



afar

**Paul B. Beeson
Emerging Leaders
Career Development
Awards in Aging**

2018 Report featuring
the 2016 Scholars



About Paul B. Beeson, MD (1908-2006)



Dr. Paul B. Beeson, a renowned physician, researcher, and teacher, was the inspiration behind the creation of the Paul B. Beeson Emerging Leaders Career Development Awards in Aging Program. It was his vision to increase the number of physicians with a combined clinical, academic, and scientific expertise to care for a growing older population.

At the time of his death, Dr. Beeson was professor emeritus of medicine at the University of Washington. Although “retired,” he remained active in the field of aging research, attending meetings and advising many Beeson Scholars. In his long and distinguished career, he profoundly influenced the career paths of many physician-scientists and was stalwart in his concern for the care and dignity of patients.

To date, 233 scholars supported by the Beeson Program have become leaders in geriatric medicine and aging research throughout the United States and the Island of Ireland. The careers of these remarkable Scholars serve as a lasting testament to Dr. Beeson’s enduring legacy as they seek to provide the best possible care for older adults and train the next generation of leaders in aging research and geriatrics.

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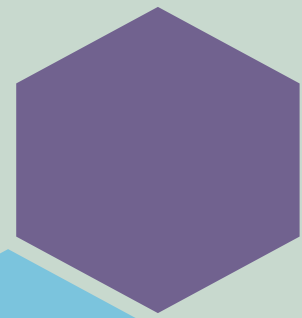
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Letter from Thomas M. Gill, MD

Chair of the Program Advisory Committee

With nine awardees, the 2016 Beeson Scholars are one of the larger classes of recent years—and they may also be the most diverse. They represent nine institutions and eight different disciplines. The class includes four women and five men. In addition, the scholars come from four racial and ethnic groups. This diversity, among scholars all committed to advancing aging research, makes our program strong.

It's also remarkable that, with this class, we have our first Beeson Scholars in the fields of dermatology and gynecology. Another 2016 scholar is a trauma surgeon, one of the few surgeons in more than 20 years of the program. These new scholars have the exceptional opportunity to be leaders in bringing an aging focus to their respective disciplines.

We have been very successful in having former Beeson scholars in one field mentoring scholars in a different field—a necessity for new scholars in fields that are “young” in aging research, and an effective way of leveraging the wide network of Beeson alumni. More traditional within-discipline mentorship remains strong in the Beeson family as well. With the 2016 class, we have a third-generation Beeson scholar—mentored by a scholar who was in turn mentored by a member of the first Beeson class. The continued involvement of Beeson alumni in the program is a testament to its long-term value throughout a scientist's career, and to the strength of our network in aging research.

As in most years, the 2016 Beeson scholars are pursuing diverse approaches to research, from the most basic to the most applied, and also translational research. There is a significant focus on Alzheimer's disease, aligned with the National Institute on Aging's increasing investment in this area. The Beeson program is clearly an outstanding mechanism to achieve major advancements in this field.

The scholars in this year's stellar group demonstrate the wide opportunities within aging research broadly, and also within the specific areas that they investigate. We are delighted to introduce them here.



Thomas M. Gill, MD



NIA Conference Grant provides additional support to the Beeson Annual Meeting

Late last year, the American Federation for Aging Research (AFAR) received funding from the National Institute on Aging (NIA) to support the Beeson Annual Meeting from 2017 to 2021. The grant comes as part of the National Institutes of Health (NIH) Research Conference Cooperative Agreement (or "U13") Program. The NIA already is the primary sponsor of the Paul B. Beeson Emerging Leaders Career Development Awards in Aging with additional support from The John A. Hartford Foundation.

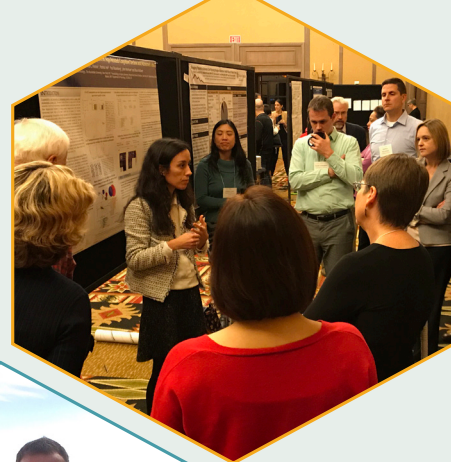
"The Beeson Program is special, and the Annual Meeting is the 'special sauce'" says Kristine Yaffe, MD. "People love coming to it because it's really small, people are engaged, and you've got different generations of scientists—you have some of the pioneers in the field, and you've got current leaders, and a lot of up and coming folks." Dr. Yaffe and Thomas M. Gill, MD, wrote the grant together as multiple PIs.

