The 2005 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 2005 awards.

Robert L. Metzenberg

The 2005 Thomas Hunt Morgan Medal

Robert L. Metzenberg

IT is completely fitting that Robert L. Metzenberg be chosen to receive the 2005 Thomas Hunt Morgan Medal. In addition to making a full lifetime's worth of impressive contributions to genetics in his years as Professor at the University of Wisconsin (1958–1996), he has also made stunning research contributions as Emeritus Professor, at Stanford University, at UCLA, and working in his home laboratory. Metzenberg's more than 120 publications include many gems. But equally important are his countless intangible contributions to members of the scientific community. If you have met Bob even just once, you know what we mean. As Bob once said (although not about himself), "The calendar ticks by at very different rates in different people, and here and there, a scientist is a human Stradivarius."

One remarkable thing about Bob is his breadth of interests and abilities. In addition to being one of the most gifted Neurospora geneticists ever, he is completely at ease with all aspects of biochemistry. Indeed, he was an award-winning teacher of biochemistry at the University of Wisconsin School of Medicine. A partial explanation comes from a glance at his training. Bob majored in chemistry at Pomona College, with minors in physics and biology (which he has pointed out were almost "immiscible" with chemistry at the time). As a graduate student in the laboratory of Herschel Mitchell at Cal Tech, he worked on the biosynthesis of amino acids in Neurospora, and as a postdoc with Philip Cohen in Wisconsin he studied enzymatic reactions involved in urea synthesis in mammals and amphibia. Next, curiosity about the underlying genes led him to spend a year with Ernst Hadorn in Zurich, soaking up developmental genetics. He then made the important decision to return to Neurospora to study "the genetics of regulation of enzyme synthesis in a simple eukaryote."

He chose to work on regulation of carbon, sulfur, and phosphorus utilization at a time when little was understood regarding regulatory differences between eukaryotes and bacteria. His identification of multiple regulatory mutants that were defective in phosphorus or sulfur utilization and his demonstration that the underlying genes exist in a hierarchy to turn on a family of unlinked structural genes was a major advance. Indeed, Bob was the first to discover a cascade of positive- and negative-acting products of regulatory genes acting to govern eukaryote gene expression. These studies fore-

shadowed the discovery of similar regulatory systems in other organisms.

In writing about "Thomas Hunt Morgan and His Legacy," Ed Lewis (http://nobelprize.org/medicine/articles/lewis/) noted that Morgan and his famous students (A. H. Sturtevant, C. B. Bridges, and H. J. Muller) remained at the bench throughout their careers: "The investigator must be on top of the research if he or she is to recognize unexpected findings when they occur." Bob also managed to stay at the bench, even when it required installing a bench in his office or in his spare bedroom. He is a natural tinkerer, overflowing with interesting ideas to tinker with. As a consequence, his research contributions have been broad and have not been limited to conceptual advances. Throughout his career Bob has also been responsible for numerous innovations and improvements in practical techniques, reflecting his continued activity at the bench and the pleasure he takes in carrying out experiments with his own hands. As examples, he devised improvements in procedures for isolating nucleic acids, preserving Neurospora stocks, analyzing tetrads, recovering and purifying fungi from soil samples, introgressing genes from one species to another, and testing whether particular genes are essential.

In part to ensure that he could stay at the bench, Bob generally kept his group small. One of us (E.U.S.) discovered this personally about 30 years ago. After becoming inspired by a fantastic seminar given by Bob at Reed College, on the phosphorus system of Neurospora, I wrote to inquire about the possibility of doing graduate work with him. He promptly wrote back a kind letter suggesting that I consider another lab in his department because his lab was full. About a year later, while visiting Wisconsin to help establish λ-cloning in his lab, I discovered that Bob's definition of "full" was rather different from that of most principal investigators. His lab was physically quite empty and his group consisted of one technician, one postdoc, and himself. Bob confided that he had recently come to realize that entry into molecular biology may require that he expand his group, but he still felt a responsibility to not add to the population explosion caused by investigators training huge numbers of graduate students.

