The Paul B. Beeson Career Development Awards in Aging Research

A joint program of the National Institute on Aging (NIA), the NIH Office of Dietary Supplements, and several private foundations, the Beeson program encourages and assists the development of future leaders in the field of aging. It deepens the commitment of academic medicine to research in aging and to translating research outcomes into advances in treatment, prevention, and service. The program, which is administered by the NIA and the American Federation for Aging Research, makes approximately 10 awards annually—126 since the program’s inception in 1994. Today, these awards are worth between $600,000 and $800,000 over three to five years.

The benefits of the award for Beeson Scholars are numerous and in many cases career-changing. They include:

- Flexible, generous funding with ample resources to pursue an innovative research program.
- Protected time for research.
- An outstanding support system. Senior faculty in each Scholar’s institution agree to serve as mentors, and Scholars are also matched with senior leaders in the field, who serve as members of the Beeson Program Advisory Committee.
- Extensive networking opportunities.
- Alumni participation through continued attendance at the annual meetings, where they can assume leadership roles in the program and even become mentors to other Beeson Scholars, offering guidance to the next generation of leaders.

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The National Institute on Aging
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The National Institute on Aging
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About the American Federation for Aging Research

AFAR is a nonprofit organization whose mission is to support biomedical research on aging. It is devoted to creating the knowledge that all of us need to live healthy, productive, and independent lives. Since 1981, AFAR has awarded nearly $93 million to more than 2,200 talented scientists as part of its broad-based series of grant programs. Its work has led to significant advances in our understanding of the aging process, age-related diseases, and healthy aging practices. AFAR communicates news of these innovations through its organizational web site www.afar.org and educational web sites Infoaging (www.infoaging.org) and Health Compass (www.healthcompass.org).

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Editorial direction was provided by Strategic Communications & Planning, Wayne, PA.

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In 1994, in response to an Institute of Medicine report calling for more support for geriatrics research and training, several private foundations— including the John A. Hartford Foundation, the Commonwealth Fund, and The Atlantic Philanthropies— developed a generous, multi-year fellowship program intended to support talented junior investigators working in the field of aging research. Seeking a name for the program, they looked no further than Paul B. Beeson, MD, one of the great physician-scientists of the 20th century and a champion of the importance of geriatrics research and education. “By naming the award after Paul Beeson, we didn’t have to say, ‘This is a program for excellence,’” says William Hazzard, MD, professor of medicine at the University of Washington School of Medicine and Beeson Award Program Committee Chair 1997–2002. “Everyone knows that’s what he stood for.”

Late last summer, Dr. Beeson passed away at the age of 97, and it is fitting that this year’s report of the program that continues to bear his name is dedicated to his memory and his extraordinary lifetime of service. As a professor and later chair of the Department of Medicine at Emory University in Atlanta, he became well-known for his key discoveries in infectious disease. Dr. Beeson was also well-loved and respected by his students, who strove to emulate his thoughtful, caring attitude toward his patients.

Recruited by Yale in 1952, Dr. Beeson eventually spent more than a decade at the university as chair of the Department of Medicine. Then, in the mid-1960’s, he accepted a position as the Nuffield Professor of Medicine at Oxford University in England. During his stay abroad, he was exposed to the practice of geriatrics as a separate discipline, which was practically unknown in the United States at that time. A few years later after returning to the U.S., the Institute of Medicine asked Dr. Beeson to head a study of the state of geriatric medicine in the United States. The 1978 report was the first to warn that U.S. medicine was unprepared to provide care for the growing number of older adults demographers predicted. Dr. Beeson and his colleagues called on the nation’s medical schools to expand their geriatrics training dramatically.

When Dr. Beeson returned to the United States, he served as the Veterans Administration Distinguished Professor of Medicine at the University of Washington School of Medicine. Although he retired in 1981, he remained active in the field, serving as editor in chief of the Journal of the American Geriatrics Society and attending rounds at the VA Hospital in Seattle. In addition to being a role model as a physician-scientist, Dr. Beeson was also the “epitome of successful aging,” says Mary Tinetti, MD, professor of medicine, epidemiology, and public health at Yale University School of Medicine and chair of the Beeson Program Advisory Committee. “He remained engaged, contributing to the field almost until the end of his life.”

Along with the rest of the medical community, all of us involved with the Beeson program will dearly miss Paul Beeson, and we will ensure that our collective efforts honor his memory and his lifetime of service to medicine, and particularly the care of older adults.
Through the Paul B. Beeson Career Development Awards in Aging Research Program, now in its thirteenth year, we have seen how a new and expanding generation of physician-scientists has focused its talents to prevent disease, reduce disability, and improve the quality of life for older adults.

The success of the Beeson program and its dedicated investigators is notable in several ways:

• The program has brought a considerable number of physician-scientists into aging research. Since 1995, some 126 Scholars from 39 institutions nationwide have been selected, directing their academic careers to research, teaching, and practice in the field.

• The program has benefited all areas of aging research. The cadre of Beeson Scholars has turned its attention to basic biology and social and behavioral aspects of aging, as well as clinical gerontology and geriatrics. The Beeson program, together with pre-Beeson support from some foundations, has allowed sustained research efforts by physician-scientists in a number of areas not previously drawn to aging research, including nephrology, emergency medicine, and oncology.

• The program has proved an effective base for physician-scientists to move on to independent research support in a highly competitive environment. Analyses conducted by the American Federation for Aging Research of 1995 through 2002 Scholars found that 80 percent of alumni received competitive grants funding. Thirty-seven percent of the current Scholars have similar support.

• The Beeson annual meeting has proven itself a fertile ground for fostering research collaboration. Scholars have developed several projects through contacts at this meeting, as they share ideas and network. This is an increasingly valuable part of the Beeson experience, the Scholars say.

These achievements continue to be possible because of the unique partnership behind the Beeson program. Now four years old, the collaboration among the National Institute on Aging (NIA), The Atlantic Philanthropies, the John A. Hartford Foundation, The Starr Foundation, and the National Institutes of Health Office of Dietary Supplements, in affiliation with the American Federation for Aging Research, is an effective blend of public and private effort.

In 2006, the first baby boomer turned 60, signaling the unprecedented aging of the population in the United States and worldwide. The Beeson program is needed now more than ever, and it is a fitting tribute to Paul Beeson that the program continues to grow and flourish. Through this endeavor, we honor Dr. Beeson’s legacy of dedication to aging research and to better health and well-being with advancing age for all of us.

