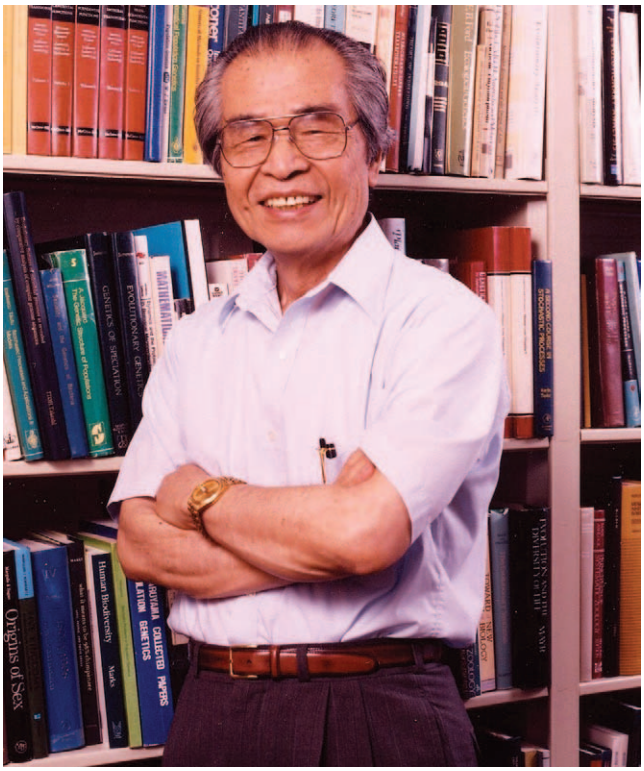
The 2006 GSA Honors and Awards

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 2006 awards.



Masatoshi Nei

The 2006 Thomas Hunt Morgan Medal

Masatoshi Nei

MASATOSHI Nei has been a major contributor to population and evolutionary genetics theory throughout his career. He is one of a select group to have a statistic named for him: "Nei's genetic distance" is a cornerstone of population genetic analyses. His body of work includes two influential textbooks and a remarkable 55 (of nearly 300) articles with over 100 citations each, 9 of which have over 1100 citations and 1 of which has over 12,000.

When Nei received the International Prize for Biology in 2002, the Japan Society for the Promotion of Science said: "Through these achievements, Dr. Nei has not only made the latest findings at the molecular level available to evolutionary biologists, but has contributed greatly to the birth of molecular evolutionary biology and its establishment as a positive science in which hypotheses can be verified quantitatively, rather than being discussed solely on a conceptual level."

Nei's work on genetic distances began with an American Naturalist article in 1972. He presented an elegant statistic involving allele frequencies from two populations that, under the infinite alleles mutation model, had an expected value proportional to the time since those populations had diverged from an ancestral population. The measure therefore provided a natural basis for reconstructing phylogenies and it was quickly adopted for distance-based methods for building evolutionary trees. Nei provided further discussion of the sampling properties of his distance statistic in Genetics in 1978. His most widely cited work is his 1987 article with Saitou in Molecular Biology and Evolution, which introduced the "neighbor-joining method" for phylogeny reconstruction. This method starts with a star-like tree and produces a unique tree by minimizing the sum of branch lengths at each stage of a recursive clustering of the taxonomic units.

Nei's early work came at the height of the selection *vs.* neutrality debate that followed the discovery, by starch-gel electrophoresis, of large amounts of genetic variation for protein variants. Nei and his students devised

and applied several tests of the neutral hypothesis and so contributed to an acceptance of this theory in many situations. His 1975 book *Molecular Population Genetics* laid out much of the theory known at that time and was followed by the masterly *Molecular Evolutionary Genetics* in 1987 and three other jointly written books.

Although Nei has produced a great body of work in statistical genetics, he was trained as a biologist and has been able to translate his data analyses into increasing our understanding of the mechanisms of evolution. He posited an African origin of modern humans in a 1974 article in the American Journal of Human Genetics and has provided details on the geographic pathways of human expansion in several subsequent articles. He has had a particular interest in the generation and maintenance of variation in the vertebrate immune system. His 1988 Nature article on patterns of nucleotide diversity at MHC class I loci suggested the action of overdominant selection. Nei's work on MHC multigene families led him to formulate a "birth-and-death evolution" model for the fate of members of a multigene family after gene duplication. His thinking over the past 40 years has led him to a view of evolution that he terms "neomutationism," whereby the driving force of evolution is mutation, with natural selection being secondary. This view is argued very clearly in a 2005 review article in Molecular Biology and Evolution that is likely to become a major reference for future workers.

