

PUSHING BOUNDARIES

Dear friends and colleagues,



We all hope to fully embrace life, fit and free of infirmity, as we pass the boundary into our later years. It's a boundary that keeps shifting, expanded further and further out by advances in science and medicine. Older adults today live active and independent lives far beyond the age of their parents and grandparents.

The work of moving that boundary inexorably forward is part of the mission of UF Institute on Aging faculty, who have always strived to lift the veil on the processes of aging.

The past several years have been challenging for us all as we navigate a relentless pandemic that has caused all too much suffering. COVID-19's worst consequences disproportionately target older adults. This plague's tragic repercussions, reaching into so many lives, reinforce the importance of our work. By better understanding the biology of aging and the nuances of clinical care, medicine is ever better positioned to respond to a health crisis.

I am proud that our team has maintained through the pandemic its mission to promote the health, independence and quality of life of older adults through research, clinical care and education. There is an honorable calling that ultimately benefits all Floridians.

As the coronavirus pandemic began in 2020, we had just celebrated our 15th anniversary. Our work never stopped, despite myriad challenges. And we look forward to a robust future.

Indeed, we welcomed four new faculty members in 2021: **Stephanie Wohlgemuth, Ph.D.**; **Christopher N. Kaufmann, Ph.D.**; **Dejana Braithwaite, Ph.D.**; and **Sudeshna Chatterjee, Ph.D.**

The UF Institute on Aging continues to be a leader in aging research.

Marco Pahor, M.D.
Director, UF Institute on Aging





NO PAIN, NO GAIN

It's a conundrum that often faces people with peripheral artery disease, or PAD, a condition involving a narrowing of arteries that restricts blood flow to the limbs.

Rigorous walking is usually recommended as the only useful therapy to maintain and improve mobility for those with PAD. But a stroll often causes severe leg pain and discomfort, which leads to less walking.

Might people with PAD walk at a slower, painless pace while still benefiting from the exercise? A study co-authored by UF Institute on Aging researchers suggests no pain, no gain.

A randomized, multi-institutional clinical trial involving about 300 patients with PAD found those who walked briskly with pain were able to dramatically improve their walking ability compared with those who walked at a slower, pain-free pace. In fact, the group walking at a more leisurely pace showed no greater improvement in mobility than a control group who didn't walk at all.



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Christiaan Leeuwenburgh, Ph.D., works in a UF Institute on Aging lab.

"High-intensity walking is a treatment, and sadly, not all treatments are comfortable," said Todd Manini, Ph.D., a professor in the UF Institute on Aging. "Nobody wants to push themselves to the point where they feel discomfort. This study was the test of the idea that, if you don't feel that discomfort, then you aren't going to get the benefit."

Even though this slower group could walk for twice as long as those in the faster group because

they weren't in pain, nonetheless they did not improve.

"This study is a huge step forward," said Christiaan Leeuwenburgh, Ph.D., a professor at the institute. "Physicians sometimes say, 'Hey, don't go over the threshold of pain. Slow down.' But no pain, no gain."

BREAST DENSITY AND CANCER RISK

Physicians have long recognized that women with denser breasts are at increased risk of invasive breast cancer, heightening the importance of mammography screenings.

A paucity of data, however, established such a risk in women age 65 and older, and virtually no data existed for women age 75 and older.

A large study led by a UF Institute on Aging population scientist examined data from more than 193,000 women age 65 and older, including more than 70,000 who were at least 75, and found a positive association between breast density and breast cancer risk.

The study fills a gap of information with possible implications on the decision-making of older women considering a breast cancer screening mammography, said the study's senior author, Dejana Braithwaite, Ph.D, the associate director of population sciences at the UF Health Cancer Center and a professor in the UF Institute on Aging.

“
Our goal is to develop the evidence that helps personalize breast cancer screening for older women.”

— Dejana Braithwaite, Ph.D.

“This study provides evidence that breast density remains an important risk factor in older women and should be included in risk prediction models that also consider life expectancy to help identify women who may benefit most from continued screening,” said study co-author Diana L. Miglioretti, Ph.D., a researcher at the University of California, Davis.

Advani SM, Zhu W, Demb J, Sprague BL, Onega T, Henderson LM, Buist DSM, Zhang D, Schousboe JT, Walter LC, Kerlikowske K, Miglioretti DL, Braithwaite D; Breast Cancer Surveillance Consortium.