Richard J. Hodes
Director
National Institute on Aging
Career Development, Cutting-Edge Science, Leadership
The Beeson Program: Past, Present, and Future

Since the Beeson program’s inception, several surveys and evaluations have reflected the program’s many benefits and ever-expanding impact. Perhaps most importantly, these reviews have allowed us to chart the hopeful progress of the growing number of Scholars, as they build their careers, develop new research insights, and provide leadership in a wide range of academic, medical, and healthcare settings.

For example, a 2005 survey of Beeson Scholars found that:

- 66 percent had received promotions;
- 79 percent had taken on increased responsibilities including serving on local and national committees and heading up divisions and centers on aging; and
- 63 percent are faculty members of a gerontology division or aging.

This track record has been heartening to all involved, and particularly the private foundations that helped launch the program and continue to sustain the initiative in collaboration with the National Institute on Aging. From so many vantage points, “the program has been enormously successful,” says Corinne Rieder, executive director of the John A. Hartford Foundation, noting the achievements of Scholars appear more and more regularly in the nation’s top scientific journals and newspapers. “For a foundation, it gives tremendous satisfaction to fund the best and brightest people out there.”

“One of the program’s unique— and perhaps underappreciated— aspects,” says Brian Hofland, director of the aging program at The Atlantic Philanthropies, another of the original private foundation partners, “is its ability not only to fund the cream of the crop, but to tap scientists pursuing a diversity of approaches to research on aging. This multi-disciplinary, interdisciplinary strategy is extremely valuable. It is where a lot of cutting-edge advances in science are coming from today.”

To foundations, the public-private partnership with the National Institute on Aging has also been a critical factor in sustaining the program and leading to a sense of a bright future. The kind of financial commitment needed to support a program like Beeson is difficult to maintain for one or even a few foundations over time. As Florence Davis, executive director of The Starr Foundation notes, NIA’s involvement has been crucial, not only in terms of dollars “but as a seal of approval, to encourage the medical community to take geriatrics and gerontology more seriously.”

Perhaps the most exciting part of the program is that the Beeson Scholars continue to make important strides in developing the knowledge our nation so desperately needs to provide high quality care to the growing number of older adults. “There is so much potential wrapped up in the Scholars,” says Stephanie Lederman, executive director of the American Federation for Aging Research. “We look forward to big things.”
As always, it is a pleasure to introduce the group of Beeson Scholars featured in this report. Every year, the program selectors focus on research excellence and try to identify a dynamic mix of basic and clinical researchers from a wide range of institutions around the country. Perhaps not surprisingly, the 2005 class of Beeson Scholars is pursuing research in everything from imaging, Alzheimer’s disease, and breast cancer to gait variability and the effect of neighborhoods on the management of chronic conditions. This breadth is indicative of the wide range of issues surrounding the healthcare needs of older adults. It is also the reason this class of Scholars is almost equally split between geriatricians and specialists, with all Scholars using the technology of their respective disciplines to advance our knowledge of aging.

On a sadder note, I must mention the passing of Dr. Paul Beeson. The program was named after him because he was such a role model as a physician-scientist and an outstanding leader in medicine. I believe the program is living up to his legacy. It has fostered the careers of so many leaders in aging research around the country, and it has also encouraged the spirit of scientific sharing and collaboration that Dr. Beeson expected from his own students. As just one recent example of his ethos, alumnus Ned Sharpless lent some mice he developed to some of his colleagues—leading to a major three-way discovery of a genetic relationship between cancer and aging, published in Nature. This spirit of open, interdisciplinary sharing of ideas and thoughts is a central theme of the Beeson program, and as we honor Dr. Beeson’s memory, I hope it can become a model for all science.

Mary Tinetti
Yale University
Before people ever reach a state of full-blown Alzheimer’s disease (AD), they may experience an intermediate state of deterioration called mild cognitive impairment (MCI). People with MCI show no obvious dysfunction, but neuropsychological testing reveals subtle changes in their ability to remember or reason. Although not everyone with MCI goes on to develop dementia, many do, and Dr. Liana Apostolova believes that MCI may represent our best opportunity for early intervention. “Alzheimer’s is a devastating disease,” she says. “If we can intervene before symptoms occur and stop disease pathology and progression, then we have won our war with it.”

To help win that fight, the Beeson program has funded her study of MCI patients, using state-of-the-art magnetic resonance imaging (MRI) techniques to develop an AD biomarker. The techniques allow her to create three-dimensional models of the hippocampus, a part of the brain that plays a major role in memory, and the cerebral cortex and analyze any changes that occur. So far, she has been able to demonstrate changes that herald the beginning of AD in two areas of the hippocampus called CA1 and the subiculum, and these changes can enable doctors to distinguish between people with MCI who will eventually develop dementia and those who will not.

“My research is involved with very advanced, computational anatomy techniques,” she says. “These allow for extremely accurate and powerful three-dimensional analysis and represent an extension of what imaging research has been able to accomplish up to now. There are only a few techniques like ours—I would say two or three really. Here at UCLA, I work with the person who pioneered our approach, Dr. Paul Thompson. He’s one of my mentors. I’m extremely grateful to be in such an environment.”

The human brain first began to intrigue Dr. Apostolova while doing a neurology rotation during her clinical years at medical school in Bulgaria. Neurology, with its deep dependence upon both clinical and logical reasoning, proved so intellectually stimulating that she decided to make it her life’s work. Cognitive function, in particular, attracted her interest, which meant her path could take her in one of two directions: cognitive development in children or cognitive decline in older adults—the study of strokes and dementias. As a physician, she felt her role fell clearly into the area of curing and preventing these illnesses.

After graduating from medical school, she left Europe for the United States, as had her mother, a biochemist, several years before. Dr. Apostolova completed her neurology training at the University of Iowa, and then moved on to the University of California, Los Angeles, where she completed a two-year dementia fellowship and began doing research on MCI. She was awarded the Beeson upon fellowship graduation.

Since then she has enjoyed a steady stream of successes, including the presentation of 19 abstracts at various professional meetings and three platform presentations—at the 36th Annual Meeting of the Society for Neuroscience and at the 58th and 59th American Academy of Neurology Meetings.