Masatoshi Nei has played many leading roles in population and evolutionary genetics. He has trained >40 graduate and postdoctoral students, who themselves read like a Who's Who in the field. In addition to his publications, he and his group have written and distributed software packages, including MEGA and MEP.

Nei received his formal training at Miyazaki and Kyoto universities in Japan and held positions in Japan before moving to the United States. He had postdoctoral training at the University of California at Davis and at North Carolina State University and was on the faculty briefly at Brown University. For 18 years, from 1972 to 1990, he was at the heart of a very productive group at the Center for Demographic and Population Genetics of the University of Texas at Houston. In 1990 Nei moved to Penn State University to become Director of the Institute of Molecular Evolutionary Genetics and later also became the Evan Pugh Professor of Biology. Nei has been honored by election to the National Academy of Sciences of the United States of America and by fellowship in the American Academy of Arts and Sciences and the American Association for the Advancement of Science. Among his many other honors, he received the 2002 International Prize for Biology, presented in the presence of the Emperor and Empress of Japan. In his remarks at the ceremony, the Emperor said that he himself had used neighbor-joining to construct a phylogenetic tree for the gobioid fishes that he studies. In what must be at least as satisfying a recognition from his peers, the Society for Molecular Biology and Evolution, of which Nei is the cofounder, has established the Masatoshi Nei Annual Lecture.

Masatoshi Nei is a long-time member of the Genetics Society of America and a frequent publisher in Genetics. He has served on the Editorial Board of this journal. The Society is pleased to present him with the 2006 Thomas Hunt Morgan Medal, and I know that Masatoshi is proud to receive the award: in Chapter 14 of his *Molecular Population Genetics* he quotes a passage from Morgan's *The Scientific Basis of Evolution*, which shows both Morgan's deep understanding of evolution and the consistency of Nei's own work with that of Morgan's.

Bruce Weir

Victor Ambros

The 2006 Genetics Society of America Medal

Victor Ambros

In 1990, Victor Ambros faced a conundrum. The search for the heterochronic gene *lin-4* had led him to a 700-bp DNA fragment. This fragment could rescue a *lin-4* mutant but contained no apparent open reading frame (ORF). The few small ORFs that could be detected were either not conserved in other nematodes or not essential for rescue. Two years and several RNAse protection experiments later, Victor Ambros was forced to conclude that the *lin-4* gene product was not a protein at all, but a very small ~20-base RNA—the first microRNA!

Geraldine Seydoux

THE 2006 GSA Medal is awarded to Victor Ambros in recognition of his seminal discovery of microRNAs and his many contributions to the field since. Victor did his graduate work at MIT with David Baltimore, where he studied mechanisms of poliovirus replication. In 1979, Victor joined the lab of Bob Horvitz, who had recently returned to MIT after 5 years at the MRC where he had helped launch Sydney Brenner's new model system, *Caenorhabditis elegans*. Among the many mutants that Bob Horvitz brought back from the MRC was *lin-4(e912)*. *lin-4* mutants have complex lineage defects with many cells repeating division patterns characteristic of early larval stages. *lin-4* mutants cannot lay eggs, so Victor decided to screen other egg-laying defective mutants for similar "heterochronic" defects. The screen yielded mutations in three new loci: *lin-14*, *lin-28*, and *lin-29*. Remarkably, while some mutations caused "retarded" phenotypes similar to *lin-4*, others caused "precocious" phenotypes, with many cells skipping ahead to cell division patterns characteristic of older larval stages. *lin-14*, in particular, could mutate to both phenotypes, depending on whether the alleles caused loss of function or gain of function. These findings not only identified the first genes regulating developmental timing in a multicellular organism, but also hinted at how mutations in key genes might underlie heterochronic variation between species (Ambros and Horvitz 1984).

