

About the American Federation for Aging Research

The American Federation for Aging Research (AFAR) is a nonprofit organization whose mission is to support and advance healthier aging through biomedical research. Through partnerships with foundations, corporations and individuals and the National Institute on Aging, AFAR has provided approximately \$100 million to more than 2,400 early and mid-career scientists from many of the nation's leading academic institutions.

AFAR supports a wide range of basic, clinical, and health-services research, necessary to increase our chance of living healthier, longer. AFAR programs also make a substantial investment in developing medical faculty for careers in geriatric medicine, with the goal of attracting a cadre of physicians who will ultimately care for a growing aging population and serve as mentors to the next generation of researchers and clinicians.

Our work has led to significant advances in the understanding of aging processes, agerelated diseases, and healthy aging practices. AFAR communicates news of these innovations to the public through our consumer newsletter *Lifelong*, organizational web site www.afar.org, and two educational web sites, Infoaging (www.infoaging.org) and Health Compass (www.healthcompass.org).



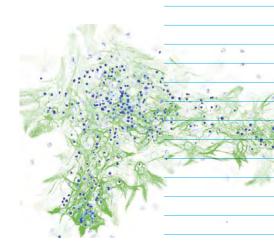
This annual report is dedicated to T. Franklin Williams, MD, a long-time advocate of AFAR and its scientific director from 1992 to 2002.

Dr. Williams began his medical career with a sub-specialty in diabetes but later transitioned to geriatrics and helped create the prestigious geriatrics program at the University of Rochester School of Medicine and Dentistry, where he now holds the title of professor emeritus. From 1983 to 1991, Dr. Williams served as director of the National Institute on Aging at the National Institutes of Health. In 1995, he received an appointment of Distinguished Physician from the Veterans Administration. During his career, he has received numerous awards, among them the Distinguished Service Medal from the U.S. Public Health Service; the Institute of Medicine Gustav O.

Lienhard Award from the National Academy of Sciences; and the Irving S. Wright Award from the American Federation for Aging Research.

We extend our profound gratitude to Dr. Williams for his contributions to AFAR and his work on its behalf, and we express our pride in and appreciation for our long association with him.

Back to Basics



Research is linked to two words: cures and hope. Research is where cures originate, and hope is the catalyst for funding science.

Diana Jacobs Kalman, Chair of the Board

The outcome of medical research is often unpredictable. Scientists who begin an investigation with a hypothesis frequently find themselves moving in directions they never anticipated. Time and again, basic discoveries that at first appear to have little clear practical relevance evolve into important clinical breakthroughs. Jonas Salk's polio vaccine, for example, owed its development to the laboratory work of Boston scientists who discovered how to cultivate the polio virus in human tissue. The development of statin drugs, now ubiquitous in medicine cabinets throughout the United States, began in 1971 as a series of laboratory experiments to find ways to inhibit the body's molecular process for producing cholesterol.

Even now, the race to find future treatments and potential cures for Alzheimer's disease, cancer, arthritis, and many other age-related conditions depends upon the efforts of basic research scientists. In fact, the most medically significant and cost-effective way of preventing these disabilities and diseases may be to focus first of all on the basic processes of aging itself.

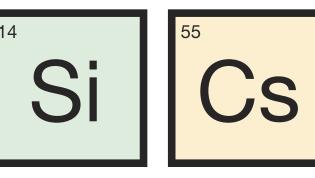
For more than 25 years, AFAR has supported scientists examining many of the most fundamental mechanisms in aging. Their research is opening up new vistas in our understanding of how and why we age. Throughout this report, you will read stories about the new, basic science that researchers are conducting in laboratories every day. This is critically important work. AFAR continues to maintain its faith in, commitment to, and support of this basic research. It is an effort we believe is already yielding the insights that—once translated into new drugs and other therapies will help all of us live healthier, longer.

Adult neural stem cells stained for markers of stem cells and for differentiated progeny.

Image source: Anne Brunet, PhĐ

Building on the Basics

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The American Federation for Aging Research is proud of the contributions it has made in the complex effort to extend human health span—the number of years we live vitally and independently. In fact, 2007 marked a milestone in AFAR's giving. Since our founding in 1981, AFAR has now awarded approximately \$100 million in grants to more than 2,400 talented researchers. A significant portion of those funds have supported basic research. This work will continue to serve as the foundation for new and exciting breakthroughs in the care of the growing number of older adults.

Maintaining a longstanding commitment to fundamental science through the AFAR Research Grant program is more important than ever in light of the current downturn in federally sponsored funding. Basic research is risky. Promising avenues of study may lead to dramatic advances, but they may also lead to disappointment and dead ends. Taking those risks is difficult, even career-threatening for researchers just starting out, especially when research funds are increasingly scarce and competitive.

In this light, we take particular satisfaction in AFAR's grantmaking and our grantees' accomplishments. Our grant programs continue to expand, enabling greater numbers of scientists to forge new discoveries in age-related research. And once again, in 2007, AFAR received high praise from Charity Navigator, which rates our impact and administration at the highest rank.