Although the first priority of her Beeson project is developing a diagnostic biomarker for dementia progression, Dr. Apostolova hopes she can use the advanced imaging techniques to discover other biomarkers that measure success in therapeutic trials. Toward that end, she will be submitting an R01 proposal in 2007.

She credits the Beeson program, and particularly her mentors, with much of the progress she has made in her career. “The Beeson mentors emphasized the importance of planning ahead and taking full advantage of what the Beeson program offers—networking, presenting work, discussing ideas with the Beeson audience composed of different geriatric subspecialties, career development advice, and support among many others. It’s been a wonderful experience.”
Malaz A. Boustani, MD, MPH
Assistant Professor of Medicine
Indiana University School of Medicine

Enhancing Care for Hospitalized Older Adults with Cognitive Impairment

Dr. Malaz Boustani does not like the idea of dying, and he is not afraid to say so. “It scares me very much, and I would love to live as long as possible,” he says. “But at the same time, I understand that living long may make me vulnerable to one of the main enemies of quality of life—losing cognition. It was from that irony—my own individual obsession with death versus my concern about living with cognitive loss—that I decided to do research to help modify the current system.”

Dr. Boustani’s decision has led him well beyond his own mortality to look closely at outcomes for cognitively impaired patients, 65 years and older, who turn to hospitals for medical care. He began with his own institution, Wishard Memorial Hospital in Indianapolis, Indiana. What he learned was unsettling. For patients with cognitive impairment (CI), the average hospital stay was one to two days longer, the cost $8,500 more, and returns to the hospital two months earlier than with other older adult patients. Patients with CI were especially vulnerable to hospital-acquired complications such as falls, injuries, pressure ulcers, restraints, and delirium. “We think part of it is because people don’t look at CI patients as a more vulnerable population having special needs. You need to treat them differently,” he says.

As Wishard already offers a well-established geriatrics program, called Acute Care for the Elderly (ACE), which proactively seeks out older patients to provide them with appropriate care, Dr. Boustani believes the statistics are probably even worse for hospitals where no similar program exists. He is using his Beeson award to run a clinical trial, called Enhancing Care for Hospitalized Older Adults with Memory Problems (e-CHAMP), which will test an upgrade of the ACE program that more fully integrates information technology into its systems and is available around the clock, seven days a week.

The new version is called Virtual ACE or ACE 24/7. He conceived it from a systems perspective. “I think the real world is nonlinear and to me much more exciting than the laboratory world,” he says. “For me to better understand that nonlinearity, I have become very interested in social science and non-traditional sciences such as chaos theory and complexity science. So I began learning from these perspectives, and I started to become very interested in system theories.”

In the e-CHAMP study, a point-of-contact healthcare professional assesses every patient 65 years or older for CI and then randomly allocates him/her to either the new ACE or the older model. Virtual ACE alerts medical personnel about a patient’s CI status and level each time a new drug or diagnostic test order is entered into the hospital’s Computerized Order Entry and makes recommendations regarding the patient’s care. It also screens for contraindicated medications, gives warnings about the appropriateness of certain medical practices, and offers alternative suggestions to the use of physical restraints.

“We’re hoping that if this Virtual ACE system works, the patient will stay fewer days in the hospital, cost the system less, and not return so quickly,” says Dr. Boustani. “In other words, we will improve overall quality and safety.”

In related research, Dr. Boustani is working with his primary mentor, Dr. Christopher M. Callahan, a 1996 Beeson Scholar, to enhance the primary care system for patients with CI, using a program called Providing Resources Early to Vulnerable Elders Needing Treatment for Memory Loss (PREVENT for Memory Loss). Over the next few years, he hopes to connect PREVENT and Virtual ACE to create a continuum of care across hospital, home, and primary care settings.

Like many Beeson Scholars, Dr. Boustani expresses immense gratitude to the Beeson program for keeping him on a career track of independent research. “I tried to get support for my research many times before but failed, and I was about to give up. Then the Beeson award came along and changed my life.”
As you might expect, varying the length of your step as you walk can put you at higher risk for balance problems, but as physical therapist Dr. Jennifer Brach has discovered, step length is not the only variable. How wide apart your feet are and how much you vary that distance can also make a difference. And difficulties do not always arise from having too much variability—they can come from having too little.

“You need to be able to adjust the width of your step to maintain your balance,” Dr. Brach explains. “If you’re always taking steps the same width apart, you’re unable to compensate for any challenges that might come up.”

An inability to compensate can develop in older adults when small system failures in the body begin to add up. These can include white matter changes in the brain, numbness in the feet, weakness in the legs, difficulty seeing, and a host of other conditions that might seem innocuous individually, but in combination can change walking from a simple pleasure to an arduous, and sometimes perilous, effort. For some individuals, progressive walking disability (PWD) can mean the end of most physical activity.

Dr. Brach is focusing her Beeson research on learning how to identify people with gait variability that leads to PWD and to develop interventions that will help them remain physically active. To measure and assess gait, she uses a four-meter-long, computerized, hard-surface walkway embedded with small switches that open and close, rendering a picture of subjects’ footprints as they move forward. The picture, which appears on a computer screen, provides information about step length, step width, and stance time (the time from heel-strike to toe-off with each step).

She is currently adding challenges to gait in her experimental regimen, such as walking slowly, walking over carpet, or walking while holding a cup of water. And after discovering the related work of fellow Beeson Scholars, Dr. Joe Verghese (2004) and Dr. Catherine Sarkisian (2004), at an annual Beeson meeting, Dr. Brach has broadened the scope of her research even further. She has begun to incorporate Dr. Verghese’s idea that splitting an individual’s attention with difficult mental tasks while walking may affect gait, and Dr. Sarkisian’s theory that personal expectations about age-associated conditions—such as losing balance and falling—may become self-fulfilling prophecies.

Results so far have not only confirmed the work of previous researchers who found that gait variability can predict how likely an individual is to experience a fall in the future, but have also demonstrated that researchers can actually determine how likely an individual is to develop PWD as well.

She and her colleagues are now trying to determine what kinds of interventions would work best to prevent falls and PWD. Their initial focus is on stance time variability. For that, they are using a treadmill, which enforces a regular stepping pattern and sets pace. The moving contact surface also forces the leg to go back into extension, which then sets off a biomechanical chain of events that forces a more regular stepping pattern.