Association of Breast Density With Breast Cancer Risk Among Women Aged 65 Years or Older by Age Group and Body Mass Index. JAMA Netw Open. 2021 Aug 2;4(8):e2122810. doi: 10.1001/jamanetworkopen.2021.22810.





The long-term effects of statins on skeletal muscle and the brain are not well documented. PREVENTABLE is designed to address these important questions.”

— Marco Pahor, M.D.

STATIN BENEFIT EXPLORED

Can taking a statin a day keep heart disease and dementia away in seniors ages 75 and older?

Researchers at University of Florida Health and the OneFlorida Clinical Research Consortium have joined a nationwide clinical trial to find out whether taking atorvastatin (Lipitor®), a drug commonly used to lower cholesterol, can help prevent dementia, disability and heart disease in older adults who haven’t already been diagnosed with those ailments.

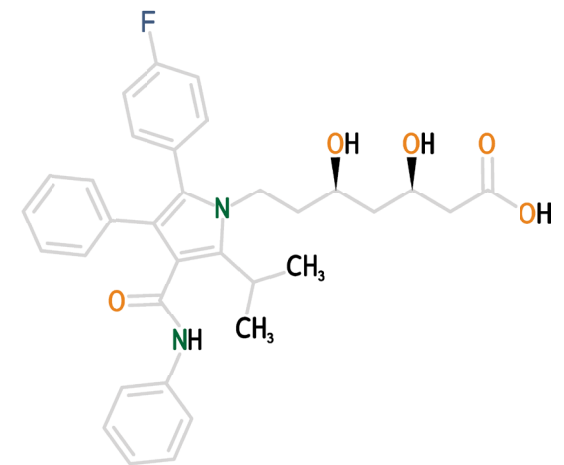
The study, expected to become one of the largest clinical trials ever conducted in older adults, will include more than 20,000 participants and 100 sites across the U.S., including UF Health and several other OneFlorida Clinical Research Consortium partner sites.

Recent studies suggest statins may continue to protect the heart and vascular system even after age 75. Preliminary evidence also suggests statins may protect against Alzheimer’s disease and contribute to overall well-being in adults ages 75 and older.

“There’s so much we don’t know about the benefits versus risks of using statins in older people,” said Marco Pahor, M.D., director of UF’s Institute on Aging and UF Health site principal investigator for the PREVENTABLE trial. “The long-term effects of statins on skeletal muscle and the brain are not well documented. PREVENTABLE is designed to address these important questions.”

During the PREVENTABLE study, participants without heart disease and dementia will be randomly assigned to receive either atorvastatin or a placebo. Researchers will follow participants for up to five years and test their memory, thinking and physical abilities. Participants will also be monitored for events such as heart attacks or strokes.

Researchers hope the large size of the study population will help them identify subgroups of older adults who are most likely to benefit from taking statins to prevent dementia, disability or cardiovascular disease.



UNDERSTANDING BRAIN MATTER LOSS

A new UF Health study of non-Hispanic Black and non-Hispanic white adults links chronic knee pain and key demographic factors to differences in areas of the brain tied to memory.

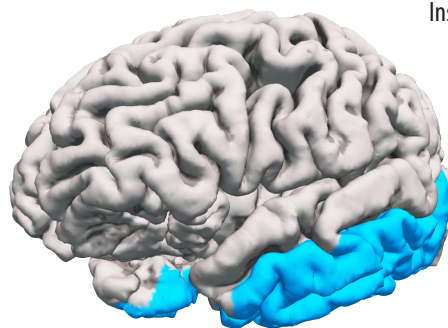
Participants who reported higher stages of pain and lower levels of income and education and less access to health insurance had thinner gray matter in these regions than those also experiencing higher stages of pain but who reported higher levels of income, education and greater access to health insurance.

Participants with higher stages of pain and lower sociodemographic factors had about 4% less gray matter in the temporal lobe than those in the same sociodemographic group with lower stages of pain.

"As we get older, typically starting around our mid-50s to mid-60s, we lose about half a percent of our gray matter per year," said Jared Tanner, Ph.D., the study's lead author and an assistant professor of clinical and health psychology in the UF College of Public Health and Health Professions. "So a 3%-4% difference could be thought of as an additional six to eight years of aging in the brain."

The area of the brain where the gray matter loss occurred is predictive of cognitive decline, indicating a greater risk of dementia or Alzheimer's disease.

