppressiveness: a new factor in the genetic determinism of the synthesis of respiratory enzymes in yeast. *Proc. Natl. Acad. Sci. U.S.A.* 41:1065-71.

With M. M. Phillips and S. M. Sands. Studies of polyploid segregations in Saccharomyces. I. Tetraploid segregation. *Genetics* 40:546-61.

1956

Studies of gene mutation in Saccharomyces. *Cold Spring Harbor Symp. Quant. Biol.* 21:175-85.

1957

With F. Jacob. Effet de la lumière ultraviolette sur la récombinaison génétique entre alleles chez la levure. *C. R. Acad. Sci.* 245:1032-34.

1958

With F. Jacob. A comparison of spontaneous and ultraviolet induced allelic recombination with reference to the recombination of outside markers. *Cold Spring Harbor Symp. Quant. Biol.* 23:155-60.

A system selective for mutations affecting the synthesis of adenine in yeast. *C. R. Lab. Carlsberg Ser. Physiol.* 26:299-314.

Sur les récombinaisons non-reciproques chez *Saccharomyces cerevisiae* et sur les problèmes posés par ces phénomènes. *Ann. Génét.* 34:11-17.

1963

With F. Sherman. Evidence of two type of allelic recombination in yeast. *Genetics* 48:255-61.

1968

With J. Friis. The effect of the mating-type alleles on intragenic recombination in yeast. *Genetics* 59:33-36.

1973

Studies of recombination in yeast. *Stadler Symp.* 5:35-48.

1976

Recombination in *Saccharomyces cerevisiae*: a DNA repair mutation associated with elevated mitotic gene conversion. *Proc. Natl. Acad. Sci. U.S.A.* 73:2828-32.

1977

With F. Fabre. Genetic evidence for inducibility of recombination in yeast. *Proc. Natl. Acad. Sci. U.S.A.* 74:1667-71.

1979

With F. Fabre. Evidence that a single DNA ligase is involved in

replication and recombination in yeast. *Proc. Natl. Acad. Sci. U.S.A.* 74:4586-88.

1983

With F. Fabre. Gene conversion and associated recombination are separable events in vegetative cells of *Saccharomyces cerevisiae. Proc. Natl. Acad. Sci. U.S.A.* 80:6912-16.

1984

A comparison of induced and spontaneous gene conversion in mitotic and meiotic cells of *Saccharomyces cerevisiae. Carlsberg Res. Commun.* 49:351-58.

With F. Fabre and A. Boulet. Gene conversion at different points in the mitotic cycle of *Saccharomyces cerevisiae. Mol. Gen. Genet.* 195:139-43.

1986

The early days of yeast genetics: a personal narrative. *Annu. Rev. Genet.* 20:1-12.

1990

With M. M. Ruzinski. Mechanisms of gene conversion in *Saccharomyces cerevisiae. Genetics* 124:7-25.