As the first non-physician ever to receive a Beeson award, Dr. Brach is particularly grateful to the program for all the ways in which it has helped both her research and career. “I’ve certainly gained prestige within my profession,” she says, “especially being the first non-MD to receive a Beeson award. It’s a pretty big coup for a physical therapist to be in such a select group.”

As to her future plans, she admits that while she has spent a lot of time studying “longitudinal associations,” as a physical therapist, she is driven to do interventions. She hopes her research will increasingly focus on defining evidence-based, effective, doable, and affordable interventions for older adults who have difficulty walking.
Among older adults, physical exercise is often the first line of therapy for age-associated, chronic conditions such as diabetes, heart disease, hypertension, and arthritis. In some urban neighborhoods, however, even so simple an exercise as going for a walk can be harrowing. Dr. Arleen Brown recalls one patient, a woman in her 70s, who had been recently diagnosed with diabetes. Rather than depend on medication, the patient tried treating her condition with exercise and dietary changes. Her new eating habits caused her to lose weight, and her daily walk through the neighborhood made her feel stronger and more energetic. But there was, she said, a problem: that stick was really heavy. What stick? Dr. Brown wanted to know. Her answer: The one she carried to beat off unleashed neighborhood dogs.

Perhaps more than any other group, older adults with chronic diseases are subject to poor health outcomes because of challenges— from unruly dogs to lack of transportation— posed by their local environments. Dr. Brown is looking for ways to help them meet these challenges and benefit from evidence-based dietary and physical activity interventions shown to improve the health of older adults with chronic conditions. “What I’m trying to do with the Beeson award,” she says, “is to assess how the neighborhood you live in influences not only the type of healthcare that you get, but also your ability to engage in health-related behaviors, which include everything from exercise to getting the healthy foods and medications that you need.” Ultimately, she would like to identify ways to build community support for chronic disease management.

To better understand these questions, she has gathered data from several sources: the Los Angeles Family and Neighborhoods Survey, an ongoing study of neighborhood influences on health, and focus groups and one-on-one interviews with older adults in low-income Los Angeles County neighborhoods. Her research shows that living in a poor area is a predictor of poorer health status, even after adjusting for age, sex, race, ethnicity, income, and other variables that can influence health. Simply put, if you have a chronic condition and live in a low-income neighborhood, you are far worse off than people with similar conditions living in wealthier areas. Why? Dr. Brown’s research pinpoints several contributing factors: your local supermarkets are less likely to carry the healthful foods you need at prices you can afford, safety issues may make venturing onto the streets to exercise a health hazard in itself, and getting to medical providers via public transportation may be difficult or impossible.

Dr. Brown is working with community groups to identify and implement interventions that would be most beneficial to older adults with hypertension, diabetes, or coronary disease. “The areas we’re going to focus on are diet, physical activity, and medication management,” she says. “For example, we’ve been encouraging restaurants in low-income areas to provide meals for seniors— heart-healthy, low-fat, low-carb, low-sugar meals.”

Her interest in the effects of the urban environment on chronic disease management grew out of her experiences as a child with the Los Angeles transportation system, which proved less than adequate in helping her family members reach the healthcare resources they needed. She left the area to pursue undergraduate studies at Harvard and then medical school and residency at the University of California, San Francisco, but when she returned to establish a clinical practice in internal medicine, she quickly recognized that her patients still faced the same problems she and her family once had.

She credits the Beeson award for making her current research possible. “The basic thing it does is pay for time— time to think, time to talk to people who ordinarily you don’t have time to talk to or can’t track down. It has also helped me buy equipment and bring in students as research assistants to really get projects moving. In fact, one of the nicest things is having those students... they’re well trained and understand the projects, and they’re really motivated. And some have become very interested in geriatrics. One wants to practice geriatrics law. Watching them develop and thrive in the environment that I’ve been able to create here has been one of the biggest benefits of the Beeson award.”
Some studies have suggested that the family of cholesterol-lowering medications called statins may reduce an individual's risk for Alzheimer's disease (AD) by more than 70 percent. Unfortunately, other studies have shown just the opposite—that statins have little or no benefit at all where AD is concerned. To complicate matters, no one can say for certain whether the reduced prevalence of AD is actually an effect of statin use or derives from some other factor such as following healthful lifestyle practices or taking medications for other conditions. To unravel the knot, Dr. Cynthia Carlsson is investigating the effect of statins on various Alzheimer's-associated biological markers in the brain, blood, and cerebrospinal fluid of adult children of people with AD.

Specifically, Dr. Carlsson and her lab are looking at the effect of one drug, simvastatin, on the volume of an AD biomarker, beta-amyloid (Aβ), in the spinal fluid. Aβ is a protein that gathers into sticky plaques in the brains of people with AD and may be responsible for many of the disease's devastating symptoms, including confusion and memory loss. In addition to measuring Aβ volume in the spinal fluid, Dr. Carlsson also is observing how simvastatin affects inflammation in the spinal fluid and blood. To determine whether subjects' memories have improved, she administers cognitive tests to participants.

In yet another aspect of the study, the Beeson award has allowed Dr. Carlsson to add in brain imaging components. “We’re using MRI perfusion,” she says, “a technique that will let us see if certain parts of the brain related to memory get an improved blood flow with statins.” It has also allowed her to work with a team of very talented investigators at the University of Wisconsin who specialize in medical physics, cardiology, neuroradiology, neuropsychology, and other neuroimaging specialties. “We’re hoping eventually to carry the investigation further and see if we can do a larger clinical trial with more clinically relevant outcomes for a longer period of time,” she says. “That would tell us what the larger impact of some of these interventions could be. It’s been exciting.” The implications of her results may be enormous for AD patients. Statins are already widely prescribed to help prevent heart attack and stroke, so if they prove effective in treating mechanisms related to AD, it would be relatively simple to establish a medical standard of care for prescribing them to people at high risk for the disease. The drugs could find their way into clinical use very rapidly. And although her own work emphasizes their use in people at high risk before clinical symptoms appear, there are other studies that suggest they may even improve the cognitive status of people with full-blown disease.