In 1985, Victor joined the faculty in the Department of Cellular and Developmental Biology at Harvard University. Taking advantage of the opposite phenotypes of retarded and precocious mutants, Victor set out to dissect the epistatic relationships among *lin-4*, *lin-14*, *lin-28*, and *lin-29*. With keen insight, he focused his analysis on a single, easy-to-score, stage-specific event: the larval-to-adult switch (L/A switch). At the transition between the last larval stage and adulthood, certain cells in the skin of the worm cease division, fuse with one another, and produce a characteristic ridged structure in the cuticle (alae). Victor constructed double, triple, and quadruple mutants and scored the L/A switch in each combination. The results were published in a single-author article (Ambros 1989), now renowned as a classic "epistasis" study, a favorite among teachers of genetics! This publication laid out the core hierarchy of the *C. elegans* heterochronic pathway: *lin-4* negatively regulates *lin-14* and *lin-28*, *lin-14* and *lin-28* inhibit *lin-29*, and *lin-29* activates the L/A switch (Ambros 1989).

With the genetics sorted out, it was time to determine the molecular identities of the heterochronic genes. Cloning in the pregenomic era was not an easy task and the article reporting the cloning of *lin-14* (a collaboration among Gary Ruvkun, Victor Ambros, Bob Horvitz, and the future leaders of the *C. elegans* genome project, Alan Coulson, Bob Waterston, and John Sulston) was an elegant demonstration of how to use linked RFLPs to clone genetic loci in *C. elegans* (Ruvkun *et al.* 1989). Soon after, Victor set his sights on *lin-4*, the negative regulator of *lin-14*. At the time, *lin-4* was defined by only a single allele, raising the possibility that *lin-4* might be

a small gene or, worse, a complicated rearrangement. Nothing, however, had prepared Victor and his lab for what followed. By the spring of 1992, Rosalind Lee and Rhonda Feinbaum in Victor's lab had mapped *lin-4* down to a 60-nt hairpin RNA (*lin-4L*). A smaller ~20-nt species *lin-4S* had also been detected but was initially dismissed as an artifact, until Feinbaum found a second *lin-4* allele that turned out to be a single-base-pair change in the *lin-4S* sequence. But how could such a small RNA regulate *lin-14* and *lin-28*?

In the meantime, the lab of Gary Ruvkun had continued the molecular analysis of *lin-14* and shown that *lin-14* gain-of-function mutations affect conserved sequences in the *lin-14* 3′-UTR. Gary and Victor exchanged the *lin-14* and *lin-4* sequences and, on the same day in June 1992, both realized that *lin-4S* was complementary to a repeated sequence in the *lin-14* 3′-UTR. They immediately shared their discovery over the phone and published their findings back to back the following year in an exemplary demonstration of open collaboration and fair play (Lee *et al.* 1993; Wightman *et al.* 1993).

The cloning of *lin-4* did not immediately trigger the microRNA frenzy that we know today. For many years, *lin-4* remained an oddity, an interesting but nematode-specific quirk. Undaunted, Victor and his lab continued the analysis of *lin-4* and its targets. In 1997, postdoctoral fellow Eric Moss showed that *lin-4* regulates *lin-28* through a 3′-UTR element similar to the ones found in *lin-14*, demonstrating that *lin-4* regulates more than one mRNA (Moss *et al.* 1997). Two years later, postdoctoral fellow Phil Olsen discovered that *lin-4* blocks translation of the *lin-14* mRNA while still on polysomes, suggesting that *lin-4* inhibits a step after translation initiation (Olsen and Ambros 1999). It was not until the Ruvkun lab cloned a second microRNA (*let-7*) and showed it to be conserved across many species (Pasquinelli *et al.* 2000; Reinhart *et al.* 2000), and until the Ambros lab and others discovered scores of microRNAs in *C. elegans* and other animals (Lee and Ambros 2001), that the microRNA world came into its full glory. Today microRNAs are recognized as major players in the regulatory programs that orchestrate the development of organisms as diverse as plants and mammals. Since their discovery through their roles in developmental timing in *C. elegans*, microRNAs have been implicated in many other processes from cell proliferation to cell death and from hematopoiesis to neuronal patterning (Ambros 2004). The spotlight on microRNAs and their connection to RNA interference has led to a renewed interest in the many RNA species that exist in cells.