"I can't think of anything else like this meeting, in that it's all aging related but it's diverse," adds Dr. Yaffe.

"This conference grant further strengthens the partnership with the NIA," says Dr. Gill, who is chair of the Beeson Program Advisory Committee. Going forward, the Annual Meeting will feature a sub-theme aligned with one of the four divisions of the NIA. In 2018 the focus will be neuroscience, and Scott A. Small, MD, director of the Alzheimer's Disease Research Center at Columbia University, will deliver the keynote address.

At subsequent meetings, participants will explore "mini-themes" of geriatrics and clinical gerontology, social and behavioral sciences, and the biology of aging. "These are all very important areas within aging research and gerontology more broadly. So this will provide the scholars with different perspectives and different opportunities across the four divisions within the NIA," says Dr. Gill.

"Our hope is that we'll have greater representation from the NIA scientists who we're going to encourage to come to the meeting, to network and interact, and potentially collaborate, with the scholars," he adds.



In another enhancement to the Annual Meeting made possible by the conference grant, early-stage investigators who are not yet advanced enough in their careers to be Beeson scholars can apply to attend the meeting. In 2017, six of these awards were made. "It's a way of broadening our reach to underrepresented minorities and to people in specialties outside of geriatrics, who may not know much about the Beeson Program, and encouraging them to apply down the line," says Dr. Yaffe.

"The annual meeting is an extraordinary opportunity for an outstanding group of scholars to meet each other and discuss their research in the company of mentors and NIA staff," says Robin Barr, DPhil, director of the NIA Division of Extramural Activities. "It has repeatedly resulted in cross-disciplinary collaborations and new ideas being translated into exciting research. The atmosphere generated by a common determination to advance the field of aging and geriatrics to improve the health and well-being of older Americans is stimulating, invigorating, and just plain fun."

Nathan E. Brummel, MD, MSCI

Assistant Professor of Medicine,
Vanderbilt University Medical Center

Mentors: E. Wesley Ely, MD, MPH, and Thomas M. Gill, MD

LONG TERM OUTCOMES OF PHYSICAL ACTIVITY IN OLDER ADULTS WITH CRITICAL ILLNESS



Some 1.4 million older adults in the U.S. who are hospitalized in an intensive care unit (ICU) for critical illness each year survive. But their bouts with pneumococcal pneumonia, severe sepsis, and other illnesses represent a turning point: up to 75 percent will emerge with new or worsened disabilities that compromise their independence.

For decades, deep sedation and bed rest were believed to be necessary for treating critical illness, practices now known to leave patients in worsened physical and cognitive condition. Today patients are allowed to be awake more and to move around in the ICU. As a result, “some people can reduce the amount of disability they have when they leave the hospital,” says Nathan E. Brummel, MD, MSCI. “But we don’t know if that matters for them long-term.”

Dr. Brummel’s Beeson project is the first study to objectively quantify patients’ activity during critical illness and investigate how it is associated with disability, and with physical and cognitive function. The study will enroll 312 critically ill patients from medical and surgical ICUs at Vanderbilt University Medical Center. During their stay in the ICU, participants will wear a type of motion sensor, called an ActiGraph, which records their movement.

After three and twelve months, Dr. Brummel and his research team are following-up with in-person assessments of participants’ health, to find out how well they can move around, care for themselves, and take care of daily activities. They will also evaluate participants’ thinking and memory.

To better understand risk factors for disability after critical illness, Dr. Brummel is also seeking out the physiological mechanisms that underlie declines in a person’s ability to function. “The area that we are studying right now is inflammation,” he says, which is measured by biomarkers in blood samples drawn from participants at the time of hospital admission and shortly before discharge.

“Critical illness is a huge inflammatory insult,” he says. “It may be that some people resolve their inflammation and do well after critical illness, whereas others develop chronic inflammatory states leading to disability.”

Understanding these relationships “is an important step toward returning ICU survivors to independent function,” says Dr. Brummel, and the need is urgent. The number of people who are developing sepsis and who need mechanical ventilators has been increasing for a number of years.

Older adults account for part of this increase. But Dr. Brummel notes that overall, patients in the ICU are sicker—the number of people developing organ failures, including kidney and respiratory failure, is also rising. In addition, older adults who are frail before admission to the ICU have more difficulty afterward—and frailty, too, is not limited to people older than 65. In other research supported by his Beeson award, Dr. Brummel and colleagues found that about 20 percent of younger patients entering the ICU are frail, and these frail patients experience declines in function after a critical illness the same as older adults.