Bob was not content to confine his work to any one problem and he has made significant contributions in areas other than biochemistry and classical gene regulatory mechanisms. Spin-off projects came naturally from his ability and regular habit of recognizing valuable nuggets in random scientific observations. As Bob put it, "What we call 'luck' in research is mostly a matter of recognizing an opportunity . . . when it comes along." Like everyone else in the early days of genomic DNA cloning, Bob and his first "molecular" postdoc, Steve Free, cloned ribosomal DNA many times over. But instead of simply discarding this as junk, they examined it in sufficient detail to discover that the tandemly repeated rDNA of Neurospora lacks a gene for 5S RNA, unlike the arrangement in yeasts. Moreover, results of a Southern hybridization suggested that the 5S genes might be dispersed in the genome, a novel possibility. If so, this might reveal whether members of a repeated gene family must be tandemly arranged to maintain sequence homogeneity. Recognizing that he did not have the time to work on all the interesting things he uncovered and that this visiting graduate student's chosen thesis project was on the rocks, Bob offered to turn over this incipient project. We should also note that Bob is a gifted salesman (so good that he can sometimes convince himself when perhaps he should not). Thus he had no trouble sending me home with a new project, which produced enjoyable and productive collaborations for many subsequent years, and which spawned numerous additional projects for each of us. For example, the project led Bob to devise an efficient RFLP mapping procedure for Neurospora and to use this to construct the first extensive RFLP map in fungi. Additional studies on dispersed 5S rRNA genes ultimately led to the discovery of DNA methylation in Neurospora and then to repeat-induced point mutation (RIP). Research on the tandemly arranged rDNA of Neurospora led Bob and his colleagues to discover position-dependent differences in DNA methylation and dramatic premeiotic modulations in copy number of the rDNA.

In another area of research, Bob and his associates examined the structure and function of the *A* mating-type gene in Neurospora in studies that were coordinated with those on mating type *a* in Charles Yanofsky's lab. In these pioneering studies, the two labs showed that the so-called mating type "alleles" *A* and *a* consist of completely nonhomologous elements. After consulting with a colleague in the Classics Department, Bob proposed to call the genes *idiomorphs* rather than alleles. In further studies related to mating type, genes that are expressed preferentially during the sexual phase were identified and mutated, and idiomorph-linked sequences were compared in species related to Neurospora.

Immediately before "retiring," Bob and his postdoctoral fellow, Rodolfo Aramayo, discovered a remarkable and unexpected new epigenetic phenomenon in Neurospora, meiotic silencing (also called "meiotic transvection" and MSUD for meiotic silencing by unpaired DNA). Elegant work by Bob and his colleagues showed that sequences that are unpaired during meiosis elicit an RNAi-like mechanism that silences all homologous sequences for the duration of meiosis. The discovery that meiotic silencing is mechanistically related to RNAi came from one of Bob's characteristically imaginative genetic schemes for selecting suppressor mutations.

A statement by Ed Lewis about Morgan's frugality applies equally well to Metzenberg: "Morgan was very thrifty when it came to purchasing laboratory equipment and supplies—but, according to Sturtevant, generous in providing financial help to his students" (http://

nobelprize.org/medicine/articles/lewis/). As Bob wrote in a budget justification, "I have always worked with a fairly modest grant, consistent with my needs." He spent taxpayers' pennies wisely while enjoying continuous support from an NIH grant renewed repeatedly to cover a period of more than 40 years. Although frugal, Bob has been generous in sharing strains, materials, clones, and, most important, ideas. He seems to generate a continual flow of interesting ideas, new ways of looking at problems, and fresh ways of stating them. This is apparent in his articles, reviews, and lectures, but is most obvious in conversation. A colleague pointed out that "Metzenberg is the type of scientist whose interactions and insights make those around him better scientists."

Bob's unique style gives a special character to his achievements. His originality is reflected in felicitous figures of speech and colorful use of words. A small set of examples cannot do justice to his style, but here are a few selections from our correspondence with him:

Finally, we cannot be permanently content with experimental material obtained by accident.

[Regarding an advantage conferred by heterokaryon incompatibility, this serves to prevent] . . . *corruption or subversion by goldbricks.*

Here are some strains—a day late and a dollar short—which you might want to analyze for methylation. Let me tell you about the dollar short part, and maybe you'll feel it's a lot of dollars short.

We are sitting in Kennedy [airport] *waiting for our plane to Madrid. I had turned off all thoughts of the lab but something intruded anyway—a possible, remotely possible way to recognize N-6 methyl adenine in conjunction with the Church-Gilbert genomic sequencing method. It requires several things working rather well in tandem, but for what it's worth, here it is . . .*

To my patient and tolerant colleagues: Here is a more than slightly speculative hypothesis . . . It has only one virtue: It is easily testable.

