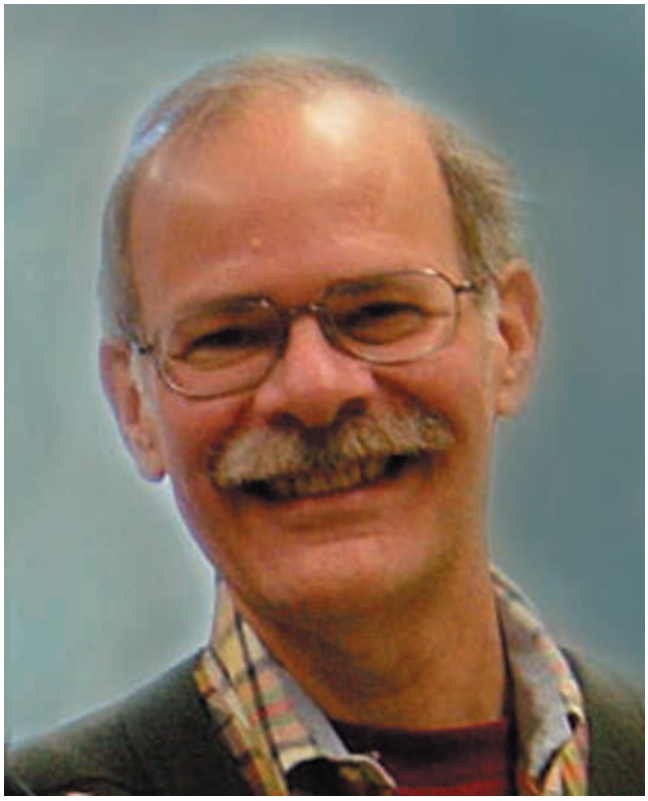
The 2002 GSA Honors and Awards

The Genetics Society of America annually honors members who have made outstanding contributions to genetics. The Thomas Hunt Morgan Medal recognizes a lifetime contribution to the science of genetics. The Genetics Society of America Medal recognizes particularly outstanding contributions to the science of genetics within the past 15 years. The George W. Beadle Medal recognizes distinguished service to the field of genetics and the community of geneticists. We are pleased to announce the 2002 awards.



Ira Herskowitz

The 2002 Thomas Hunt Morgan Medal

Ira Herskowitz

IRA Herskowitz is the richly deserving recipient of the 2002 Thomas Hunt Morgan Medal, the highest honor awarded by the Genetics Society of America. This award recognizes 33 years of outstanding achievement since the publication of his first research paper in 1970. We are sad to note that Ira Herskowitz succumbed to pancreatic cancer on April 28, 2003.

Ira's research career started during his undergraduate days at Cal Tech, where he characterizes his experience as "I was 20 minutes late for my first class and I never caught up." Fortunately for genetics, he found his way into a research project on bacteriophage with Robert Edgar and Jonathan King, where he developed a passion for experimental genetics. Perhaps more importantly he gained a deep appreciation of experimental contexts in which intellectual rigor could be matched by experimental care, as this, he believed, was the best way to train scientists.

Imprinted by the gospel of microbial genetics, Ira found his way to graduate school at MIT, where he joined Ethan Signer's lab for graduate work. There he developed an interest in the biology of λ phage and its interaction with the physiology of its host. Lambda appealed to Ira deeply because of the alternate fates, lysis or lysogeny, that were controlled by genes of λ and of *Escherichia coli*. This study of alternative fates was to be a theme that continued throughout his career.

After completing his Ph.D. in 1971, Ira enjoyed a brief stint with yeast and Cold Spring Harbor Laboratory during a postdoctoral year with David Botstein before beginning as an Assistant Professor in the Institute of Molecular Biology at the University of Oregon. The institute at that time was an odd mixture of geneticists and biophysicists. Two of his colleagues who made a deep impression on Ira were George Streisinger and Frank Stahl, top figures in microbial genetics and molecular biology.

Ira's approach to science was a refreshing change of pace for the graduate students first attracted by more biophysical interests. Indeed his first six graduate students were walk-ons who gave up their original interests to follow Ira's research agenda and style. As the seventh

member to join the lab, I remember Ira's uncanny ability to take any result and help you see how it could be developed into a much bigger story with great significance. There was more to Ira's appeal than intricate hypotheses on chalkboards, toothpicks, and Petri plates. His passion for both music and ping pong enlivened many occasions, and the track meets in Eugene were always fun and occasionally dry. Joining his lab was the easiest decision that most of us had made.

