



THE UNIVERSITY
of
WISCONSIN
MADISON

Laboratory of Genetics

Milestone Celebrations • MAY 2010

WE HAVE MILESTONES TO CELEBRATE — MARK YOUR CALENDARS

The Laboratory of Genetics contains two sibling departments, and both departments have anniversaries to celebrate. The Department of Genetics, which is the oldest genetics department in the United States, is one hundred years old this year. The Department of Medical Genetics is a tad over fifty.

We hope you will join us for our Milestones Celebration, a three-day symposium on May 20-22, 2010. The theme of our celebration is “One hundred years of genetics — What’s next?” Most of the speakers in the symposium will be people who were students here in Madison or who are currently members of our faculty. Here’s the schedule:

May 20, 2010

The annual Smithies Seminar (sponsored by our distinguished ex-faculty member and Nobel Laureate, Oliver Smithies):

Martin Chalfie, Professor and Chair, Department of Biological Sciences, Columbia University

Gerald R. Fink, Professor of Genetics, MIT; member of the Whitehead Institute

May 21, 2010

Morning session: Neuroscience/Neurogenetics

Barry Ganetzky, Professor of Genetics and Medical Genetics, University of Wisconsin-Madison

Ching Kung, Professor of Genetics and Molecular Biology, University of Wisconsin-Madison

Stephanie Ceman, Associate Professor of Molecular and Cellular Biology, University of Illinois at Urbana-Champaign

Jerry C-P. Yin, Professor of Genetics and Neurology, University of Wisconsin-Madison

Afternoon session: Evolutionary Genetics

William Engels, Professor of Genetics and Zoology, University of Wisconsin-Madison

Daniel L. Hartl, Higgins Professor of Biology, Harvard University

John F. Doebley, Professor of Genetics, University of Wisconsin-Madison

Sean B. Carroll, Professor of Molecular Biology, Genetics, and Medical Genetics, University of Wisconsin-Madison

May 22, 2010

Morning session: Agricultural Genetics

Margaret (Molly) Jahn, Dean, College of Agricultural and Life Sciences; Professor of Genetics; University of Wisconsin-Madison; and Deputy Undersecretary of Research, Education, and Economics, United States Department of Agriculture

Russell Malmberg, Professor of Plant Biology; Associate Dean, Franklin College of Arts and Sciences, The University of Georgia

L Curtis Hannah, UFRF Professor of Horticultural Science, University of Florida

William H. Stone, Professor Emeritus, Trinity University, San Antonio



Afternoon session: Medical Genetics

Paul M. Sondel, Professor of Pediatrics and Human Oncology, School of Medicine and Public Health, University of Wisconsin-Madison

William F. Dove, Professor of Oncology and Medical Genetics, University of Wisconsin-Madison

Julie R. Korenberg, Professor and Director of the Center for Integrated Neurosciences and Human Behavior, Brain Institute, University of Utah

Jon A. Wolff, Vice President and Site Director, Roche Madison, Madison, Wisconsin, and Clinical Professor, School of Medicine and Public Health, University of Wisconsin-Madison

About the speakers:

Martin Chalfie studies the genetics of nervous system development and function in the roundworm *C. elegans*. Professor Chalfie received the Nobel Prize in Chemistry in 2008 for his part in developing the use of Green Fluorescent Protein as a molecular marker for gene expression.

Gerald Fink is a pioneer in yeast research who, among many other accomplishments, discovered means to achieve genetic transformation in yeast. He has also contributed to the introduction of *Arabidopsis* as a model organism in genetics.

Barry Ganetzky has studied the mechanisms of meiotic drive in *Drosophila* and has been a leader in studying the molecular biology of the nervous system through the use of *Drosophila* behavioral mutants.

Ching Kung has studied sensory functions in a variety of organisms — *Paramecium*, *E. coli*, and yeast — by doing patch clamp studies of ion channels.

Stephanie Ceman studies the molecular biology of Fragile X Mental Retardation and has evidence that the FMRP protein is involved in RNA expression and the regulation of translation. She is also studying the role of FMRP in song-learning in the zebra finch.

Jerry Yin studies learning and memory in *Drosophila* by using genetic, biochemical, and cell biological methods.

Bill Engels has done landmark studies of transposable elements in *Drosophila* and on the mechanisms of transposition of these elements. These studies have shed light on the mechanisms of recombination and DNA repair.

