

THE ARCHITECTS OF AGING: 2016 ANNUAL REPORT



GLENN FOUNDATION



AFAR dedicates our 2016 Annual Report to Paul F. Glenn, a true architect of aging.

Paul F. Glenn founded the Glenn Foundation for Medical Research in 1965. In the decades since, the Foundation has significantly built the field of aging research through its mission to "extend the healthy years of life through research on mechanisms of biology that govern normal human aging and its related physiological decline, with the objective of translating research into interventions that will extend healthspan with lifespan."

Through his continued vision, in addition to supporting a range of grant programs and fostering the acclaimed Glenn Centers for Research on Aging nationwide, the Glenn Foundation has partnered with AFAR for over 30 years.

We are grateful not just for his support and collaboration, but more importantly, for his commitment to building a future where we can live healthier as we grow older.

IN MEMORIAM | AFAR remembers our colleagues. We are grateful for their contributions to the field and support of our work:

Michal Arbel, PhD, Instructor in Neuroscience, Massachusetts General Hospital 2014 New Investigator Awards in Alzheimer's Disease grantee

Chad Dickey, PhD, Associate Professor in Molecular Medicine and Psychiatry, University of Southern Florida Byrd Alzheimer's Institute Chair, New Investigator Awards in Alzheimer's Disease Selection Committee 2007 New Investigator Award in Alzheimer's Disease grantee 2013 Collaborative Research Award in Alzheimer's Disease grantee

Senator John H. Glenn, Honorary Director, AFAR Board of Directors

THE ARCHITECTS OF AGING: INNOVATORS AT WORK

In laboratories across the nation, researchers are developing life-changing drug interventions that may someday prevent many of the health conditions associated with older age. More than 30 drugs shown to influence the aging processes in animal studies are moving toward clinical trials. Many others are sure to follow.

This innovative research could reshape the way we age. It rests on a firm foundation of more than three decades of studies conducted in yeast, fruit flies, worms, and mice that have clearly established the connection between the biological mechanisms of aging and the chronic diseases of aging—including cancer, heart disease, diabetes, and Alzheimer's.

Translating science into clinical practice is crucial—and promising. But we still need basic biological research. The next generation of therapies that target fundamental mechanisms of aging, and the generations after that, will be constructed on that same solid foundation of basic studies. There are no shortcuts.

Since its founding more than 35 years ago, AFAR has supported the basic biological research that is now being translated into exciting new interventions that can help people live healthier longer. Therapies that attack specific molecular targets identified by this basic research are on the verge of moving into human trials.

In this report, we spotlight a few of the Architects of Aging who are driving this exciting moment for aging research: Accomplished scientists affiliated with AFAR whose cutting-edge work is leading to interventions that will extend healthspan—our years of good health as we age—by modifying the fundamental processes of aging.

With one person turning 65 every eight seconds in America today, we need to expedite translation of this science so it can enhance human health. On the following pages, you will read about AFAR Board members and grantees whose research is ushering in this new era of innovation.

We celebrate the Architects of Aging, yet know that there is still much work to do. As it has for more than three decades, AFAR stands ready to provide leadership and expertise to advance the science of healthy aging.



William J. Lipton Chair, Board of Directors



Stephanie Lederman Executive Director

BUILDING THE FUTURE

Today, new drug interventions being translated from the lab to our lives have the potential to profoundly alter the architecture of health care in America. By targeting the fundamental processes of aging that underlie major age-related chronic diseases, these innovations promise to produce significant social, economic, and health benefits for ourselves and our nation.



"Every day in my practice, I witness the toll that diseases such as Alzheimer's, cancer, diabetes, and heart disease take on the lives of my older patients," says AFAR Board President Mark S. Lachs, MD, MPH, who is the Director of Geriatrics for the New York Presbyterian Health System and Professor of Medicine and Co-Chief of the Division of Geriatrics and Gerontology at Weill Medical College.

"Having drug interventions that delay the onset of multiple, age-related diseases at once would alleviate suffering and likely lessen the amount of care people need as they age," Dr. Lachs says. "In turn, we could expect health care costs to decrease, perhaps dramatically. Extending years that we can live free from frailty, disability, and chronic disease would vastly improve the quality of life."





An AFAR-commissioned 2013 study published in *Health Affairs*, co-authored by AFAR Board member S. Jay Olshansky, PhD, concluded that targeting the fundamental processes of aging could increase life expectancy by 2.2 years, most of which would be spent in good health. Dr. Olshansky is a Professor in the School of Public Health at the University of Illinois at Chicago and Research Associate at the Center on Aging at the University of Chicago and at the London School of Hygiene and Tropical Medicine.

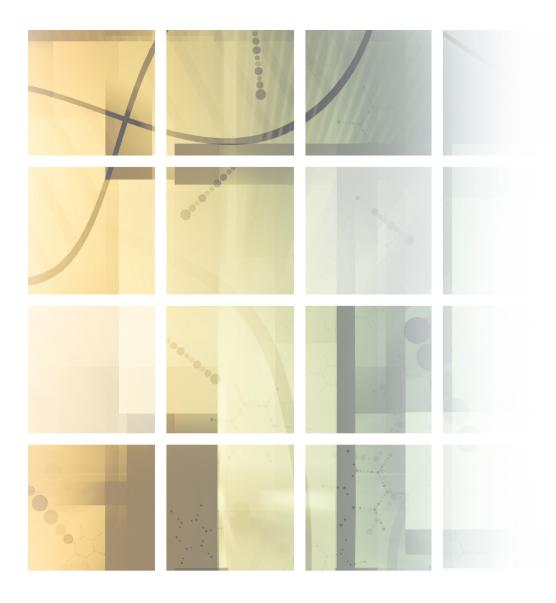
The study authors conservatively estimated that the resulting economic value would be \$7.1 trillion over 50 years in the United States alone. This figure does not factor in "cognitive benefits to individuals that could arise from these interventions," according to the study. These cognitive benefits include retaining memory, reasoning, perception, and the language skills necessary for such essential functions as managing medications and finances.