It's hard to say with certainty what any great scientist's principal strength is. With Ira, certainly the ability to choose compelling research problems was one of them. He described his strategy as one in which he looked for situations in which there are two or more observations that all parties agree upon, yet the observations are mutually incompatible. This philosophy led Ira directly into a central mystery in the biology of the Saccharomyces yeast. Everyone agreed that the *MAT***a** and *MAT*α alleles of the mating-type locus were codominant. Yet everyone also agreed that Don Hawthorne had a deletion that converted an α cell into an **a** cell. Clearly, the conversion of one codominant allele into another challenges all normal conventions in genetic thinking.

This insight led to an amazingly beautiful set of experiments, initiated by Jim Hicks and Jeff Strathern, which proposed and proved that yeast switch mating types by way of transposable cassettes. This body of work may well represent the last great problem in biology that was fundamentally resolved purely by classical genetic analysis.

In 1979, Ira spent a sabbatical at UC San Francisco; in 1981 he joined the faculty at UCSF, where he remained. From 1981 to 2001, he headed the Division of Genetics and from 1982 to 1995, served first as Vice Chairman and then Chairman of the Department of Biochemistry and Biophysics. This early period in Ira's career at UCSF was heavily influenced by the pervasive strength in cell biology at UCSF and the experimental facility that yeast lent his lab in tackling these issues with genetics. The leading example from this period was his lab's contribution to understanding the cascade of events that enable two yeast cells of opposite mating types to engage in *preconjugal* communication, coordinating their cell cycles to facilitate mating. This process is now understood from the receptors, through the G protein, through a cascade of MAP kinases, to the transcription factors that are the targets of the signal. By looking for mutants in the classic way that could still respond to the ligand but did not arrest the cell cycle, Ira and his colleagues worked out the coordination between signaling and cell cycle progression.

Other examples include a detailed dissection of how the expression of the HO gene is regulated. His lab has been one of the principle contributors to our understanding of how the HO endonuclease is expressed only in G1, and then only in mother cells and not in their daughters. Understanding the genetic basis of asymmetry at HO expression was particularly gratifying to Ira, both as a capstone to his lab's discovery of the asymmetry in mating-type switching, but also as the first well understood example of a problem fundamental to developmental biology: how new cell types can be programmed to appear at the right place at the right time.

More recent studies include an analysis of why the budding pattern of haploid and diploid cells is different, which has blossomed into other aspects of cell polarization, and studies of the role of chromatin components and chromatin remodeling factors on gene expression. As in all cases, Ira came to these interests not by reading the papers of others. Instead he simply allowed the mutants isolated in his own lab to reveal the stories they had to tell.

His most recent work continued an interest in signaling of other types, including pathogenesis in Ustilago, and moved into more central medical problems. He had begun a study of prion autocatalysis in yeast and became interested in the significance of polymorphisms in human genes that encode molecules involved in drug transport and metabolism.

Prior to the Morgan Medal, Ira had already received substantial recognition from his peers including election to the National Academy of Science in 1986, a MacArthur Foundation Fellowship in 1987, the Genetics Society of America Medal in 1988, and election to the Institute of Medicine in 2002. He served the field at the highest levels including service on the NIH study section, where he had great influence on the articles that appear in this journal. He performed great service on many different editorial boards, including five years as Associate Editor of Genetics, on the Scientific Review Board of the Howard Hughes Institute, and as a jury member for the Albert Lasker Medical Research Board.

I suspect that these and the many other awards and honors he received were of secondary importance to Ira at best. He led a career in which excellence in teaching was always a goal and in which teaching people how to ask the right question is of paramount importance. There can be no better sign of his success than the thousands of students whose appreciation of genetics was born in the classes that Ira taught and the perhaps unprecedented success that Ira's students have had in their own independent careers following their training in his lab. As a community, we warmly applaud the selection of Ira Herskowitz as the recipient of the 2002 Thomas Hunt Morgan Medal of the Genetics Society of America.

Jasper Rine

Andrew Fire

The 2002 Genetics Society of America Medal

Andrew Fire

ANDY Fire is awarded the GSA Medal for 2002 for his discovery that introducing double-stranded RNA into an animal can activate a process that leads to the destruction of its own complementary mRNA. This discovery, known as RNA interference (RNAi), is now having a profound effect on biological research in many organisms and has immense potential for disease treatment in humans. RNAi can now be used to inhibit gene function in many research organisms including *Caenorhabditis elegans*, Drosophila, and mice. RNAi screens have now nearly replaced conventional mutagenesis screens in some fields of research, and because it is much faster than current methods, RNAi will probably come to play a major role in the genetic analysis of mice and other mammals. Because the targeting process is so specific, RNAi may eventually be used to inactivate human disease genes, such as the oncogenic forms of genes responsible for human cancers. Already a number of biotechnology companies have been formed specifically to develop this therapeutic strategy. Andy discovered RNAi when he began to ask why preparations of sense as well as antisense RNAi were able to inhibit gene function in conventional antisense-RNA experiments in *C. elegans*. On closer inspection, he discovered that the active species was actually double-stranded RNA, which had been contaminating both the sense and antisense RNA preparations. Since then, Andy's laboratory has gone on to elucidate many of the key steps in the mechanism by which double-stranded RNA leads to the destruction of endogenous mRNA.