Dan Hartl studies evolution in a variety of model organisms by using genomics data. In addition, he has written popular textbooks in genetics and population genetics.

John Doebley studies the evolution of plants — in particular trying to understand the genetic changes that account for the differences between corn and its ancestor, teosinte. How many genes, and what sorts of genes, are involved in speciation?

Sean Carroll studies the genetics of speciation with special attention to the effects of genetic changes on developmental processes. He is a pioneer in “evo-devo” and, in addition, has written several outstanding books on evolution, including the recent Phi Beta Kappa prize-winner, “The Making of the Fittest” and the National Book Award finalist, “Remarkable Creatures.”

Molly Jahn, before becoming Dean of the College of Agricultural and Life Sciences, was busily engaged in research on plant breeding and crop improvement. She developed new vegetable varieties for Asia, Africa, and Latin America and worked overseas on six continents to apply the fruits of plant breeding to the improvement of human nutrition and health.

Russell Malmberg studies the molecular evolution of plants with special emphasis on insect-eating pitcher plants, and he is doing bioinformatics studies on non-coding RNAs.

Curt Hannah studies the genetic control of starch production in maize and has developed new methods for manipulating the genes responsible for this vital function.

Bill Stone is one of the early leaders in immunogenetics. He developed immunological methods for studying inheritance in cattle, a tool that proved extremely valuable in commercial animal breeding. More recently, at the Hospital Sant Pau in Barcelona, he has been working on the genetics of thrombosis in humans.

Paul Sondel is an oncologist working on immunotherapy for cancer.

Bill Dove has done landmark research on bacteriophage lambda, on slime molds, and, most recently, on the genetics of cancer in mice.

Julie Korenberg has been a major contributor to the cytological and functional mapping of the human genome. She is currently involved in research on the genetic basis of Williams Syndrome, a human genetic disorder that affects behavior and cognition.

Jon Wolff is a pioneer in gene therapy and is currently leading research at Roche Madison, a pharmaceutical company developing methods for treating inherited disease in humans.



The Genetics Department in 1943. This photo was submitted by Rose E. Frisch (front row, third from left) and she is standing to the right of her PhD adviser, Leon J. Cole. Dr. Frisch is currently an associate professor of population sciences emerita at the Harvard School of Public Health. Her long term research is on female fertility and body fat connection.

A Fabulous Century

We can't begin to list all the important achievements of the Laboratory of Genetics since its birth in 1910, but here are a few highlights.

1910s

The Department of Genetics was established — as the “Department of Experimental Breeding” — in 1910. It was the first such department in the United States. The department owes its creation to the vision and persuasive powers of William D. Hoard, who was largely responsible for making Wisconsin “America’s Dairyland.” In 1871, Hoard suddenly realized that the soil of Wisconsin was more suitable as pasture than as wheat land, and he became “the apostle of the dairy cow” in Wisconsin. In 1885, he founded Hoard’s Dairyman, a trade magazine that still serves the dairy industry today. Hoard’s fame grew, and, in 1889, he became governor of Wisconsin. Eight years later, he became a UW regent and used his considerable influence to pressure for the creation of a department devoted to the study of agricultural animal breeding. Harry L. Russell, the Agriculture Dean, enthusiastically supported Hoard’s suggestion and hired a promising young animal geneticist, Leon J. Cole, to serve as the first chair (and, for eight years, the sole member) of a new Department of Experimental Breeding. So our celebration includes W. D. Hoard, Harry L. Russell, and Leon J. Cole as the visionaries who helped to make Wisconsin a world-renowned center in genetics.



1910: Leon J. Cole becomes the first chair of the Department of Experimental Breeding, which later becomes Genetics.

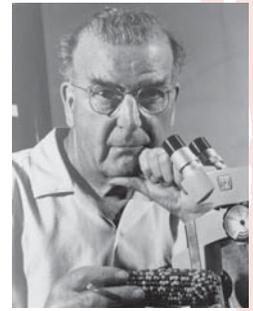
Cole, a gifted educator, was a leader in establishing the academic standards that made Wisconsin one of the world’s leading centers for graduate education in biology. He launched pioneering research programs on the genetics of birds and fur-bearing mammals. His unique collection of virtually every paper published in genetics before 1939 remains a wonderful resource for people interested in the history of genetics. And bird lovers will be pleased to learn that he founded the American Bird-Banding Association.

