The 2001 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 2001 awards.

Yasuji Oshima

The 2001 Thomas Hunt Morgan Medal

Yasuji Oshima

MANY great geneticists have contributed to making yeast genetics the remarkable experimental system that it has become. Dr. Yasuji Oshima's contributions stand out, however, because he has provided the genetic groundwork for two major pathways of cell physiology and gene regulation (phosphate regulation and mating-type switching) and has made fundamental contributions to another (galactose regulation).

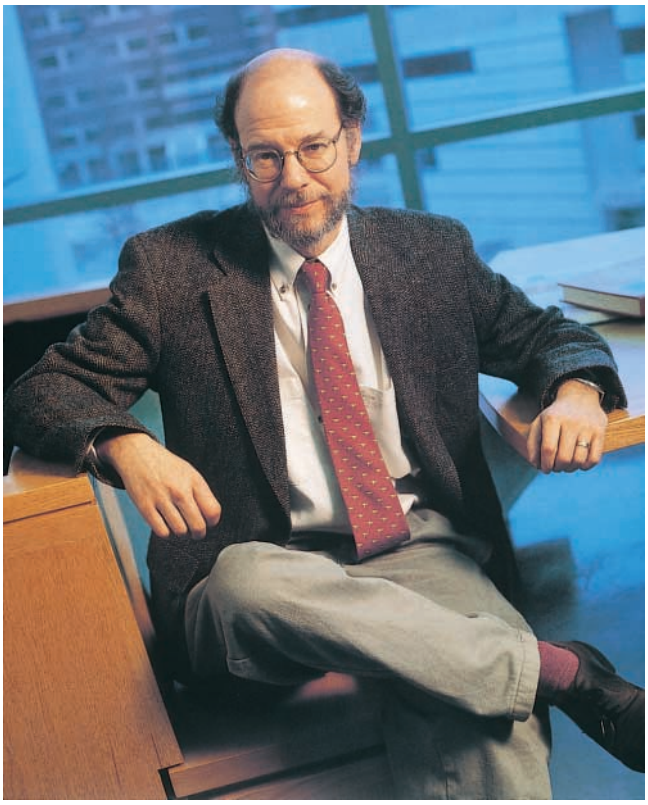
Yasuji Oshima was born in Japan in 1932. He graduated from the Department of Fermentation Technology in the Faculty of Engineering of Osaka University in 1955 and went on to receive his doctoral degree there in 1960. He then moved to Carbondale, Illinois, for postdoctoral research with the pioneering yeast geneticist Carl Lindegren from 1963 until 1965. He returned to Japan and worked in the research laboratories of Suntory Ltd. until 1970, when he assumed a faculty position in the Department of Fermentation Technology at Osaka University. In 1990 he became Director of the International Center of Cooperative Research and Development in Biotechnology at Osaka, and in 1996 he moved to his present position as Professor at Kansai University. Throughout his career, Professor Oshima has been active in the Society of Fermentation and Bioengineering (formerly the Society of Fermentation Technology), serving as Director and Member of the Council since 1973. He has also been awarded several prestigious prizes.

What is particularly notable in all of the work from Professor Oshima's laboratory is the unerring logic and critical analysis that led to the discovery of essentially all of the genes of the phosphatase pathway and their organization by incisive epistasis analysis. These studies provided the pathway that has subsequently been mined

by others to understand in exquisite detail how the genes discovered by Oshima regulate nuclear import and export of a transcription factor. Oshima's incisive studies of the galactose regulatory genes exploited fine-structure mapping to place a dominant constitutive mutation among the null mutations that inactivate the *GAL4* gene and result in an uninducible phenotype. This observation, together with the judicious use of temperature-sensitive mutants and temperature-shift experiments, overturned a dogma that had grown up around this pathway and set the stage for the galactose genes (and their positive regulatory protein, Gal4, in particular), to become one of the most fertile grounds for studies of gene regulation in yeast. Finally, the contributions of the Oshima laboratory to mating-type switching were pioneering and remarkable. His earliest studies began in 1967 to understand the unusual life cycle of *Saccharomyces oviformis*, in which only one of the two mating types can switch. In a series of rigorous papers published with his students I. Takano and S. Harashima in Genetics, Oshima proposed that mating-type switching results in a genetic change at the mating-type locus and that the *HM*α and *HM***a** genes were transposable elements that associated with the mating-type locus to confer **a** or α mating type. In a remarkable 1974 paper, Harashima, Nogi, and Oshima demonstrated that the simplest explanation for mating-type switching is that actual **a** or α information resides in the donor *HM* loci, that the information in the donor loci can be either **a** or α, depending on the strain, and that the genetic information for mating type is actually transferred from the donor into the mating type locus itself to effect the change in mating type. These studies of unstable genes represent a pinnacle of genetics and led to subsequent genetic and molecular studies in other laboratories that revealed this system to involve transposable structural genes governed by a double-strand break repair process.