Yet most medical personnel in the ICU are not well versed in aging principles, including the risks of critical illness to older or frail patients. To “bring an aging message into the ICU,” Dr. Brummel is working with 2017 Beeson Scholar Lauren Ferrante, MD, MHS, of Yale University. In an endeavor that is true to the Beeson program’s goals of fostering emerging leaders and promoting collaboration, they have formed the Aging in Critical Care Interest Group within the American Thoracic Society, the largest international society of pulmonary and critical care doctors in the world.

“Aging research and geriatric care have not been the focus in the ICU,” says Dr. Brummel, “but they should be as the population ages.”

Zara Cooper, MD, MSC, FACS

Assistant Professor of Surgery,
Harvard Medical School / Brigham and Women's Hospital



Mentors: Susan L. Mitchell, MD, MPH, and Ronnie A. Rosenthal, MD

BEYOND 30-DAYS: PATIENT-ORIENTED OUTCOMES AMONG OLDER ADULTS AFTER EMERGENCY GENERAL SURGERY

For older adults, the hazards of emergency surgery are well-documented: the risk of death is three times higher than after elective surgery, and two to seven times higher than for younger emergency surgery patients. Up to half of older adults experience complications after emergency surgery, and most are discharged to nursing homes.

Yet little is known about patients' well-being beyond these specific surgery-related outcomes, usually evaluated 30 days after the procedure. "For older adults who may just have a number of months to live, that 30-day mortality number isn't quite as valuable as, what will that time be like?" says Zara Cooper, MD, MSC, FACS.

"We really don't have any great understanding of, what will your function be like?" she continues. "What kinds of activities will you be able to do? Will you still be living at home versus being in a nursing facility? How many times will you be re-admitted to the hospital? And then, what is that experience like for your family?" These questions are critical for older adults, because maintaining function and independence often are what they value most.

Dr. Cooper's Beeson research strives to enhance understanding of quality of life in the year after surgery. Ultimately, the goal is to help older people undergoing emergency surgery to be involved in making informed decisions about their care.

Identifying factors associated with better outcomes is the first step. To this end she is analyzing data from more than 650,000 Medicare claims, including survival, nursing home use, rehospitalization, and hospice use, among older adults 12 months after emergency surgery. Then she will compare the results to data from similar patients hospitalized for three common medical conditions: pneumonia, congestive heart failure, and heart attack.

This comparison could help in communicating with patients about the long-term impact of their surgery. In research that led up to her Beeson award, Dr. Cooper used Medicare data to investigate outcomes of patients with a broken neck sustained in a fall. She compared the results to those for patients with hip fracture.

"Both physicians and the lay public understand the impact of a hip fracture on an older adult," says Dr. Cooper. But her study found that that patients with cervical spine fracture were more likely to die—and this point of comparison proved especially helpful in bringing the future into focus during conversations with patients and families. "If you can relay the information to the family that this is worse than hip fracture, they seem to understand better what the impact will be," she says.

For her Beeson research, Dr. Cooper is also using surveys to follow-up with a cohort of 150 older adults after emergency general surgery every three months for up to a year, "so that we can understand aspects of their trajectory, including cognition, physical function, symptoms, quality of life, and depression."

With a smaller group of 20 patients and their care partners, Dr. Cooper is carrying out semi-structured interviews to elicit a more in-depth understanding of their experience—and identify ways to improve a host of issues that arise in the year after emergency surgery including doctor-patient communication, advance care planning, managing symptoms, negotiating transitions in care, and taking care of caregivers.

Dr. Cooper credits her Beeson mentors with helping to strengthen the methodology that guides her research, and with providing the opportunity to be involved in creating national standards of care for geriatric surgery patients. Mentorship through the Beeson award has "helped my work evolve toward thinking about those things specifically for palliative care and surgery," she says, "which is a passion of mine."

Eleni Linos, MD, MPH, DrPH

Associate Professor of Dermatology,
University of California, San Francisco

Mentors: Kenneth E. Covinsky, MD, MPH, Mary-Margaret Chren, MD,
and Louise C. Walter, MD

INVOLVING OLDER ADULTS IN DECISION MAKING FOR SKIN CANCER



Each year American dermatologists treat tens of millions of slow-growing skin lesions, such as basal and squamous cell carcinoma, and actinic keratosis. These skin cancers and pre-cancers result from exposure to the sun over a lifetime, so it's no surprise that they are more common among older adults.