1920s

Alex Brink, who joined Genetics in 1922, initiated a program for developing hybrid corn for Wisconsin, a program later largely taken over by Norman Neal. Later, Brink developed a winter-hardy variety of alfalfa, called Vernal. These two projects had enormous impact on the profitability of farming in the state.

1930s

Bob Irwin, who joined the department in 1930, was a pioneer in immunogenetics — indeed, he coined the term. Irwin and collaborators provided tools for paternity testing in cattle, tools that proved invaluable to the development of the dairy industry in the Dairy State.



1926: Winter hardy alfalfa (Vernal), developed by R. A. Brink, is released to Wisconsin farmers.

In 1938 W.K. Smith and R. A. Brink showed that fermented sweetclover was toxic to cattle because it contained a bitter substance, coumarin, that, when the sweetclover was stored at high temperature, was converted to a poison causing a fatal bleeding disease in cattle that ate the fermented feed. Smith managed to produce a non-bitter, coumarin-free sweetclover that could safely be used for cattle feed. This work led to the development, by Karl Paul Link, of Warfarin, a rodenticide, and dicoumarol, an anticoagulant used to prevent dangerous blood clotting in human patients.

1940s

Ray Owen discovered that non-identical twin cattle with blood cells that were genetically like those of both twins. As adults, similar cattle would have rejected transfusions from each other, but embryos developed tolerance to cells originating in their genetically distinct twins. When the discovery of immunological tolerance received a Nobel Prize many years later, Peter Medewar, one of the recipients, wrote to Owen to acknowledge his original contribution and to express regrets that the prize committee failed to recognize Owen’s pioneering work.



1945: Ray Owen discovers immune tolerance in twin cattle.

Bill Stone, who joined the department in 1948 as a graduate student and remained here for 35 years, was one of Bob Irwin’s collaborators in taking the science of immunogenetics to the agricultural and medical fields. And he developed both of our 100-level introductory genetics courses.

In 1948, James Crow became a member of the department. He became a legendary teacher, textbook author, and researcher — and to this day remains key member of the Laboratory of Genetics and productive scholar.

1950s

In 1950, *Genetics Notes* by James F. Crow made its appearance. This became one of the most popular genetics textbooks of all time and was translated into many languages. The 8th and last edition of the book appeared in 1983. Problems from the book continue to be used in genetics courses to this day.

In the early 1950's, Alex Brink initiated studies of unstable genetic loci in maize, working on this problem at about the same time as Barbara McClintock. The basis for the genetic instability turned out to be transposable genetic elements. McClintock received the Nobel Prize for her work on this subject, and Brink affirmed that she deserved credit for the discovery of these elements. But Brink undoubtedly deserves credit for having written much more easily understood papers on this subject.



1951: Lester Casida (left), William Stone, (right) and colleagues report the first successful implantation of an *in vitro* fertilized embryo resulting in the birth of a calf.

Joshua Lederberg joined the Department of Genetics in 1947 as a brand new Ph.D. graduate of Yale University. His thesis research on bacterial genetics, together with the work that he did in Madison over the next eight or nine years, earned Lederberg the Nobel Prize in Medicine in 1958. Lederberg had begun his journey to the Ph.D. degree as a medical student and believed that genetics research would transform medical science. He urged the University of Wisconsin Medical School to create a Department of Medical Genetics, which was established, with Lederberg as its first chair, in 1957. Although



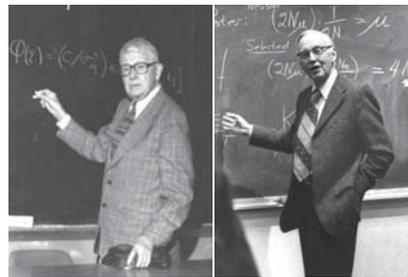
1952: Joshua Lederberg and colleagues discover plasmids in bacteria and transduction of genes by bacterial viruses.

it was not the first such department in the country, it was among the earliest. After he won the Nobel Prize in 1958, Lederberg was offered an irresistible position at Stanford University and moved to California in 1959. The department that he founded here in Madison flourished and is now part of the renowned Laboratory of Genetics.

