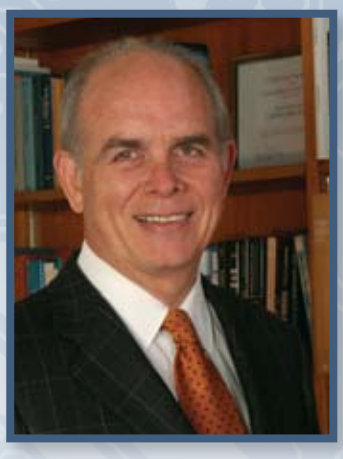


Bernie Machen, President

"Inventiveness" Spurs Florida Economy

UF spin-off companies foreshadow state's high-tech future

Last March, President Obama gave a speech at the White House titled "Investing in Our Clean Energy Future."

His main point was that the nation's clean energy innovators will help bring about energy independence — while creating new jobs and industries to drive economic recovery.

One of his leading examples was Sinmat, a Gainesville startup featured in this issue. Sinmat is engineering better ways to build microchips used in smart energy systems such as efficient lighting. The president introduced Deepika Singh, who founded Sinmat with her husband Rajiv, a UF professor of materials science and engineering.

President Obama told Deepika and the other innovators, "It's said that necessity is the mother of invention. At this moment of necessity, we need you. We need some inventiveness."

What's true for the nation is also true for this university, for this region and for Florida.

Like most other universities, UF faces severe cuts due to the state's steep fall-off in tax dollars. At the statewide level, Florida is struggling to find its way now that the mainstays of housing and tourism are in such sad shape.

People in the tech community say successful commercialization rests on four pillars: exciting technology, entrepreneurship, investment, and good location.

Research, technology transfer, startups — in Obama's word, "inventiveness"— all offer a proven path to a better future.

For evidence, we need only look to the past.

People in the tech community say successful commercialization rests on four pillars: exciting technology, entrepreneurship, investment, and good location.

We have demonstrated success in all four areas here at the University of Florida.

"The Today Show" this winter featured WiPower, another UF spin-off profiled in this magazine. Also, the BBC was in town not long ago to film a segment on Sharklet Technologies, which makes a unique antimicrobial coating for medical devices. These are just two of several startups that have drawn national attention in recent years.

Win Phillips,
Vice President for Research

Progress Corporate Park

Sid Martin Biotechnology Development Incubator

"It's said that necessity is the mother of invention. At this moment of necessity, we need you. We need some inventiveness."

— President Obama

We also have a track record of successful entrepreneurs.

Look no further than Progress Corporate Park, adjacent to the Sid Martin Biotechnology Development Incubator. Some 1,200 people work in the park currently — 85 percent at successful UF spin-offs.

Investment is another strength. To be sure, the downturn has made it tough to attract angel and venture funding, but last year UF spin-offs cracked the $100 million mark in venture funding. And, since the Sid Martin Incubator was founded in 1995, its current and former occupants have brought in at least $300 million in private investment dollars as well as $100 million in grants.

Last but not least, there is a lot going on in this region.

We are part of the Florida High Tech Corridor Council, which works to bolster the technology industry in a 23-county region throughout central and North Florida. More locally, the Sid Martin Biotechnology Development Incubator is full, with nine companies occupying all of its space.

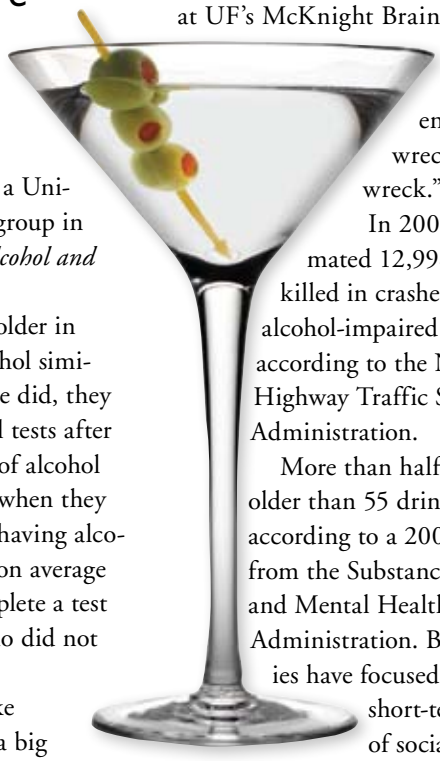
The City of Gainesville's incubator, the Gainesville Technology Enterprise Center, is also full, with nine of its own companies.