Earlier, in a 2006 paper in *The Scientist*, Dr. Olshansky and his co-authors coined the term "Longevity Dividend." This describes the societal and economic benefits of moving from a disease-specific focus in research and medicine toward a model that targets the fundamental biological processes of aging, and thus delaying the onset of agerelated chronic diseases.

"A lot of people still think that getting sicker as we grow older is inevitable," notes Dr. Olshansky. "That's simply not true. We can modify aging, we can intervene, and we can live healthier for longer as we grow older."

The Architects of Aging highlighted in this report begin with a foundation of basic biological research supported by AFAR for more than 35 years. Their blueprint for clinical trials and drug interventions will transform aging from a period of sickness to a time of vitality.





THE GEROSCIENCE NETWORK: LAYING THE FOUNDATION

For a drug that targets a single, specific disease, it currently takes about 17 years from discovery in the lab to completion of clinical trials. It takes eight more years for physicians to adopt the drug, making it available to people who need it. That's 25 years in all. The cost: \$500 million to \$1 billion, on average.

Over the past three years, the Geroscience Network has brought together leading aging researchers from 18 aging centers and academic groups in the United States to design the strategic infrastructure needed to dramatically cut the time and cost required to gain regulatory approval for a new class of drugs that tackle fundamental aging processes.

"We feel there's an urgent need for these particular drugs," says James L. Kirkland, MD, PhD, Professor of Medicine and Physiology at the Mayo Clinic in Rochester, Minnesota, a 2012 Glenn/AFAR Breakthroughs in Gerontology (BIG) Award recipient, and AFAR President Elect. Led by Dr. Kirkland with AFAR Scientific Director Steven N. Austad, PhD, and AFAR Deputy Scientific Director Nir Barzilai, MD, the Geroscience Network is funded by a National Institutes of Health (NIH) R24 planning grant.

Through the grant, the Geroscience Network is working to identify the fastest, most efficient, and most effective ways to move ahead drugs that can keep us healthier longer.

Advancing Trials, Building Frameworks

Already, there are more than 30 drugs that affect fundamental aging processes in studies in mice and other animals. Since aging processes in mice and humans are similar, this suggests that these drugs may be formulated to prevent or alleviate multiple chronic diseases in humans—including cancer, heart disease, diabetes, and Alzheimer's disease and other forms of dementia.

Through a series of seven retreats with colleagues from 51 other institutions around the world, the core Geroscience Network has developed strategies to conduct:

- Phase 1 and Phase 2 trials that enroll fewer than 100 people and run from one month to a year to test new drugs that have little or no track record in humans, and
- The more advanced Phase 3 trials that enroll up to 3,000 people and run for several years to test established drugs that have shown evidence of extending healthspan and/or lifespan.

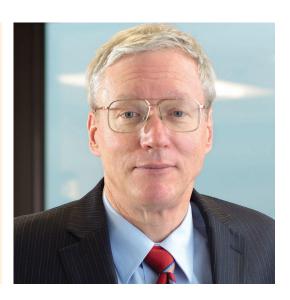
Senolytics, drugs that kill senescent cells (see page 6), are a good example of the newer drugs moving into Phase 1 and Phase 2 trials. Led by Dr. Barzilai, the TAME (Targeting Aging with Metformin) Trial (see page 8) grew out of one of the Geroscience Network retreats, where researchers selected metformin for the initial Phase 3 trial. The goal, Dr. Kirkland says, is to use metformin to "prepare the regulatory landscape" for a range of drugs that target fundamental aging processes.

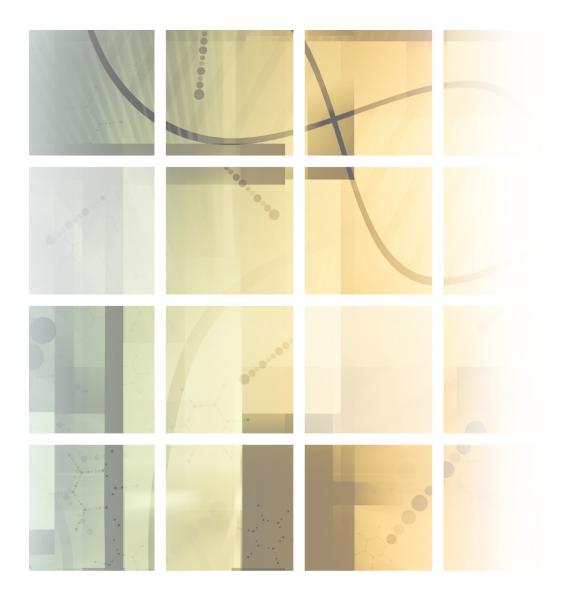
The Geroscience Network also has published a framework for short-term, proof-of-concept trials that take on age-related diseases, geriatric syndromes, and loss of resilience (the ability to fully recover function following surgery, chemotherapy, falls, infections, and other stressors). The team is now devising plans to train a cadre of geriatrics researchers to be expert in both researching basic biological science and working within the regulatory system. It also is devising plans to build a national system of aging centers to work cooperatively and in parallel on clinical trials to cut the time it takes to approve a drug for human use.

"The field of aging research really is at an exciting point," says Dr. Kirkland. "If these drugs can indeed target multiple, age-related chronic conditions, it would be transformative for all of medicine."

"The field of aging research really is at an exciting point. If these drugs can indeed target multiple chronic conditions, it would be transformative for all of medicine."

- James L. Kirkland, MD, PhD





SENOLYTICS: TARGETING "ZOMBIE"CELLS

As a young assistant professor at the Dana Farber Cancer Institute, Judith Campisi, PhD received an AFAR Research Grant for Junior Faculty in 1990. Soon after, she first encountered senescence, the process by which cells are unable to proliferate further. Many believed senescence protects us against cancer.

"In the face of myriad types of stresses, cells will enter a state in which they no longer divide," says Dr. Campisi, now a Professor at The Buck Institute for Research on Aging. "When that happens, cells are protected from becoming cancerous. The whole process is designed to suppress cancer, and it does a pretty good job."

During senescence, cells also begin to secrete molecules that alert surrounding tissue to potential danger and repair cellular damage.

However, research has also confirmed a link between senescence and multiple agerelated diseases.