"The body and the brain are adaptive to stress to a certain point," said the study's senior author, Kimberly Sibille, Ph.D., an affiliate faculty member of the UF Institute on Aging and an associate professor in the UF College of Medicine's departments of physical medicine and rehabilitation and anesthesiology. "But with persistent stressors that are more intense and longer duration, eventually the body's response is no longer adaptive and changes start occurring in the other direction." More research is needed. But findings suggest some people at risk of gray matter loss might benefit from earlier identification and pain treatment, researchers said.



GARLIC AND GOOD HEALTH

Researchers at the UF Institute on Aging are testing the ability of aged garlic extract, or AGE, to reduce levels of chronic inflammation and improve cognitive and physical performance in older adults at 60 years in age.

Growing evidence strongly indicates chronic low-grade systemic inflammation might play a significant role in contributing to sarcopenia (muscle loss from aging), functional decline and ultimately disability.

Inflammation is a vital part of the body's immune response. It is the body's attempt to heal itself after an injury; defend itself against foreign invaders, such as viruses and bacteria; and repair damaged tissue. Without inflammation, wounds would fester, and infections could become deadly. So in many ways, acute inflammation is "good" and helps the body heal itself when injured.

If inflammation does not subside, however, it can be problematic. Research increasingly indicates that chronic inflammation does indeed increase the risk of many chronic diseases, and also negatively affects cognitive and physical function as people age. For this reason, treatments are needed that can help reduce the rise in chronic inflammation that seems to occur with aging.

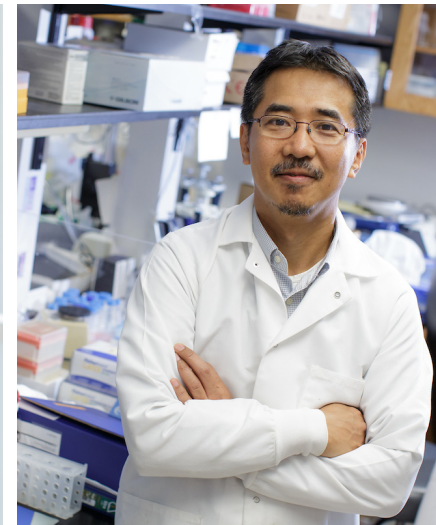
AGE is a natural health food made of fresh garlic under regulated temperature and humidity conditions and is generally recognized as safe by the U.S. Food and Drug Administration. AGE has been found in preclinical studies to enhance cognitive functions, including spatial learning and memory, as well as protect neurons against free radical damage.

The goal of the AGE study is to examine whether these beneficial effects transfer to older adults. The study's principal investigator is Steve Anton, Ph.D., a UF Institute on Aging faculty member.

EXCELLENCE IN GERIATRICS



A much-watched ranking of health system specialties is again recognizing UF Health geriatrics as one of the best programs in the nation. U.S. News & World Report's 2022-23 survey listed the program as the 45th best in the United States. Geriatrics is one of five UF Health adult specialties ranked nationally by U.S. News. An additional five pediatric specialties placed among the nation's elite. The rankings are based on a range of measures, including survival rates, patient safety and specialized staff. They also include survey responses from thousands of physicians. More than 4,000 hospital systems are evaluated nationwide.



Pictured, from left to right, are UF undergraduate student Natalia Evripidou; UF Institute on Aging faculty member Todd Manini, Ph.D.; institute faculty member Shinichi Someya, Ph.D.; and institute faculty members Stephanie Wohlgemuth, Ph.D., and Christiaan Leewenburgh, Ph.D.

UF CLAUDE D. PEPPER OLDER AMERICANS INDEPENDENCE CENTER: 2021 KEY RESEARCH FINDINGS

Prescribing cascade

Dihydropyridine calcium channel blockers, or DH CCBs, are among the first-line drug options to treat hypertension. However, they can cause swelling in the lower legs or hands, which is often treated with a loop diuretic. When a drug is prescribed to treat a side effect of another medication, it is commonly called a prescribing cascade. We analyzed data from 5.4 million people who were prescribed DH CCBs, including 185,000 who were given loop diuretics after starting DH CCB. We found that loop diuretics were associated with lower physical functioning among DH CCB users. These findings suggest this prescribing cascade might cause a significant decrease in health-related quality of life for many adults, making it important for clinicians to avoid or better manage this cascade when possible.

