BUILDING ON CELLS

Surviving Cancer, Saving Fertility

Old Bones Explained

Aiming at a Failing Heart

Unmasking Sleeping Sickness

Huntington’s Deadly Relatives

Putting Stem Cells To The Test

Ovarian Cancer Marker Found?
The ‘Founding Fathers’ of Ubiquitin
Receive ASCB’s Top Scientific Medal

It was named ubiquitin because the tiny protein is found in all organisms, even if its purpose was a mystery. It took the separate but complementary discoveries of researchers Avram Hershko and Alexander Varshavsky to reveal that this ubiquitous molecule is critical to nearly every significant activity in the cell. Ubiquitin is at the center of one of the hottest fields in medical research, as scientists strive to understand ubiquitin’s role in many human diseases, including cancer and neurodegenerative disorders.

For their discovery of the ubiquitin system and its crucial functions, the American Society for Cell Biology will present the E.B. Wilson Medal, the Society’s highest scientific honor, to Varshavsky and Hershko, at 6 p.m. Sunday in Room 103 of the Moscone Convention Center. Both will speak after the medal ceremony.

Hershko, 64, is Distinguished Professor of Medicine at the Technion-Israel Institute of Technology, in Haifa, Israel. Varshavsky, 55, is the Smits Professor of Cell Biology at the California Institute of Technology, in Pasadena.

Tiny but powerful, ubiquitin keeps order in the cell by tagging unnecessary proteins for destruction. It was Hershko who first uncovered ubiquitin’s role in protein degradation and delineated the ubiquitin conjugation pathway by which a healthy cell regulates the degradation of its proteins. In the meantime, Varshavsky who was then at MIT was studying ubiquitin conjugates in chromosomes. With Daniel Finley and Aaron Ciechanover, Varshavsky demonstrated that ubiquitin was essential for protein degradation in living cells essential for cell growth and division. Any substance which can regulate cell division has enormous potential in medicine.

“The complementary discoveries by the laboratories of Hershko and Varshavsky transformed the realm of intracellular protein degradation from a relative backwater of cell biology into a broad and dynamic subject of great importance,” wrote Caltech biologist and ASCB member Seymour Benzer, in his nomination of Hershko and Varshavsky for the ASCB’s E.B. Wilson Medal. “At the present time, ubiquitin studies are one of the major arenas in modern biology, the point of convergence of many disparate disciplines. It is rare in the history of science that a huge, complex, and singularly important field is founded in the main by just two laboratories.”

The scientific story of ubiquitin is nearly as interesting as the personal histories of its discoverers. Both medallists were refugees. Hershko was born in Hungary in 1937. His father was sent to one concentration camp, Avram and his mother to another. Amazingly, father, mother and son were reunited after the war. The family emigrated to Israel when Avram was 13. Hershko earned his medical degree at the Hebrew University-Hadassah Medical School and served as a doctor in the Israeli Defense Forces before returning to Hebrew University to earn his Ph.D. in 1969. He worked as a postdoctoral fellow with Gordon Tompkins at the University of California, San Francisco and returned to Israel to join the faculty of Technion in 1972.

Varshavsky was born in Moscow in 1946, earning his B.S. in Chemistry at Moscow University in 1970 and his Ph.D. in Biochemistry at Moscow’s Institute of Molecular Biology in 1973. He managed to escape from the Soviet Union in 1977 by attending a scientific meeting in Finland, from which he made his way via Sweden to the American Consulate in Frankfurt. Having briefly met the American Nobel Laureate David Baltimore years before, Varshavsky was able to contact Baltimore, who helped Varshavsky procure a visa to the U.S. In America, Varshavsky became a full professor at MIT by 1986. He moved to Caltech in 1992.

The Society’s E.B. Wilson Medal, named for an early 20th century pioneer of American biology who advocated the chromosomal theory of inheritance, is awarded by scientific peers to those whose careers have made highly significant contributions to cell biology.

Who: Avram Hershko of Technion-Israel and Alexander Varshavsky of Caltech
What: The “fathers” of ubiquitin receive the E.B. Wilson Medal
When: Sunday, Dec. 15, 6 PM
Where: Room 103, Moscone Convention Center
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Cell Biology 2002 is published by the Public Information Committee of the American Society for Cell Biology. Katherine L. Wilson is chair. Its members are Simon Atkinson, Rex Chisholm, Mary Dasso, Tom Egelhoff, Robert Goldman, Lynne Maquat, Robert Palazzo, Gregory Payne, Joel Rosenbaum, and Michael Shelanski. In reviewing and editing this press book, the PIC had help from ASCB members Kerry Bloom, Laura Robles, and Meg Titus. The ASCB Science Writer is John Fleischman.
In a year when there was no business as usual, can there be science as usual? For some answers, the American Society for Cell Biology invites you to cover its 42nd Annual Meeting, the largest and most influential meeting of research cell biologists in the world, on December 14-18, 2002 at the Moscone Convention Center in San Francisco. Working Press can register through the ASCB Newsroom (www.ascb.org) until Dec. 10 and thereafter in person at the Annual Meeting.

Bioterrorism, stem cells, bioethics, and cell biology in a genomic world are the subjects of this year’s unusual Keynote Symposium, “Opportunities and Challenges in Cell Biology,” (Saturday, Dec. 14 at 6 p.m.) featuring three scientists and a law professor: Steven M. Block of Stanford, Ron McKay of NIH, and Andrew W. Murray of Harvard plus R. Alta Charo, a professor of law and bioethics at the University of Wisconsin Law School.


This press book, Cell Biology 2002, highlights a baker’s dozen of what we think are the top news “picks,” chosen from more than 3,000 abstracts submitted for the Annual Meeting. As usual, all stories in this press book are embargoed until 5 p.m., pst, Dec. 13, the evening before the meeting opens. Instead of a single large press conference, this year we will invite two or three “Press Book” authors each day to be on hand in Room 212 for our all-new Ten A.M. Press Briefing, on Saturday, Sunday, and Monday. (Which authors and which day will be announced on site.)

Media credentials are for WORKING PRESS ONLY. This means reporters, news producers, desk editors, science freelancers, research institution PIOs, journalism teachers, and journalism students on assignment. The ASCB welcomes card-carrying members of the National Association of Science Writers (NASW), International Science Writers Association (ISWA), and the Canadian Science Writers Association (CSWA). Other freelancers should bring a letter of assignment from an editor or producer. Full-time professional editors of scientific journals may register as media. Academics who serve as journal editors should register as regular members of the Society.

All others including publishers, sales representatives, and media senior management are invited to register as paying guests. Anyone with questions should contact John Fleischman (jfleischman@ascb.org) immediately. We look forward to seeing you in San Francisco and helping you to cover the world’s liveliest science.

Elizabeth Marincola, Executive Director
John Fleischman, Science Writer
Katherine L. Wilson, Chair, Public Information Committee
Kevin Wilson, Director of Public Policy

“"If You Liked Us in San Francisco, You’ll Love Us in Denver.”

AAAS Annual Meeting, Denver, Colorado
Monday, February 17, 2003; 10 AM–1 PM

The American Society for Cell Biology presents a seminar:
The “New” Nucleus: Mothership of the Human Genome
Taking Aim at the Failing Heart

If the golden dream of molecular medicine is to treat disease on the cellular level, what better target could there be than the failing human heart? In heart failure, cardiomyocytes are caught in a vicious spiral of damage, declining efficiency, and then apoptosis or cellular suicide. As more failing cardiomyocytes kill themselves, the heart’s ability to contract weakens, the damage spreads, and the process accelerates. Intervening precisely in a basic cell process such as apoptosis would be an incredible step forward in treating heart disease.