We feel particularly connected to Dr. Oshima since our own research has built so heavily on his pioneering studies in phosphate regulation and in mating-type interconversion. We and many others in yeast genetics have truly stood on the shoulders of a giant.

Ira Herskowitz
Erin O'Shea



H. Robert Horvitz

The 2001 Genetics Society of America Medal

H. Robert Horvitz

THE 2001 GSA Medal is given to H. Robert Horvitz to honor his many contributions to genetics research and training. One of the pioneers in the *Caenorhabditis elegans* system, Bob has cut a genetic swath through many areas of developmental biology, cell biology, and neurobiology, discovering new gene families and defining genetic pathways. Along the way Bob has trained many of the current leaders in the *C. elegans* field. This award specifically recognizes Bob's accomplishments during the past 15 years in two important areas: the analysis of vulval development and function, and the elucidation of the pathway controlling programmed cell death.

After undergraduate studies at the Massachusetts Institute of Technology, Bob pursued graduate studies at Harvard University with James Watson and Walter Gilbert on the regulation of *Escherichia coli* RNA polymerase by bacteriophage T4. He then joined Sydney Brenner at the MRC Lab of Molecular Biology in 1974 to learn the then-new *C. elegans* system. While there, he developed interests in two processes that have driven much of the work in his lab: programmed cell death and vulval development and function. He had planned to study muscle development, and upon arrival he joined forces with John Sulston in an ambitious project to determine postembryonic cell lineages. The programmed cell deaths that occurred in the lineage kindled an interest that Bob would return to after his postdoc studies. In a pioneering study, Horvitz and Sulston applied genetics to the complex problem of understanding how the cell lineage was specified. They tried a variety of screens and found a fascinating set of cell lineage mutations that they reported in a 1980 GENETICS article. Bob realized that one class of mutants that emerged in the screens, egg-laying defective mutants—visualized by their "bag-of-worms" phenotype—would provide an entry point to several aspects of development and behavior. The "bags of worms" arose either from failure of development of the vulva, the epidermal egg-laying apparatus, or from failure in development or function of muscles and nerves required for egg laying. After moving to MIT in 1977, Bob recruited a group of talented students and postdocs to help him saturate the genetic map for mutations affecting vulval development and egg laying. These genetic studies set the groundwork for defining pathways of developmental control, as well as many aspects of neuronal development and function.

Bob's genetic studies on the development of the egg-laying system have had a major impact in developmental biology. The analysis of the vulva defective mutations led to what is arguably the most complete understanding of a developmental induction and contributed significantly to the elucidation of the conserved EGF-receptor/RAS signaling pathway for fate specification. As an example, consider the first three of the cell lineage genes found. *lin-1* encodes an ETS domain protein at the nuclear end of the RAS pathway, *lin-2* is necessary for EGF-receptor localization, and *lin-3* encodes the

EGF-like vulval inductive signal. In addition, Bob's studies of egg-laying mutants that affected sex muscle precursor development identified the *C. elegans* FGF-receptor and, in 1992, *sem-5*, the key missing link in the signaling pathway from transmembrane "receptor" tyrosine kinases to RAS activation. The key result was based on the placement of *sem-5* upstream of RAS in a genetic pathway. Following up on an elegant bit of genetic sleuthing Bob reported in the 1980 cell lineage paper, in 1989 he and student Edwin "Chip" Ferguson defined two apparently redundant pathways involving the "synthetic multivulva" genes. When worms are defective in any of the "A" class of genes as well as in any of the "B" class of genes, they display a "multivulva" phenotype. While these two pathways remain a fascinating genetic puzzle after a decade, Bob has found that some of these genes in the B pathway encode Rb pathway proteins, putting a molecular face on one of the two pathways.

Many of the genes identified in the egg-laying screens defined new gene families involved in a host of biological phenomena, after they were positionally cloned in Bob's lab or in the labs of his students. The vulval lineage gene *lin-11* is the L in the LIM homeodomain family. The cell lineage regulator *unc-86* is the U in POU domain transcriptional regulators. *lin-12* is a founding member of the Notch family of receptors. *lin-4*, necessary for developmental timing, encodes the first of the recently expanded families of micro-RNAs. *egl-10*, a regulator of egg-laying behavior, was a founding member of the RGS family of regulators of G protein signaling.