Dr. Campisi admits she was initially skeptical of the connection, but her research led her to believe that the molecules produced by senescent cells "really could be a driving force behind aging. So, as with most science, you go where the data leads you, not the other way around."

The data led Dr. Campisi to found Unity Biotechnology Inc. with Jan Van Deursen, PhD of the Mayo Clinic. Today, Unity is at the forefront of efforts to develop senolytics: drugs that have been shown in mice to target age-related chronic diseases by killing senescent cells.

The Link to Chronic Inflammation

Senescent cells may protect against cancer and repair damaged tissue, but there is a reason they are sometimes referred to as "zombie cells."

"The problem with senescent cells is they tend to not die," Dr. Campisi says. "And consequently, they increase with age. When people begin to accumulate them above certain thresholds, their secretions can drive what we term chronic inflammation. And chronic inflammation is a part of virtually every major age-related disease, from neurodegeneration to, ironically, late-life cancer."

Unity—under the vision of its CEO Nathaniel "Ned" David, PhD—as well as other biotech companies are working on getting senolytic drugs into clinical trials with specific disease indications, such as osteoarthritis and glaucoma.

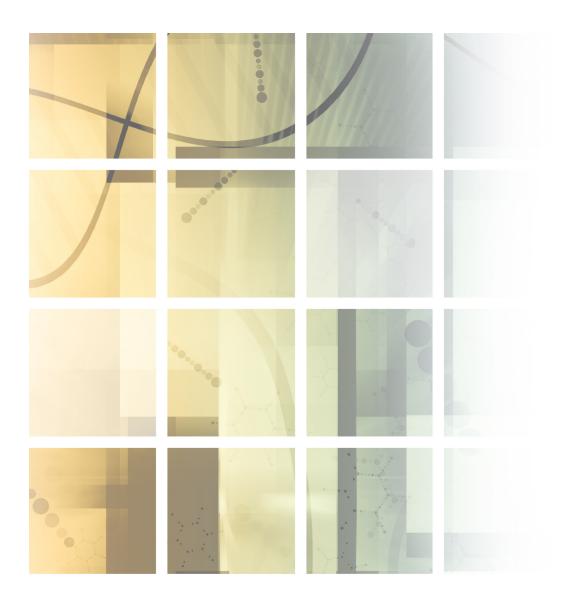
"Then the drugs, if approved, will be used off label by other researchers, and it's going to take time before the senolytics are recognized as hitting multiple age-related diseases," Dr. Campisi says. "I know Unity would like to have something at least in the first stages of a trial within a year. So we're not talking decades down the road. I think most people who are thinking about drug interventions are thinking about it in terms of a couple of years—not a couple of decades."

Dr. Campisi is an excellent example of why AFAR's support for promising young scientists with a passion for understanding the biological processes of aging is so crucial. She says: "AFAR's support at the beginning of my career fueled my passion for basic biological research and set me on the path to this fascinating and potentially life-changing work with senolytics."

"I think most people who are thinking about drug interventions are thinking about it in terms of a couple of years—not a couple of decades."

- Judith Campisi, PhD





THE TAME TRIAL: USHERING IN A NEW ERA OF DRUG INTERVENTIONS

"In the lab, we've been increasing healthspan every day," says Nir Barzilai, MD, AFAR Deputy Scientific Director and multiple-AFAR grantee, as well as Director of the Institute for Aging Research at Albert Einstein College of Medicine.

"We've done it in cells, we've done it in worms, we've done it in flies, we've done it in mice, we've done it in rats, we've even done it in monkeys. And we've done it by doing genetic manipulation, by working with the environment, or by using drugs. Some of those drugs, like metformin and others, are actually in human use. But they're used for other specific indications—not to treat or target aging."

The reason? The U.S. Food and Drug Administration (FDA) does not recognize aging as an indication, a medical term that refers to the use of a drug to treat a specific disease.

"A Very Big Picture Study"

Dr. Barzilai is principal investigator on a groundbreaking clinical trial designed to change the regulatory landscape by demonstrating that metformin—which has been used effectively and safely for 60 years as a front-line drug to treat type 2 diabetes—can delay the onset of multiple chronic age-related diseases, including cancer, heart disease, Alzheimer's, and others.

Managed by AFAR, the TAME (Targeting Aging with Metformin) Trial will offer the FDA the opportunity to review whether aging can be made an indication. TAME is a series of clinical trials over six years that is projected to enroll 3,000 people between the ages of 65 and 80 nationwide. The goal: to see whether those taking metformin experience delayed development or progression of age-related chronic diseases compared with those who take a placebo.

"TAME is a big picture study," Dr. Barzilai says, "and we are all limited now by the fact that there is no indication for targeting aging or age-related diseases. If TAME can convince the FDA to make aging an indication, a range of drugs that target aging can move ahead into human trials."

The TAME trial has the potential to unleash the powerful research and development engine of the pharmaceutical industry to generate next-generation drugs, individually or in combination, to prevent and delay multiple age-related diseases.

The researchers know that no single drug will work for everyone. "There are several pathways for aging, and eventually you have to do something in combination or at a different time in order to really make strides in healthspan," Dr. Barzilai says.

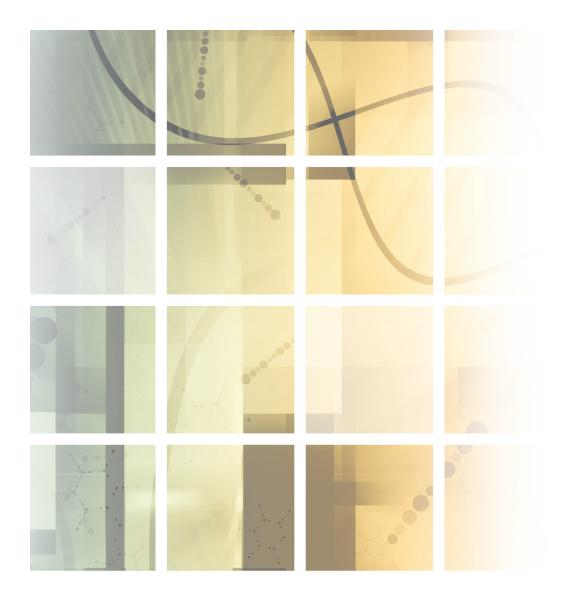
Scientists believe that other drugs in the research pipeline—including senolytics (see page 6), rapamycin (see page 10), and NAD boosters (see page 12)—may hold the potential to be even more effective and powerful than metformin in extending healthspan.