Indeed, there is so much demand for startup support that earlier this spring we made the decision to pursue another incubator on the Alachua General Hospital property.

In our proposal to the federal Economic Development Administration for a major grant, we argued that nurturing small, innovative companies is essential to restoring and diversifying Florida's economy. The more we can do on this score, the better, and this new incubator can add another vital pillar of support.

Extracts

Study: Alcohol Affects Older Adults More



Older, active people who have a drink or two might be more impaired afterward than they think, according to a report from a University of Florida research group in the *Journal of Studies on Alcohol and Drugs*.

Although people 50 or older in the study metabolized alcohol similarly to how younger people did, they performed worse on special tests after having moderate amounts of alcohol and did not always realize when they were impaired. Soon after having alcohol, older adults also took on average five seconds longer to complete a test than their counterparts who did not have a drink.

"That doesn't sound like much, but five seconds is a big difference if you're in a car and need to apply the brakes," said lead author Sara Jo Nixon, a psychiatry professor at UF's McKnight Brain Institute. "It can mean the difference between a wreck and not-a-wreck."

In 2007, an estimated 12,998 people were killed in crashes involving alcohol-impaired drivers, according to the National Highway Traffic Safety Administration.

More than half of adults older than 55 drink socially, according to a 2008 report from the Substance Abuse and Mental Health Services Administration. But few studies have focused on the short-term effects of social drinking among older adults.

Previous research mainly investigated consumption of large amounts of alcohol at one time, and generally in young people. But results from studies of younger adults might not be applicable to older people because of age-related declines in cognitive skills, as well as changes in how alcohol is metabolized and removed from the body.

Nixon's group aimed to expand understanding of the effects over time of moderate levels of alcohol consumption in healthy, active older adults.

"You want to know how long does it take for them to become sober enough to engage in potentially dangerous activity such as driving," Sullivan said.

The study involved 68 nonsmokers — one group ages 50 to 74 and a comparison group ages 25 to 35 — who had at least one drink a month. Within each group, some individuals

Mite Could Put The Bite On Chilli Thrips

Amblyseius swirskii

Chilli thrips sound more like a snack food than an agricultural menace, but these tiny insects threaten many of the Sunshine State's most important crops. Fortunately, University of Florida research shows a predatory mite gobbles them up like popcorn.

On bell pepper plants in greenhouses, the mite consumed enough chilli thrips to keep the population to less than one per leaf, compared with 70 per leaf on control plants. Similar results were obtained with peppers grown outdoors. The study was published in April in the journal *Biological Control*.

Native to Asia, the invasive pest attacks more than 100 host plants, including corn, citrus, peanuts and tomatoes. Established first in the Caribbean, it spread to Florida in 2005 and then to Texas. Adult chilli thrips are about 1 millimeter long.

According to a U.S. Department of Agriculture estimate, if chilli thrips become more widely established in the U. S., they could cause agricultural losses of almost $4 billion per year.

Chilli thrips

For greenhouse crops — including bell peppers, strawberries, basil and flowers such as Gerber daisies — the mite could provide a much-needed alternative to pesticides, said Lance Osborne, a professor with UF's Institute of Food and Agricultural Sciences and an author of the study.

"This mite has a lot of potential for greenhouses, which is where it's used now," Osborne said. The mite, which has no common name but is known scientifically as *Amblyseius swirskii*, is available commercially to manage whiteflies and broad mites.

Because the mite is already approved for use in Florida, growers can try it against chilli thrips, he said. Osborne cautioned that the mite is not likely to be successful on every crop the pest attacks. Researchers were happy

were given alcohol while others were given a placebo beverage that did not elevate their breath alcohol levels.

When a person consumes alcohol, concentration in the blood builds to a peak, then dissipates. During the first phase of the metabolic process, alcohol has a stimulating effect. During the second phase, there is a sedative or depressive effect.

During each phase — at 25 minutes and 75 minutes after alcohol consumption, respectively — participants were given tests that required them to draw lines connecting numbered and lettered dots on a paper, in chronological order, without lifting the pen from the paper. They were timed and evaluated for how many errors they made.

The first test involved numbers, while the second involved alternating between numbers and letters. Those tests give clues about a person's mental processing related to movement, and about the ability to mentally shift from one problem-solving strategy to another. The researchers also asked participants to rate on 10-point scales how intoxicated they felt, and how much they thought the alcohol impaired their performance.