The kind of success AFAR has experienced does not happen on its own. It depends upon two precious resources: people and partnerships. Our people include eminent scientific and lay leaders who serve on our board and review committees. In 2007, we honored two of these extraordinary volunteers—board members T. Franklin Williams, MD and Diane A. Nixon recognizing their dedicated commitment and generosity to AFAR at our gala dinner. Unquestionably, their leadership and vision have contributed to AFAR's continued success.

Other critical people are the AFAR grantees, who continue to receive recognition in numerous academic journals and in the popular media for their important work. With fewer than 20% of research proposals funded, AFAR's selectiveness ensures that its grantees are scientists of the highest caliber. This includes people such as Nir Barzilai, MD, director of the Institute for Aging Research at the Albert Einstein College of Medicine, who is investigating the metabolic decline associated with aging. This research has demonstrated that we inherit at least part of our longevity through our DNA. And it includes David Sinclair, PhD, associate professor of pathology at Harvard Medical School and co-director of the Paul F. Glenn Laboratories for the Biological Mechanisms of Aging, who is studying compounds that activate another group of these so-called "longevity genes." The vast majority of these talented researchers remain within the field of aging research. Many continue to maintain their relationship with AFAR beyond the tenure of their grants. Grantees help the organization by mentoring younger scientists and serving on scientific review committees and the AFAR board, taking their places alongside some of the

The image (opposite page) shows a red fluorescent protein (RFP) reporter of poly-ubiquitin expression in adult Caenorhabditis elegans. Ubiquitin is involved in degrading damaged proteins, a process important for longevity and protection against ageassociated diseases.

<u>Image source:</u> Matt Kaeberlein, PhD

Biomarkers of Aging

most esteemed scientists in the field of aging research. These include George M. Martin, MD, AFAR's scientific director, Terrie Fox Wetle, PhD, former deputy director of the National Institute on Aging and AFAR's board president, and Roger McCarter, PhD, chair of AFAR's review committee.

AFAR's partnerships are similarly broad and diverse. These collaborations extend to the public, foundation, and corporate sectors and not only make our grant programs possible but also allow them to move in new directions. For example, the Hartford/AFAR Collaborative Research Award extends and enriches the longstanding Paul B. Beeson Career Development Awards in Aging Research, funding joint projects for the program's alumni and encouraging incorporation of all of the Beeson Scholars' promising research into a shared information database.

We wish to acknowledge the contributions received from all of our major funding partners in 2007 as well. In particular we are pleased to note: The Atlantic Philanthropies; Basic Element Company; The Ellison Medical Foundation; The Rosalinde and Arthur Gilbert Foundation; Glenn Foundation for Medical Research; David W. Gore; The John A. Hartford Foundation; Marion Esser Kaufmann Foundation; F.M. Kirby Foundation; The Ambrose Monell Foundation; Pfizer Inc; Fannie E. Rippel Foundation; Goldman Sachs; The Starr Foundation; John L. (Launny) and Weezie Steffens; and the National Institute on Aging. All of these organizations and individuals have shown extraordinary, ongoing faith in the value of basic research in aging.

A biomarker of aging is a biochemical indicator that can help identify rates of aging, predict longevity, and reveal susceptibility to disease. Researchers have made important progress in finding biomarkers of aging in lower life forms, such as roundworms, by looking at genes that turn on and off in age dependent ways. Locating them in humans has proven more difficult, but researchers have made significant progress through studying stem cells and tumor suppressor genes. And exciting

new fields such as epigeneticsthe study of alterations in gene expression/regulation that go beyond the genetic sequenceare leading to a cascade of new discoveries. Although most scientists agree that finding a single biomarker for the entire complex process of human aging is a long way off, developing a group of them that can predict risk for age-related diseases, such as cancer, Parkinson's disease, and Alzheimer's disease, is well within our reach and generating great interest among scientists.

Liana Apostolova, MD



Working at the Geffen School of Medicine, University of California, Los Angeles, with the support of AFAR and its partners through a 2005 Paul Beeson Career Development Award in Aging Research, Liana Apostolova, MD, is in the vanguard of the search for Alzheimer's disease biomarkers. By using cutting-edge

magnetic resonance imaging technology to look for atrophy in particular regions of the brain such as the hippocampus and the cortex, she is developing techniques for identifying who will develop the disease long before symptoms appear. This should prove a particularly important tool, as once signs of Alzheimer's disease begin to appear, significant damage has already occurred in the brain. Thus far, Dr. Apostolova and her colleagues have successfully identified predictable patterns of change in the brains of people who go from mild cognitive impairment-a subtle and often sub-clinical form of neurological impairment-to full-blown Alzheimer's disease.