But the TAME Trial is an essential first step. If the trial is successful, it will serve as the framework to what some believe would be the most important medical intervention in the modern era since antibiotics—a new category of drugs that add years of healthy life as we age.

"If TAME can convince the FDA to make aging an indication, a range of drugs that target aging can move ahead into human trials."

- Nir Barzilai, MD





RAPAMYCIN: REALIZING ITS FULL POTENTIAL

Over the past four decades, rapamycin has advanced from its discovery as a rare antibiotic, collected in soil on Rapa Nui (Easter Island), to a drug that has been shown to extend lifespan in mice by 25 percent.

Since 1999, rapamycin has been approved by the U.S. Food and Drug Administration (FDA) as a drug for transplant patients. It also is used in some cancer chemotherapy regimens. Today, AFAR-supported scientists are working to realize the drug's potential to increase the number of healthy years in humans.

"There have been probably a dozen studies in mice that all show that rapamycin extends life, even when administered at fairly advanced ages—the human equivalent of 70 years," says Steven N. Austad, PhD, AFAR Scientific Director. "That's been the most remarkable finding because we always assumed that if people were going to really affect their later-life health and longevity, they would probably have to start doing something in their 30s or 40s. I think what the rapamycin research suggests is that interventions in the aging process could start quite late in life, but still have a dramatic effect."

This finding on rapamycin helped pave the way for the TAME Trial (see page 8), which will test the generic type 2 diabetes drug metformin with people aged 65-79 over an exceptionally concentrated time frame: just six years. In the past, one of the biggest obstacles facing researchers considering testing drugs that influence fundamental aging mechanisms was the assumption that the tests would take 50 or 60 years to get results.

The ability of rapamycin to extend healthspan and lifespan in mice—even older mice—"started us thinking in a different way," Dr. Austad says. "We realized we could give these drugs that target fundamental aging processes to older people and expect to get quite a substantial effect."

'Like Airplanes Waiting to Take Off'

The main questions that must be resolved concerning rapamycin in humans involve the correct dosage and eliminating serious side effects. For example, rapamycin suppresses the immune system, which is a good thing in transplant patients but not in vulnerable older adults. However, in a new study of people aged 65 and older, researchers found that rapamycin actually boosted the efficacy of a flu vaccination by 20 percent, with minimal side effects.

"Now, whether that dose is going to be a dose that also affects healthspan, we don't know," Dr. Austad says.

Rapamycin is also now being tested in the Dog Aging Project—led by two, two-time AFAR grantees, Matt Kaeberlein, PhD, and Daniel Promislow, PhD, at the University of Washington—to see if it achieves similar results in canines as those achieved in mice.

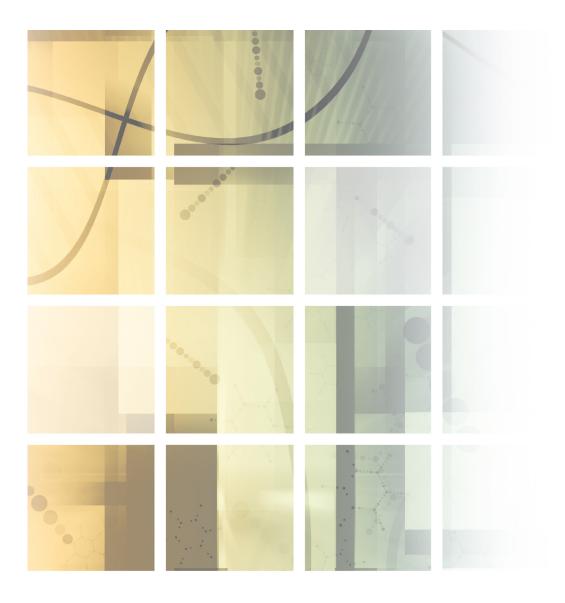
"It's gratifying to see two AFAR grantees, Matt and Daniel, moving our knowledge of rapamycin forward with the promising early results of the Dog Aging Project," says Dr. Austad. "Their study is also garnering national media attention, which helps raise awareness of aging research in general and the potential of age-targeting drugs."

Scientists at pharmaceutical companies continue to work on rapamycin to tweak the dosage and improve its safety. Dr. Austad says drugs that target fundamental aging processes "are lining up like airplanes waiting to take off, and metformin is just the first one. I do think that rapamycin would be a logical next step. If the dog trial shows a great deal of promise, a human trial designed much in the spirit of the TAME Trial would be next."

"I think what the rapamycin research suggests is that interventions in the aging process could start quite late in life, but still have a dramatic effect."

- Steven N. Austad, PhD





FROM RESVERATROL TO NAD BOOSTERS: ADDRESSING THE HALLMARKS OF AGING

Think of sirtuins as the body's cellular defenders.

"Sirtuins protect everything from the brain to the heart to skin," says David Sinclair, PhD, a 2000 AFAR Research Grant for Junior Faculty recipient and current board member. "Every aspect of aging—the 'hallmarks of aging,' as they're called—is counteracted by the sirtuins."

There are seven types of sirtuins in all, each with a role to play in a kaleidoscopic range of important processes that have been linked to aging: from improving mitochondrial function, autophagy (a natural physiological process dealing with cell destruction), and DNA repair, to lessening epigenetic change (the biological mechanisms that switch cells on and off), and protecting telomeres (the specific DNA–protein structures found at both ends of each chromosome).

The molecules that activate sirtuins degrade as we age. More than a decade ago, Dr. Sinclair—a Professor of Genetics at Harvard Medical School and Professor in the School of Medicine at the University of New South Wales in Sydney, Australia—started working on resveratrol, a natural compound found in red wine that can activate one particular sirtuin. Today, he is working with "synthetic molecules that are thousands of times more potent than resveratrol and that activate all of the sirtuins."