Older adults who had alcohol took longer to complete the tasks than younger adults who had alcohol. But there was no such age difference between the older and younger groups that had not had alcohol. The researchers found that even though blood alcohol levels for participants in both groups rose at a similar rate right after drinking and reached the same peak, the older adults did worse on tests. That suggested the performance gap seen after moderate amounts of alcohol was not because of age-related differences in how the body processes the substance, but rather because of other factors influencing how alcohol affected the individuals.

In the test portion during the "stimulating" alcohol phase, older adults who had alcohol were slower than those who had not had any. In contrast, alcohol seemed to give the younger group a performance boost during that phase.

During that same post-drinking phase, when the older adults were impaired, they didn't think they were. And in the second phase — an hour and 15 minutes after having alcohol — older adults thought their performance was impaired, even when it wasn't.

"An older person might say 'Really, I feel all right, I'm sure I can drive,'" Sullivan said. "But the study shows that you can't always take someone at their word."

So what advice would Nixon give to active, older adults?

"If you have a couple of drinks at dinner, sit around, have dessert — don't drive for a while."

Czerne M. Reid

to find the mite held up well outdoors on bell peppers. Previous attempts to establish the mite outside on rose bushes have been unsuccessful, he said. "Maybe there is a plant issue — they prefer peppers, but not roses," Osborne said.

An upcoming project will investigate the use of peppers as "banker plants" — the mite equivalent of birdhouses, said Cindy McKenzie, a research entomologist with the USDA's Horticultural Research Laboratory in Fort Pierce.

In the project, ornamental peppers will be planted outdoors among rose bushes to see if they can harbor mite populations that protect both plant species, said McKenzie, another author of the study.

If successful, this approach could be helpful to rose gardeners, especially in the Orlando area, hard-hit by chilli thrips. And if you've never heard of ornamental peppers, McKenzie said they make a nice addition to the landscape.

"We screened more than 20 ornamental peppers and narrowed it down to four," she said. "They're very pretty varieties, with dark purple and green leaves."

Researchers also hope to develop a pesticide-resistant strain of the mite, Osborne said.

"That way, if a grower has to come in and spray, it won't disrupt the biological control," he said. Osborne previously developed a resistant strain of another predatory mite.

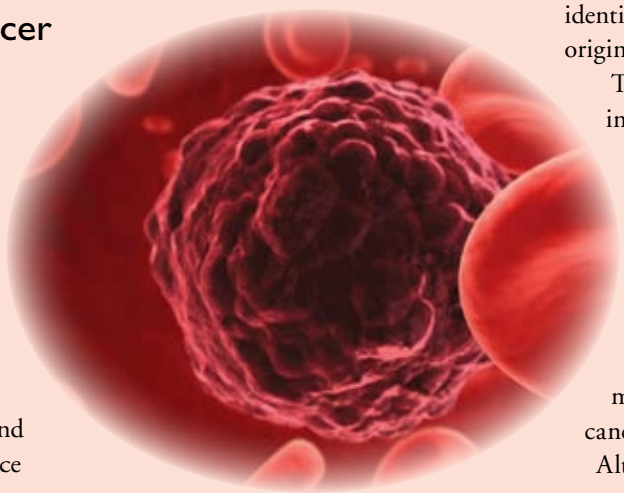
The current study was part of an ongoing collaboration between scientists with UF and the USDA, aimed at minimizing chilli thrips damage.

Lance Osborne, lsosborn@ufl.edu

Tom Nordlie

Extracts

Biomarker May Show 'Root' Of Colon Cancer



To truly kill colon cancer and eliminate the risk of recurrence, it is important to kill the "root" of the disease, according to a University of Florida College of Medicine surgeon.

"It's like a dandelion — if you don't kill the root it just keeps coming back," said Dr. Emina Huang, a UF colorectal surgeon, who added that colon and rectal cancers have high recurrence and spread rates, especially if the disease is not found until advanced stages.

Her findings, featured in April in the journal *Cancer Research*, identify a biomarker for colon cancer stem cells that she believes will help researchers further evaluate the cancers' origins and progression. The discovery sheds light on the cancer stem cell theory, an idea that has arisen because cancer cells and stem cells share many qualities, including the ability of cancer stem cells to demonstrate self-renewal.

The research determined a protein called aldehyde dehydrogenase 1, or ALDH1, can be used to identify, isolate and track these ultra-resilient cells throughout the development of malignant colon or rectum disease. Previously used markers cannot as precisely track colon cancer stem cells.

"Without a better handle on what cells might be contributing to cancer metastases and recurrence, we won't have any targets to go after," said Huang, an associate professor in the UF department of surgery and a member of the Program in Stem Cell Biology and Regenerative Medicine at the UF College of Medicine. "This gives us a potential target."