Beyond Basics: Program Highlights Events and Education

Sustaining the Momentum: AFAR Annual Awards Dinner

Nearly 200 people joined AFAR at its awards dinner honoring leaders in the corporate, scientific, and lay communities for their efforts to sustain the momentum of aging research. The dinner, held October 1, 2007, at the University Club in New York City, coincided with AFAR's annual grantee conference and served as a kick-off event for AFAR's scientific meeting, Seeking Biomarkers of Aging and *Diseases of Aging* (see below). Among the awardees were Richard A. Miller, MD, PhD, professor of pathology and associate director of the Geriatrics Center at the University of Michigan and AFAR board member; Diane A. Nixon, AFAR board member; Allen D. Roses, MD, senior vice president, Pharmacogenetics, GlaxoSmithKline; John L. (Launny) Steffens, former vice chairman of Merrill Lynch, and current managing director of Spring Mountain Capital; and T. Franklin Williams, MD, professor of medicine emeritus & VA Distinguished Physician, University of Rochester, former director, the National Institute on Aging (1983-1991) and AFAR board member emeritus.

The Twentieth Annual AFAR Grantee Conference

Recent grantees participated in this year's meeting, moderated by AFAR president Terrie Fox Wetle, PhD. Some of the nation's leading scientists in the field addressed these talented investigators, including Steven Austad, PhD, University of Texas Health Science Center at San Antonio; Thomas Johnson, PhD, University of Colorado at Boulder; Karen Bandeen-Roche, PhD, Johns Hopkins Bloomberg School of Public Health; and Anna McCormick, PhD, National Institute on Aging. A highlight of the program was the poster session, which provided grantees with an opportunity to share their research with these leaders as well as other grantees and meeting participants.

Seeking Biomarkers of Aging and Diseases of Aging

More than 200 AFAR grantees, mentors, and industry representatives joined AFAR for a high-level scientific meeting focused on the now decades-long search for these elusive indicators of aging. The interactive conference featured presentations highlighting the resources available for aging-related biomarker research and the kind of biomarkers needed to provide improvements to the human condition by alleviating disease and extending healthy lifespan. A forum with industry discussed public-private partnerships for the development of more useful biomarkers and effective interventions that could ultimately identify, treat, and track age-related diseases and disorders.

Richard Hodes, MD, director of the National Institute on Aging, presented the keynote address, "The Outlook for Biological Research on Aging." Other speakers included: Stephen L. Helfand, MD, Brown University; Donald Ingram, PhD, Pennington Biomedical Research Center/ Louisiana State University; Gerald McClearn, PhD, Penn State University; Richard A. Miller, MD, PhD, University of Michigan; Richard L. Sprott, PhD, The Ellison Medical Foundation; and Richard Weindruch, PhD, University of Wisconsin.

Aging, Genome Maintenance, and Metabolism

In a joint presentation with the Albert Einstein College of Medicine, on December 6, 2007, AFAR hosted a conference focusing on the intersection between aging, genome maintenance, and metabolism at the New York Academy of Sciences. Speakers included preeminent experts on genomics and metabolism, including Albert Einstein's Nir Barzilai, MD, a Beeson alumnus and AFAR research grantee; and AFAR research grantees Judy Campisi, PhD, from the Lawrence Berkeley National Laboratory; and David Sinclair, PhD, of Harvard Medical School.

New Grant Programs

AFAR and its partners created the following new grant programs in 2007. The first recipients will be selected in 2008 unless otherwise noted.

Beeson Annual Meeting

AFAR held the 2007 annual meeting of the Paul B. Beeson Career Development Awards in Aging Research, June 21–24, 2007, at the Tarrytown House Estate & Conference Center, Tarrytown, New York. This event, a key aspect of the Beeson program, offers Scholars an opportunity to present their findings to their colleagues, develop their scholarship and leadership skills, and network with other Scholars as well as important senior researchers in their field.

Infoaging Update and Expansion

Since 1999, Infoaging.org has served as an easy-to-understand, consumer web resource on the latest research about the biology of aging, age-related diseases, and healthy aging. This year, with additional support from Pfizer Inc, AFAR installed a variety of new interactive capabilities to better serve thousands of people who use the site each year. We are also updating the site's 35 information centers to ensure that Infoaging.org continues to provide the most up-to-date, credible news possible on the field.

Centers of Excellence Network Resource Center

Since 2005, with support from The John A. Hartford Foundation, AFAR serves as the Network Resource Center for the Foundation's 27 Centers of Excellence (COEs), recognized for their considerable capacity to recruit and develop physician leaders in geriatrics. The role of the Network Resource Center is to facilitate communications among the COEs and to identify and disseminate best practices in geriatrics recruitment and career development. Three major publications on recruitment of medical trainees to careers in geriatrics; recruitment to advanced fellowship training and academic careers; and managing geriatrics programmatic growth and development are currently under production.