But dermatology as a specialty does not yet tailor its practices to older adults, according to Eleni Linos, MD, MPH, DrPH. And a one-size-fits-all approach to treating skin lesions fails to account for the different needs, priorities, health issues, and life expectancies of older adults.

"For many frail, older adults at the end of life, the risks of treatment of these low-risk but highly prevalent tumors may often outweigh the benefits," says Dr. Linos. As a resident, she was struck by one patient in particular. "It was my job to call him every time I diagnosed yet another basal cell carcinoma, and tell him he had to come back in for surgery, again. I had to do this every couple of months, and I didn't feel we were offering the best care given his other medical circumstances," she says.

So with her mentors, Dr. Linos began to "think critically and in a data-driven way" about these issues. In research that preceded her Beeson award, she found that among older adults treated, mostly surgically, for skin cancer, more than a quarter said they had a problem afterward—a complication like bleeding or infection. "That number is huge," she says, "even though not all of those were true medical complications the way a physician would classify them."

Dr. Linos is testing the hypothesis that older adults who are fully informed and engaged in making decisions about their treatment will choose more conservative options for treating skin lesions. This choice would likely lead to fewer complications and better quality of life.

First, using the Health and Retirement Survey, a national database, Dr. Linos is gathering data on how skin cancers are treated in patients who are nearing the end of life. She also is conducting focus groups and interviews with

patients, caregivers, and physicians to better understand what they know about basal cell skin cancers and their preferences for treatment.

Ultimately the research will lead to an evidence-based tool to help patients, families, and caregivers make better decisions about their skin cancer treatment. "I'd love to be able to offer older adults with skin disease better care, and change the way we approach this problem with them so that it is much more a shared decision. I want patients to really be aware of risks and benefits and feel empowered to make decisions in the context of their own health."

In addition to funding the research, the Beeson award supports career development, which played a role for Dr. Linos in her promotion to associate professor. She adds that, "The mentorship I have received as part of the Beeson program has been incredible—not only because of the inspiration and excitement that comes with joining this phenomenal group of researchers, but also because of the practical and focused advice I received," she says. "The Beeson program has also taught me what exceptional mentorship looks like, so that I can pass this forward to my own mentees." Dr. Linos was selected as a Tideswell Emerging Leader in Aging in 2018 and was invited to give the Keynote lecture at the 2018 annual meeting of the the British Association of Dermatologists in Edinburgh, UK on this topic.

As a trailblazer for geriatric dermatology, Dr. Linos has created the first American Academy of Dermatology (AAD) Geriatric Dermatology Expert Resource Group, which is planning to meet at the 2019 annual AAD meeting. She already has the opportunity to support junior researchers. "Before receiving the Beeson award I didn't know of anyone interested in this field of geriatric dermatology, and now it feels like there's just tremendous enthusiasm," she says. "I hope this is the beginning of a field that will have major impact on the care of older adults with skin disease, and that I can continue to support other dermatologists to join the Beeson program in the future."

Brendan P. Lucey, MD

Director, Sleep Medicine Center,
Assistant Professor of Neurology,
Washington University in St. Louis



Mentors: Randall J. Bateman, MD, and David M. Holtzman, MD

SLEEP QUALITY AND HUMAN AMYLOID-BETA KINETICS

"It's been known for a long time that Alzheimer's patients have a disturbed sleep-wake cycle," says Brendan P. Lucey, MD. "They're up at night, or they're napping during the day. Anyone who has taken care of someone with Alzheimer's can attest to that."

In the last decade, research has found that that disrupted sleep can develop years in advance of Alzheimer's dementia. It may even be a risk factor for the disease or a marker for the underlying changes in the brain.

In 2012, Dr. Lucey, a neurologist, joined the faculty of Washington University in St. Louis to work with two researchers who pioneered studies of the relationship between sleep and beta-amyloid protein, which forms the hallmark plaques found in the brains of people with Alzheimer's disease (AD).

Both were former Beeson scholars. David Holtzman, MD, a member of the first Beeson class, was the first to show in laboratory animals that brain levels of beta-amyloid protein normally rise and fall with the sleep-wake cycle. Randall Bateman, MD, who was mentored by Dr. Holtzman, discovered a similar diurnal fluctuation in beta-amyloid in healthy people. Further studies showed that, in laboratory animals, sleep deprivation accelerates the formation of beta-amyloid plaques in the brain. The opposite holds true as well—inducing the animals to sleep more results in less beta-amyloid, and fewer plaques.