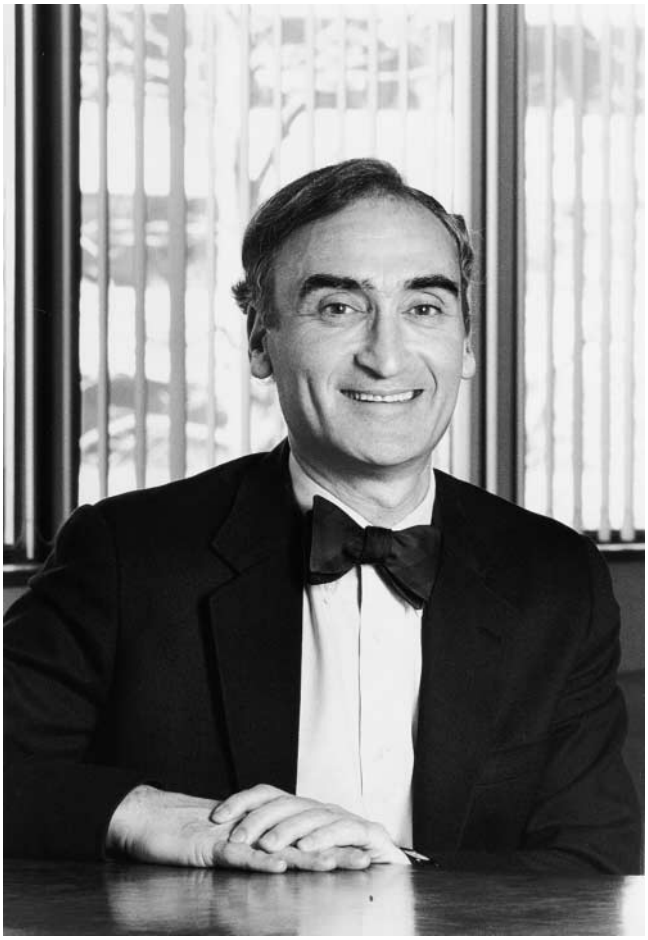
At the same time that Bob was collecting and analyzing the egg-laying defective mutations, he began his study of the poorly understood developmental phenomenon of programmed cell death or apoptosis. His genetic studies led to the identification of the core players in the canonical pathway that controls apoptosis. In a clever screen published in 1986, Hilary Ellis and Bob discovered *ced-3* and *ced-4* as genes required for most apoptosis in *C. elegans*. These genes defined the beginning of a cell death pathway. Additional screens for cell death genes filled out the pathway. Analysis of mutations identified in screens for worms with persistent cell corpses defined about 10 genes involved in the phagocytosis of the apoptotic cells. Continuing screens for mutations that block cell death identified a dominant mutation in *ced-9*. Reversion of the dominant mutation and epistasis analysis led to the understanding that *ced-9* protects against cell death by antagonizing the action of *ced-3* and *ced-4*. The cloning of *ced-9* revealed that it was homologous to the mammalian cell death gene *bcl-2*. This discovery was a major advance in the cell death field because it linked genetic pathway analysis in *C. elegans* to biochemical and oncogenetic studies in human and mouse. This advance rapidly led to the discovery of caspases (*i.e.*, *ced-3*) and an explosion in the apoptosis field because the results from *C. elegans* led directly to new discoveries in mammalian systems. Bob's screens of egg-laying mutants also contributed to the cell death analysis. A dominant mutation in *egl-1* proved to result from an inappropriate programmed cell death of neurons that innervate the vulval muscles and was subsequently found to be required for all cell deaths. Indeed, this phenotype of *egl-1* mutants allowed screening for mutants defective in cell death pathways genes such as *ced-9*.

Bob also has had a longstanding interest in inherited human diseases, especially Huntington's disease and amyotrophic lateral sclerosis. He has been a major advisor to the Hereditary Disease Foundation and the ALS Association. Bob was a major player in the collaborative cloning of the first ALS gene and in a series of related molecular and genetic studies.