Hartford/AFAR Collaborative Research Awards

This one-time award encouraged teams of current and former Beeson Scholars to collaborate on translational and multi-disciplinary research on aging. Five research teams received \$400,000 each to probe a variety of aging-related issues, including preventing Alzheimer's disease, rehabilitating intensive care unit patients, and examining the role of inflammation in central nervous system dysfunction, among others. Recipients were selected in 2007 and include the teams: Wes Ely, MD, Vanderbilt University School of Medicine, and Helen Hoenig, MD, Duke University Medical Center; Martin Sadowski, MD, New York University School of Medicine, and David Holtzman, MD, Washington University School of Medicine; Scott Small, MD, Columbia University College of Physicians and Surgeons, and Frank Longo, MD, PhD, Stanford University Medical Center; Laura Dugan, MD, University of California, San Diego, and Jeremy Walston, MD, Johns Hopkins University School of Medicine; and Joshua Hare, MD, University of Miami Miller School of Medicine, and Michael Schwarzschild, MD, PhD, Harvard Medical School.

The Ellison Medical Foundation Increases Funding for AFAR Grants

In an effort to attract and retain more talented scientists at a time when government funding is scarce, The Ellison Medical Foundation has increased funding for two critical AFAR grant programs: the new Ellison Medical Foundation/AFAR Postdoctoral fellows in Aging Research Program and the Julie Martin Mid-Career Awards in Aging Research. The Ellison Medical Foundation has awarded AFAR more than \$2.8 million to support 45 postdoctoral fellows (both MDs and PhDs at any level of postdoctoral training) over the next three years in the fundamental mechanisms of aging. With this new commitment, The Ellison Medical Foundation/ AFAR partnership has increased five-fold the number of researchers it will support. Ellison's additional contribution to the Julie Martin Award will allow that program, established in 2005, to support more mid-career investigators engaged in innovative, often risky aging research or a related field that could lead to new insights into the biology of aging. For more information on these awards, see page 12.

New Grant Awards

In 2007, the first recipients of the following grant programs were selected:

The Paul Beeson Career Development Awards in Aging Research Program: Extension to the Island of Ireland

The Paul Beeson Career Development Awards in Aging Research Program continues to create a cadre of leading physician-scientists committed to academic careers in aging-related research, teaching, and practice. This year, the program went international, with support from The Atlantic Philanthropies, providing awards of up to approximately \$450,000 to two outstanding junior physician faculty members in Ireland: Patricia M. Kearney, MB BCh BAO, PhD, Trinity College Dublin, and Bernadette McGuinness, MD, MRCP, Queen's University of Belfast.

Rosalinde and Arthur Gilbert Foundation/ AFAR New Investigator Awards in Alzheimer's Disease

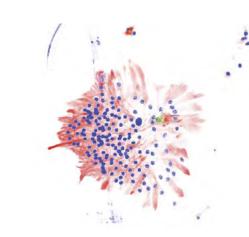
This program supports research into the prevention, diagnosis, and treatment of Alzheimer's disease. The program also encourages junior investigators in the United States and Israel to pursue research and academic careers in the neurosciences, and Alzheimer's in particular. Six talented Israeli and American researchers received these one- to two-year awards of \$60,000 each in 2007, including: Yaniv Assaf, PhD, Tel Aviv University; Olivier Boutaud, PhD, Vanderbilt University Medical Center; Chad Anthony Dickey, PhD, University of South Florida; Isabella A. Graef, MD, Stanford University; Indu Kheterpal, PhD, Pennington Biomedical Research Center; and Grace Stutzmann, PhD, Rosalind Franklin University.

<u>The Fannie E. Rippel Foundation/</u> <u>AFAR New Investigator Awards on Gender</u> <u>Differences in Aging</u>

To address the need for more study about the effects of aging on men and women, AFAR partnered with the Fannie E. Rippel Foundation to create this award, which supports early-career scientists using a gender-based approach to aging research. In 2007, the program's two \$60,000 awards went to Jennifer S. Lee, MD, University of California, Davis, and Rebecca C. Thurston, PhD, University of Pittsburgh School of Medicine. This program will not be offered in 2008.

AFAR-GE Healthcare Junior Investigator Award for Excellence in Biomarker Research

In conjunction with AFAR's conference on biomarkers, AFAR and GE Healthcare teamed up to award four talented early-career scientists \$1,500 each in recognition of their innovative scientific accomplishments in the area of biomarker research. Their work illuminates fundamental aspects of cell aging and their regulation as key aspects of health and fitness of aging individuals. The 2007 awards went to Ying Liang, PhD, University of Kentucky; Krishnamurthy Janakiraman, PhD, University of North Carolina at Chapel Hill; Stuart M. Chambers, PhD, Baylor College of Medicine; and Carolina Ibáñez-Ventoso, PhD, Rutgers University.



Affiliate Program

Through partnerships with local philanthropic and community-based organizations, corporations, and medical schools, AFAR's Affiliate Program develops resources to distribute more research grants to scientists in local regions. Each year, AFAR matches up to two \$30,000 grants per affiliate and also provides fundraising and public relations support. Since its inception, the Affiliate Program has granted more than \$720,000 to 12 scientists in upstate New York, Ohio, and the southeastern U.S. Currently, the AFAR Affiliate Program has two offices in operation.