[Regarding the desirability of publishing details of methodology rather than relying on private communication] . . . *without needing to know the secret handshake.*

Bob's discussions have animated seminars and meetings—whether in fungal or general genetics, in biochemistry, microbiology, or biology—with imaginative insights. Much of this is done in a playful, clear, and challenging style that makes observers remember what was said. His command of the biological lore and his deep insight into chemistry and physics enable him to see the "landscape" of a hypothesis quickly and bring it to bear on the subject under discussion.

This is not the first time Bob Metzenberg has received an award named after T. H. Morgan. Nearly 50 years ago, in 1956, he received a Thomas Hunt Morgan Award conferred by Cal Tech in recognition of his accomplishments as a graduate student. His more recent contributions have been recognized by numerous honors, including a Guggenheim Fellowship, an NIH Merit Award, and election to the National Academy of Sciences. He was President of the Genetics Society of America in 1989–1990.

Eric U. Selker
Rowland H. Davis
David D. Perkins

Steven J. Elledge

The 2005 Genetics Society of America Medal

Steven J. Elledge

THE 2005 GSA Medal is awarded to Steven J. Elledge for his seminal contributions to the study of the regulation of the cell cycle, especially in cellular responses to DNA damage. One of the most impressive aspects of Elledge's work has been the facility with which he and his colleagues have carried out studies both with a model organism, budding yeast *Saccharomyces cerevisiae*, and with mammalian cells. In both cases he has combined powerful genetic screens with innovative molecular biology and biochemistry to characterize the way cell cycle progression is coordinated and regulated. In addition to the many genes and regulatory pathways his lab has identified and characterized, Steve Elledge has enriched his colleagues by his passion for the development of many genetic tools and reagents.

Elledge's interest in the way cells cope with DNA damage began with his graduate work with Graham Walker at MIT, where he identified the *UmuC* bypass DNA polymerase. During this time Elledge also developed phasmids, the first of several novel recombinant DNA-cloning systems he has devised. Steve's interest in biotechnology drew him to the lab of Ron Davis, at Stanford, in 1984. There, he devised several new genetic tools, including both shuttle vectors allowing easier cloning and transfer of genes from yeast to *Escherichia coli* and an inducible gene library that made possible the study of dominant mutations. But his future direction was launched by a fortuitous result: While trying to clone the yeast homolog of the bacterial recombinase Rec A, Elledge instead identified a subunit of ribonucleotide reductase. With his finding that the RNR genes were both cell cycle regulated and damage inducible, Steve was on his way.

It is hard to trace Steve's contributions in a linear fashion, because his work has ramified in so many directions. After having moved to Baylor Medical School in

1989 as an Assistant Professor, Steve used the new cloning and expression vectors he had devised to identify Cdk2, a paralog of the one known mammalian cell division kinase, Cdc2. Cdk2 proved to be the key regulator of the G1-to-S transition in mammalian cells. Elledge then teamed up with Wade Harper, a collaboration that continues today, to identify and characterize p21 as an inhibitor of Cdk2, simultaneously with the Vogelstein lab's demonstration that p21 was regulated by the cancer gene p53. Among the many findings that Elledge made in the mid-1990s was the identification of cyclin F and the finding that degradation of this cyclin is dependent on a specific protein sequence, the F-box. Steve's lab then both identified and characterized the SCF ubiquitin ligase complex that regulates protein degradation and identified a number of new specificity factors that target proteins for timely destruction. One important recent article implicates the F-box ubiquitin ligase Fbw7 in defective cardiovascular development in the mouse, accompanied by elevated levels of cyclin E.