Victor Ambros, now a professor at Dartmouth in his hometown of Hanover, New Hampshire, is a soft-spoken and unassuming scientist, always eager to give credit to his collaborators. A strong supporter of the *C. elegans* community, he has organized four East Coast *C. elegans* meetings and the International *C. elegans* Conference in 1993, which he will lead again in 2007. He recently received the 2005 Lewis S. Rosenstiel Award in Basic Medical Science from Brandeis University. Victor Ambros's accomplishments exemplify what is most compelling about genetics: the power to discover what nobody knew existed—starting with a handful of interesting mutants.

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Geraldine Seydoux

Fred Sherman

The 2006 George W. Beadle Medal

Fred Sherman

FRED Sherman has been awarded the 2006 George W. Beadle Medal for distinguished service to the field of genetics and to the genetics community. Professor Sherman is honored for his fundamental contributions to molecular biology, his service to the scientific community, and his key role in the education of budding yeast geneticists.

Sherman is one of the "fathers" of modern yeast genetics. He conducted key postdoctoral studies with Herschel Roman and Piotr Slonimski before embarking on his life-long exploitation of the *Saccharomyces cerevisiae* iso-cytochromes c and their modifiers to address fundamental questions of genetics. A few of the major discoveries resulting from his work include: (1) establishment of the universality of the genetic code in eukaryotes by deducing the codons of the *CYC1* gene through analysis of amino acid changes caused by mutations and their reversion; (2) comprehensive analysis of tRNA informational suppressors; (3) establishment of the rules for translational and transcriptional start sequences in yeast; (4) identification of transcriptional stops and 3′ mRNA processing sites; (5) discovery of a family of N-terminal protein acetyltransferases; (6) key insights into mechanisms of DNA recombination and gene conversion and how these processes affect evolution; and (7) establishment of a yeast model for Batten disease. In addition to generating this substantial body of knowledge, Sherman was one of the early contributors to development of the methodology and genetic logic that all subsequent yeast molecular biologists have employed.

A theme throughout Sherman's career has been service to the scientific community. He was the chairman of the Department of Biochemistry and Biophysics at the University of Rochester from 1979 to 1988. He served as an associate editor of three journals: Genetics, Molecular and Cellular Biology, and Yeast. He served on numerous review panels for the National Institutes of Health, the American Cancer Society, the National Research Council of Great Britain, and the Israel Cancer Research Fund and as chairperson of the Howard Hughes Evaluation Panel. Sherman has also played an important role in the genetics community as a member of the Board of Directors of the Genetics Society of America and as Chairman of the Genetics Section of the National Academy of Sciences. He was elected to the National Academy of Sciences in 1985.

Fred is legendary in the yeast community because of his extraordinarily generous training of yeast geneticists and molecular biologists. In 1970 he and Gerald Fink established the Cold Spring Harbor Laboratory course on yeast genetics and molecular biology. This course served as the most important training vehicle for students, postdoctoral scholars, and faculty members who wanted to learn the ins and outs of the budding yeast model system. Fred indoctrinated students in this course in the yeast community's "etiquette" of sharing of information and ideas and materials and methods. The course was one of the main reasons that a collegial community of yeast researchers quickly materialized, and it played a major role in establishing budding yeast as an important model organism for genetic analysis.

Fred invested his time and his considerable energy in this course for 17 consecutive summers, through 1987! He has also trained numerous students and postdoctoral fellows in his laboratory, many of whom have become leaders in the field. The Genetics Society of America gratefully acknowledges Fred Sherman for his seminal scientific discoveries, his service to the scientific community, his good humor, and his many years of unselfishly training subsequent generations of yeast geneticists.

Anita Hopper

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 Botstein 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
2002	Ira Herskowitz	Andrew Z. Fire	Robert Mortimer and André Goffeau
2003	David S. Hogness	Jeffrey C. Hall	Gerald M. Rubin and Allan C. Spradling
2004	Bruce N. Ames	Trudy F. C. Mackay	Norbert Perrimon
2005	Robert L. Metzenberg	Steven J. Elledge	Thomas C. Kaufman