According to the American Cancer Society, about 150,000 Americans are diagnosed each year with colorectal cancer, and more than 50,000 die from the disease. In addition to the potential advances in therapeutic strategies, Huang said having a more direct target to explore will benefit progress in the areas of diagnostics and prevention.

In collaboration with Dr. Bruce Boman, a professor of medical oncology at Thomas Jefferson University in Philadelphia, Huang chose to evaluate ALDH1 because of its known association with breast, brain and other cancers. In addition to being a strong marker for malignant colon stem cells, the researchers believe ALDH1 may be a marker for benign colonic stem cells. Whether these two types of colonic stem cells are one of a kind still needs to be determined.

Researchers implanted human colon tissue cells into mice and analyzed the resulting growth. Although normal cell tissue was evaluated, it never replicated in the mice — only the tissue that was malignant grew. Comparing ALDH1 patterns with that of the previously used markers, the researchers found ALDH1's presence was much more targeted, suggesting a way to more definitively identify colon cancer stem cells in the original tissues.

They also noted that ALDH1 indicated an increasing number of colonic stem cells throughout the progression of colon tissue's transformation from normal cells to premalignant cells to cancerous cells. These findings support the theory that an increase in ALDH1 expression marks the tumor growth in colon cancer stem cells.

Although the theory that cancers are seeded by cancer stem cells is still becoming scientifically accepted, Huang said she thinks that in every cancer there is a small fraction of cells capable of reproducing the cancer. If these unique cells are not killed or removed during treatment, the cancer will not be entirely destroyed.

While changes in patient care are most likely years away, she says the findings give researchers an immediate target to focus on as they try to develop new medical interventions and optimize treatment regimens to completely kill the disease.

Potentially, tumors could be examined to determine if there is an overwhelming expression of the biomarker, or tests taken to determine if the biomarker may be circulating in the bloodstream — scenarios that could possibly indicate a worse outcome, thus signaling the need for more aggressive treatment.

"The next step is to look at some of the predisposing conditions and see if the pattern is suggestive of anything we can do in the prevention mode," said Huang, who noted that people with inflammatory bowel disease, for example, have a higher risk of cancer.

Emina Huang, EminaHuang@surgery.ufl.edu

Jennifer Brindise

Vitamins Might Help Prevent Hearing Loss

Vitamin supplements can prevent hearing loss in laboratory animals, according to two new studies, bringing investigators one step closer to the development of a pill that could stave off noise-induced and perhaps even age-related hearing loss in humans.

The findings were presented at the Association for Research in Otolaryngology's annual conference by senior author Colleen Le Prell, a researcher at the University of Florida.

The supplements used in the research studies are composed of antioxidants — beta carotene and vitamins C and E — and the mineral magnesium. When administered prior to exposure to loud noise, the supplements prevented both temporary and permanent hearing loss in test animals.

"What is appealing about this vitamin 'cocktail' is that previous studies in humans, including those demonstrating successful use of these supplements in protecting eye health, have shown that supplements of these particular vitamins are safe for long-term use," said Le Prell, an associate professor in the UF College of Public Health and Health Professions' department of communicative disorders.

About 26 million Americans have noise-induced hearing loss, according to the National Institute on Deafness and Other Communication Disorders, the agency that funded the studies.

In the first study, UF, University of Michigan and OtoMedicine scientists gave guinea pigs the vitamin supplements prior to a four-hour exposure to noise at 110 decibels, similar to levels reached at a loud concert. Researchers assessed the animals' hearing by measuring sound-evoked neural activity and found that the treatment successfully prevented temporary hearing loss in the animals.

In humans, temporary noise-induced hearing loss, often accompanied by ringing in the ears, typically goes away after a few hours or days as the cells in the inner ear heal. Because repeated temporary hearing loss can lead to permanent hearing loss, the scientists speculate that prevention of temporary changes may ultimately prevent permanent changes.

In the second, related study in mice, UF, Washington University in St. Louis and OtoMedicine researchers showed that the supplements prevented permanent noise-induced hearing loss that occurs after a single loud sound exposure. The researchers found that the supplements prevented cell loss in an inner ear structure called the lateral wall, which is linked to age-related hearing loss, leading the scientists to believe these micronutrients may protect the ear against age-related changes in hearing.