In a study underway before receiving his Beeson award, Dr. Lucey began testing the findings from animal studies in research with human subjects. He found that in people who were completely sleep-deprived, the overnight levels of beta-amyloid protein in cerebrospinal fluid (CSF) increased up to 30 percent compared to control participants who were allowed to sleep. The result suggests a mechanism by which disrupted sleep could increase the risk of AD.

"But no one is going to be completely sleep deprived for long enough to increase the risk of AD," he says. "The missing piece is that no one has shown that in humans you can improve sleep and decrease beta-amyloid levels."

Dr. Lucey's Beeson research aims fill in that piece. With Drs. Holtzman and Bateman as his mentors in carrying the work forward, he says, "I'm a third generation Beeson Scholar; a Beeson grandson."

Dr. Lucey's study, which is enrolling 45 volunteers, parses the differences in CSF beta-amyloid between good sleepers and poor sleepers, and between poor sleepers who take a sleeping aid and those who don't. For two weeks, study volunteers wear an actigraph, a device that measures activity and light exposure, on their wrists to monitor when they go to bed and to sleep. Each volunteer also keeps a sleep diary to back up this data.

"The end goal of these projects," says Dr. Lucey, "is to provide the preliminary data to support doing a clinical trial using sleep to prevent beta-amyloid deposition or progression of beta-amyloid deposition."

Once a person has dementia and sleep problems, it's difficult to study the connections or to intervene. "What's exciting about these developments," says Dr. Lucey, "is to use sleep therapy to prevent Alzheimer's." Yet he cautions that, even if his Beeson project is successful, improving sleep likely will not be simple or disease-altering for all people at risk of AD.

About the Beeson program, Dr. Lucey says "the annual meeting is one of the best things about it. It's always so exciting to interact with people who are doing great work. And I really like being exposed to aging research in areas that I'm not thinking about all the time."

Hillary Lum, MD, PhD

Assistant Professor of Medicine,
University of Colorado School of Medicine and
VA Eastern Colorado GRECC

Mentors: Cari Levy, MD, PhD, and Jean S. Kutner, MD, MSPH

REFINING AN ADVANCE CARE PLANNING GROUP VISIT INTERVENTION: A NOVEL INTERVENTION TO ENGAGE



"I've personally seen how advance care planning can benefit the lives of my family members," says Hillary Lum, MD, PhD. "During difficult conversations with my grandmother, I realized the importance of honoring her preferences, even when I wouldn't have chosen that for myself. It's important, as a physician, to really hear what someone wants—and make it easier for them to share that with the people around them."

Although advance care planning helps people receive treatment that aligns with their values, only about a third of Americans have completed at least part of the process. In the healthcare system where she works, Dr. Lum says just 12 percent of people have an advance directive on file in their medical record.

Dr. Lum's research aims to engage older adults in this process. "We really want to provide opportunities to make it easier for patients," she says. To that end, she is testing the feasibility of group medical visits for advance care planning.

Supplementing one-on-one visits with group visits is an idea that has gained traction in recent years, especially for patients with chronic diseases. During group visits, medical staff can provide additional care and address patients' questions at length. Family medicine practices are increasingly arranging group visits that allow people with a chronic disease, like diabetes, to find out how to manage their condition and learn from the experiences of others.

"We adapted that model to talking about advance care planning—even for individuals with very different health needs," says Dr. Lum.

Advance care planning requires many steps, over time. In addition to having conversations with their doctors, people need to consider their own wishes and values, have conversations with family members, complete documents, and ensure that their documents are on file in their medical records.

"We recognized that patients often have questions that they aren't able to get answered in the one-on-one clinic or by going to their lawyer," says Dr. Lum. "Also, the support of the group dynamic is encouraging to patients. There's an opportunity to learn from someone else's situation."

In earlier work, Dr. Lum demonstrated that participating in a prototype group visit for advance care planning increased family discussions and filing of documents in the medical record for older adults. Her Beeson project takes the next step toward standardizing this intervention.

This pilot study is evaluating whether the advance care planning group visit model is feasible and acceptable to patients, and also to primary care provider staff. It compares participants who take part in group medical visits with participants who receive advance care planning materials by mail. At three months and six months after baseline, the researchers will interview participants and examine their medical records to find out whether they have had conversations with family about their planning, and have documents on file. The research lays the groundwork for a larger scale, multi-site, randomized clinical trial of implementing the group visit.