Repairing DNA

Sirtuins are dependent on nicotinamide adenine dinucleotide (NAD), and our NAD levels drop by half as we age. Dr. Sinclair is currently working on NAD-booster molecules, which "restore those NAD levels to youthful levels."

Research led by Dr. Sinclair has identified a critical step in a molecular chain reaction responsible for cellular DNA repair, cell degeneration, and aging in mice. Sinclair and his team found that giving old mice a certain NAD precursor, called NMN, restored their cells' ability to repair DNA to the levels seen in young mice. They published their study in the journal *Science* in March 2017.

For the proof-of-concept study in human trials expected to begin in 2017, Dr. Sinclair's research team is using a stabilized version of the natural NMN molecule. "We also have a lot of synthetic molecules on the horizon that we will be putting into clinical trials in 2018," he says.

Dr. Sinclair believes that developing an intervention that addresses as many aspects of aging as possible, such as the NAD boosters, is the key to extending healthy lifespan.

"If an intervention didn't have such broad effects, it wouldn't stand a chance of having a major effect on healthspan," he says. "Aging is the combination of many systems breaking down. If you only address one of the hallmarks of aging, something else will end up killing you shortly thereafter. I don't think it's sufficient to just protect the telomeres or prevent DNA damage or improve proteostasis (the process that regulates proteins within the cell to maintain the health of both the cellular proteome and the organism)."

Dr. Sinclair advocates for approaches that target multiple, age-related biological processes. "Addressing one of the hallmarks of aging may buy you a little more time and health, but to have a really big impact, you want to slow down—or even reverse—all of them."

"Addressing one of the hallmarks of aging may buy you a little more time and health, but to have a really big impact, you want to slow down—or even reverse—all of them."

- David Sinclair, PhD



AFAR GRANTS: A FOUNDATION OF RESEARCH

AFAR has created the foundation of biomedical research on aging through our rigorously reviewed grant programs, which to date have given over \$172 million to more than 4,000 talented investigators and students nationwide.

Our volunteer **Scientific Review Committee** members—hundreds of highly acclaimed scientists, representing a wide range of expertise within aging research—meticulously review hundreds of grant applications each year to fund proposals that have the greatest likelihood of making a significant contribution to helping us stay healthier longer as we age. Our grant review processes are highly regarded in the field, and we are grateful for our reviewers' time and talent.

AFAR's **Biology of Aging grant programs** fuel the research pipeline of researchers who are working to understand the basic biology of aging and age-related diseases and disorders in order to extend our years of health and decrease periods of sickness. Several grant programs help young scientists acquire the knowledge, skills, and experience they need to obtain higher-level grants as they build a body of research. Just as critical are grants tailored to mid-career and senior investigators, which allow them to remain focused on aging as they advance their careers. While maintaining a core investment in basic biomedical research, these grants help advance translational interventions that are moving from labs into our lives.

AFAR's **Physician Training grant programs** help medical student and faculty researchers become academic and clinical leaders prepared to meet the growing health care needs of an ever-growing older population. Across the country, few medical schools offer mandatory courses or rotations in geriatrics, yet there are 46 million adults age 65 and older in need of specialized care. The necessity to sensitize physicians to the needs of older patients could not be clearer, and these programs continue the legacy of AFAR's founder Dr. Irving S. Wright, a visionary in the field of aging research and care.

Scientists who received AFAR grants early in their careers are now advancing discoveries in translational research. AFAR grantees are building the future of healthy aging.

AFAR RESEARCH GRANTS FOR JUNIOR FACULTY SELECTION COMMITTEE

Pinchas Cohen, MD, *Chair* University of Southern California

Sean Curran, PhD University of Southern California

Brian Kennedy, PhD Buck Institute for Research on Aging

Richard Miller, MD, PhD University of Michigan

Coleen Murphy, PhD Princeton University

David Sinclair, PhD Harvard Medical School

NEW INVESTIGATOR AWARDS IN ALZHEIMER'S DISEASE SELECTION COMMITTEE

Chad Dickey, PhD, *Chair* University of Southern Florida Byrd Alzheimer's Institute

Kim Green, PhD University of California, Irvine

Orly Lazarov, PhD
The University of Illinois at Chicago

Beth Stutzmann, PhD Rosalind Franklin University

BREAKTHROUGHS IN GERONTOLOGY (BIG) AWARDS SELECTION COMMITTEE

Arlan Richardson, PhD, *Chair* University of Oklahoma Health Science Center

James L. Kirkland, MD, PhD Mayo Clinic

David Marcinek, PhD University of Washington Medical Center

Nicolas Musi, MD University of Texas Health Science Center at San Antonio

Charlotte Peterson, PhD University of Kentucky

GLENN/AFAR POSTDOCTORAL FELLOWSHIP PROGRAM FOR TRANSLATIONAL RESEARCH ON AGING SELECTION COMMITTEE

Norman Sharpless, MD, Chair University of North Carolina

James Galvin, MD Florida Atlantic University

Margaret Goodell, PhD Baylor College of Medicine

Salvatore Oddo, PhD Arizona State University

Bruce Troen, MD University at Buffalo – SUNY

Jeremy Walston, MD Johns Hopkins University School of Medicine

THE PAUL B. BEESON EMERGING LEADERS CAREER DEVELOPMENT AWARDS IN AGING PROGRAM ADVISORY COMMITTEE

Thomas Gill, MD, *Chair* Yale University School of Medicine

Liana Apostolova, MD, MSc., FAAN Indiana University School of Medicine

Kenneth Covinsky, MD, MPH University of California, San Francisco School of Medicine Wes Ely, MD, MPH, FCCP Vanderbilt University