*Morris EJ, Brown JD, **Manini TM**, Vouri SM.*

*Differences in Health-Related Quality of Life Among Adults with a Potential Dihydropyridine Calcium Channel Blocker-Loop Diuretic Prescribing Cascade. **Drugs Aging.** 2021 Jul;38(7):625-632. doi: 10.1007/s40266-021-00868-0. Epub 2021 Jun 7.*

Exercise and the circadian clock

The disruption of circadian rhythms and circadian clocks is an emerging risk factor for cardiometabolic disease, which includes cardiovascular disease and diabetes. Skeletal muscles, one of the largest organ systems, have an intrinsic circadian clock whose disruption can lead to detrimental effects on the body. Our research review shows such disruption causes a preferential shift toward lipid oxidation while reducing carbohydrate oxidation. Resulting effects include insulin resistance and glucose intolerance and fasting hyperglycemia, among others. Exercise has been shown to modify muscle clock function, thus we hypothesize that exercise might rebalance carbohydrate and lipid metabolism to the benefit of health.

*Erickson ML, **Esser KA**, Kraus WE, Buford TW, Redman LM.*

*A Role for Exercise to Counter Skeletal Muscle Clock Disruption. **Exerc Sport Sci Rev.** 2021 Jan;49(1):35-41. doi: 10.1249/JES.0000000000000235.*

Environmental exposures and COVID-19

Little is known about the risk factors of severe COVID-19 beyond older age and conditions such as hypertension, diabetes, cardiovascular diseases, asthma and chronic lung diseases. Mortality, however, is not always associated with any of these factors. We conducted an analysis of the potential association of a wide variety of environmental factors with COVID-19 mortality. We confirmed a previously reported association involving nitrogen dioxide and identified novel environmental factors associated with COVID-19 mortality. Those included air toxins methyl bromide, benzidine and chloroform. Among other findings, we show that U.S. counties with less vacant land are associated with less COVID-19 mortality. Greater vacant land has previously been shown to be associated with negative health outcomes, including chronic stress and less social interaction. Future study is needed to understand the mechanisms underlying these associations.

*Hu H, Zheng Y, Wen X, Smith SS, Nizomov J, Fische J, Hogan WR, **Shenkman EA**, Bian J.*

*An external exposome-wide association study of COVID-19 mortality in the United States. **Sci Total Environ.** 2021 May 10;768:144832. doi: 10.1016/j.scitotenv.2020.144832. Epub 2021 Jan 7.*

Disc degeneration of the spine

Intervertebral disc degeneration occurs, as the name implies, when one or more of the discs separating the vertebrae composing the spine breakdown. This often can lead to intense pain in the arms and legs. The mechanism of this degeneration remains unclear. An inflammatory cytokine called lymphotoxin- α , or LT α — cytokines are proteins that play a role in cell communication — is associated with various pathological conditions. Our study explored the relationship between LT α and disc degeneration. We found that LT α is closely associated with intervertebral disc degeneration and might induce cell death in the nucleus pulposus, which is the inner core of a disc. In a sense, it acts as a shock absorber for the spine.

Guo Z, Qiu C, Mecca C, Zhang Y, Bian J, Wang Y, Wu X, Wang T, Su W, Li X, Zhang W, Chen B, Xiang H.

*Elevated lymphotoxin- α (TNF β) is associated with intervertebral disc degeneration. **BMC Musculoskelet Disord.** 2021 Jan 13;22(1):77. doi: 10.1186/s12891-020-03934-7.*

2021 HIGHLIGHTS:

58
faculty

105
affiliate
members

5
clinical
physicians

89
active
research
grants

\$182.1
million in research
grant funding

124
peer-reviewed
publications

Long-term cost benefit of exercise

The Lifestyle Interventions and Independence for Elders, or LIFE, study found that physical activity is a cost-effective way to prevent major mobility disability in older adults compared to health education. But the long-term effects of the intervention after the conclusion of the study were unknown. We conducted a secondary analysis of LIFE data linked to Medicare claims information to determine if the cost benefits of exercise were maintained over time. Our analysis of health care utilization and costs found no statistically significant difference between physical activity and education interventions poststudy. These findings highlight the challenge of impacting long-term health care costs using physical activity interventions.

Brown JD, Wang CY, Groessl EJ, Pahor M, Manini TM.