Amazingly, the principle has already been demonstrated. In earlier laboratory experiments using cultured heart muscle cells, an enzyme involved in anti-apoptotic signaling, Akt kinase, was delivered to the cell surface of damaged cardiomyocytes by using the fatty acid, myristolate, as a kind of anchor. The Akt performed beautifully, inhibiting cell death and preventing the spread of new pathogenic signals. However, the myristolated form had undesirable side effects for cardiac structure and function that limited its potential for therapy. Now the cellular delivery of Akt has been further refined. This time, an international team of Japanese and American researchers has targeted Akt even more precisely, using an adenovirus as the vector to aim the anti-apoptotic kinase directly at the cell’s nucleus.

Accumulation of activated Akt in cardiomyocyte nuclei was first discovered by Mark Sussman at the Children’s Hospital Medical Center, Cincinnati. Reasoning that the nucleus might be the biologically relevant target for Akt, Isao Shiraishi who is now at the Children’s Research Hospital in Kyoto, Japan worked with Sussman and other collaborators at the Boston University School of Medicine and the Massachusetts General Hospital, developing a targeted Akt construct to be aimed at the cell nucleus. An adenovirus turned out to be the ideal vehicle to deliver the targeted Akt gene.

After confirming by confocal microscopy and immunoblot analysis the safe delivery of their Akt construct, the researchers checked for signs of morphological damage and found none. They did find significantly higher levels of Akt in the nuclei of targeted cells compared to controls that received an adenovirus delivering an irrelevant nuclear-targeted protein. Shiraishi and colleagues then subjected their nuclear-targeted cells to the insults of hypoxia (low oxygen) and hypoglycemia (low glucose). The nuclear-targeted cardiomyocytes resisted as strongly as those that had received the myristolated Akt, but without the side effects. In all, it was an amazing shot and a possible preview of a new kind of treatment to be delivered where it will do the most good.

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Nuclear Targeting of Akt Enhances Kinase Activity and Survival of Cardiomyocytes. I. Shiraishi,1,2 J. Melendez,1 S. Welch,1,1 E. Schaefer,3 K. Walsh,4 A. Rosenzweig,5 M. A. Sussman;1,1 Molecular and Cardiovascular Biology, Children’s Hospital Medical Center, Cincinnati, OH, 2 Division of Pediatrics, Children’s Research Hospital, Kyoto Prefectural University of Medicine, Kyoto, Japan, 3 Biosource International, Hopkinton, MA, 4 Whitaker Cardiovascular/Molecular Cardiology, Boston University School of Medicine, Boston, MA, 5 Program in Cardiovascular Gene Therapy, Cardiovascular Research Center, Massachusetts General Hospital, Harvard Medical School, Boston, MA

At the ASCB Meeting: Program 915, Poster B86, Apoptosis II. Author presents: Monday, December 16, 1:30 —3:00 PM.
Bone Marrow Stem Cells Renew Muscle and Brain

It was long thought that once cells differentiate, that is, once they begin expressing the genes of a specialized cell type, they cannot change—their identity is fixed and irreversible. This dogma has been challenged in the past few years with the discovery of “stem cells” in the adult. Recent studies have suggested that adult bone marrow cells and their progeny may be extremely plastic. Stanford University’s Helen Blau has been at the forefront of this work, her results strengthening the idea that these naturally occurring changes in cell fate may be ongoing at some level throughout life, and that they may be involved in repair of damage, a function that could potentially be strengthened.

The question remained whether adult bone marrow cell plasticity was a rare event or whether it figured significantly in the normal upkeep and repair of the organism. Blau’s latest results in transplanting fluorescently-labeled bone marrow cells in mice revealed a robust response in muscle fibers, far stronger than any previously reported. She also found that her mice with labeled bone marrow cells contributed to what appear to be fully developed neurons involved in balance and motor function.

In a series of experiments, Blau’s research group transplanted mouse bone marrow cells containing a gene for the green fluorescent protein (GFP) into irradiated mice. The transplanted cells, which glow green, could be readily tracked over time to assess the location and morphology of the new cells. The GFP+ marked cells were found in the brain (in the olfactory bulb) and in muscle. All appeared morphologically similar to their neighbors. In certain muscles, as many as 5 percent of total muscle fibers contained GFP+ cells. This percentage is significantly higher than any reported for other muscles to date. In neurons, numerous GFP+ Purkinje cells with their characteristic cell bodies, axons, and full dendritic trees were detected, suggesting that bone marrow cells can yield fully functional neurons in adult mice. These results suggest that cells for the repair of nervous system damage may be readily obtained from the marrow and that one day it may be possible to mobilize these cells to go from the bloodstream to specific tissues in need of repair.

In all, Blau says, “Our data suggest that adult stem cells in blood may contribute throughout life to brain and brawn in a previously unrecognized manner. Once the underlying mechanisms are elucidated, we may be able to exploit them to target specific organs and diseases.”
A Pregnancy-Induced Stem Cell: Is It the Clue to Pregnancy’s Anti-Cancer Effects?

The baby may seem the prime beneficiary but a mother’s milk has an unexpected benefit for the mother. Studies have shown that early pregnancy confers a lifelong, two-fold reduction in breast cancer risk in women regardless of race, creed, or nationality. Mice and rats also enjoy this increased protection against mammary cancer even when challenged with cancer-inducing chemicals.

The biological problem is how. It was commonly held that all milk-producing breast cells were lost when nursing stops and that the gland reverts to its virginal state. But if these parous (i.e. breeding) females no longer have their distinctive milk-producing cells, where does their anti-cancer protection come from? The common theory, it turns out, is wrong. Gil Smith and his colleagues at the National Cancer Institute in Bethesda, Maryland, in collaboration with Dr. Kay-Uwe Wagner at the Eppley Cancer Center in Omaha, Nebraska, have discovered a new pregnancy-induced epithelial cell population present in the mammary glands of parous mice. This discovery could help unlock their anti-cancer protective mechanism, possibly for all women.

Instead of dying out completely, a proportion of milk-producing cells survive cell death after lactation and the reversion to pre-pregnancy conditions, say the researchers. With subsequent pregnancies, the proportion of surviving cells increases within the glands. Similar cells were not found in females that were never pregnant (nulliparous). Therefore, says Smith and colleagues, the mammary cell population in breeding animals is fundamentally different than those in virgin females.

This new pregnancy–dependent epithelial population was found in the mammary glands of mice by using a reporter gene that could be triggered only by the expression of a milk protein gene. The cells thus identified were isolated and grown in culture so they could be transplanted into epithelium-free mammary fat. There, the pregnancy-induced mammary cells acted like stem cells, multiplying and differentiating into most, if not all, of the epithelial subtypes recognized in the gland. Now the question becomes, how do these pregnancy-induced stem cells protect women when they are no longer pregnant? This raises the possibility of a common mechanism to protect all women against breast cancer.