In spring 2008, AFAR will celebrate the official launch of a new Florida Affiliate. Partnering institutions include Florida State University; the Center on Aging at the University of Miami; University of Florida; University of South Florida; Nova Southeastern University; Sarasota Memorial Hospital; and the Mayo Clinic. AFAR board member and immediate past president Mark Beers, MD, will chair the Florida Affiliate Board of Directors.

The Affiliate Program supported exciting new science in 2007. Our Southeastern Affiliate at Emory University awarded two grants. The first went to Mark A. Eckert, PhD, Medical University of South Carolina, for research on brain imaging and age-related changes in speech recognition. The second was presented to Mauricio Rojas, MD, Emory University, for investigation into the effects of age on the stem cells' ability to localize in the lung and promote repair after an injury.

We strive to broaden our outreach and to trigger excitement in being involved with aging research. Ultimately, support for basic research has a direct effect on population health.

Terrie Fox Wetle, PhD, AFAR President and Associate Dean of Medicine for Public Health and Public Policy at Brown University

Dorothy Dillon Eweson Lecture Series on Advances in Aging Research

The Eweson Lecture Series on Advances in Aging Research was established in 1997 by late AFAR board member Dorothy Dillon Eweson in an effort to bring the issues of aging and age-related diseases and conditions to the forefront of medical association conferences. The Eweson Lecturers strive to increase awareness of aging issues within specialty areas by presenting cutting edge papers and research on topics directly relating to specific disciplines. The series provides funding of up to \$1,500 to cover travel expenses and honoraria for up to six lectures each year. The 2007 recipients include: James Galvin, MD, MPH, Washington University School of Medicine; Thomas Gill, MD, Yale University School of Medicine; Daniel Goldstein, MD, Yale University School of Medicine; and Jeffrey Hausdorff, PhD, Harvard Medical School.

From AFAR's Labs: Grantee Highlights

Many AFAR grantees are gaining broad attention both in top scientific journals and high-profile consumer media, expanding the knowledge we all need to live well longer. Some highlights from 2007 include:

2000 Beeson Scholar <u>Catherine Sarkisian, MD</u>, of the University of California at Los Angeles, was cited in *Reuters Health* December 5, 2007, in an article about older adults who had experienced lower expectations about aging. Those who expected to experience more health-related decline as they grew older, were more likely to report spending less time engaging in physical activity than those with higher age expectations. These observations were from her study of 636 adults aged 65 and older. Her research was originally published in the October, 2005, issue of the *Journal of General Internal Medicine*.

Laura E. Niklason, MD, PhD, of Yale University and a recipient of the 2001 AFAR Research Grant and a 2002 Beeson Scholar, was profiled in the *Charlotte News & Observer* in November, 2007. The article profiled her research on replicating blood vessels that can be used for dialysis patients and in heart bypass surgery.

Thomas Perls, MD, MPH, 1998 Beeson Scholar, of Boston University, and <u>David Sinclair</u>, PhD, 2000 AFAR Research Grant recipient, of Harvard University, discussed their recent work in longevity and healthy aging on the November 11, 2007, broadcast of *CBS News Sunday Morning*. Dr. Perls is currently investigating the effects of lifestyle choices on the longevity of centenarians. Dr. Sinclair is working to develop a pill that will mimic the health enhancing effects of caloric restriction in the human body. The research of 2000 Pfizer/AFAR Research Grant recipient and University of California Irvine researcher <u>Frank LaFerla</u>, <u>PhD</u> about the restorative effects of stem cells to reduce memory problems was covered in *New Scientist* and *Scientific American.com* November, 2007.

On October 31, 2007, <u>Gordon Lithgow, PhD</u>, of the Buck Institute and 2006 Glenn/AFAR Breakthroughs in Gerontology (BIG) Award recipient, <u>Gawain McColl, PhD</u>, formerly of the Buck Institute and now at the Mental Health Research Institute of Victoria, Australia, and 2003 Glenn/AFAR postdoctoral fellow, and <u>David Killilea, PhD</u>, of Children's Hospital Oakland Research Institute and 2003 Glenn/ AFAR postdoctoral fellow, were featured in *Science Daily*. The article discussed the researchers' work regarding the use of lithium, a drug to treat mood affective disorders, in increasing lifespan in nematode worms.

The October 8, 2007, edition of the *Los Angeles Times* featured 2000 Pfizer/AFAR Research Grant recipient, <u>James Lah, MD, PhD</u>, of Emory University, who discussed potential genetic markers for diagnosing Alzheimer's disease.

The New York Times (October 7, 2007) cited University of Pennsylvania researcher and 2000 Beeson Scholar, Jason Karlawish, MD, who pointed out that a diagnosis of a mental disease does not mean the person is incapable of working, making decisions, or voting.

Anne Louise Oaklander, MD, PhD, of the Massachusetts General Hospital and 1999 Beeson Scholar, was featured on *CNN.com* on September 24, 2007. This piece focused on treating patients with chronic pain that do not have an obvious cause of the pain and do not respond to medicine. Elizabeth Phelan, MD, of Harborview Medical Center and 2003 Beeson Scholar, was featured in the *Seattle Times* on September 10, 2007, offering recommendations on helping older adults avoid falls.