Jean Kutner, MD, MSPH University of Colorado Health Science Center

Mark Lachs, MD Weill Medical College of Cornell University

Alison Moore, MD, MPH University of California, San Diego

Raymond L. Yung, MBChB University of Michigan, Ann Arbor

MEDICAL STUDENT TRAINING IN AGING RESEARCH (MSTAR) PROGRAM NATIONAL SELECTION COMMITTEE

Julie Bynum, MD, *Chair* Dartmouth Medical School

Theodore Johnson, MD, MPH Emory University

Kamal Masaki, MD University of Hawaii

Lillian Min, MD, MSHS University of Michigan

Alexander Smith, MD, MS, MPH University of California, San Francisco

Kathleen Unroe, MD Indiana University

Heather Whitson, MD, MHS Duke University School of Medicine

GLENN/AFAR SCHOLARSHIPS FOR RESEARCH IN THE BIOLOGY OF AGING SELECTION COMMITTEE

Paul Agris, PhD, *Chair* State University of New York at Albany

Rebecca Butcher, PhD University of Florida

Danica Chen, PhD University of California, Berkeley

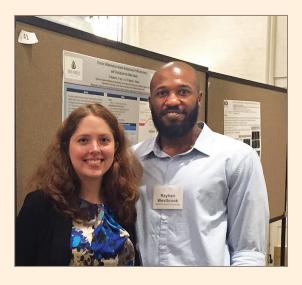
Dena Dubal, MD, PhD University of California, San Francisco

John Newman, MD, PhD University of California, San Francisco

Joshua Shulman, MD, PhD Baylor College of Medicine

2016 SCIENTIFIC MEETINGS

Grantees, senior leaders in the field, and representatives from foundations convened in Santa Barbara, California for AFAR's annual Grantee Conference, June 5-8. The conference was held in conjunction with the annual meeting of the New Investigator Awards in Alzheimer's Disease program and the Glenn Foundation for Medical Research's annual workshop and dinner. Grantees reported on their AFAR-supported research, and senior investigators from top institutions nationwide presented on emerging research in the field.





above: 2015 Glenn/AFAR Postdoctoral Fellows Lynda Wilmott, PhD and Reyhan Westbrook, PhD shared insights at the 2016 poster sessions.

below: The scenic Santa Barbara setting inspired an india ink drawing by 1993 AFAR Research Grant Recipient, Felipe Sierra, PhD, Director of the Division of Aging Biology at the National Institute on Aging of the National Institutes of Health.

BIOLOGY OF AGING GRANTS

AFAR RESEARCH GRANTS FOR JUNIOR FACULTY

Hua Bai, PhD Assistant Professor, Iowa State University

Gabrielle Fredman, PhD Assistant Professor, Albany Medical College

Jennifer Garrison, PhD Assistant Professor, Buck Institute for Research on Aging

Eric Greer, PhD Assistant Professor, Harvard Medical School

Guo Huang, PhD Assistant Professor, University of California, San Francisco

Changhan Lee, PhD Assistant Professor, University of Southern California

Scott Leiser, PhD Assistant Professor, University of Michigan

Joseph Rodgers, PhD
Assistant Professor,
The Keck School of Medicine of USC.

Brian Zid, PhD Assistant Professor, University of California, San Diego

NEW INVESTIGATOR AWARDS IN ALZHEIMER'S DISEASE

Bess Frost, PhD Assistant Professor, University of Texas Health Science Center at San Antonio

Yonatan Savir, PhD Assistant Professor, Technion

Yin Shen, PhD Assistant Professor, University of California, San Francisco

GLENN/AFAR BREAKTHROUGHS IN GERONTOLOGY (BIG) AWARDS

Rozalyn Anderson, PhD Associate Professor, University of Wisconsin, Madison

Shin-Ichiro Imai, MD, PhD Professor, Washington University School of Medicine

GLENN/AFAR POSTDOCTORAL FELLOWSHIP PROGRAM FOR TRANSLATIONAL RESEARCH ON AGING

Jenna Bartley, PhD University Postdoc Fellow 1, University of Connecticut

John Collins, PhD Postdoctoral Fellow, University of North Carolina at Chapel Hill

Evgeni Frenkel, PhD Postdoctoral Fellow, Massachusetts Institute of Technology

Jessica Hoffman, PhD Postdoctoral Scholar, University of Alabama at Birmingham

Liam Hunt, PhD Postdoctoral Fellow, St Jude Children's Research Hospital

Timothy Jarome, PhD Postdoctoral Researcher, University of Alabama at Birmingham

Jamie Justice, PhD Postdoctoral Research Fellow, Wake Forest University School of Medicine

Su Jeong Kim, PhD Postdoctoral Fellow, University of Southern California

Marissa Schafer, PhD Postdoctoral Fellow, Mayo Clinic

Xiaoai Zhao, MD, PhD Postdoctoral Research Fellow, Stanford University

GLENN FOUNDATION FOR MEDICAL RESEARCH



GLENN/AFAR SCHOLARSHIPS FOR RESEARCH IN THE BIOLOGY OF AGING

Meredith Course Stanford University

Allessandra Dall'Agnese Sanford-Burnham Medical Research Institute

Victoria Dominguez Ohio State University

Linna Guan Stanford University Chelsea Hays University of California, San Diego

Richard Jin University of Buffalo

Sun Kim Brown University

Mai Nakamura Johns Hopkins University School of Medicine

Dean Nehama University of North Carolina at Chapel Hill

Justin Nicholatos Cornell University

Raghav Ramabadran Baylor College of Medicine

Jimi Rosenkrantz Ohio State University

SANTA BARBARA FOUNDATION / AFAR COLLABORATIVE RESEARCH AWARD IN ALZHEIMER'S DISEASE

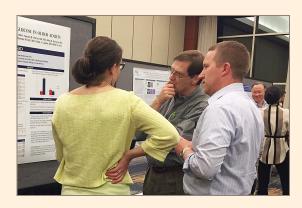
Jason Hinman, MD, PhD Assistant Professor, University of California, Los Angeles

Kenneth Kosik, MD Professor, University of California, Santa Barbara

2016 BEESON MEETING

AFAR hosted the Annual Meeting of the Paul B. Beeson Emerging Leaders Career Development Awards in Aging program from November 9 to 12.

Over 100 current and former Beeson scholars, mentors, and foundation supporters convened in Itasca, Illinois to review their research progress and share insights on career development, while fostering collaborations.





above: Beeson scholars Kasia Lipska, MD (2014), Steven Prior, MD (2012), and Brock Beamer, MD (2000) discuss research presented during the poster sessions.

below: 2016 Beeson scholar Hillary Lum, MD, PhD, meets with her Beeson mentor, AFAR board president and 1995 Beeson scholar Mark Lachs, MD, MPH.