Dr. Carlsson’s current research in AD is the fruition of an interest that extends back to her early adolescence, when her grandmother first showed symptoms of the disease. Though watching someone she loved slowly deteriorate was difficult, it also ignited in her a passion to find ways to understand and fight the disease. That passion persisted through medical school at the University of Michigan and fellowships in geriatrics and women’s health at the University of Wisconsin.

In addition to her research responsibilities, Dr. Carlsson also serves as Medical Director of the Memory Assessment Clinic at the William S. Middleton Veterans Memorial Hospital in Madison, Wisconsin. Through her work in the clinic, she has developed a curriculum to train students, residents, and fellows in the interdisciplinary team care of patients with dementia. She feels the clinical component of her work is invaluable to her research. “One of the things I like to do,” she says, “is clinical trial design. Being involved with the clinical care of patients helps me realize what’s feasible and what’s not, and what is and isn’t an important clinical outcome.”

Seeing what people go through with AD and the suffering they and their families endure also motivates her to work harder to try and find ways to prevent the disease. She expresses gratitude for the help she has received that allows her to do that: “I applaud Dr. Beeson and all of his work,” she says. “We’re really thankful for all he invested in people, and though he recently passed away, we’re confident that his work will continue to help aging research far into the future.”
Perhaps more than any other age group, older adults need vaccines to help them fight off malignancies and infections. Yet as several clinical studies have shown, aging itself reduces immune function and makes vaccination less effective. Understanding the cell biology behind this immune system degradation is the focus of Dr. Daniel Goldstein’s Beeson research.

It is a complex problem. Immune response is the result of interplay between two different components. The first, innate immunity, defends the body in a general way against microscopic interlopers. It does not make specific responses to specific invading organisms but rather uses physical barriers such as the skin to protect the body, and it attacks foreign substances, called pathogens, with chemicals and immune cells. It also activates the second component of immune function, adaptive immunity, which creates armies of immune cells designed to fend off specific pathogens.

Dr. Goldstein’s hypothesis proposes that aging has a greater impact on T cells—important role-players in the adaptive immune system—than on the innate system. So far, his work seems to confirm this idea. His initial research, based on a viral infection model in mice, has demonstrated that one subtype of innate immune cell function, which activates T cells, does not change with age. This implies that any age-related degradation in T cell function probably occurs either in the T cells themselves or in some other component of the innate immune system. It is a critical finding, but one that at first met some initial resistance in the scientific community.

“I had a hard time convincing people of the value of the study. It’s a lot of negative data in a sense, finding no differences due to age in certain priorities of the innate immune system. But it’s a result that gives us hope. It suggests that we may eventually be able to activate and use innate immune functions to recover T cell immune responses.” One way to do this would be to use agonists, or adjuvants, substances that can stimulate the innate immune system to create more inflammation during a pathogen attack, temporarily allowing T cells to mount a more powerful response.

Dr. Goldstein also points out that although the particular subtype of innate immune function he has studied does not change with age, other components might, and he and his colleagues are in the preliminary stages of pursuing that area of research as well.

As a practicing heart-failure transplant cardiologist, Dr. Goldstein first discovered his interest in aging cells and immunity a long way from the laboratory bench. His work in transplantation aroused his interest in some intriguing questions: Does the aging process exert any influence on transplant rejection? And if so, is that due to its having a negative effect on innate immunity? The questions have important practical, as well as theoretical applications, as more and more people in their 60s and 70s are undergoing transplantation, not only of the heart but of the kidneys and other organs as well.

Expanding his research to include broader issues of aging and immunity seemed a natural progression. “I became interested in aging through my transplantation work, but now I’m very committed to developing an active research program that looks at all aspects of the relationship between immunity and aging, which includes conducting the work supported by the Beeson award. It has been extremely helpful, and I feel very lucky and grateful to be part of the program. It’s absolutely instrumental in getting me into this field.”

The work he and his colleagues have done with the help of the Beeson award resulted in the publication of his first paper in the aging field: “Murine myeloid dendritic cell-dependent toll-like receptor immunity is preserved with aging.” (Aging Cell. 2006: 473-486.) He expects that many more will follow.
In the world of Dr. Wendolyn Gozansky’s research, pears turn into apples, and that presents a problem. More specifically, the typical pear-shaped body silhouette many women acquire when they gain weight often becomes more apple-like when they reach menopause and begin accumulating fat around their midsection rather than their hips and legs. It’s called central adiposity, and it’s a problem because fat above the waistline is associated with—and can be predictive of—the development of serious medical conditions such as hyperlipidemia, hypertension, cardiovascular disease, and diabetes.

Presumably, estrogen plays a role in protecting younger women from central adiposity, but no one is quite certain how it does its job. Dr. Gozansky hypothesizes that it affects the function of an enzyme called 11b-HSD1 that converts cortisone, a relatively inactive hormone, into cortisol, which causes fat cells in the midsection to expand.

To study the process, Dr. Gozansky uses a microdialysis technique. Tiny probes that look like pieces of dental floss are inserted into a subject’s abdomen, and then salt water is perfused through the probes in the abdominal fat. The fluid that comes out can reveal information about the fat tissue’s background production of cortisol. On the experimental side, she perfuses cortisone along with the salt water and measures how much cortisol comes out, which can yield information about how the enzyme is working in the abdominal fat. She also gives some subjects either estrogen or placebo for a short period of time to see how it affects the cortisone to cortisol conversion.

Animal studies have already given a strong indication of the kinds of effects over-activity of 11b-HSD1 can induce. “When mice over-express the enzyme,” Dr. Gozansky says, “they end up looking like they have metabolic syndrome—they get central obesity, high blood pressure, and insulin resistance or pre-diabetes. However, when you take mice and knock out the gene responsible for expressing 11b-HSD1, you get animals that are resistant to developing metabolic syndrome.”

Dr. Gozansky is currently working with a population of post-menopausal women, comparing obese subjects with those at normal weight to see how enzyme activity in the conversion of cortisone to cortisol is affected by the volume of body fat. She plans in the future to do studies of sex hormone suppression in pre-menopausal women, and she has already acquired grant funding for the study. This model of drug-induced menopause will allow Dr. Gozansky to isolate the effects of sex hormone suppression from the effects of aging. Her hope is that this work will lead to medications that can modulate the activity of the enzyme in the way estrogen does, but that don’t have the negative side effects associated with estrogen replacement therapy.