In addition, Dr. Lum has developed an implementation manual, which takes into account her research team's observations of how clinics might want to adapt the model to meet the needs of their patients or resources. For example, different patient populations or clinics may prefer particular advance directives or decision aids, require materials in different languages, or need materials written for varying levels of health literacy.

For Dr. Lum, the Beeson award has opened the door to collaborations with former Beeson scholars. In addition, she says, "one of the great things about having a career development award is the time and space to develop knowledge, research expertise, and leadership skills."

Ana Pereira, MD

Assistant Professor of Neurology and Neuroscience,
Icahn School of Medicine at Mount Sinai

Mentors: Bruce S. McEwen, PhD, John H. Morrison, PhD, and
Patrick R. Hof, MD



ENHANCING GLUTAMATE TRANSPORT IN AGE-RELATED COGNITIVE DECLINE AND ALZHEIMER'S DISEASE

While Ana Pereira, MD, was a medical student in Brazil, she had the opportunity to translate the classic textbook, *Principles of Neural Science*, by Nobel laureate Eric Kandel and colleagues. "I was fascinated by how complex the brain is," she says, "and I really wanted to understand how memory, learning, emotion, language—all those cognitive processes—happen in the brain."

That experience set her on the path to becoming a physician-scientist focusing on Alzheimer's disease (AD), the most common neurodegenerative disorder, and one that dramatically affects cognition. "I knew I wanted to do research—and I wanted to expand my training so that I could do research that is also relevant to improving human health," says Dr. Pereira.

Her work today investigates changes in the brain that occur with both aging and AD; in particular, deterioration of the brain's synapses, the points of communication between neurons. The cells most affected are in areas that are critical to learning and memory, and use a chemical messenger called glutamate to carry signals across synapses. With aging, these connections weaken; and with AD, they are significantly lost.

Dr. Pereira is researching at the molecular level how synapses fail. It turns out that glutamate levels are regulated by another molecule, called glutamate transporter, which ferries glutamate to the synapse and ensures that it is in the right place, at the right time, and in the right quantity, for learning and memory to occur. In both aging and AD, the brain decreases its production of glutamate transporter.

Faulty glutamate signaling can have many consequences. For example, if glutamate spills into the wrong place, neurons can be damaged. Recent research also suggests that changes in glutamate activity can increase the toxicity of amyloid-beta and tau proteins in the brain, which are hallmarks of AD.

"If you can efficiently target the degenerating synapse, that could potentially have a very important impact in terms of cognition," says Dr. Pereira. In research published before her Beeson award, she and colleagues stud-

ied glutamate signaling in the brains of aged rats. They found that boosting glutamate transporter could prevent age-related cognitive decline, and they discovered a mechanism to explain how synapses were strengthened.

Dr. Pereira's Beeson project further investigates the role of glutamate transporter in cognitive aging and AD. In studies with laboratory mice genetically engineered to develop AD, she and coworkers are testing the effects of increasing glutamate transporter on cognition and on levels of beta-amyloid, tau, and other molecules. Other experiments focus on cognition in mice engineered to lack glutamate transporter to further understand its function.

Ultimately, new therapies for AD might be aimed at the glutamate transporter. In animal studies, Dr. Pereira and coworkers have increased glutamate transporter using riluzole, a drug that is FDA-approved to treat amyotrophic lateral sclerosis (ALS). They also are testing riluzole in a small clinical trial with participants already diagnosed with AD.

"Riluzole enhances these transporters, but modestly," says Dr. Pereira. For a drug that could potentially treat AD, "we want something much more efficacious. So we have started a drug screening program for more efficient enhancement of the transporters."

"Launching a scientific career depends on success at so many levels," she adds, and the Beeson award helps with all of them. "You have to do great science, you have to collaborate with the right people, you have to navigate the process of writing successful grants." At the Beeson annual meeting, "You get to know these people who are future leaders in aging very well. It's critical for collaborations, and for getting advice. The Beeson scholars really form a community."

Tony E. Rosen, MD, MPH

Assistant Professor of Medicine,
Weill Cornell Medicine

Mentors: Mark S. Lachs, MD, Karl A. Pillemer, PhD, and
Terry Fullmer, PhD, RN, FAAN

IDENTIFYING INJURY PATTERNS AND FORENSIC BIOMARKERS DIAGNOSTIC OF PHYSICAL ELDER ABUSE



A cognitively impaired older man arrives in a hospital emergency department with a large bruise around his left eye socket. The son who brought him in says the man fell, but a physical exam is inconsistent with this explanation. Was the bruise caused by an accident or an intentional injury? What happens next?