To follow undifferentiated epithelial cells through lactogenesis (see diagram), Smith and colleagues used female mice with two transgenes, WAP-Cre to report cell differentiation and Rosa-lox-LacZ to monitor cell survival. After lactation ends, fully differentiated, milk-producing aveolar cells undergo apoptosis as the mammary gland involutes to its virgin state. It was thought that all aveolar precursors perished as well. Instead, the reporter genes showed the survival of a new type of pregnancy-induced epithelial stem cell. Early in pregnancy (top left), the reporter genes show under blue stain in mammary tissue section. Yet even after involution, blue stain in small ducts shows the survival (left) of aveolar precursor cells.

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Identifying Multilineage Mammary Epithelial Progenitors, In Vivo. G. H. Smith,1  K. Wagner,2  and C. Boulanger3; 1NCI, NIH, Bethesda, MD, 2Eppley Institute, University of Nebraska, Omaha, NE, 3NCI, NIH, Bethesda, MD

At the ASCB meeting: Presentation 2352, Minisymposium 26: Stem Cells. Author presents: Wednesday, December 18, 2002, 3:45 —4:05 PM.
Putting Stem Cells to the Test

Toti-, pluri-, or multi-, stem cells are supposedly sortable by potency. The truth is, four years into the stem cell era, we are still exploring stem cell potential and still finding surprises. Here’s another. A team led by Suzanne Kirby and colleagues at the University of North Carolina at Chapel Hill and the Duke University Medical School has demonstrated for the first time cross-species hematopoietic transdifferentiation of a cloned and easily genetically-altered liver stem cell line from a male rat into functional bone marrow cells in female mice.

The rat stem cells, naturally marked by the y-chromosome and artificially marked by transgenes, were injected into female mice whose bone marrow had been damaged by radiation. Six to eight weeks later, mouse bone marrow was harvested and analyzed for cells with the rat-specific markers. Then individual colonies of blood-making cells from the transplanted mice were cultured for closer examination. Half the colonies were examined genetically for two key types of multipotent blood stem cells, myeloid and lymphoid progenitors.

Compared to control results, rat-markers—the rat Y-chromosome and an inserted transgene—turned up in 59 percent of the colonies with myeloid cells and in 90 percent of the colonies with pre-B (pre-lymphocyte) cells. Examined by microscope, the stem cell-transplanted colonies had developed into a wide complement of blood cell types—including neutrophils, monocytes, megakaryocytes, macrophages, erythroid, and pre-B cells¾, although T cells have not yet been found at these early time points.

The researchers’ cloned rat liver stem cell line, WB-F344, had been used in earlier experiments where liver stem cells were shown to transdifferentiate into cardiac myocytes. By transplanting to another species, they hoped it would be easier to track the stem cells and thus demonstrate a complete “proof of concept” that stem cells derived from one tissue line could be cloned and transplanted to a host where they would transdifferentiate into new tissue without fusing with the host’s cells. This, they have accomplished, says Kirby and colleagues, adding with traditional scientific restraint, “This transdifferentiation of adult stem cells could prove useful for tissue repair.”

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Hematopoietic cell transdifferentiation of cloned adult liver-derived stem cells. Suzanne Kirby1,2, Stuart Bentley2, James Fry2, William Walton1, Niyati Desai2, Ann Latour3, William Coleman2, Page Anderson4, Joe Grisham2, and Nadia Malouf2. Departments of Medicine1, Pathology2, and Genetics3, University of North Carolina at Chapel Hill and Department of Pediatrics, Duke University Medical Center4

At the ASCB Meeting: Program 680. Poster B660, Stem Cells. Author presents: Sunday, December 15, 1:30 —3:00 PM.

Morphology of G418 resistant, Y-chromosome + colonies. A) erythroid, B) megakaryocyte, C) macrophages, D) immature myeloid and neutrophils.
Unmasking Sleeping Sickness: ‘Old’ Antibiotics May Offer New Ways to Treat a Third World Plague

All parasites are tricksters but *Trypanosoma brucei*, a single-cell parasite that cycles between an insect form that lives in the tsetse fly and a bloodstream form that lives in the human host, is a master of the game. To move from fly to human host, the *T. brucei* must slip into an effective disguise to hide from the immune system. Now researchers at the Johns Hopkins School of Medicine led by Kimberly S. Paul have blown the cover of *T. brucei*, catching the human bloodstream form dressed in a self-synthesized coat of fatty acid-linked proteins. Further, Paul and her colleagues found that the molecular pathway in the parasite that generates the fatty acid coat is highly vulnerable to a commonly used antibiotic. This opens the possibility of a new cheap and effective treatment, a development that could have significant impact on human health, especially in Africa. The bloodstream form of *T. brucei* causes African sleeping sickness, a disease that afflicts nearly 500,000 people today. If left untreated, it is fatal.

Although it was known for years that the insect form of *T. brucei* could synthesize fatty acids, it was thought that the bloodstream form could not. Paul and her Hopkins collaborators, Y. Morita, J. Stephens, and P. T. Englund, discovered that the bloodstream form does, indeed, synthesize fatty acids, specializing primarily in the fatty acid myristate. Myristate is a critical component of the outer protein coat that protects the parasite from attack by the host’s immune system.

The researchers then looked for ways to disrupt the process. Using data from the *T. brucei* genome project, they identified several genes that may encode the enzymes that catalyze fatty acid synthesis (FAS). Interestingly, they found that some of these genes were structurally similar to the FAS genes of bacteria (prokaryotes) rather than to those of animals (eukaryotes), which was surprising because *T. brucei* is eukaryotic. Experiments that switched off or suppressed expression in some of these genes indicated that the FAS pathway was essential for the parasite’s growth and survival.

Given this pathway’s apparently vital role and its structural difference from the human host’s FAS pathway, the Hopkins researchers decided to test the effect of known inhibitors of bacterial FAS on *T. brucei* including Triclosan, an antibiotic commonly found in toothpaste and soap. Triclosan directly inhibited the FAS pathway in cell-free enzymatic assays and inhibited the growth of *T. brucei* living in laboratory cell cultures. “These data suggest that Triclosan and other antibiotics that target bacterial FAS could represent a ready-made pool of new drugs to combat this lethal disease,” says Paul.

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*Prokaryotic Fatty Acid Synthesis in the Eukaryote Trypanosoma brucei: A Pathway with Potential for New Drug Therapy.* K. S. Paul, J. Stephens, P. T. Englund; Biological Chemistry, Johns Hopkins School of Medicine, Baltimore, MD 21205.

At the meeting: Program 2309, B463, Structure & Function of Membrane Proteins II. Author presents: Wednesday, December 18, 12:00 —1:30 PM.
The Geologist’s Delight, the Biologist’s Dilemma

There is nothing new under the sun, or for that matter under the cell membrane. Bacteria invented the magnetic compass billions of years before any human being sailed the ocean blue, eyes on the binnacle. Magnetotactic bacteria are an ancient and diverse group of prokaryotes with the unique ability to align themselves in the earth’s magnetic field, apparently to guide themselves to low oxygen microenvironments. Their compass is an organelle called the magnetosome that consists of an inorganic magnetite crystal surrounded by a lipid bilayer. Magnetosomes usually form a single chain near the cell membrane of the bacterium, creating a larger magnet that is sensitive to external magnetic fields.

For geologists, magnetosomes are a gift. Their shape and magnetic properties are so distinctive that geologists can identify them in samples that are billions of years old. These “magnetofossils” have been used to trace the history of life on earth and the evolution of the earth’s magnetic field over time.