In the late 1950s, Stanley Peloquin, Bob Hougas, and collaborators developed new methods for the genetic improvement of potatoes, which affected not only Wisconsin agriculture, but also had worldwide impact.

Sewall Wright came to Wisconsin in 1955 after reaching mandatory retirement age at the University of Chicago and remained active in science until he was almost 100 years old. He is widely recognized as one of the “Fathers of Population Genetics.” In the years he spent in Madison, he wrote the immense and definitive four-volume, “*Evolution and the Genetics of Populations*,” the first volume of which was published in 1968. The fourth volume appeared in 1978. Professor Wright published his last paper in 1988, the year in which he died at the age of 99.

In 1959, Jim Crow and colleagues (especially Yuichiro Hiraizumi) discovered and characterized meiotic drive in *Drosophila*. This is caused by *Segregation distorter (Sd)*, a “selfish” mutation that violates the rules of Mendelian genetics.



Over the years, the Genetics faculty has included some of the most important figures in population genetics. These have included Sewall Wright (left) and James F. Crow (right). Other brilliant mathematical geneticists — Newton Morton, Charles Cotterman, and Carter Denniston — made important contributions in applying mathematics to human genetics.

Robert DeMars joined the Genetics faculty in 1959 and did pioneering work in developing methods for studying human genetics by using laboratory cultured cells. This work led to many important discoveries about genetic disorders, including cancer, and about gene regulation in humans. In 1980, DeMars reported the isolation of deletion mutations affecting the human major histocompatibility locus. These mutations have been used by DeMars and other labs around the world to analyze the workings of the immune system. In 2007, Bob DeMars, in his retirement, and colleagues demonstrated recombination by genetic transfer in *Chlamydia*.

1960s

From 1957 until 1965, the Departments of Genetics and Medical Genetics were distinct administrative units, each with its own chair and its own executive committee. This cumbersome arrangement ended in 1965 when the two departments were given permission to create an umbrella organization, the Laboratory of Genetics, which contains both departments but has a single chair and a single executive



1961: Klaus Patau and colleagues discover two trisomies in humans.

committee. Although the Laboratory still reports to two deans and answers to two college-level business offices, this administrative duality has almost no effect on the daily lives of staff and students.

In 1960 Oliver Smithies, already famous for his invention of starch gel electrophoresis, joined the faculty.

Julius Adler used genetic methods to discover the receptors on bacterial surfaces that account for the ability of the bugs to sense attractive or repulsive chemicals in the environment, and subsequently identified the components of the signal transduction machinery that connects the swimming apparatus to the sensory apparatus.



In the 1960s, Masayasu Nomura (left) and colleagues demonstrate self-assembly of small ribosomal subunit. Julius Adler (right) discovers the receptors responsible for chemotaxis in bacteria.

At the beginning of the 1960's, faculty in the growing Laboratory of Genetics were housed in several buildings scattered across campus. In 1963, the Laboratory was unified in the newly built building at 445 Henry Mall.

1970s

During the 1970's, Renata Laxova organized the Statewide Genetic Services Network, a coordinated system of service providers with a "genetics contact" in every county of the state. This was the first such service in the nation and served as a model for numerous such services later established throughout the country. In 1972 John Opitz and Jurgen Herrmann founded the Clinical Genetics Unit.



Renata Laxova organizes the Statewide Genetic Services Network in the 1970s.

In 1975 the interdepartmental PhD Training Program in Genetics was initiated. This is the oldest and largest such training program in the United States.

In 1979, William Engels showed that transposable elements, the so-called P

elements, were responsible for the abnormalities — infertility, high mutation rate, chromosome instability — that occur in the offspring of wild-caught *Drosophila* males mated to females from laboratory stocks. P elements have subsequently become a widely-used vector for genetically engineering flies. Engels's studies of the insertion and transfer of P elements have shed light on DNA repair and recombination mechanisms.



In 1978, Jerry Kermicle makes fundamental discoveries in epigenetic effects ("imprinting") that affect gene expression in corn.

1980s

Oliver Smithies was an early leader in genetic engineering and ultimately invented a method for "targeted" gene replacement in mice, thus making it possible to produce specific "knockout" mice that could be used to reveal the phenotypic effects of any chosen gene. For this work, he received the Nobel Prize in 2007.