Three-Year, Postintervention, Follow-up Comparison of Health Care Resource Utilization and Costs in the Lifestyle Interventions and Independence for Elders (LIFE) Study. J Gerontol A Biol Sci Med Sci. 2021 Jan 18;76(2):272-276. doi: 10.1093/gerona/glaa088. 0.

Muscle wasting and aging

The world's population is rapidly aging and the number of adults 65 years and older is expected to double by 2050. In this aging society, frailty has become an important health issue. Unfortunately, the cause of sarcopenia, or muscle wasting, remains unclear. Vascular calcification — the buildup of mineral deposits in the arteries and veins — is prevalent in older adults and is a risk factor for cardiovascular disease and death. Emerging evidence

suggests vascular calcification can affect skeletal muscle perfusion, or capillary blood flow. Our review of the scientific literature demonstrates a simplified conceptual model of vascular calcification contributing to sarcopenia.

Jeon YK, Shin MJ, Saini SK, Custodero C, Aggarwal M, Anton SD, Leeuwenburgh C, Mankowski RT.

Vascular dysfunction as a potential culprit of sarcopenia. Exp Gerontol. 2021 Mar;145:111220. doi: 10.1016/j.exger.2020.111220. Epub 2020 Dec 26.

Resveratrol and exercise

Maintaining physical function while aging is critical to ward off disability and extend independent living. Research has shown that exercise is a necessary, yet insufficient, part of interventions to prevent a decline of physical function due to age. With a rapidly aging world population, the costs associated with this physical decline will be enormous. So it is essential to develop adjuvant therapies to optimize the efficiency of exercise and ultimately help prevent disability. In this small, randomized controlled trial, we show that combining exercise with resveratrol, a compound commonly found in red grapes, can be safe and feasible for older adults with functional limitations. The pilot study shows that exercise with a 1,000 mg dose of resveratrol might benefit physical and mitochondrial function. A larger, fully powered trial is necessary to determine the combined effectiveness of resveratrol and exercise.

Harper SA, Bassler JR, Peramsetty S, Yang Y, Roberts LM, Drummer D, Mankowski RT, Leeuwenburgh C, Ricart K, Patel RP, Bamman MM, Anton SD, Jaeger BC, Buford TW.

Resveratrol and exercise combined to treat functional limitations in late life: A pilot randomized controlled trial. Exp Gerontol. 2021 Jan;143:111111. doi: 10.1016/j.exger.2020.111111. Epub 2020 Oct 15.

Biomarkers and sepsis

Sepsis has been called the “quintessential disease of the elderly.” Indeed, sepsis increases the mortality of hospitalized patients over the age of 65 exponentially. In the past decade, however, in-hospital death from sepsis has substantially declined. While most younger survivors of sepsis rapidly recover, many older patients progress into a clinical trajectory of chronic critical illness, or CCI, involving long ICU stays, with dismal long-term outcomes. Our study compared biomarkers for persistent inflammation, immunosuppression and catabolism syndrome, or PICS, in younger and older sepsis patients more than 14 days after disease onset. We found that, compared with younger patients, a greater number of older adults develop CCI and have higher mortality after 12 months. Older patients demonstrated early biomarker evidence of the underlying pathobiology of PICS.

Jeon YK, Shin MJ, Saini SK, Custodero C, Aggarwal M, Anton SD, Leeuwenburgh C, Mankowski RT.

Vascular dysfunction as a potential culprit of sarcopenia. Exp Gerontol. 2021 Mar;145:111220. doi: 10.1016/j.exger.2020.111220. Epub 2020 Dec 26.

The intersection of sleep and pain

Sleep and pain have previously been shown to be independently associated with cognitive performance. We sought to preliminarily investigate the interactive associations of sleep and pain with cognitive performance in middle-aged and older adults. These associations have been studied only on a limited basis. Our study shows that in sedentary adults age 50 and older, pain and sleep interact in their associations with executive function tasks. Higher sleep efficiency — the time we spend in bed trying to fall asleep — might be associated with better

reasoning and working memory in those with the highest pain. Lower total sleep time might be associated with better reasoning in those people with the lowest amount of pain. More study is recommended to examine this topic.

Curtis AF, Dzierzewski JM, Buman MP, Giacobbi PR, Roberts BL, Aiken-Morgan AT, Marsiske M, McCrae CS.

Preliminary investigation of interactive associations of sleep and pain with cognition in sedentary middle-aged and older adults. J Clin Sleep Med. 2021 Feb 1;17(2):233-242. doi: 10.5664/jcsm.8856.