For cell biologists, the magnetosomes are a problem. Prokaryotes are not supposed to have organelles. Membrane-bounded organelles, such as the nucleus and endoplasmic reticulum, are supposed to be strictly the province of eukaryotes. Yet magnetosomes, which are a distinctly prokaryotic organelle, share many features of eukaryotic organelles. For example, each magnetite crystal is formed within a membranous vesicle made of a lipid bilayer. This vesicle contains unique proteins that are not found in any other part of the cell while the number of vesicles and even their position within the cell is tightly regulated. Clearly magnetotactic bacteria, like eukaryotic cells, possess mechanisms for the biogenesis, assembly and maintenance of their organelles. Being so ancient, could magnetotactic bacteria offer insights into organelle biogenesis in eukaryotes?

To answer these and other questions, Arash Komeili and Dianne Newman of the Geological and Planetary Sciences Department at Caltech have been applying genetic, cell biological, and biochemical approaches to magnetotactic bacteria. They have identified several mutants that cannot form magnetite, and are now looking for the specific defects that interfere with vesicle formation or protein targeting. The genes affected in these mutants localize to a previously identified cluster that seems to be unique to magnetotactic bacteria. This gene cluster codes for several proteins that have interesting homologies to serine proteases, PDZ proteins, and even actin. These are all players in some of the most fundamental processes in eukaryotic cells, and genomic connections at this level could, indeed, throw light on the common origins of organelles. 

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At the ASCB Meeting: Presentation 1594, Minisymposium 21: Organelle Biogenesis and Inheritance. Author presents: Tuesday, December 17, 5:05 —5:25 PM.

Thin section electron micrographs of wildtype and magnetite mutants (mnm1 and mnm2) of Magnetospirillum magnetotacticum sp. AMB-1. The two mutants have distinct phenotypes; mnm2 is devoid of any minerals whereas mnm1 contains small mineral inclusions arranged in a chain within the cell.
Safe from Harm: A New Agent to Protect Fertility During Cancer Therapy

Chemotherapy and radiotherapy are strong medicine but they can be harsh treatment. Along with a cancer diagnosis, a female patient must also face the possibility of infertility and premature menopause. For a girl or a woman of reproductive age, a routine side effect of these common anti-cancer treatments is the inadvertent destruction of the eggs stored in her ovaries since birth.

The American Cancer Society estimates that one in 52 females younger than 40 (i.e., the years when their fertility is vulnerable) will be diagnosed with cancer. Although some will be cured by surgery, the vast majority of these young girls and women will receive chemotherapy, radiation or a combination of the two. For the past five years, a major collaborative effort between the laboratory of Jon Tilly at the Massachusetts General Hospital in Boston and groups headed by Richard Kolesnick and Zvi Fuks at Memorial Sloan-Kettering Cancer Center in New York to find an agent that would protect the ovaries from the ravages of anti-cancer therapies has centered on sphingosine-1-phosphate (S1P). In major studies published in *Nature Medicine* in 1997 and 2000, the collaborators showed that when this fatty chemical produced naturally in the body was injected into female mice, it could protect their eggs from the lethal effects of radiotherapy, and potentially chemotherapy. Now comes a vital test of the protective effects of S1P; whether the eggs protected by S1P would be fertile and whether oocytes derived with S1P-protected eggs would have levels of genetic damage that would endanger the health or fertility of any offspring that resulted. The results, which are also published in *Nature Medicine*, are promising.

To assess S1P's impact on genetic stability, Kolesnick led a multi-institutional team of researchers in a study of DNA damage in three generations of female mice, irradiating the first generation to compare S1P-treated females to untreated females, and both groups to non-irradiated controls. The studies showed the fertility of the unprotected but irradiated females falling by as much as 85%. Those protected by S1P maintained normal fertility throughout their adult lives. Secondly, a screening of nearly 500 first- and second-generation offspring conceived by these protected females found no evidence of genetic damage or defects.

To measure potential DNA damage, eggs from S1P-protected females were closely examined for breaks in chromosomes or inappropriate recombination events between chromosomes that should not normally pair with each other, both important signs of DNA damage. None were seen. The scientists also looked to see if there were any signs of genetic damage in other cells in the first-and second-generation offspring, by looking for fragmented chromosomes in blood cells. The offspring of the S1P-treated mothers did not show any increased signs of damage.

Taken with the previous studies, Kolesnick and colleagues—Jon Tilly and Gloria Perez at Harvard Medical School, Fuks at Sloan-Kettering, William Morgan at the University of Maryland, Baltimore, and Pat Hunt at Case Western Reserve in Cleveland—believe this new report is critical evidence that S1P might be capable of preserving ovarian function during cancer therapy without causing genetic mayhem afterward.

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*Sphingosine 1-phosphate Preserves Fertility in Irradiated Female Mice Without Propagating Genetic Damage in Offspring.* R. N. Kolesnick, F. Paris, G. I. Perez, Z. Fuks, A. Haimovitz-Friedman, M. Bose, A. Ilagan, P. Hunt, W. Morgan, J. L. Tilly; Pharmacology, Memorial Sloan-Kettering Cancer Center, New York, NY, Obstetrics and Gynecology, Harvard Medical School, Boston, MA, Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY, Radiation Oncology, University of Maryland, Baltimore, MD, Genetics, Case Western Reserve, Cleveland, OH

At the ASCB Meeting: Presentation 819, Minisymposium 13: Apoptosis and Cellular Senescence. **Author presents:** Monday, December 16, 4:25 —4:45 PM.
Genes Tied to Ovarian Cancer Could Be Long-Sought Early Markers

All cancers can be cruel but few are as swift as ovarian cancer, partly because diagnosis is usually made at such a late stage. Only 25 percent of ovarian cancers are caught before the disease spreads beyond the ovaries, the point at which current therapy is mostly ineffective. The survival rate for the advanced disease is only 20-30 percent. Yet ovarian cancer caught in its early stages can be cured in up to 90 percent of cases. A reliable early warning test could have enormous impact on a disease that is still the sixth leading cause of cancer-related deaths among women. A reliable test, though, needs a reliable disease marker.

Against this background comes the announcement by Pat Morin and Leticia Rangel of the National Institute on Aging in Baltimore and other collaborators that they have identified four ovarian-specific genes they call HOSTs (Human Ovarian Specific Transcripts) consistently expressed only in ovarian tumor tissues. The four HOSTs are rarely expressed in normal tissues including normal ovary tissue or in cancers in other organs of the body. This makes them prime candidates as markers for ovarian cancer and thus targets for an early diagnostic test.

Using a technique called SAGE, or serial analysis of gene expression, that identifies all the genes that are switched on in a particular cell or tissue, the researchers discovered many genes that are specifically activated in malignant ovarian tissue. Morin and colleagues zeroed in on the HOST genes by wading through the long list of human genes activated in ovarian cells whose functions are unknown. The researchers then took cells microdissected from ovarian tumors and, using PCR amplification to see which genes were “upregulated,” found the four HOST genes fully activated in all four major kinds of ovarian cancer.

A marker for a disease is not necessarily the cause. But whatever role the HOST genes actually play in the onset of ovarian cancer, if they show up early enough and reliably enough in ovarian tumor cells, the HOST genes become prime suspects for earlier diagnostic tests and even as targets for new drugs. For thousands each year, their appearance in an early screening could be just in the nick of time.