Barry Ganetzky identified genes that affect the nervous system of fruit flies, and Ching Kung did similar work with yeast, bacteria, and ciliates. In 1989 Barry Ganetzky and colleagues cloned the gene for sodium ion channel in *Drosophila*.

Michael Culbertson (in yeast) and Philip Anderson (in *C. elegans*) discovered the first genes of the nonsense-mediated mRNA decay pathway.



Oliver Nelson joined the department in 1969. He produced the first fine structure map of a plant gene. In 1984 he cloned the first plant gene.

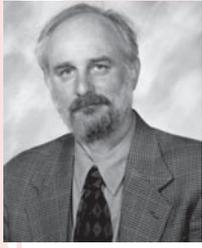
Richard Spritz, who was on the faculty from 1981 until 1998, studied the molecular basis for human genetic disorders. In 1982, he described a number of mutations that caused thalassemia, including an interesting mutation located in an intron which interfered with mRNA splicing.

In 1986, Raymond Kessel launched the Wisconsin Teacher Enhancement Program (WisTEP) for middle school and high school teachers of biology. It offered hands-on instruction in up-to-date biology techniques and has greatly enriched biology education throughout the state of

Wisconsin.

1990s

Fred Blattner was one of the first geneticists to tackle the DNA sequencing of entire genomes; it was his lab that produced the first total sequence of *E. coli*.



1997: Fred Blattner and colleagues complete DNA sequence analysis of *E. coli*.

Tomas Prolla, who joined the Genetics faculty in 1997, has used genetic arrays to study changes in levels of gene expression that are correlated with aging and with factors that alter the rate of aging in mice and primates.

In 1996, many of the faculty moved their labs to the new Genetics Biotechnology Center.

2000s

By 2004 the second phase of the Genetics/Biotechnology Center Building was finished and all faculty and staff were housed in the completed complex. This is just one of many new biological science buildings that have been built in the 2000s. Construction continues to this day. Henry Mall appears to be in a constant state of construction.

John Doebley, who joined the faculty in 1999, has analyzed the genetic relationships between modern corn and its ancestor, teosinte, and has identified many of the genetic changes that account for the differences between the two.

The Present

Research interests of current Genetics faculty

Phil Anderson - Targeted degradation of specific messenger RNAs in the nematode *C. elegans* and its role in regulating normal gene expression.

David Baum - The developmental genetics of plant evolution — searching for genes that underlie the divergent phenotypes of closely related species.

Frederick Blattner - Understanding the genetics of *E. coli* by determining in detail the sequence of its genes, the regulation of gene expression, and the interactions among genes. Genomic studies of bacterial evolution.

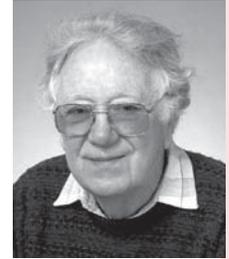
Sean Carroll - The mechanisms of pattern formation in animal development and the evolution of those mechanisms.

Qiang Chang - Genetic and epigenetic regulation of brain functions in mammals.

Nansi Jo Colley - Genetic control of protein trafficking and signal transduction in the eye of *Drosophila melanogaster*.

Michael Culbertson - Transcriptional, translational, and post-translational mechanisms controlling gene expression.

Judith Kimble has been a world leader in describing the genetic regulation of development and sex determination in the roundworm, *C. elegans*, and Phil Anderson has made major discoveries on how gene expression is controlled in roundworms. Sean Carroll has studied the genetic “toolbox” that produces pattern development in insects (and other complex organisms) and has analyzed the genetic changes that have occurred during the evolution of the varied species that share a common ancestral toolbox.



1987: Oliver Smithies and colleagues achieve targeted gene replacement in embryonic stem cells of the mouse.

And that’s only a superficial description of some highlights. What is described in these pages is the “tip of the iceberg” of the rich, scientific heritage of the Laboratory of Genetics. Graduates from our graduate program are among the most distinguished scholars in the field of genetics, and, in recent years, we have seen the growth of the popularity of our undergraduate program. In the 1970’s, we had just a handful of undergraduate majors; now we have about 275. There is good reason to think that the next one hundred years will be just as exciting as the previous century we will be celebrating in May.

John Doebley - Evolutionary genetics of maize and its relatives.

William Dove - The genetics of colon cancer in mice, rats, and humans.