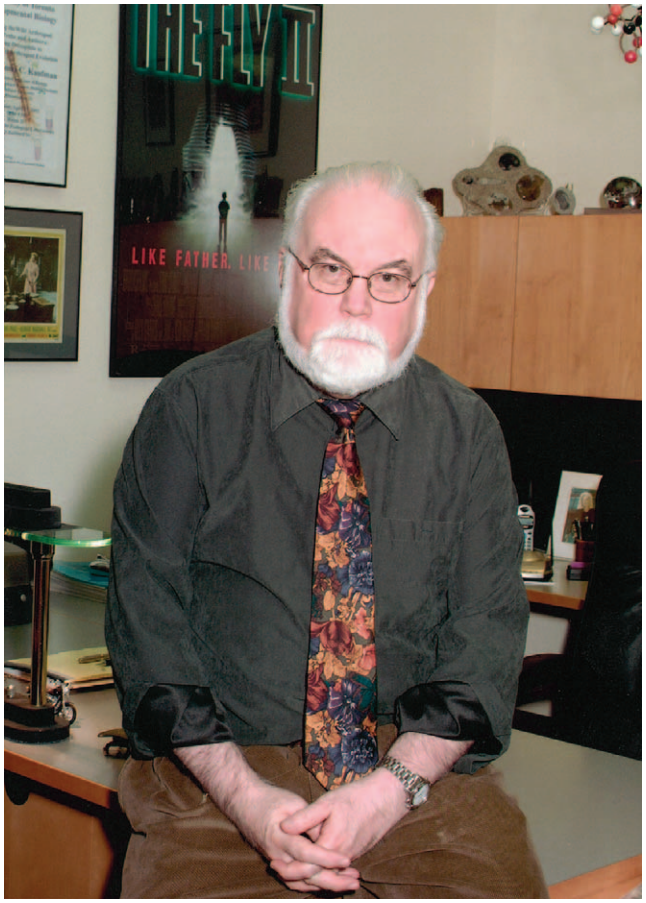
Steve has also made key contributions to the study of the DNA replication and damage checkpoints. Screens of yeast mutants sensitive to the ribonucleotide reductase inhibitor hydroxyurea identified S-phase arrest-defective mutants; these have implicated the Rad53/Chk2 protein kinase and DNA polymerase epsilon protein in preventing mitosis in the presence of stalled replication forks. Another hydroxyurea-sensitive mutant led Elledge into studying aspects of the mitotic spindle. Steve's lab found the human and budding-yeast homologs of the *Schizosaccharomyces pombe* Chk1 protein kinase and showed that the yeast Chk1 regulated cell cycle progression in a parallel pathway with Chk2/Rad53. His lab has made major contributions to understanding the roles of damage response proteins in mammalian cells. Many articles have focused on the way DNA damage is sensed and how these signals are transduced into altered gene expression and cell cycle arrest. The finding that the essential Chk1 gene in mice exhibits haplo-insufficiency for tumor suppression opens up still more avenues.

And still more useful tools emerged from Steve's lab, including the univector plasmid-fusion system, for rapid construction of recombinant DNA without restriction enzymes and, most recently, new tools for large-scale RNA-interference-based screens in mammals.

The GSA medal honors a remarkable scientist in midcareer. Steve Elledge has been a powerful force in understanding how cells deal with the stresses of replication and DNA damage. He has harnessed the "awesome power of yeast genetics" to trace pathways of cell cycle regulation and then used all of his skills as a molecular biologist to learn the similarities and differences in these processes in mammals. We anticipate many more surprises from Steve Elledge's inventive mind and his passionate love of genetics.

Since 1993, Steve has been an investigator of the Howard Hughes Medical Institute. In 2003 he moved to Harvard Medical School as Professor in the Departments of Genetics and as Geneticist in the Department of Medicine, Brigham and Women's Hospital. Steve has been honored for his many contributions by his election in 2003 to both the U.S. National Academy of Sciences and the American Academy of Arts and Sciences. He has received the DAMD Breast Cancer Innovator Award (2003), the National Academy of Sciences Award in Molecular Biology (2002), the John B. Carter, Jr. Technology Innovation Award (2002), and the Paul Marks Prize for Cancer Research (2001), among others.

James E. Haber



Thomas C. Kaufman

The 2005 George W. Beadle Medal

Thomas C. Kaufman

THOMAS C. Kaufman has been awarded the 2005 George W. Beadle Medal for outstanding contributions to the genetics research community. It is a fitting tribute for Thom to receive a prize named in honor of George Beadle. Beadle is best known for the pioneering work that he carried out with Edward Tatum to explore the relationships between genes and enzymes. This work led to the "one gene–one enzyme" concept, a Nobel Prize to Beadle and E. Tatum in 1958, and a description in every modern genetics textbook. As recently described by Singer and Berg (2004), Beadle should be remembered not only for his foundational work in genetics, but also for the dedicated leadership roles he played for scientific and academic communities.