Dr. Gozansky’s Beeson project is not her first foray into the study of older women’s health. In the earliest days of her medical career, a colleague suggested that she consider combining her love of internal medicine, interest in menopausal women’s health, and attraction to treating older people into one specialty: geriatrics. It became her passion, and she has never looked back. “I think it was the perfect decision,” she says, “and it works for me because I like the medical minimalism approach of geriatric medicine. To me, the idea of trying to keep people healthy and functional longer is a really good research goal.”

The Beeson award has helped her not only by providing funding to get her research up and running, but also in her career development. “Linda Fried, who’s my external Beeson mentor, has been very helpful in career counseling, particularly around the concept of learning to negotiate and prioritize,” she says. “At the last meeting, we talked about issues of promotion, the sort of things you usually get to talk about only a little now and then. But we had a couple of days to focus on those things specifically, as well as to hear what other people have done and gone through. It’s invaluable.”
Cardiac anesthesiologist Dr. Leanne Groban has three passions in her work: learning about the aged human heart, increasing medical knowledge that will improve the lives of older adults, and sparking excitement about the subject of aging in other researchers. For her Beeson project, she is using all three to develop a deeper understanding of a particular type of heart failure.

Like any pump, the heart compresses and relaxes. Its compression is called **systolic** function and its relaxation, **diastolic** function. Problems—dysfunctions—can occur during either phase, but as people grow older, diastolic dysfunction of the heart’s left ventricle, the chamber that accepts blood from the left atrium and then forces blood into the aorta, becomes more common, especially among older women. Diastolic dysfunction, or the inability of the aged left ventricle to relax and fill adequately between beats, can lead to heart failure symptoms, particularly during exercise. In addition, age-related architectural changes of the left ventricle lead to chamber stiffness, further contributing to the disease progression.

To learn how diastolic dysfunction develops, Dr. Groban is investigating the potential roles of growth hormone (GH) and its circulating blood protein mediator, insulin-like growth factor-1 (IGF-1)—major players involved in the aging process. Age-related diminishing supplies of GH/IGF-1 may further lead to imbalances in a system that helps control blood pressure, and, in part, heart structure. That system is called the renin-angiotensin system (RAS).

Dr. Groban uses animal models in her research that closely mimic healthy human aging. “We study normal, healthy, aged rats,” she says. “We study them anywhere from 24-35 months of age—which is probably equivalent to a 75–80 year old person—and what we’ve found is that they have early signs of diastolic impairment.” The models’ close mimicking of diastolic dysfunction in humans may eventually allow researchers to develop interventions that can reverse or at least control the problem. Currently, no treatment exists.

Finding the right animal model has been critical to Dr. Groban’s work. She credits Professor William Sonntag with first piquing her interest in using specific animal models to study age-related cardiovascular changes. He donated some of his own rats, specially bred to study GH and IGF-1, for use in her first project, and she continues to learn from him the importance of animal models in aging research.

With the data she gathered from those early studies, she was able to obtain a small Merck starter grant through the Society of Geriatric Cardiology, and then a small research grant (R03) through the National Institute on Aging, which allowed her to procure more animals. After three years, she had created a large enough data set to put together a grant for the Dennis W. Jahnigen Career Development Award, an American Geriatrics Society grant for researchers who are not in geriatrics per se, but are in surgical subspecialties that work with aged patients.

“Having this Beeson award has allowed me to protect my time to work in the laboratory, and also to make some awesome research collaborations within my own campus at Wake Forest,” says Dr. Groban. “For example, I’m now working with people who have expertise in hypertension and the renin angiotensin system from the Hypertension and Vascular Disease Center. In short, I’m building collaborations, I’m doing laboratory work, I have a technician, and I have a bench, and, just as important, I’m disseminating, communicating, and exciting other medical science professionals about this untapped area of aging—diastolic dysfunction. I feel like that’s part of the reason why I received the Beeson award—to disseminate an interest in aging and aging research among trainees and professional colleagues within and outside of my discipline as well as to advance the knowledge of diastolic dysfunction.”

Her passion seems to be working. Recently, a group of cardiac surgeons asked her to help them understand the utility of echocardiographic indices of diastolic function in their evaluation of how well specific-types of aortic valve replacements perform in elderly patients. And with typical enthusiasm, Dr. Groban jumped at the chance.
Sixty percent of all cancers and 70 percent of cancer deaths occur in patients over the age of 65, yet older adult patients are the most under-treated age group for the disease. Often, that is because oncologists, whose training focuses on choosing the best medical intervention for physically fit younger patients, presume that older patients are at greater risk for toxicity from treatment and require less aggressive intervention. Dr. Arti Hurria, however, believes that factors other than age can more accurately predict who will tolerate treatment well and who will not. These factors include, among others, a patient’s activity levels in the home and community, social support network, coexisting medical problems, nutritional status, psychological state, and perhaps most importantly, general performance level.

“A 40-year old person who is bed-bound probably won’t tolerate therapy well; but an 80-year old person who is a marathon runner probably will,” says Dr. Hurria. With help from the Beeson program, she has developed a questionnaire to help determine which patients would prove the best candidates for more aggressive approaches to treatment.

The first hurdle was to demonstrate the feasibility of obtaining the needed information from an older adult population with cancer. Oncologists have traditionally been concerned that gathering adequate data from each patient for this kind of assessment would prove too time consuming to be practical. Dr. Hurria’s studies, however, have shown that the majority of patients or their caregivers can complete the questionnaire before ever walking into the doctor’s office. Studies to determine whether the instrument can successfully predict toxicity from treatment are still underway, and after that, the hope is to use the instrument to develop interventions that will improve patients’ outcomes.

The Beeson award has allowed Dr. Hurria to hire research assistants, bring a biostatistician onboard, and protect her research time by limiting her clinical practice to one day a week. It has also broadened the scope of her work by bringing her into contact with other Scholars and mentors pursuing similar ideas. In particular, she and Dr. Cary Gross, a 2004 Beeson Scholar who is studying the impact of co-existing medical conditions on cancer patients, have become close colleagues and have even co-authored a paper on the benefits of radiation therapy in an older patient population. “I think the collaboration will continue to flourish over time,” she says. “We’ve talked about protocols that we want to open for each other. The Beeson program’s annual meeting has been an amazing opportunity to link with other investigators with similar research interests.”