Research by 1999 Beeson Scholar <u>Thomas</u> <u>Rando, MD, PhD</u>, of Stanford University School of Medicine, indicates that a stem cell's ability to reproduce, regardless of its age, is dependent on the age of the cell's environment. The study was published in the August, 2007, issue of *Science* and featured in articles on *Forbes.com*, *Voice of America*, and *Science Daily*.

Malaz Boustani, MD, MPH, of Indiana University School of Medicine and 2005 Beeson Scholar, was featured in *WebMD*, *Medical News Today*, the *Los Angeles Times*, and other media outlets for his study published in the Journal of the American Geriatrics Society, in August, 2007. Dr. Boustani's work looked into the effect of long-term H2 blocker use in the development of cognitive impairment.

Wes Ely, MD, of Vanderbilt University School of Medicine and 2001 Beeson Scholar, was featured in *U.S. News & World Report* on July 18, 2007. The article focused on Dr. Ely's research on detecting and preventing delirium in older hospitalized patients.

A July 3, 2007, *Washington Post* article on palliative care cited 2000 Beeson Scholar <u>Sean Morrison, MD</u>, from the Mount Sinai School of Medicine, on how the use of palliative care not only provides very ill patients with the care they need but also lowers hospital costs at the same time.



(1) Catherine Sarkisian, MD; (2) David Sinclair, PhD; (3) Frank LaFerla, PhD;
(4) Gordon Lithgow, PhD; (5) James Lah, MD, PhD; (6) Jason Karlawish, MD;
(7) Thomas Rando, MD, PhD; (8) Sean Morrison, MD; (9) Dellara Terry, MD,
MPH; (10) Anne Cappola, MD; (11) Scott Pletcher, PhD; (12) Nir Barzilai, MD

In order to understand the diseases of aging, you first have to understand the processes of aging. That's why it's so important for us to fund as many basic scientists early in their careers as possible, to maintain the drive toward new discoveries in the field.

Stephanie Lederman, Executive Director

Dellara Terry, MD, MPH, of the Boston University School of Medicine and a 2005 Beeson Scholar, was noted in the August, 2007, issue of *Real Simple* magazine, offering tips on living healthier longer.

Bernadette McGuinness, MD, MRCP,

Queen's University of Belfast, first recipient of the Paul B. Beeson Career Development Award Extension to the Island of Ireland, was featured in the June 25, 2007, issue of the *Belfast Telegraph*. Her research focuses on the neuropsychological changes and genetics of early Alzheimer's disease.

A March 26, 2007, *Newsweek* cover story about exercise and the brain featured two AFAR-supported scientists: <u>Scott Small, MD</u>, of Columbia University and <u>Kristine Yaffe</u>, <u>MD</u>, of the University of California, San Francisco, both Beeson Scholars. Dr. Small discussed the results of his research, which showed that humans who exercised regularly during a three-month period grew new brain cells in the areas of the brain that controlled learning and memory. Dr. Yaffe commented about the additional cognitive benefits of exercise. Dr. Small's research about the effects of exercise on cognition was also featured in an August 19, 2007, *New York Times* article. Anne Cappola, MD, of the University of Pennsylvania School of Medicine and <u>Mark</u> <u>Lachs</u>, MD, of The New York Presbyterian Health System/Weill Medical College of Cornell University appeared on the *WABC-TV* program *Viewpoints* on March 18, 2007, to discuss the different ways men and women age. Dr. Cappola is a 2001 recipient of the AFAR/Pfizer Research Grant in Hormones and Aging. Dr. Lachs is a recipient of the Beeson award and a current AFAR board member.

Research conducted by <u>Scott Pletcher, PhD</u>, at Baylor College of Medicine and the first recipient of the Glenn/AFAR Breakthroughs in Gerontology Award (BIG), showed that the life-lengthening effects of caloric restriction were negated by the odor of yeast paste in fruit flies. The study, reported in the journal *Science* in February, 2007, found that the flies that could smell rich food in the environment lived shorter lives than flies that ate the same amount of food but were not exposed to the odor. Dr. Pletcher's research was featured in *The Scientist*, *Scientific American*, *Nature and Slate*.

NOVA scienceNOW, the PBS science series, featured a 13-minute broadcast segment on aging and longevity genes. The segment, which aired January 9, 2007, included interviews with <u>Nir Barzilai, MD</u>, of the Albert Einstein College of Medicine (1994 AFAR Research Grant recipient and 1997 Beeson Scholar) and <u>David Sinclair, PhD</u>, of Harvard University (2000 AFAR Research Grant recipient).



Biology of Aging

Studying the underlying mechanisms of aging may be the most efficient and least expensive way to extend the human health span and relieve the suffering that results from age-related diseases. Some of the field's most exciting areas include research into the metabolic characteristics of aging, especially at the cellular level, and how interventions such as caloric restriction manipulate them. Scientists

are taking particular interest in growth hormone, insulinlike growth factor, and the interaction between DNA and mitochondria—the organelles in cells that convert nutrients into energy. Other hot topics include oxidative damage, telomeres and tissue engineering, DNA damage and repair, cellular senescence, immune response, and longevity variations both among and within species.