“Victims of elder abuse present to emergency medicine physicians commonly—but we’re treating their medical complaint and not identifying that they’re victims,” says Tony E. Rosen, MD. “Developing a multidisciplinary approach for doing this, and measuring its efficacy and impact, is an important future step in improving care for these victims.”

In fact, most elder abuse goes undetected, even though between 5 and 10 percent of older adults are the victims of neglect or physical, sexual, or psychological abuse. As the baby boomers age, the number of people affected will increase.

With his Beeson award, Dr. Rosen is developing a clinical prediction rule, a tool to help busy emergency department staff identify, report, and intervene in cases of elder abuse. Emergency departments are already on the front-lines of screening for child abuse. In Rosen’s view they provide a unique opportunity to identify signs of elder abuse as well.

For example, because emergency visits are unplanned, medical staff can readily see if a patient’s personal hygiene needs have been regularly attended to. In addition, paramedics bringing in the patient often have had the opportunity to see inside the person’s home and could assess whether it is a safe environment. Nurses who provide bedside care have the opportunity to talk with, and observe, patients and family members. Patients also have conversations with technicians and others who transport them within the hospital.

Still, it can be difficult to be certain whether injuries are accidental or inflicted. Emergency department staff need both training and a reliable way to identify injury patterns, physical findings, and other signs associated with elder physical abuse. To create such a tool, Dr. Rosen is

carrying out a prospective study to compare physical findings in abuse victims to those of geriatric patients who have been injured in accidental falls. He will add to that a comparison of laboratory and radiology exam results in the two groups.

Identifying and recruiting study participants is a team effort, carried out through partnerships with the New York City Elder Abuse Center, the New York City Department for the Aging, Adult Protective Services, prosecutors’ offices, and Emergency Medical Services, as well as through emergency department evaluation.

Within the emergency department, Dr. Rosen’s research is highly collaborative as well, utilizing the knowledge and participation of emergency medical services providers, triage providers, nurses, radiologists, radiology technicians, social workers, and case managers.

The project builds on Dr. Rosen’s long-term relationships with these experts and agencies, and his earlier research focusing on injury patterns gleaned from the legal files of cases of elder abuse. In those studies he and colleagues developed a comprehensive classification system for acute geriatric injuries and a protocol for standardized photography of acute injuries.

“For me, one of the exciting things about the Beeson Award has been joining such an extraordinary community of scholars that is focused on collaboration,” says Dr. Rosen. As a Beeson scholar, he also is pursuing formal training in forensic sciences and medico-legal investigation of death. In addition, the Beeson award provided him the opportunity to develop policy-making expertise by attending the John A. Hartford Foundation Policy Institute in Washington DC.

“Ultimately, we want to improve the ability of health care providers to identify and protect victims of physical elder abuse, who are among the most vulnerable older adults,” he says.

Phillip P. Smith, MD, FPMRS

Associate Professor of Surgery
University of Connecticut, Farmington



Mentors: George A. Kuchel, MD, FRCP, AGSF, Lori A. Birder, PhD,
Laura Haynes, PhD, and Eric S. Levine, PhD

REGULATORY MECHANISMS IN A HOMEOSTATIC MODEL OF GERIATRIC VOIDING PROBLEMS AND INCONTINENCE

"Urinary symptoms, especially as we age, are a critically important problem," says Phillip P. Smith, MD. "Urinary incontinence, frequent and urgent needs to urinate, and difficulty emptying, are distressing and costly, exceeding the total costs of all cancer care in the United States."

However, although symptoms in older people contribute to social isolation and institutionalization, too often they have not received the attention they deserve. But attitudes towards urinary control problems are changing. "If our grandparents got wet, they chalked it up to old age. But I think the baby boomers and beyond are going to be highly intolerant of this problem," says Dr. Smith.

Aggravating the problem is that available therapies are less than optimal, especially in the elderly. Dr. Smith points out that this might be because the idea behind current therapies is overly simplistic. "The idea that symptoms indicate overactive and underactive bladder muscle is clearly untrue," says Dr. Smith. Furthermore, in research leading up to his Beeson award, he showed that the bladder muscle does not necessarily lose strength as it gets older, and confirmed that the sensitivity to what's in the bladder actually decreases.

Dr. Smith's Beeson research is investigating the aging bladder, and mechanisms why older people are more likely to become symptomatic. Dr. Smith has re-framed urinary control as an adaptive system. "Thinking of urinary symptoms as something wrong with the bladder is too limiting," says Dr. Smith. "Urinary control is really evidence of an adaptive system working well," he says. "It explains why some people do well and others don't. Whether it's genetic or environmental, some people just have better adaptive systems than others." Designing new ideas for prevention and treatment means thinking less about what is wrong with the bladder, and more about what went wrong with the aging system. In results of his Beeson research published this year, Dr.