Like Beadle, Thom Kaufman discovered genetics early in his scientific career. As an undergraduate at California State University at Northridge, Thom joined the laboratory of George Lefevre. This early experience convinced him of the amazing power of a mutational analysis to deduce the function of genes and firmly hooked him on the use of Drosophila as a model system. Thom did his graduate work with Burke Judd at the University of Texas at Austin. Their studies on saturation mutagenesis and developmental genetics of a small region of the Drosophila X chromosome, known as the *zeste-white* region, became a classic study in genetics. The objective was to test the "one gene–one chromomere" hypothesis (Judd 1998). The results, published mostly in the early 1970s, made the *zeste-white* region one of the best understood regions in the fly genome and contributed to estimates of gene number in Drosophila before the era of genome sequencing. Thom joined David Suzuki's group at the University of British Columbia as a postdoctoral associate and explored how temperature-sensitive mutations might be used to dissect complex processes in Drosophila. As an independent researcher in Vancouver, and continuing as an assistant professor at Indiana University, Thom began a long-term and fun-filled collaboration with Rob Denell that focused on a rather odd set of mutations that caused dominant defects in the fly's head and anterior thorax (Denell 1994). An early prediction by Thom that these genes were functionally related and developmentally critical could not have been truer. Through extensive genetic, developmental, and molecular studies, Thom defined the antennapedia gene complex (ANT-C) as a

cluster of genes controlling the identity of the anterior segments in the embryo and adult. This work beautifully complemented and extended Ed Lewis's work on the bithorax complex. Over the course of several decades, Thom's research group has elucidated the role of each homeotic gene in the ANT-C and unraveled complex regulatory interactions. Thom has broadened his work to examine the role of the homeotic gene clusters, or HOX genes, in insect evolution. He is truly a leader in the field of evolutionary developmental biology and his work has inspired many scientists to broaden their work to include comparative biology. In parallel with the work on homeotic genes, the Kaufman lab has also pursued other research topics, including the regulation of tubulin gene families and studies of the composition of the centrosome. In all cases, the starting point has been to establish a solid genetic framework for testing hypotheses about gene functions and interactions.

Thom's research career has been accompanied by a dedicated commitment to the Drosophila research community. He has been a constant and dedicated force behind many major projects that are extensively used by Drosophilists worldwide. He is one of the initial founders and designers of FlyBase, the electronic database that organizes data on Drosophila genes, mutations, and other biological features in a comprehensive way. Thom was also instrumental in the development of both the Bloomington Drosophila Stock Center and the Drosophila Genomics Resource Center and he continues to codirect these resources with colleagues at Indiana University. These centers provide tens of thousands of genetic stocks and molecular reagents to researchers across the globe each year and they have added impressively to the fame of Bloomington and Indiana University. Recently, Thom played a prominent role in garnering support for the genome projects to sequence multiple Drosophila species, an important initiative that will provide a paradigm for comparative genomics. He has worked tirelessly on these projects and with the best interests of the research community in mind. His mission follows in the tradition of the early Drosophilists to provide fair and equal access to research materials and findings.

Thom's service extends to the larger community of geneticists and developmental biologists. He has served leadership roles for numerous professional societies, including the Genetics Society of America. He has garnered prestigious awards in recognition of his scientific achievements. Among these are Distinguished Professor of Biology at Indiana University (1993), the Conklin Medalist (1998), and Fellow of the American Academy of Arts and Sciences (1999). Thom has trained approximately 50 graduate students and postdoctoral fellows thus far. There is perhaps no greater evidence of Thom Kaufman's impressive impact on science than the knowledge that his mentorship has inspired a deep love of genetics in so many of his trainees and associates.

LITERATURE CITED

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Judd, B. H., 1998 Genes and chromomeres: a puzzle in three dimensions. Genetics **150:** 1–9.

Singer, M., and P. Berg, 2004 George Beadle: from genes to proteins. Nat. Rev. Genet. **5:** 949–954.

Barbara Wakimoto

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 Fire	Robert Mortimer and André Goffeau
2003	David S. Hogness	Jeffrey C. Hall	Gerald M. Rubin and Allan C. Spradling
2004	Bruce Ames	Trudy F. C. Mackay	Norbert Perrimon