Dr. Hurria has also found the Beeson program to be a rich source for mentorship. Scholars work both with the mentors they named in their applications and with an external mentor assigned by the Beeson Advisory Committee, who can objectively evaluate work and provide advice about career transitions. Perhaps just as important, she has discovered that many other senior people in the program have generously given advice and help whenever she has needed them. “William Hazzard and Mary Tinetti have provided me with invaluable advice and guidance,” she says.

Although Dr. Hurria began her current research at Memorial Sloan-Kettering Cancer Center in New York City, she is now pursuing the research at City of Hope, a National Cancer Institute-designated comprehensive cancer center in Duarte, California, where she directs the cancer and aging research program. She sees her work there as a way of fulfilling the Beeson goal of moving Scholars into leadership positions, where they can work to increase the presence of geriatrics and its subspecialties in the medical research community.
Breast cancer is a disease of older women. The media may pay more attention to cases among their younger peers, but post-menopausal women, especially those over age 65, make up the vast majority of patients. Although medical science can now offer some valuable therapies to these patients, the most effective way to decrease the impact of this cancer is to stop it before it starts.

Unfortunately, the only current recommendation for women at higher risk, such as those with a family history or abnormal breast tissue, is to start using the anti-cancer drug tamoxifen. For many, this may not be an acceptable choice. Tamoxifen can have serious, even life-threatening side effects. But for whom? If patients could know who among them are most likely to benefit from and respond well to preventive therapy, they and their physicians could make treatment decisions that are safer and more rational. That information could also help researchers test newer, less expensive therapies for efficacy.

Dr. Pearl Seo hopes to develop a diagnostic test that can obtain that information by finding breast cancer biomarkers in DNA taken from cancer patients’ blood samples. Having such a biomarker might do more than simply predict who is most likely to develop the disease. A relatively non-invasive test might also be created that could determine the developmental stage of existing tumors, which in turn could help to improve outcomes for patients.

“When initially I was interested how people do with therapy and how to get them through their chemotherapy,” says Dr. Seo. “Then I thought, wouldn’t it be great if I could work on the other side and increase the impact of treatment on the numbers or the incidence of cancer?”

When she has gathered enough data, she hopes to do a pilot study in the clinic to see if her diagnostic test can be performed in a time-effective manner, that is, whether it can return results within 24–48 hours. She hopes to use the study as the basis for an NIH R01 Research Project Grant.

Dr. Seo’s interest in both geriatrics and oncology blended well from the start. She felt that geriatrics represented the wave of the future in medicine, and she particularly enjoyed “the detective part of it— thinking out of the box, figuring out how to make geriatrics’ principles work for patients on an individual basis.” But her interest extended beyond the intellectual. She quickly discovered that she really enjoyed working with older people.

“They’re gracious, and they’ve been through a lot in their life,” she says. “The thing is, you want to retire and have this great life, and then the time comes and you get breast cancer.”

She is particularly grateful for all the benefits the Beeson award has given her, including protected research time, the opportunity to work at the laboratory bench and pay for the help of a statistician.

Ultimately, Dr. Seo sums up her work this way: “With heart disease you can make changes in your lifestyle management to improve your condition, but it’s hard to know exactly what you need to do for cancer. We do have great therapies for older women, of course, but the real way to decrease breast cancer’s impact is to decrease its formation. So that’s why I chose this field. I want to give people more than hope and help every woman live as long as possible.”
If you want to know how to live to the age of 100 and beyond, don’t just look at people who have already done it. That is like trying to learn how to win a marathon by only observing the winners at the trophy ceremony. It makes sense to also observe the best runners—that is, the people most likely to reach the furthest extremes of old age—while they are still in the race.

That is why Dr. Dellara Terry is conducting studies into the phenotypes (the observable physical characteristics) of the children of centenarians. Not all of them will live as long as their parents, but some will, because longevity does seem to run in families.

Dr. Terry has been conducting the research for a long time. She started during her medical residency with a pilot study of 80 people, maintained the work throughout her fellowship and continues it today. Her method has been straightforward: observing the health characteristics of her subjects and comparing them to those of a control group comprising the children of people who did not live to age 100.

Although intuitively it might seem that the control group would suffer more health problems from all causes than did the centenarian offspring, over the years a different picture has emerged. The centenarian offspring consistently showed a lower prevalence of cardiovascular disease and its risk factors. Surprisingly, there was not much difference in the two groups’ cancer rates. By the time Dr. Terry sees her subjects, they are in their 70s and 80s, and differences in cancer prevalence in her research subjects tend to happen before that age.

Her research group gathers data nationally through mail questionnaires and phone interviews, and follows subjects over time to observe changes in phenotype. The Beeson award, however, has helped extend her research to a group of local patients who come to the clinic for an entire day to undergo detailed vascular and cognitive assessments, as well as body composition measurements (weight, height, and hip and waist circumference, etc.).

Although Dr. Terry recognizes that the results of her work may not translate immediately into clinical practice, she hopes that eventually they will significantly improve the quality of life of older individuals by extending good health into their later years. “I think ideally we’re trying to figure out how vascular disease plays a role in age-related diseases, and in turn, how much of that is driven by genetics, versus environment, versus lifestyle. The next step is to learn how we can use that information to extend the health span of individuals and to help them maintain their function, independence, and good health for as long as possible.”

Although Dr. Terry takes great intellectual satisfaction in her research, she also finds fulfillment in working with older people, a population she feels is generally underserved. “I find them very inspiring,” she says, and adds with obvious pleasure: “People used to tell me that when you go into practice, your patients hug you. I couldn’t imagine that. But they do! And just hugging them makes such a difference, because many of these people don’t get any physical contact, so when they reach out to hug me, it’s just wonderful.”