At the Stanford Center on Longevity at Stanford University, 2005 AFAR Research Grant recipient Anne Brunet, PhD, and her colleagues are working to understand molecular mechanisms that influence longevity. In the past, she has used AFAR's support to identify mechanisms at work in caloric restriction, a well known way to extend life and health in many invertebrate and vertebrate species. She and her colleagues are

currently investigating how pro-longevity FOXO transcription factors (proteins that bind to DNA and help regulate the creation of RNA molecules) act within cells to help extend the life of mammals. In particular, she is investigating their importance in the nervous system with regard to stem cell maintenance and agedependent behaviors such as learning, cognitive function, and locomotor abilities. In another important project, she and her colleagues are developing a novel model for aging in vertebrates—a rapidly aging African killifish (Nothobranchius furzeri) that lives only nine weeks, which is 15 times shorter than mice. She hopes that studying this new model will help identify genes that regulate vertebrate lifespan.

Career Building Blocks: Grant Programs

In 2007, the American Federation for Aging Research conducted a range of grant programs for medical and graduate students, fellows, and junior faculty. All of these efforts have been designed to attract the most talented new scientists to the field and help them launch careers in aging research. Information about the newest additions to our grant programs as well as the first recipients of new programs created in 2006 can be found in our "Program Highlights" section on pages 5-7.



AFAR Research Grants

AFAR's flagship program provides junior faculty MDs and PhDs with up to \$60,000 one- to twoyear grants to conduct research that will serve as the basis for longer term research efforts. AFAR-supported investigators study a broad range of biomedical topics related to the biology of aging. Thirteen grants were awarded this year.

AFAR-GE Healthcare Junior Investigator Award for Excellence in Biomarker Research

For a description and more information, please see page 6.

Affiliate Grants

For a description and more information, please see page 7.

Ellison Medical Foundation/AFAR Senior Postdoctoral fellows Research Program

This program encourages and furthers the careers of postdoctoral fellows (both MDs and PhDs) with at least three and not more than five years of prior postdoctoral training in the fundamental mechanisms of aging. Three to four two-year fellowships of \$100,000 are awarded annually.

The Fannie E. Rippel Foundation/AFAR New Investigator Awards on Gender Differences in Aging

For a description and more information, please see page 6.

<u>Glenn/AFAR Breakthroughs in Gerontology</u> (BIG) Award

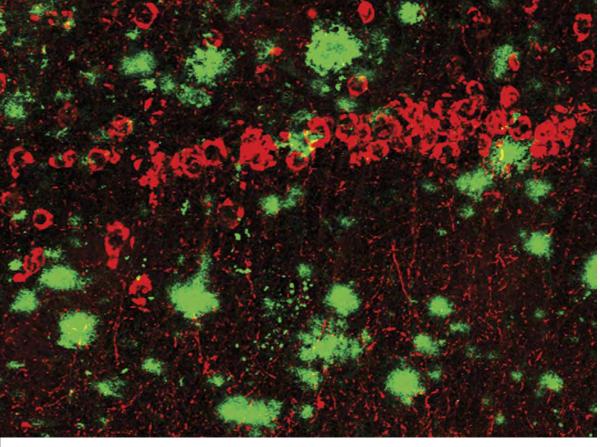
Sponsored by the Glenn Foundation for Medical Research, the BIG awards provide timely support to a small number of pilot research programs that are considered higher risk but which offer significant promise of yielding transforming discoveries in the fundamental biology of aging. Four two-year grants of up to \$200,000 were awarded in 2007.

Hartford/AFAR Collaborative Research Awards

For a description and more information, please see page 5.

The Julie Martin Mid-Career Award in Aging Research

Sponsored by The Ellison Medical Foundation, this program encourages outstanding midcareer scientists—both those actively engaged in the study of aging and those in related areas whose research has the potential for high payoff in advancing our understanding of the basic biology of aging. Two four-year awards of \$550,000 are made annually.



Alzheimer's disease brains are characterized by two major lesions, amyloid plaques and neurofibrillary tangles. Using DNA technology, it is possible to induce these in mice, such as the 3xTg-AD mice, which exhibit both lesions, with amyloid plaques and neurofibrillary pathology shown in green and red, respectively.

Image source: _____ Frank LaFerla, <u>PhD</u>

Medical Student Training in Aging Research (MSTAR) Program

To encourage medical students—particularly budding researchers—to consider a career in geriatrics, this program awards short-term scholarships to more than 100 medical students each year. AFAR has partnered with the NIA and several foundations to continue and strengthen the program, an extension of the original Hartford/AFAR Medical Student Geriatric Scholars Program.