William Engels - Transposable elements in *Drosophila* and the mechanisms of DNA repair and recombination.

Barry Ganetzky - Mechanisms regulating synaptic development and maintenance of neuronal viability in *Drosophila*.

Audrey Gasch - Genetics and evolution of the stress responses in fungi.

Philip Giampietro - Genetic and environmental factors associated with vertebral column abnormalities.

Michael Hoffmann - TGF cellular signaling factor and genetic influences on cancer, wound healing, immunoregulation, and other cell functions.

Akihiro Ikeda - The role of genetics in the formation and function of sensory synapses in the mouse nervous system.

Scott Kennedy - The role of small RNAs in the regulation of gene function in *C. elegans*.

Judith Kimble - Molecular genetics of development in *C. elegans*.

Ching Kung - Genetics of ion channels and their role in sensory responsiveness of bacteria, yeast, and ciliates.

Allen Laughon - Cellular signaling by TGFbeta and the genetic control of development in *Drosophila*.

Patrick Masson - Mechanisms of plant (*Arabidopsis*) responses to gravity and touch.

Kate O'Connor-Giles - Developmental genetics and plasticity of synapse formation in *Drosophila*.

Bret Payseur - Population genetics of mice and genetic studies of speciation.

Francisco Pelegri - Developmental genetics of zebrafish with special emphasis on maternal genes that affect early embryogenesis.

Nicole Perna - Genomic studies of bacterial evolution.

Tomas Prolla - Largescale gene expression surveys to study the genetics mechanisms of aging, DNA repair, and carcinogenesis.

David Schwartz - Human genome structural variation, cancer genomics, revealed by new single molecule systems.

Ahna Skop - The role of membrane trafficking in cell polarity and cytokinesis in the *C. elegans* embryo.

Paul Sondel - Immunological approaches to the treatment of cancer.

Xin Sun - Genetic control of organogenesis and pattern formation in the mouse.

Richard Vierstra - The role of protein turnover in the regulation of cellular function in *Arabidopsis* and the genetic control of that turnover.

Jerry Yin - Molecular genetics of sleep, memory formation, and diseases related to their dysfunction, in *Drosophila*.

JaeHyuk Yu - Molecular genetics of development and signal transduction in fungi (*Aspergillus*).

Current faculty who are members of the National Academy of Sciences

James Crow	1961
Julius Adler	1978
Judith Kimble	1995
William Dove	1998
John Doebley	2002
Barry Ganetzky	2006
Sean Carroll	2007

The Future



Our entering class is pictured: (first row l-r) Anna Rissman, Alison Muir, Sbarolyn Kawakami, Jennifer Pleiman, (second row l-r) Elizabeth Hines, Kari Forshey, Elise Walck-Shannon, Yang Cao, Katie Clowers, (third row l-r) David Gemperline, Daniel Woods, Amanda Henning, (fourth row l-r) John Hivala, Scott Gratz, Celeste Eno, Therese Rytz, Virginia Lamb.

Our future rests in the hands of our graduate students and their dedicated mentors. The University of Wisconsin-Madison ranks first in the nation for training grants funded by the National Institutes of Health. The Genetics predoctoral training grant is the oldest and largest grant for Genetics graduate students. The written review for our most recent renewal recognized the PhD program for: incorporating a number of novel and innovative training mechanisms; maintaining a cohesive training program while offering the students a wide range of research opportunities including interdisciplinary projects; a distinguished faculty including many members of the National Academy of Sciences and holders of national leadership positions; and exceptional programmatic identity and cohesion.

Genetics

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Laboratory of Genetics Milestone Celebrations • MAY 2010

Department of Genetics
• 100th Anniversary •

Department of Medical Genetics
• 50th Anniversary •

We look forward to renewing friendships. Visit our website to learn more and to share your memories of your days in Madison:
<http://www.genetics.wisc.edu>

CELEBRATE WITH US

MAY 20

Annual Symposium sponsored by Nobel Laureate Oliver Smithies

MAY 21-22

Symposium: "100 Years of Genetics – What's Next"
Featuring Madison's research contributions in

- Agricultural Genetics • Evolution •
- Medicine • Neuroscience •

and the anticipated outburst of genetic innovation

MAY 22

Centennial and Golden Jubilee Banquet

For registration, visit our website at <http://www.genetics.wisc.edu>