Cynthia Kenyon

Robert Mortimer

André Goffeau

The 2002 George W. Beadle Medal

Robert Mortimer and André Goffeau

THE 2002 Beadle Medal of the Genetics Society of America is awarded to Robert Mortimer and André Goffeau for their outstanding contributions to the development of the yeast *Saccharomyces cerevisiae* as an experimental organism. The availability of genome resources for this important model organism, which is now taken for granted, is in large part due to the extraordinary efforts of these two individuals. Bob Mortimer launched the yeast genome project in the early 1950s, when he began to produce a genetic map of the yeast genome. The project was brought to fruition through the efforts of André Goffeau, who initiated and successfully led the yeast genome sequencing project.

It is difficult to exaggerate the importance of *S. cerevisiae* as an experimental organism. The results of decades of studying the organism form a cornerstone of our knowledge base of cellular and molecular biology. Mortimer and his colleagues provided genetic tools for analyzing yeast that fueled development of the organism as an experimental system for several decades. By revealing all the genes of the organism, the yeast genome sequence determined by Goffeau and his collaborators opened the way to the systematic study of gene function. In addition, it stimulated scientists working with other organisms to address their biological problems through incisive experiments with yeast, offering the opportunity

to realize a much deeper understanding of cell function. The completion of the yeast genome sequence transformed experimental biology by ushering in the current era of whole genome analysis that is providing great insights into global gene regulation, gene function, and genome evolution. Clearly, Bob Mortimer and André Goffeau have had a huge impact on biological research.

Bob Mortimer is the person most responsible for development of the yeast genetic map, which he pursued from the 1950s right until the genome sequence became available in the middle 1990s. This indispensable resource cemented the position of yeast as a premier experimental organism. The Yeast Genetic Stock Center he founded was the forerunner of the yeast genome resources available today. Mortimer's discovery of an easy method of digesting asci made tetrad analysis a technique accessible to many scientists. His generosity with the reagents he developed and the information he learned set a standard of collegiality that is still enjoyed by everyone working with yeast.

Mortimer's early characterization of the radiation biology of yeast laid the groundwork for the widespread use of Saccharomyces in understanding DNA repair. He and his colleagues identified the major *RAD* genes involved in DNA repair. His contributions to our understanding of meiotic recombination, especially gene conversion in yeast, was crucial for subsequent model building and theoretical understanding of recombination mechanisms. Mortimer was one of the first people to identify and characterize translational suppressors in yeast, which are now part of the genetic landscape of the organism, and have been widely used to understand the nature of prions. Even in retirement, he continues to make significant contributions to our understanding of the ecology and natural history of yeasts.

André Goffeau had already achieved international recognition as a world expert in yeast energetics and membrane proteins when he turned his attention to sequencing the yeast genome. Goffeau's discovery of the plasma membrane H^+-ATPase opened to research an important area of yeast cell biology. Much of what we know about the ABC (ATP binding cassette) transporters in yeast cells, which informs how human cells become resistant to anticancer drugs, stems from Goffeau's work. Goffeau was one of the first people to foresee the importance of knowing the DNA sequence of entire genomes. He and Steve Oliver began to advocate for sequencing the yeast genome in the middle 1980s, when many people were skeptical of (indeed, even hostile to) the idea that an organized effort to sequence the yeast genome was advisable. Goffeau organized and led the successful worldwide effort to determine the sequence of the yeast genome. He first convinced his colleagues in Europe to mount the sequencing effort, and he was effective in securing the necessary funding for this project from the European Commission. The success of Oliver, Goffeau, and their European colleagues in determining the sequence of yeast chromosome III stimulated others around the world to join the project, which was completed, ahead of schedule, in 1996. André Goffeau's collegial, cooperative, and capable leadership of this international project was recognized by his position as the first of 633 authors of *The Yeast Genome Directory*, a special issue of Nature published in 1997.

André Goffeau's vision of how the sequence of the yeast genome should be determined—by many investigators collaborating worldwide—was followed by the Human Genome Project. It stimulated yeast research worldwide and fostered a collaborative spirit that continues today. Goffeau played a major role in setting the standards for the entire field of genome sequencing by his insistence on high standards for sequence quality and completeness. Largely because of his leadership, the yeast genome sequence is very accurate and still stands as the most complete genome sequence on record.