Contact: Patrice J. Morin, National Institute on Aging, NIH, 5600 Nathan Shock Drive, Baltimore, MD 21224, (410) 558-8506, morinp@grc.nia.nih.gov

Characterization of Novel Ovarian-Specific Genes Identified by Serial Analysis of Gene Expression (SAGE). Leticia B. A. Rangel1,2, Cheryl A. Sherman-Baust1, Donald R. Schwartz3, Kathleen R. Cho3 and Patrice J. Morin1,4, 1Laboratory of Cellular and Molecular Biology, National Institute on Aging, Baltimore, MD, 2Department of Basic and Clinical Pharmacology, National Institute on Aging, Baltimore, MD, 3Department of Pathology, The University of Michigan Medical School, Ann Arbor, MI, 4Department of Pathology, The Johns Hopkins Medical Institutions, Baltimore, MD. *Corresponding author.

At the ASCB meeting: Program 1353, B555, Tissue-Specific Gene Expression II. Author presents: Monday, December 16, 12:00—1:30 PM.

Immunohistochemical analysis of an ovarian tumor using an antibody directed against an overexpressed product identified by SAGE. The dark brown positive staining is clearly restricted to the surface of cancer cells.
Well-done Meat and Herbal Tonics Affect Important Breast Cancer Cell Growth Pathways

The growth of many breast cancers depends on estrogen. Thus, any factor that affects estrogen-dependent pathways is potentially important for cancer development or treatment. Now, a new study suggests that two herbal tonics used as alternative therapy for breast cancer contains active ingredients that may interact with a naturally-occurring, mutation-inducing compound found in well-cooked meats. In combination, these particular herbal tonics and overcooked meat may sharply increase the activity of the cellular estrogen receptor in breast cancer cells, and be harmful to breast cancer patients.

The mutagenic compound found in well-cooked muscle meats is called PhIP (2-amino-1-methyl-6-phenylimidazo[4,5-b] pyridine). Exposure to PhIP alone is known to alter DNA in mammalian cells, and causes breast and prostate tumor formation in rats. In human studies, consumption of well-done meat is linked to increased breast cancer risk in women. The herbal tonics, Flor-Essence® and Essiac®, are complementary and alternative medicines that are taken in addition to, or instead of standard chemotherapy. Both tonics are widely available at health food stores and on the Internet, and are frequently recommended to women with breast cancer by word-of-mouth.

Working with breast cancer cell lines in the laboratory, Kristen S. Kulp and colleagues in the Biology and Biotechnology Research Program at the Lawrence Livermore National Laboratory in Livermore, California used assays that monitor cell growth and estrogen receptor activation to study the interaction of known mutagens such as PhIP with other dietary compounds. They found that breast cancer cell lines exposed to PhIP increased their estrogen receptor activation 1.8-fold more than untreated cells, a milder effect than the 5-fold increase typically seen with estrogen treatment alone. PhIP also caused a 20-30% increase in growth in the cancer cell lines. Flor-Essence® and Essiac® herbal tonics both contain herbal extracts known or suspected to stimulate the estrogen pathway. When added individually, each tonic stimulated the growth of breast cancer cells as much as 2-fold higher than controls, and was as potent as estrogen in activating the estrogen receptors.

However when breast cancer cells were incubated with PhIP and Flor-Essence® together, the activity of estrogen receptors increased 6-fold, a level greater than either compound or estrogen alone. Researchers, including L.M. Bennett at the National Cancer Institute in Bethesda, Maryland, believe these results raise concerns about interactions between dietary carcinogens and alternative medicines in breast cancer survivors.

Contact: Kristen S. Kulp, Lawrence Livermore National Laboratory, Biology and Biotechnology Research program, 7000 East Ave., L-452, Livermore, CA 94550, (925) 422-6351, kulp2@llnl.gov

Dietary constituents affect estrogen receptor activation and cell proliferation in MCF-7 cells. K. S. Kulp,1 J. L. Montgomery,1 E. R. Latham,1 J. S. Felton,1 L. M. Bennett2; 1 Biology and Biotechnology Research Program, Lawrence Livermore National Laboratory, Livermore, CA; 2 Center for Cancer Research, National Cancer Institute, Bethesda, MD (This work was performed under the auspices of the U. S. Department of Energy by the University of California, Lawrence Livermore National Laboratory under Contract No. W-7405-Eng-48)

At the ASCB Meeting: Program 1616, Poster B1, Growth Factors & Receptors. Author presents: Tuesday, 12/17/02, 12:00 —1:30 PM.
Tracing a Deadly Family Resemblance

They form an unhappy family, an extended clan of fourteen different genetic brain diseases, all under the seemingly innocent name of “trinucleotide repeat disorders.” The most infamous is Huntington’s, an inherited, progressive neurodegenerative disease. Huntington’s belongs to an immediate subfamily of eight “repeat” disorders that share a common defect—a mutated gene that contains extra copies of the repetitive DNA nucleotide code “CAG”. The genes in question vary from disorder to disorder but the biochemical result is the same, a mutant protein containing a long tract of misfolded glutamine. Yet each glutamine disorder has its own signature, devastating a different region of the brain or nervous system. Why the same defect should be so destructive in so many different ways is one of the central mysteries underlying Huntington’s and its seven terrible relations.

Now a Canadian-American collaboration led by R. Truant of McMaster University in Hamilton, Ontario, together with Harry Orr at the University of Minnesota, has taken a closer look at one of them, spinocerebellar ataxia type I or SCA1, and discovered that the signature mutant repeat protein of SCA1 is so unwieldy that it gets stuck in the nucleus, trapping an associated protein along with vital pieces of messenger RNA inside. The researchers believe that a very similar mechanism may be at work in Huntington’s.

Ataxin-1, the protein defective in SCA1, normally resides in the cell nucleus where it was thought to bind messenger RNA, the genetic instructions for the cell’s protein-making machinery, but for unknown reasons. Using lasers and microscopy on living cells, Truant and colleagues were able to watch normal ataxin-1 move in and out of the nucleus together with another protein, LANP. It’s the LANP that turns out to be critical to the export of key messenger RNAs. But the oversized mutant ataxin-1, with its long chain of glutamine repeats, so gums up the exits of the nucleus that it gets stuck in the nucleus, trapping an associated protein along with vital pieces of messenger RNA inside. The researchers believe that a very similar mechanism may be at work in Huntington’s.

Contact: Ray Truant, McMaster University, Biochemistry, HSC 4H45, 1200 Main Street West, Hamilton, ON L8N 3Z5 Canada, (905) 525-9140 ex.22450, truantr@mcmaster.ca

Polyglutamine Neurodegenerative Disease Protein Ataxin-1 is a member of a Protein Complex Mediating the Nuclear Export of Specific Messenger RNAs J. L. Howell, 1 H. G. Serra, 2 M. Vandelft, 1 T. Zu, 2 S. Irwin, 1 J. Xia, 3 H. Y. Zoghbi, 4 H. T. Orr, 5 R. Truant 6; 1 McMaster University, Hamilton, ON, Canada, 2 University of Minnesota, Minneapolis, MN, 3 McMaster University, Hamilton, ON, 4 Howard Hughes Medical Institute, Baylor College of Medicine, Houston, TX, 5 Dept. of Genetics, Cell Biology, and Development, Institute of Human Genetics, University of Minnesota, Minneapolis, MN, 6 Biochemistry, McMaster University, Hamilton, ON, Canada

At the ASCB Meeting: Program 2138, Poster B560, Nuclear Import and Export Signals. Author presents: Tuesday, December 17, 1:30 —3:00 PM.