For a complete list of the 132 Medical Student Training in Aging Research (MSTAR) scholars that AFAR supported in 2016, visit www.afar.org/ research/grantees

PHYSICIAN TRAINING GRANTS

THE PAUL B. BEESON EMERGING LEADERS CAREER DEVELOPMENT AWARDS IN AGING

Sponsored by the National Institute on Aging, National Institute of Neurological Disorders and Stroke, The Atlantic Philanthropies, and The John A. Hartford Foundation

Nathan Brummel MD, MSCI Assistant Professor of Medicine, Vanderbilt University

Zara Cooper MD, MSc, FACS Assistant Professor of Surgery, Harvard Medical School

Eleni Linos MD, DrPH Assistant Professor, University of California, San Francisco

Brendan Lucey, MD Assistant Professor of Neurology, Washington University School of Medicine

Hillary Lum, MD, PhD Assistant Professor, University of Colorado, Denver and VA Eastern Colorado GRECC

Ana Pereira, MD Assistant Professor of Clinical Investigation, Rockefeller University

Anthony Rosen MD, MPH Instructor of Medicine, Weill Cornell Medicine

Phillip Smith, MD Assistant Professor, University of Connecticut

Andrew Teich, MD, PhD Assistant Professor, Columbia University

BEESON SCHOLARS / HARTFORD CHANGE AGENTS ACTION FUND

Cynthia Carlsson, MD Associate Professor, University of Wisconsin, Madison

Kelly Trevino, PhD Assistant Professor, Weill Cornell Medicine

THE CENTERS OF EXCELLENCE LEGACY

From 1988 to 2016, The John A. Hartford Foundation invested \$57.7 million in its Centers of Excellence (CoE) Program in Geriatric Medicine and Geriatric Psychiatry, which started with 10 centers and eventually grew to 28. AFAR played a key part in the CoE program as the national Coordinating Center from 1998 to 2009, when its role evolved into a National Program Office, responsible for building a transparent, centralized award distribution process, developing a scholar selection process, and creating a scholar database. Over the years, the CoE program supported research and academic development for a total of 1,164 fellows and junior faculty through December 2016.

"Initially the program was designed to support faculty development for people who aspired to research careers," recalls AFAR Medical Officer Richard Besdine, MD, who served as Co-Chair of the Centers of Excellence Program Advisory Committee. "But, it became increasingly apparent that in addition to supporting researchers, there was an urgent need to support the career development of academic geriatricians who would teach other physicians how to take very good care of vulnerable older people."



In March 2017, a special article in the *Journal of the American Geriatrics Society* was published online. The report, "John A. Hartford Foundation Centers of Excellence Program: History, Impact, and Legacy," shows that the CoE intiative strengtened the national network of geriatric programs and served as a major driver of increased prestige for the fields of geriatric medicine and geriatric psychiatry.

The John A. Hartford Foundation Centers of Excellence in Geriatric Medicine and Geriatric Psychiatry included:

Baylor College of Medicine

Boston University

Brown University

Cornell University

Duke University

Emory University

(Southeast Center of Excellence)

Harvard University

Indiana University

Johns Hopkins University

Mount Sinai School of Medicine

University of Alabama at Birmingham

(Southeast Center of Excellence)
University of California, Los Angeles

University of California, San Diego

(Geriatric Psychiatry)

University of California, San Francisco

University of Chicago

University of Colorado at Denver

University of Hawaii

University of Michigan

University of North Carolina at Chapel Hill

University of Pennsylvania

University of Pittsburgh

University of Pittsburgh

(Geriatric Psychiatry)

University of Rochester

University of Texas Health Science Center

at San Antonio

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Yale University





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AFAR is deeply grateful to our donors for their generous support. Their continued contributions enable us to fulfill our mission and strengthen our programs.

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35TH ANNIVERSARY DINNER

On November 2nd, AFAR celebrated its 35th Anniversary with an Awards Dinner, themed "Let's Make this the Age of Aging Better" at Le Parker Meridien in Manhattan.

AFAR presented Roger W. Ferguson, Jr., CEO of TIAA, with our *Chairman's Award*; Peter G. Peterson, Founder and Chairman of the Peterson Foundation, with our *George E. and Mary J. Doty Award*; and Johannes J. Baensch, PhD, Chief Scientific Officer of Nestlé Skin Health SA, with our *Honorary Leadership Award*. We also presented the inaugural *Icon of Aging Award* to Frances Hesselbein, President and CEO of the Francis Hesselbein Leadership Institute.

The awards were presented by special guests Paul A. Volcker, Chairman of the Volcker Alliance and former Chairman of the Federal Reserve; AFAR board member Michael W. Hodin, CEO of the Global Coalition on Aging; and Terry Fulmer, President of The John A. Hartford Foundation.

- ^{1.} 2016 Awards of Distinction honorees (clockwise): Roger W. Ferguson, Jr.; Johannes J. Baensch; Peter G. Peterson; and Frances Hesselbein.
- ² Mark S. Lachs, MD, MPH, current Board President, discusses AFAR's leadership in the field.
- ^{3.} AFAR Board Chair Emerita Diana Jacobs Kalman with Executive Director Stephanie Lederman.

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Cristine Cravens
Margaret F. Cristofalo
Catherine Cullar
Janis Cummings
Thomas De Fazio
Jeffrey Dobrinsky
David Dodd
Linda Dokas

Harold Chapman

Dwight Edwards and

Hattie Herman

Reba and Gerald Faigeles

Alan Finn

Christopher Fralic David Fussell Christi Gall

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Carl Golub

Karen A. Goraleski David W. Gore Douglas Hamilton

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Jessica Herrera-Flanigan

Gloria Ho

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Bettie Hon

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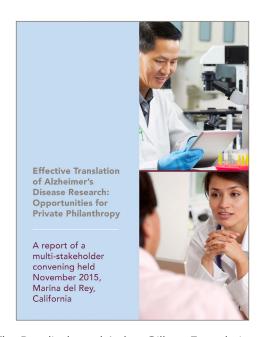
Raymond Yung Natalie Zimmer Barry Zurbuchen

PUBLICATIONS AND COLLABORATIONS

In 2016, AFAR partnered with peers in the private and public sectors to produce a range of symposia and publications to further dialogue within the field.