Mark Johnston

The 2002 George W. Beadle Medal Essay

Why I Developed the Yeast Genetic Map

Robert Mortimer

Division of Genetics, University of California, Berkeley, California 94720-3204

IN the late 1940s while finishing my degree as an honors physics major at the University of Alberta, I decided to look for future options. Fortunately, UA had a good library where I discovered the program in biophysics at the University of California, Berkeley. I wrote to Professor Cornelius Tobias, advisor of the program, and was accepted as a Ph.D. candidate with a teaching assistantship. Meanwhile, I had begun doing geophysical work with an oil survey company in Calgary at a time when large reservoirs of oil were being discovered in Alberta. The oil industry offered an adventuresome and lucrative future.

However, I opted for UC Berkeley and was married; together we headed south where I joined Tobias, who was working with Raymond Zirkle, professor at the University of Chicago, trying to determine if haploid cells were more or less resistant to ionizing radiation than diploid cells. The diploids were more resistant. Zirkle and Tobias constructed a recessive lethal model to explain this difference. To test their model I constructed and tested triploid and tetraploid cells, which, contrary to their model that predicted that they should be more resistant, became progressively more sensitive. After perusing the biology library at Berkeley regarding radiobiology and ploidy, I found that there was much to learn about the field. Subsequently, my interests focused on the area of dominant lethality, and after further research, I proposed a theory to explain the higher sensitivity in tetraploid cells: the damage was partially caused by dominant lethality, which resulted from chromosome aberrations whose frequencies increased with the ploidy of the irradiated cell. Such damage was then demonstrated in haploid and diploid irradiated cells in yeast, thus confirming my hypothesis.

The theories of dominant lethality involved chromosome aberrations and the formation of dicentric chromosomes that formed anaphase bridges. These bridges led to mechanical disruption of mitosis, which led me to try to demonstrate chromosome abberations in yeast. Yeast chromosomes were small and not subject to cytological examination so I decided to develop the yeast genetic map that I hoped could facilitate further characterization of the chromosomes. The Neurospora and Aspergillus maps had already been developed, showing that their chromosome numbers were small, 7 or 8. Additionally, Perkins had published articles describing a genetic method to detect Neurospora chromosome aberrations. I reasoned that yeast, also being a fungus, should have a similar number. I planned to take a year off to develop this map of yeast but it turned out to be a much bigger job.

In 1960 Don Hawthorne and I published our first article on yeast genetic mapping in GENETICS. It is my view that this was a seminal article in yeast genetics research that proved to lay a cornerstone for the entire field of yeast genetics research. It not only defined a number of centromere-linked genes and their associated centromeres and provided the framework map on which others could build, but also laid out clearly the way to map genes and chromosomes using unordered tetrads. It was eventually discovered that yeast had 16 chromosomes and the recombination along each of these chromosomes was high. Subsequently, I continued mapping in collaboration with other investigators until, 40 years later when the job was nearly finished, I turned the project over to David Botstein of Stanford University, for publication of the twelfth edition of the yeast genetic map. Completion of the yeast genome sequence soon followed.

I am pleased to have spent a good part of my career helping develop yeast as a model organism, which has become widely used in laboratories doing research in many fields, including detection of human diseases.

Previous Recipients of These Awards

	Thomas Hunt Morgan Medal	Genetics Society of America Medal	George W. Beadle Medal
1981	Barbara McClintock and Marcus M. Rhoades	Beatrice Mintz	
1982	Sewall Wright	Gerald R. Fink	
1983	Edward B. Lewis	Charles Yanofsky	
1984	George W. Beadle and R. Alexander Brink	David S. Hogness	
1985	Herschel L. Roman	Philip Leder	
1986	Seymour Benzer	Gerald M. Rubin	
1987	James F. Crow	Sydney Brenner	
1988	Norman H. Giles	David Boststein and Ira Herskowitz	
1989	Dan L. Lindsley	Allan C. Spradling	
1990	Charles Yanofsky	Nancy Kleckner	
1991	Armin Dale Kaiser	Bruce S. Baker	
1992	Edward H. Coe, Jr.	Maynard V. Olson	
1993	Ray D. Owen	Jonathan R. Beckwith	
1994	David D. Perkins	Leland H. Hartwell	
1995	Matthew Meselson	Eric Wieschaus	
1996	Franklin W. Stahl	Elliot Meyerowitz	
1997	Oliver Evans Nelson, Jr.	Christine Guthrie	
1998	Norman H. Horowitz	Ronald W. Davis	
1999	Salome G. Waelsch	Charles H. Langley	Michael Ashburner
2000	Evelyn M. Witkin	Jack W. Szostak	John Sulston and Robert Waterston
2001	Yasuji Oshima	H. Robert Horvitz	Gerald R. Fink