Purkinje cells from the central folia of a 27 week old SCA1 mouse expressing a mutant SCA1 gene with an expanded CAG repeat. The section was stained with an antibody to the Purkinje cell-specific protein calbindin. This image demonstrates the dendritic atrophy and disruption of the Purkinje cell body layer seen in these mice. Image courtesy of Harry Orr, Institute of Human Genetics, University of Minnesota.
Does Bone Cell Aging Cause Osteoporosis?

Our bones lengthen as we grow until as adults we take it for granted that we have the finished product, a reasonably rigid, unchanging skeleton. Unchanging, that is, until old age. Yet seen on the cellular level, bones are never still and a new look at aging bone cells by Bernard Halloran and colleagues at the Veterans Administration Medical Center of the University of California, San Francisco may throw new light on what causes the dangerous bone brittleness of osteoporosis.

Even as adults, our bones are constantly being built up and torn down, a process known as “remodeling”. It continues throughout life to insure that our bones stay strong and free of damage. Osteoblasts (OB) are the cells that make bone and osteoclasts (OC) are the cells that tear bone down. Normally, there is a balance between the formation of new bone and the destruction or “resorption” of old bone, maintained by an elegant molecular coupling between the bone forming OBs, and the bone resorbing OCs. However, with age, this balance can be upset, resulting in loss of mineral from the bone and increased brittleness.

Bone cell coupling is brought about, in part, by a unique system that bone cells use to signal to each other, involving a receptor activator of NFkB (RANK) on the OC cell surface and a ligand or protein (RANKL) on the OB cell surface that binds to RANK. When the OB touches the OC, the RANKL binds to RANK stimulating the OC to multiply and increase its bone resorbing activity. The OB also produces another protein, osteoprotegerin or OPG, which acts as a brake on the process. OPG binds to RANKL and interferes with its ability to stimulate RANK. Thus the OB controls the number and activity of OCs. Normally, the OB produces just enough RANKL and OPG to balance bone formation with bone resorption, and our bones are healthy and strong.

Halloran and colleagues wondered if the loss of bone that occurs with aging might involve a disruption of the RANKL-OPG balance. Collecting and culturing OB cells from young and old donor animals, they observed that OBs from old donors produced more RANKL and less OPG than OBs from young donors. This would increase the number of osteoclasts and produce an imbalance between bone formation and resorption.

To determine how age-related changes in OB function affect OC formation and activity, the researchers combined OBs with OC-precursor cells from young and old animals. OCs have more than one cell nucleus and also produce an enzyme known as tartrate resistant acid phosphatase or TRAP. Since the cells were growing together in culture, to tell the OBs from the OCs, the researchers counted the number of multinucleated/TRAP+ cells. The researchers found that more OCs were produced when their precursors were cultured with OBs from old animals than when they were cultured with OBs from young animals. These results show that OBs from old animals have a much greater ability to make new OCs than OBs from young animals. This suggests a mechanism to explain age-related bone loss and the development of osteoporosis.

“It appears that as we age the cells in our bones also age and as a consequence undergo a change in function,” says Halloran. “The osteoblasts are no longer able to balance bone formation with bone resorption. As a consequence, we lose bone mineral, our bones become weak and eventually fracture. We now need to learn how to interfere in this process and restore the balance.”

Contact: Bernard P. Halloran, Veterans Affairs Medical Center and University of California, San Francisco, Division of Endocrinology and Departments of Medicine and Physiology, VA Medical Center (111N), 4150 Clement St., San Francisco, CA 94121 (415) 750-6928 bhallor@itsa.ucsf.edu

Aging Alters Osteoblast-Osteoclast Interaction. L. L. Venton, B. P. Halloran, J. Cao; Division of Endocrinology and Departments of Medicine and Physiology, Veterans Affairs Medical Center and University of California, San Francisco, San Francisco, CA

At the ASCB Meeting: Presentation 2764, Poster B400, Cell–Cell Interactions II. Author presents: Wednesday, December 18, 1:30 —3:00 PM.
The Drink That Refreshes Your Mitochondria?

If you are a speed-reader of fine print, you know that advertising claims for “health” food, drinks, and supplements are often cheerfully unsubstantiated. Yet in Japan, Oolong tea—a blended, semi-fermented tea halfway between unfermented green and fermented black tea—has been the subject of an amazing amount of scientific research into its effectiveness as an anti-oxidant and in controlling fat storage. One interesting piece of physiological evidence to emerge from these studies is a reported increase in CO₂ exhalation following the ingestion of Oolong tea.

CO₂ is produced at the cellular level from oxygen consumption by mitochondria as they generate the cellular energy source ATP, suggesting to Osamu Numata and colleagues at the Institute of Biological Sciences at the University of Tsukuba in Japan that some substance in Oolong tea activates mitochondria to convert oxygen into energy. To investigate, the researchers selected two biological test models with external moving parts, the flagella-wagging mouse sperm and the cilia-waving protozoan Tetrahymena. Oolong tea extract was chemically fractionated into water-soluble and water-insoluble fractions. The two fractions and controls were used on Tetrahymena and mouse sperm. To examine effects on mitochondria, the researchers used Rhodamine 123, a fluorescent chemical tag which incorporates into the mitochondrial membrane and reports on mitochondrial activity by increasing its fluorescence in response to increases in mitochondrial membrane potential. To investigate cellular activity, they measured the swimming velocity of the Tetrahymena and mouse sperm. The movement of these external parts is highly dependent on cellular energy, so they represent sensitive indicators of cellular energy levels.

The water-insoluble fractions, which contain high concentrations of polyphenol molecules, strongly activated the mitochondrial membrane potential in both Tetrahymena and mouse sperm. The hydrophobic fractions of Oolong tea also elevated swimming velocity by up to 25-33 percent in Tetrahymena and 100 percent mouse sperm. Numata now proposes that the hydrophobic fraction of Oolong tea increases ATP production through activation of cellular metabolic pathways, such as the TCA cycle or oxidative phosphorylation, housed in mitochondria. Increased ATP elevates swimming velocity because ATP is used to drive ciliary and flagellar movement.

Contact: Osamu Numata, Institute of Biological Sciences, University of Tsukuba, Tennoudai, 1-1-1, Tsukuba, Ibaraki, 305-8572, Japan, (T) 81-298-53-6648, numata@sakura.cc.tsukuba.ac.jp

Hydrophobic Fraction of Oolong Tea Activates the Mitochondrial Membrane Potential and Elevates Swimming Velocity in Tetrahymena and Mouse Sperm. T. Fujiwara,1 S. Yoshida,1 M. Kimura,2 Y. Ishikura,2 K. Hosoda,2 O. Numata,1 ; 1 University of Tsukuba, Institute of Biological Sciences, Tsukuba, Ibaraki, Japan, 2 Suntory Limited Research Institute for New Product Development, Suntory Research Center, Osaka 618-8503, Japan

At the ASCB Meeting: Program 1072, Poster B253, Cilia & Flagella I. Author presents: Monday, December 16, 12:00 —1:30 PM.