She feels that the Beeson award has made all of this possible. “Besides providing money that allows me to carry out the research I’m doing,” she says, “the biggest gain I’ve had from the Beeson program is the way it fosters mentoring in a broad way so that you have access to many of the major aging researchers—people who before the Beeson award I only read about or would hear talk in front of an audience of a thousand people. I would never have had the opportunity to interact with them on a one-on-one basis.” That began with her primary mentor, Dr. Thomas Perls, a 1998 Beeson Scholar, and Dr. Terry credits him with first introducing her to the field of longevity and helping her to start her research.
Here are just a few of the recent findings from current or past Beeson Scholars:

**Longevity and Cognitive Function Associated with Cholesterol-Regulating Gene**
The results of a study by 1997 Beeson Scholar Nir Barzilai, MD, of the Albert Einstein College of Medicine, were published in the December 2006 issue of *Neurology*. Dr. Barzilai’s research examined whether a variant of a particular cholesterol-regulating gene, called the V-type cholesteryl ester transfer protein (CETP) gene, played a role in preserving cognitive function in 158 Ashkenazi Jews with an average age of 99.2. Sixty-one percent of those with the V type CETP gene had good cognitive function, versus 30 percent of those with another type, suggesting that this gene variant may protect individuals from various types of dementia.

**New Technique to Predict Alzheimer’s Disease Progression**
In a study published in the November 2006 issue of *Brain*, a team of University of California, Los Angeles researchers led by Liana Apostolova, MD (2005), used an innovative, 3-D imaging technique to compare the hippocampi of 31 patients with mild cognitive impairment (MCI) with 34 patients with probable Alzheimer’s disease (AD). They found that compared with the MCI patients, AD subjects showed greater atrophy of particular parts of their hippocampi that are responsible for certain aspects of memory. At this point, it is impossible to predict which cases of MCI will convert to AD and which will not. According to Dr. Apostolova, this analytic technique may help solve this problem and allow clinicians to diagnose and initiate treatment at the pre-dementia stage and have an impact on Alzheimer’s disease progression.

**Promise in Treating Alzheimer’s Disease in Mice**
For years, clinicians and physicians have had little to offer AD patients in the way of effective therapies. Current drug treatments can help manage symptoms and can even delay progression of symptoms for approximately six months, but these drugs have had no observable effect on the underlying pathology of AD. That could change if a new drug, known as PBT2, shows as much promise in humans as it has shown in mice. PBT2 is a second-generation chemical designed by a team of scientists led by Ashley Bush, MD, PhD (1995). Dr. Bush focused on PBT2 after studies revealed that PBT1 could reduce beta-amyloid plaques in mouse models of AD.

**Linking Aging and Cancer**
Beeson alumnus Norman E. Sharpless, MD, of the University of North Carolina (2003), along with colleagues Sean J. Morrison, PhD, of the University of Michigan, and David T. Scadden, MD, of Harvard Medical School, recently discovered that the tumor suppressor gene p16-Ink4a is linked to lifespan. Published online in the journal *Nature* on September 6, 2006, the researchers’ three independent articles suggest that efforts to prolong lifespan may have the unwanted side effect of increasing susceptibility to cancer.

**An Ounce of Prevention**
According to Todd Golde, MD, PhD, of the Mayo Clinic College of Medicine (1997), enough is known about the mechanisms of Alzheimer’s disease (AD) to know this: Preventing the devastating neurodegenerative disease is likely to be far easier than finding a cure for it. In a recent study in which monoclonal antibodies were given to mice predisposed to AD, Dr. Golde took a great leap forward in understanding just how it might be done.

**Drink to Your Health?**
After two major studies published in the late 1990s suggested that moderate consumption of alcohol in middle and old age reduced deaths from vascular disease by one-third, many older Americans felt a certain freedom to enjoy one or two drinks a day. But a recent study led by Alison Moore, MD, of the Geffen School of Medicine at UCLA (1998), has found that older men who drink as few as two drinks twice a week and also have certain comorbidities have higher death rates than men who drink less or do not have similar comorbidities. Who is most at risk? Men who have diseases that could be worsened by alcohol or who take medications that could interact with alcohol.
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<th>2006 Scholars</th>
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<tr>
<td>Katrin Chua, MD, PhD</td>
<td>Liana Apostolova, MD</td>
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<td>Assistant Professor of Medicine</td>
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<td>Margaret Fang, MD, MPH</td>
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<td>Alex Federman, MD, MPH</td>
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<td>Emily Finlayson, MD</td>
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<td>Stacy Fischer, MD</td>
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<td>Alfred Fisher, MD, PhD</td>
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<td>Ann O’Hare, MD</td>
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<td>Caterina Rosano, MD</td>
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<td>Assistant Professor of Epidemiology</td>
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<td>University of Pittsburgh School of Medicine</td>
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<td>Manish Shah, MD, MPH</td>
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<td>Consuelo Wilkins, MD</td>
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2004 Scholars

Sandy Chang, MD, PhD
Assistant Professor of Cancer Genetics
University of Texas MD Anderson Cancer Center

Cathleen Colon-Emeric, MD
Assistant Professor of Medicine
Duke University Medical Center

William Dale, MD, PhD
Assistant Professor of Medicine
University of Chicago School of Medicine

Lee Goldstein, MD, PhD
Assistant Professor of Psychiatry
Harvard Medical School

Cary Gross, MD
Associate Professor of Medicine
Yale University School of Medicine

John Lehman, MD
Assistant Professor of Medicine
Washington University School of Medicine

Andrew Lieberman, MD, PhD
Assistant Professor of Pathology
University of Michigan School of Medicine

Atul Malhotra, MD, PhD
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Marcin Sadowski, MD, PhD
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Catherine Sarkisian, MD, MSPH
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Geffen School of Medicine at the University of California, Los Angeles

Clemens Scherzer, MD
Instructor in Neurology
Harvard Medical School/Brigham and Women’s Hospital

Lisa Silbert, MD
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Albert Einstein College of Medicine

2003 Scholars

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Michael Irizarry, MD
Director, Epidemiology
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University of Michigan School of Medicine

S. Holly Lisanby, MD
Associate Professor of Clinical Psychiatry
Columbia University College of Physicians and Surgeons

Jack Parent, MD
Associate Professor of Neurology
University of Michigan School of Medicine

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2003 Scholars
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Henry Paulson, MD, PhD
Professor of Neurology
University of Iowa Carver College of Medicine

Elizabeth Phelan, MD, MS
Assistant Professor of Medicine/Gerontology
University of Washington School of Medicine

Wendy Post, MD, MS
Associate Professor of Medicine and Epidemiology
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Norman Sharpless, MD
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2002 Scholars

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Associate Professor of Neuroscience
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Kristine Yaffe, MD
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Continued
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Continued
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*Continued*

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Charles Thornton, MD  
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