Paul Beeson Career Development Awards in Aging Research Program

The National Institute on Aging, The NIH Office of Dietary Supplements, The John A. Hartford Foundation, The Atlantic Philanthropies, The Starr Foundation, and an anonymous donor are collaborating on this initiative to sustain and promote the careers of clinically trained individuals who are pursuing research in aging. In 2007, 11 scientists received this generous, multi-year award of \$600,000 to \$800,000. The Paul Beeson Career Development Awards in Aging Research Program: Extension to the Island of Ireland

For a description and more information, please see page 6.

Rosalinde and Arthur Gilbert Foundation/AFAR New Investigator Awards in Alzheimer's Disease For a description and more information, please see page 6.

Like so many other fields, we are taking advantage of the genomics revolution. As we increase our understanding of genetic risk factors, we'll discover the mechanisms of pathogenesis and learn how we might intervene.

George M. Martin, MD, AFAR Scientific Director and Professor Emeritus of Pathology, University of Washington

Frank LaFerla, PhD

The Aging Brain

Of all the human organ systems investigators look at in aging research, none has come under such intense scrutiny as the brain. Every day brings new insights into how the brain ages normally and what causes it to veer off into abnormal pathologies such as Alzheimer's disease and Parkinson's disease. Rapid advances in knowledge are partly due to equally rapid advances in imaging technology. Today, we no longer have to create hypotheses about brain function from post-mortem studies. Positron emission tomography, magnetic resonance imaging, and other imaging techniques allow us to actually see subtle changes in brain structure and function as they occur. We've learned that atrophy and glucose metabolism can predict future cognitive impairment, and we've been able to observe the action of new drug candidates for treating Alzheimer's disease. Other important research in the field is showing how cardiovascular risk factorsand medications-may affect the risk of dementia.



Life span extension from dietary restriction has been observed in many different organisms, but the details of this phenomenon remain poorly understood. Matt Kaeberlein, PhD, of the University of Washington and recipient of two-AFAR supported awards, the 2006 AFAR Research Grant and the 2007 Glenn/AFAR Breakthroughs in Gerontology Award, aims to understand the mechanisms underlying how reduced food consumption slows aging and increases life span in the nematode C. elegans. While dietary restriction increases life span in organisms ranging from yeast to mice, it is critical to determine whether the mechanisms of life span extension in these different organisms are similar or different. If the mechanisms are conserved, then there is a good chance these same processes will apply to humans. The discoveries from Dr. Kaeberlein's research may one day identify potential targets for therapies that will be beneficial for many different age-associated diseases in humans.



Frank LaFerla, PhD, and his lab team at the University of California, Irvine, have done some of the most provocative and promising work in the field of aging-brain research. They are credited with creating the first transgenic mouse model to develop plaques and tangles, the most important hallmark pathologies of Alzheimer's disease. Recently, they have been working to identify factors that either exacerbate or improve cognitive decline. In one surprising study, they discovered that learning not only improves cognitive function but actually diminishes neuropathological lesions. Most recently, they created a new mouse model of neurodegeneration, which can be induced to express diphtheria toxin to kill neurons selectively in particular brain regions. These mice develop deficits in learning and memory, but by transplanting neural stem cells into their brains, Dr. LaFerla has actually rescued cognitive function. He and his colleagues are now doing further studies that will determine whether stem cells can produce a similar effect in brains damaged by Alzheimer's disease. Dr. LaFerla is a recipient of the 2000 Pfizer/ AFAR Research Grant.

Finding the Best and Brightest: The AFAR Review Process

Each year, AFAR receives five times as many qualified research proposals as can be funded. We use a rigorous review process and ultimately fund a small percentage of these high quality proposals. The AFAR National Scientific Advisory Council (NSAC), consisting of more than 250 of the nation's leading researchers in aging and aging-related fields (see list on pp. 16-17), carefully considers each proposal's scientific merit. The size and expertise of the NSAC is critical as AFAR welcomes proposals from the entire spectrum of the biology of aging.

Volunteer members of this diverse panel screen, read, and score the applications before referring them to AFAR's Research Committee, currently chaired by Roger McCarter, PhD, who began his term in 2007. After another two-day deliberation, the Committee then recommends finalists.

AFAR's high-quality administrative skills and review processes are well known. Because of this, many foundations, individuals, and corporations turn to AFAR to manage their research grant programs. These grant programs have their own committees, drawn from the large pool of superb scientists committed to AFAR's important work. AFAR's excellent reputation is due in large part to the efforts of the senior researchers in our network.



We need a constant renewal of ideas in aging research. Supporting young people and bringing new people into the area is absolutely critical.

Roger McCarter, PhD, Chair, AFAR Research Committee and Professor of Biobehavioral Health, Pennsylvania State University

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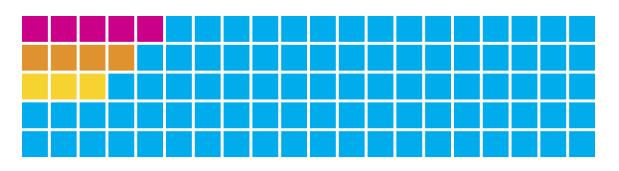
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There are several ways individuals, corporations, and foundations can show their support for AFAR's unique role in this important effort. For example, you can:

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