Below: Florescence photographs of Tetrahymena stained by Rhodamine 123. The bright dots along cilia are the signal from mitochondria. Especially, cells treated with OHF2 and OHF5 exhibited intense florescence.
Pharmacologists call the new class of synthetic stimulants “entactogens,” a coinage from the Greek meaning “to touch within,” but to the teens and young adults who wolf down the latest “club drugs,” they go by many names. The most popular entactogen—3,4-methylenedioxymethamphetamine or MDMA—is sold as XTC, Adam, and, most familiarly, Ecstasy. Increasing evidence shows that MDMA does indeed touch within. It touches the neurotransmitter serotonin (5-HT) system. In long-term use, it’s a neurotoxin.

In humans, the neurotransmitter 5-HT system regulates numerous functions, such as mood, learning, memory, sleep, and pain. MDMA’s toxic effects on 5-HT neurons could explain some long-term consequences of MDMA use including learning and memory impairment, depression, and sleeping disorders. But the exact mechanism by which MDMA changes 5-HT neurons is not fully understood. Since exploring molecular pathways is difficult in human subjects, Nathalie Thiriet and colleagues at the National Institute on Drug Abuse (NIDA) in Baltimore have turned to rats to look at MDMA’s long-term neurological consequences. The group has already shown that MDMA regulates the expression of several genes in the rat cortex. The corresponding proteins are enzymes involved in the detoxification of the cell or proteins participating in the remodeling of neuronal connections.

In their latest findings, Thiriet and colleagues take the molecular story a step farther. They now show that MDMA activates the JAK (Janus kinase)/STAT (signal transducers and activators of transcription) pathway. The JAK/STAT pathway is known to transmit information from the external membrane of the cell to its nucleus and allows a reprogramming in the pattern of expressed genes. In the nucleus, STAT proteins regulate important biologic responses including cell growth and programmed cell death. Connecting MDMA to the JAK/STAT pathway moves us closer to understanding the molecular basis of its effects. It may help explain how MDMA touches the brain so indelibly.
Eric Wieschaus: Screens, Genes and Sorting Out Front from Back

Among colleagues, Eric Wieschaus of Princeton University is famous for telling stories on himself—almost flunking out of graduate school at Yale, getting so caught up in lecturing that he stabbed himself with a pencil, or insisting that the 5:30 a.m. call from Sweden informing him that he’d won the Nobel Prize was a wrong number. But the 1995 prize in Physiology or Medicine did indeed go to Wieschaus, Christiane Nüsslein-Volhard, and Edward Lewis. Wieschaus and Nüsslein-Volhard were cited for their work on the “genetic control of early embryonic development.”

Their collaboration, 15 years before at the European Molecular Biology Lab (EMBL) in Heidelberg, involved a saturation mutagenesis screen for all the genes involved in early embryonic organization of *Drosophila*. Their unprecedented approach yielded 40,000 mutants and 15 different genes that controlled early pattern formation. Targeting all the genes in an entire process such as zygotic segmentation through a saturation mutant screening was a novel idea in 1980 and their results caused a stir in the *Drosophila* community, says Wieschaus, but it was the later perfection of gene cloning in the mid-1980s that turned their experimental insights into a genetic land rush.

Born in South Bend, Indiana, in 1947, Wieschaus was five when his father, a chemical engineer, was transferred to Birmingham, Alabama. Wieschaus went to Birmingham’s only Catholic high school, doing well in math and science although his most obvious talent was his ability to draw. For his undergraduate degree, Wieschaus went back to Indiana and his father’s alma mater, Notre Dame where his introduction to *Drosophila* was as the student fly keeper in Harvey Bender’s lab which gave Wieschaus an appetite for basic research but a strong distaste for flies. Nonetheless, Wieschaus started graduate studies under Yale’s legendary *Drosophila* geneticist Don Poulson. From Poulson, Wieschaus learned the basics of fly genetics and fly embryology, skills that turned out to be vital. But when the newly arrived Swiss embryologist Walter Gehring offered him the chance to experiment *in vivo* with *Drosophila* embryos, Wieschaus made the switch.

When Gehring went back to Basel in 1972, Wieschaus went with him. In Basel, Wieschaus finished his Yale thesis, and first met “Janni” Nüsslein-Volhard. In 1975, Wieschaus took a postdoc with Rolf Nöthiger at the University of Zurich where he acquired fluent German and kitchen French, and met Gertrud “Trudi” Schupbach, a fellow *Drosophilist* who would have an important impact on his science but a deeper one on his personal life. They would be married in 1983.

In 1978, EMBL named Wieschaus a Group Leader, a contract position targeted to young researchers. His labmate was Nüsslein-Volhard. Working at first with one technician and one fly keeper, they embarked on the development of their saturation mutagenic screen. In those days, molecular genetic analysis was far too slow for a screen of such size. To visually evaluate thousands of mutant embryos, they hit on the idea of a microscope fitted with dual eyepieces where they could sit opposite each other and, in assembly line fashion, score each one simultaneously.

Their timing was lucky, says Wieschaus. “We did it almost as a classical genetics experiment. It could have been done anytime from the 1930s onward but we did it at a time when other people were discovering how to clone genes. If we’d done it earlier, it would have been just as good an experiment but the intellectual impact would have been less. But because of cloning and molecular approaches that were suddenly possible in flies, here were all these interesting genes and their postulated functions.”

Wieschaus and Schupbach moved to Princeton in 1981 where both have since worked their way up to full professorships in Molecular Biology. Princeton was a wonderful place to raise their three science-phobic daughters, says their father. Princeton continues to offer Wieschaus a quiet place to get on with his work on embryonic morphogenesis. It’s a freedom he relished before the Nobel and has savored even more since.

“I still work in the lab. I still teach. My life is pretty much like it was before. People here are willing to tolerate my choices because they say, ‘Oh, gosh, he’s the Nobel laureate and if that’s what he wants, well, we’ll let him have it.’ Besides, in my case, what I want is pretty cheap.”
A Harvard biologist and a pioneer in molecular genetics whose long-standing warnings about chemical and biological weapons (CBW) became bitterly real during last year’s terrorist anthrax attacks is this year’s winner of the ASCB’s Public Service Award.

Matthew Meselson, 72, is a professor of Molecular and Cell Biology at Harvard University and Co-Director of the Harvard-Sussex Program on CBW Armament and Arms Limitation. He says that a hair-raising talk in 1963 with an American biological weapons arms expert who extolled the “cheapness” of biological weapons propelled him into what became a nearly 40-year campaign against CBW programs and their unexpected consequences. In October 2001, anthrax spores sent through the U.S. mails to media and government offices caused 22 cases of anthrax including five deaths, underscoring Meselson’s longheld concerns that CBW technology is hard to control in war or in peace.

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“Since 1963, Matt Meselson has dedicated much of his life to the issue concerning the development and use of chemical and biological agents for war,” says H. Robert Horvitz, an MIT biologist, this year’s Nobel laureate in Physiology, and a member of the ASCB’s Public Policy Committee that selected Meselson for its annual award. “Matt advocated that the U.S. stop the development of biological weapons during the Nixon era, and he raised critical questions about the putative Soviet biochemical weapon “yellow rain” in the 1980s. In the wake of September 11th, he’s been educating the politicians and the public of a country still in shock over the first use of anthrax as a bioterror weapon.”