Richard J. Hodes, MD, Director of the National Institute on Aging at the National Institutes of Health, welcomed guests to the *Disease Drivers in Aging: Advances in Geroscience* summit, which AFAR co-sponsored at the New York Academy of Sciences with the Gerontological Society of America and the Trans-NIH Geroscience Interest Group. Several AFAR board members and past grantees presented.



The Rosalinde and Arthur Gilbert Foundation, the Santa Barbara Foundation, and AFAR published a report exploring how the scientific and philanthropic sectors can work together to help move Alzheimer's research to translation. The report captured insights from a convening held in 2015.







AFAR managed the review and selection of the MetLife Foundation Awards for Medical Research in Alzheimer's Disease, which were presented at a plenary session in Toronto at the Alzheimer's Association International conference and celebrated at a special reception attended by many past awardees in commemoration of the Awards' 30th anniversary.

AFAR and MetLife Foundation are thankful for the 2016 Awards Advisory committee: David Holtzman, MD, Chair; Karen H. Ashe, MD, PhD; Mathias Jucker, PhD; Edward H. Koo, MD; Sangram S. Sisodia, PhD; Rudolph E. Tanzi, PhD; and John Trojanowski, MD, PhD.

As seen below, MetLife Foundation President and CEO A. Dennis White (center) presented the awards to John Cirrito, PhD; Inna Slutsky, PhD; Miia Kivipelto, MD, PhD; and Guojun Bu, PhD (left to right).



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SUMMARIZED FINANCIAL INFORMATION

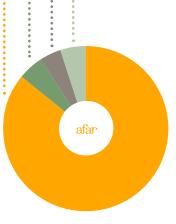
Year Ended December 31, 2016



9% management and general

7% public education and meetings

8% fundraising



AFAR is proud to maintain high fiscal standards internally, and we require the same of our grantee institutions.

SUMMARIZED OPERATING RESULTS

OPERATING REVENUE

OPERATING REVENUE		94%
Contributions	4,881,388	
Investment Income, Net	9,337	_
Endowment Earnings	274,870	5%
Other Total Operating Revenue	34,012 5,199,607	1% 100%
Research Grants and Scholarships	3,803,385	
Meetings and Public Education	366,869	
Total Program Expense	4,170,254	83%
Management and General	446,218	9%
Fundraising	389,735	8%
Total Supporting Expense	835,953	17%
Total Operating Expense	5,006,207	100%
Total Operating Income	193,400	4%
SUMMARIZED BALANCE SHEET		
Assets		
Cash	6,133,846	27%
Contributions Receivable	4,772,233	21%
Investments	10,520,421	46%
Other	1,302,428	6%
Total Assets	22,728,928	100%
Liabilities and Net Assets		
Research Grants and Scholarships Payable	2,211,770	10%
Other	44,997	_
Total Liabilities	2,256,767	10%
Net Assets		
Unrestricted	5,037,128	25%
Temporarily Restricted*	11,273,758	55%
Permanently Restricted Endowment	4,161,275	20%
Total Net Assets	20,472,161	90%
Total Liabilities and Net Assets	22,728,928	100%

^{*} Funding pledged in support of future programming

The above summarized financial information is derived from the organization's audited financial statements, which are available upon request.

BUILD THE FUTURE OF HEALTHY AGING WITH AFAR

AFAR envisions a future in which we remain healthier as we grow older, less susceptible to disease and disability. For more than three decades, AFAR has been the premiere driver of aging research, supporting innovative scientists who have defined our understanding of the basic biology of aging while conducting cutting-edge studies that have led to the drug interventions reported here.

Thanks to AFAR's leadership and vision, these discoveries that target aging are closer than ever to moving from the lab to our lives. Yet at this critical moment in the field, funding for scientific research is becoming even more scarce.

AFAR depends on private support to find and fund the best research to advance therapies that will extend healthspan—the years we will live in good health—for us all.

Private philanthropy has provided the funding for modern medical breakthroughs such as the polio vaccine, statins, and many life saving drugs. Today, we can make similar breakthroughs in aging together.

When you give to AFAR, you help shape the future of aging research!

AFAR offers a range of giving opportunities for your consideration:

- Make a gift to underwrite or endow a **named research grant**. Naming opportunities in support of AFAR research grants, new investigator, or disease-specific grants are available at multiple levels of giving.
- Make a gift to our **annual fund**, the central vehicle through which our core research grant program is funded. Gifts may be made annually, or consider becoming a sustaining donor through our monthly or quarterly gifts program.
- Sponsor an **MSTAR** (Medical Student Training in Aging Research) scholar in your local community and help us fill the urgent need to train more physicians to care for our expanding older population.
- Sponsor a **scientific conference** or public educational program. Sponsorship opportunities are available at many levels.
- Make a **planned gift** as a member of the Irving S. Wright Legacy Society.
- Make a **memorial** or a **tribute gift** to honor a loved one or special occasion.
- Make a **gift of stock** or other tangible property. This is a win-win: while supporting aging research, you avoid paying capital gains taxes.

If you wish, gifts can be made through your **donor advised fund**.

We welcome the opportunity to speak with you about how your gift can help support AFAR's researchers who are building the future of healthy aging.

If you would like more information or would like to discuss ways to support AFAR, please contact Karen Wenderoff, Director of Development, 212-703-9977 or karen@afar.org.

To make a gift online, please visit AFAR's secure website at www.afar.org/give.

Special thanks to all of the featured experts for their time and care in contributing to this report.

AFAR 2016 Annual Report Creative Team: John Chaich, MFA, Design; SCP Communications, Copywriting; and Elizabeth Hanson, Copyediting.

Photographs courtesy of featured contributors as well as Studio 7 NYC Photography (p. 1); Joseph De Sciose (p. 9); Diane Bondareff/AP Images (p. 21); New York Academy of Sciences (p. 23, upper left); and Livingface Photography (p. 23, lower right).



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