The cell and unfolded proteins

Proteins in our cells take on specific shapes that differ depending on their specific function in the body. But when these proteins become misshapen, or unfolded, and then accumulate beyond a cell's ability to rid itself of this excess garbage, consequences can include a number of diseases, such as neurodegenerative conditions, cardiovascular disease and even cancer. Cells have a survival mechanism called the unfolded protein response, or UPRs, that helps dispose of these proteins. Using the *Caenorhabditis elegans* worm, we found that the triggering of UPRs in different parts of the cell is time-dependent at distinct life stages, suggesting subcellular defense mechanisms might decline at different rates in different tissues. This might provide insights into the cellular aging processes of other species, including humans.

Sheng Y, Yang G, Markovich Z, Han SM, Xiao R.

Distinct temporal actions of different types of unfolded protein responses during aging. J Cell Physiol. 2021 Jul;236(7):5069-5079. doi: 10.1002/jcp.30215. Epub 2020 Dec 21.

NEW FACULTY

Stephanie Wohlgemuth, Ph.D., is an assistant research professor in the UF College of Medicine's department of physiology and aging. She has worked as a comparative physiologist, with a focus on metabolic and cellular responses to aging and disease, environmental stress and aging in a variety of species. These range from marine annelid worms and freshwater fish to rodents, humans and large mammals. She has previously worked in the UF department of animal sciences in the UF College of Agricultural and Life Sciences, which is part of the UF Institute of Food and Agricultural Sciences. Wohlgemuth began her career as a clinical nurse before receiving undergraduate and graduate degrees from the University of Düsseldorf.



Stephanie Wohlgemuth, Ph.D.

Dejana Braithwaite, Ph.D., is a professor in the UF College of Medicine's department of surgery and the UF College of Public Health and Health Professions' department of epidemiology. She also serves as the associate director of population sciences at the UF Health Cancer Center. Much of her research is focused on the intersection of cancer and aging, with the overarching goal to encourage a more individualized approach to cancer screening and care among older adults. Braithwaite earned a doctorate in epidemiology at the University of Cambridge and completed a postdoctoral fellowship in cancer epidemiology at the University of California, San Francisco.



Dejana Braithwaite, Ph.D.

Sudeshna Chatterjee, Ph.D. is an assistant scientist and clinician in the UF College of Medicine's department of physiology and aging. She studies how the brain contributes to the control of walking and how those contributions change due to aging and neurological disorders, such as stroke. She earned her doctorate from the University of Florida in rehabilitation science (movement science), a master's degree in kinesiology from Iowa State University and holds a license in physical therapy. She has previously received Pepper Scholar status from the UF Claude D. Pepper Older Americans Independence Center, which is competitively granted to highly qualified early-career scientists.



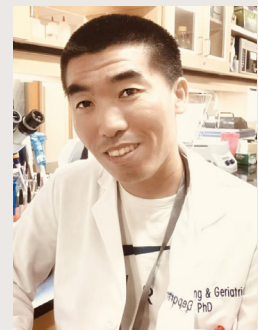
Sudeshna Chatterjee, Ph.D.

Christopher N. Kaufmann, Ph.D., M.H.S., is an assistant professor in the UF College of Medicine's department of health outcomes and biomedical informatics. He is a public health scientist with interests at the intersection of aging, sleep and health services research. His focus is on the use of epidemiologic data to identify patterns in the use of health services for sleep disorders among older adults. He is a former assistant professor at the University of California, San Diego, in its division of geriatrics, gerontology and palliative care. Kaufmann earned a doctorate in public mental health from Johns Hopkins Bloomberg School of Public Health, where he also earned his master's. His undergraduate degree is from the University of Southern California where he majored in communication and minored in performing arts studies.



Christopher N. Kaufmann,
Ph.D., M.H.S.

Yi Sheng, Ph.D., is a research assistant scientist in the UF College of Medicine's department of physiology and aging whose work is focused on the mechanisms of aging as modulated by iron metabolism, diets and neuronal aging. He was formerly a postdoctoral researcher at UF in aging and genetics. He earned his doctorate in biophysics from Huazhong University of Science and Technology in Wuhan, China, where he also received a bachelor of science degree in bioinformatics.



Yi Sheng, Ph.D.



PROGRESSES

2019

2020

2021 ◀ Annual Report

2022

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