Meselson was widely known in government and policy circles for influencing President Nixon’s 1969 decision to renounce biological weapons. In 1981, U.S. Secretary of State Alexander Hague charged that the Soviet Union had battle tested a mycotoxin known as “yellow rain” in S.E. Asia. Puzzled by the scarcity of physical evidence, Meselson and colleagues undertook an independent investigation including an arduous field expedition through Southeast Asia to collect samples and interview refugees. Meselson concluded that the “yellow rain” samples were harmless droppings from honey bee “cleansing flights” and that the claims of microtoxins were based on false positives. His 1987 report was denounced by the State Department but its evidence was never refuted.

In 1992, Meselson and a team he organized that included his wife, Jeanne Guillemin, a Boston College medical anthropologist, were the first outsiders to directly investigate the “Sverdlovsk incident,” the accidental release in 1979 of anthrax from a secret Soviet military CBW laboratory that killed 65. Their field investigation revealed new details on how anthrax behaves as a weapon as well as confirming rumors that the Soviet military had secretly pressed ahead with its CBW research in violation of international agreements. Meselson remains concerned about what happened to those CBW experts and their biological stocks in the former Soviet Union.

A native of Denver, Dr. Meselson received his bachelor’s from the University of Chicago in 1951 and his doctorate at the California Institute of Technology in 1957. Meselson was still a graduate student at Caltech under Linus Pauling when he and post-doc Frank Stahl devised what has been called “the most beautiful experiment in biology.” They tested a major prediction of Watson and Crick’s theory of double-stranded DNA, by proving the semi-conservative nature of DNA replication. Later working in collaboration with Sydney Brenner and Francois Jacob, he described one of the fundamental players in genetics, messenger RNA.

Past winners of the ASCB’s Public Service Award include actor and medical research activist Christopher Reeve, former Secretary of Health and Human Services Donna Shalala, former NIH Director Harold Varmus, and U.S. Senator Tom Harkin.
# The American Society for Cell Biology
## 42nd Annual Meeting
### December 14-18, 2002 - San Francisco
**Gary Borisy, President; John Cooper, Program Chair; Patricia Calarco, Local Arrangements Chair**

### Keynote Symposium: Opportunities & Challenges in Cell Biology
**Saturday, December 14 - 6:00 pm**

- **Steven M. Block,** Stanford University
- **Ron McKay,** National Institutes of Health
- **R. Alta Charo,** University of Wisconsin Law School
- **Andrew W. Murray,** Harvard University

### Symposia

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<td>Nuclear Trafficking and Dynamics</td>
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<td>How Cells Interact with Each Other</td>
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<td>Cell Biology of Cancer</td>
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### Minisymposia
#### Sunday, December 15
- **Cell Junctions and Signal Transduction**
  - Barry Gumbiner, Memorial Sloan-Kettering Cancer Center
  - Susan LaFlamme, Albany Medical College
- **Cell Polarity: Establishment & Maintenance**
  - Erlei Bi, University of Pennsylvania School of Medicine
  - Elisabeth Knust, Heinrich-Heine Universität Düsseldorf, Germany
- **Computational Approaches to Cell Biology**
  - Gaudenz Danuser, Swiss Federal Institute of Technology
  - George Oster, University College London, UK
- **Cytokinesis**
  - Fred Chang, Columbia University
  - John G. White, University of Wisconsin
- **Endocytosis**
  - Sandra Lemmon, Case Western Reserve University
  - Mark Mash, University College London, UK
- **Extracellular Matrix and Cancer**
  - Hynda Kleinman, NIDR
  - James McCarthy, University of Minnesota
- **Microbial Pathogenesis**
  - Vojta Dervisic, University of New Mexico
  - Michele Swanson, University of Michigan
- **Signaling and Development**
  - Alan Christian, Oregon Health Science University
  - Janet Heasman, Children’s Hospital Medical Center, Cincinnati

#### Monday, December 16
- **Apoptosis and Cellular Senescence**
  - Barbara Osborne, University of Massachusetts
  - Kristia White, Harvard Medical School
- **Control of Growth, Size and Shape**
  - Suzanne Banes, St. Jude Children’s Research Hospital
  - Martin Raff, University College London, UK
- **Cytoskeletal Processes During Development**
  - Susan Strome, Indiana University
  - William Theurkauf, University of Massachusetts
- **Integrin Signaling**
  - Jun-Lin Guan, Cornell University
  - Richard Klemke, Scripps Research Institute
- **Mitosis and Germ Cells**
  - R. Scott Hawley, Stowers Institute
  - Anne Villemeur, Stanford University
- **Nucleocytoplasmic Trafficking**
  - Larry Gerace, Scripps Research Institute
  - Maureen Powers, Emory University
- **Rafts and Other Membrane Microdomains**
  - Pico Caroni, Friederich Miescher Institute, Switzerland
  - Martin Hemler, Duke-Farber Cancer Institute
- **Regulation of Cytoskeleton Assembly**
  - Lynne Cassimeris, Lehigh University
  - Tatyana Svitkina, Northwestern University

#### Tuesday, December 17
- **Cell Biology of Angiogenesis**
  - Nancy Rudnicka, University of California, San Francisco
  - Joseph Madri, Yale University
- **Cell-Cell Junctions**
  - Eric Bayer, University of Chicago
  - Sandra CITI, University of Padova, Italy
- **Cell Cycle Regulation**
  - Orna Cohen-Fix, NIH/NIDDK
  - Dannel McCollum, University of Massachusetts
- **Cell Migration**
  - John Condeelis, Albert Einstein College of Medicine
  - Anna Huttenlocher, University of Wisconsin
- **Cytoskeletal Motors**
  - Richard Cheney, University of North Carolina
  - Richard Vallen, Columbia University
- **Organelle Biogenesis and Inheritance**
  - Benjamin Glick, University of Chicago
  - Judith Klumperman, Utrecht University Medical Centre, The Netherlands
- **Protein Folding and Quality Control in the ER**
  - Jeffrey Brundage, University of Pittsburgh
  - Linda Hendershot, St. Jude Children’s Research Hospital
- **Signaling and Cell Proliferation**
  - Jonathan Cooper, Fred Hutchinson Cancer Research Center
  - Sarah Spiegel, Virginia Commonwealth University

#### Wednesday, December 18
- **Cytoskeletal Dynamics in Living Cells**
  - Jake Nuthke, University of Dundee, Scotland
  - John Vic Small, Austrian Academy of Sciences
- **ECM Molecules and their Receptors**
  - Elisabeth Lord, University of California, Riverside
  - E. Helene Soga, Hope Heart Institute
- **Mechanisms of Cell Signaling**
  - Lewis Cantley, Harvard Medical School
  - Peter Pryciak, University of Massachusetts
- **Mitotic Spindle Assembly and Function**
  - Rebecca Heald, University of California, Berkeley
  - Tim Yen, Fox Chase Cancer Center
- **Nuclear Structure and Function**
  - Wendy Bickmore, Medical Research Council, UK
  - Sui Huang, Northwestern University
- **RNA Localization and Dynamics**
  - Anita Hopper, Pennsylvania State University
  - Mary Lou King, University of Miami
- **Stem Cells**
  - Emanuela Gussoni, Children’s Hospital, Boston
  - James Sherley, Massachusetts Institute of Technology
- **Vesicle Trafficking**
  - Joan Bonifacino, NIH/NICHD
  - Carolyn Muchamore, The Johns Hopkins University