Bob's contributions to training in genetics are as impressive as his research accomplishments. Bob set standards of genetic rigor through his papers, through his reviewing of the work of others, and through the training of students and postdocs in his lab. Thirty of his former students and postdocs now have their own *C. elegans* laboratories. The experimental approach, scientific rigor, and rapid progress in the labs of these former students and postdocs show Bob's influence. Projects in Bob's lab started with genetic screens followed by intensive definition of loss-of-function phenotypes and construction of many double mutants to infer pathway relationships. When coupled with positional cloning, these studies were key contributors to the paradigm of developmental genetics that has led to our understanding of how genes control development and is beginning to make inroads into how genes control behavior.

Bob is not only a pioneer in the use of the *C. elegans* system but has also been a leader and a spokesperson for the *C. elegans* and broader biomedical research communities. He was an organizer of three of the first six International *C. elegans* Meetings and has been a shaper of policy and practices within the community. He served as president of the Genetics Society of America and on their Board of Directors. Bob has been active in NIH Genome Council and helped pave the way for the extraordinary effort of the *C. elegans* Sequencing Consortium to deliver the first complete sequence of a metazoan. He has had a strong interest in public science policy, serving on the Joint Steering Committee for Public Policy and the American Society for Cell Biology Public Policy Committee, among other efforts. Bob has been a major advocate and cheerleader for *C. elegans* in particular and the power of developmental genetics in general through his seminars and talks at national and international meetings. He was a strong advocate for National Cancer Institute funding of model organisms such as yeast, worms, and flies as co-chair of the NCI Working Group on Preclinical Models for Cancer. Bob's most important statements, however, have been the amazing series of discoveries made in his laboratory that demonstrate how genetic analysis in a model organism help solve biological problems such as the mechanism of programmed cell death.

Paul Sternberg
Kenneth Kemphues



Gerald R. Fink

The 2001 George W. Beadle Medal

Gerald R. Fink

IT is a pleasure to honor Gerald R. Fink as the recipient of the George W. Beadle Medal for 2001. This medal recognizes the impact of Gerry's research advances, his mentoring of students in his own lab as well as in the yeast field, his contributions to the yeast community, and his commitment to science education and science policy.

Gerry's early work on the *HIS4* gene in the yeast *Saccharomyces cerevisiae* weaned us from thinking about operons in eukaryotes, established some of the genetic properties of loci that encode multifunctional proteins, and provided a rich and varied collection of mutants and mutations that he made freely available. His was the first yeast lab to combine genetics with biochemistry in a meaningful way. The *his4* mutants provided, for Gerry and his scientific descendants, entries into recombination, the general control system (*GCN* and *GCD*), the transcriptional apparatus (*SPT*), initiation of translation, Ty transposition as retrotransposition, and, of course, transformation. He and his colleagues provided definitive proof of yeast transformation, allowing the molecular genetics of yeast in all its glory to be developed. In recent years, he and his colleagues have not only deciphered the workings of the filamentation pathway and its overlap with the pheromone response pathway in budding yeast but also identified homologous genes for the pathway in the fungal pathogen, *Candida albicans*. This work has important medical implications for fungal pathogenicity. In addition to this large body of work on Saccharomyces, in recent years Gerry and his students have contributed to making *Arabadopsis thaliana* and *Candida albicans* workable genetic systems.

Gerry and Fred Sherman organized and taught the yeast genetics course at Cold Spring Harbor Laboratory for 18 years and introduced many current researchers to the organism. The several editions of the laboratory manual for that course and a subsequent *Methods in Enzymology* volume (both with collaborators) have been widely used. Gerry has been a driving intellectual force for the field and has played a major role in convincing those who work on higher/bigger eukaryotes how much yeast has to offer as a model system for important biological problems. Today this seems obvious, but there was a time when Gerry was assuring audiences that yeast cells really do have nuclei. Gerry has been in no small part responsible for the vitality of yeast genetics in the current scientific enterprise.

Gerry's energy and vision extend also to science education for the public. During his 11 years as Director of the Whitehead Institute, he instituted an educational outreach program for local high school teachers that has made a major impact. He also established an educational program for local high school students to introduce them to research in biology. In addition to these educational programs, he implemented several public policy initiatives, including efforts to inform legislators about social issues resulting from recent scientific advances. Part of this effort includes a biannual symposium on social implications of genetic research, with presentations by scientists, legislators, ethicists, physicians, members of the medical community, members of the judiciary community, and lawyers.

Gerry also has given extensive service to the larger genetics community through service on study sections and scientific advisory boards. He played a critical role in bringing the Genetics Society of America through a perilous financial period. Less easy to document has been his outspoken advocacy for and defense of genetics in various arenas, both scientific and political.

Terry Orr-Weaver
Elizabeth W. Jones

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