Smith describes a possible contributor to the risk of adaptive failure. In experiments with mice, he is investigating how a molecule called the HCN ion channel can affect how the bladder responds to brain control. HCN channels regulate electrical signals throughout the body, and were only recently found in the bladder. In other body systems, HCN declines with aging are paralleled by diminished adaptive reserve, leading Dr. Smith to suspect a similar problem in the bladder.

His research has confirmed that HCN channels play an important age-dependent role in brain control over bladder function, as well as discovering that there is a decline in HCN channels with aging. "The importance of these results is they provide evidence for a loss of controllability without requiring a sick or damaged muscle. We are hopeful that as we gain a better understanding of how this adaptive system works we will be able to define new treatment approaches," says Dr. Smith.

Dr. Smith spent many years in clinical practice before pursuing basic science. Participating in the Beeson program has provided crucial mentoring and research support to make the transition to physician-scientist. "Too often clinicians and clinical research are too far removed from understandings of basic mechanisms, yet without a clinician's input it is hard for the basic scientist to know the clinical relevance of their research directions. I believe real progress requires bridging that gap."

"The Beeson program has provided me the critical opportunity to contribute to improving our science and thus care for our older patients."

Andrew F. Teich, MD, PhD

Assistant Professor of Pathology and Cell Biology
Columbia University Medical College

Mentor: Scott A. Small, MD

AN INTEGRATIVE ANALYSIS OF DNA METHYLATION, TRANSCRIPTOMIC CHANGES, AND COGNITIVE DYSFUNCTION IN ALZHEIMER'S DISEASE



Aging is the number one risk factor for Alzheimer's disease (AD). And "diseases of aging tend to be really complicated," says Andrew F. Teich, MD, PhD. "By the time you get into your 70s and 80s the slings and arrows of an entire life add up in a complex way."

AD, for example, involves many changes in the brain that can take decades to manifest as dementia. More than any other change, however, a decline in synapses—the communication points between neurons in the brain—correlates best with memory loss and cognitive decline in AD.

What goes awry to cause brain synapses to break down in AD, and disrupt neuronal communication? Dr. Teich's research places this question in the methodological crosshairs of computer science and molecular biology.

"The increasing amount of data that's becoming available to medical researchers is really exciting," he says. One type of data is called RNA sequencing data. All of the body's cells contain the same genes, encoded in DNA. But only a portion of these genes are in use at any time, and which ones are "turned on" varies depending on the cells. RNA encodes a transient message of which genes are working, and RNA sequencing data provides a snapshot of cellular activities.

In studies that preceded his Beeson award, Dr. Teich analyzed RNA sequencing data from human brain tissue preserved in a brain bank. One result of this work was a better understanding of which genes orchestrate cellular communication at the synapses.

For his Beeson project, Dr. Teich is studying RNA sequencing data alongside well-known cellular hallmarks of AD in small pieces of brain tissue from patients with hydrocephalus. Patients with hydrocephalus sometimes undergo shunt surgery to facilitate drainage of excess cerebral spinal fluid that is causing the hydrocephalus. A tiny sample of brain tissue is sometimes removed during surgical installation of this shunt drain.

Hydrocephalus is unrelated to AD, but the aged patient population that typically undergoes this procedure is also at risk for developing Alzheimer's disease, and some of these patients show early signs of Alzheimer's pathology. Dr. Teich and his coworkers are using sequencing technologies to screen this brain tissue, find out which genes are being disrupted, and tease out changes that correlate to known markers of AD progression.

The next question will be, "can we do something about that?" says Dr. Teich. "AD tends to hit at the end of life. But if we just delay the onset by 5 years, it'll have an outsized impact on the total prevalence in our society."

The Beeson award has "afforded me time to really build my identity as a physician-scientist," says Dr. Teich. "My background is in computational biology, looking at how neurons process information, so I did a lot of work with big data sets. But I never dealt with sequencing data, or genetics or genomics. I really needed the time to learn how to analyze that kind of data."

Dr. Teich also credits the Beeson annual meeting with playing a role in his research success. "It helps you in so many ways," he says. "The best part about it is the people who come back. It's so beneficial to the trainees to be in this really small meeting with all of these successful senior people, who can offer objective advice—but you also just get to know them. And then you know people around the country who you can contact when you have a question. That's really useful."

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