The research builds on previous studies that demonstrated hearing loss is caused not just by intense vibrations produced by loud noises that tear the delicate structures of the inner ear, as once thought, said Josef Miller, who has studied the mechanisms of hearing impairment for more than 20 years and is a frequent collaborator of Le Prell's. Researchers now know noise-induced hearing loss is largely caused by the production of free radicals, which destroy healthy inner ear cells.

"The free radicals literally punch holes in the membrane of the cells," said Miller, a professor of communicative disorders at the University of Michigan.

Miller is the co-founder of OtoMedicine, a University of Michigan spin-off company that has patented AuraQuell, the vitamin supplement formula used in the studies.

The antioxidant vitamins prevent hearing damage by "scavenging" the free radicals. Magnesium, which is not a traditional antioxidant, is added to the supplement mix to preserve blood flow to the inner ear and aid in healing.

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Jill Pease

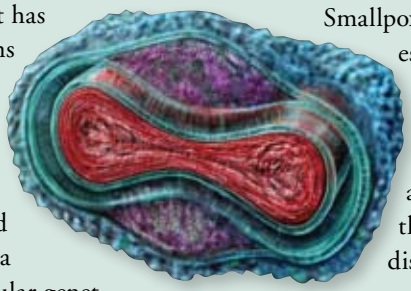
Extracts

Smallpox Shown To Inhibit Inflammation

University of Florida researchers have learned more about how smallpox conducts its deadly business — discoveries that may reveal as much about the human immune system as they do about one of the world's most feared pathogens.

In findings published in May in the *Proceedings of the National Academy of Sciences*, scientists describe how they looked at all of the proteins produced by the smallpox virus in concert with human proteins, and discovered one particular interaction that disables one of the body's first responders to injury — inflammation.

"This virus that has killed more humans than any other contains secrets about how the human immune system works," said Grant McFadden, a professor of molecular genetics and microbiology at the College of Medicine and a member of the UF Genetics Institute. "I'm always amazed at how sophisticated these pathogens are, and every time we look, they have something new to teach us about the human immune system."



Smallpox Virus

With researchers from the University of Alberta, the Centers for Disease Control and Prevention and a private company called Myriad Genetics, UF researchers for the first time systematically screened the smallpox proteome — the entire complement of new proteins produced by the virus — during interactions with proteins from human DNA.

These protein-on-protein interactions resulted in a particularly devastating pairing between a viral protein called G1R and a human protein called human nuclear factor kappa-B1, which is believed to play a role in the growth and survival of both healthy cells and cancer cells by activating genes involved in immune responses and inflammation.

"One of the strategies of the virus is to inhibit inflammation pathways, and this interaction is an inhibitor of human inflammation such that we have never seen before," McFadden said. "This helps explain some of the mechanisms that contribute to smallpox pathogenesis. But another side of this is that inflammation can sometimes be harmful or deadly to people, and we may learn a way to inhibit more dangerous inflammation from this virus."

Smallpox is blamed for an estimated 300 million deaths in the 20th century alone, and outbreaks have occurred almost continuously for thousands of years. The disease was eradicated by a worldwide vaccination campaign, and the last case of smallpox in the United States was in 1949, according to the CDC. The last naturally occurring case in the world was in Somalia in 1977.

With the exception of stores of the virus held in high-containment facilities in the United States and Russia, smallpox no longer exists on the planet. Since it was no longer necessary for prevention, and because the vaccines themselves were risky, routine vaccination against smallpox was stopped. However, public health concerns regarding the possible re-emergence of the virus through bioterrorism have led to renewed interest in the development of treatments for the disease and safer vaccines.

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John Pastor

Best Protectors From Bullies? Girls Rule!

Playground bullies may meet their match from where they least expect — in the ranks of kids who are anti-bullies — and most of them are girls, a new University of Florida study finds.

"Boys may be more likely to bully, but girls are more likely to defend those being bullied," said Jim Porter, who did the research for his doctoral dissertation in counselor education at UF. "While a lot of attention has been devoted to bully prevention programs, very little recognition is given to kids who jump in and try to stop the bullying or comfort the victim."

These playground defenders merit attention because research shows that a majority of school shootings are committed by students who have been bullied, and victims of bullying are at risk for dropping out of school, suffering from depression and bullying others,

Porter said. Thirty percent of students in sixth- through 10th-grade report some experience with bullying, either as a victim or perpetrator, he said.

Schools overlook good Samaritans as they are putting a growing number of bully prevention programs in place, in some cases relying on peer mediation where students resolve the disputes themselves, with mixed results, Porter said.

"What is missing in these programs is they don't incorporate children who are already known to help victims," he said. "Understanding kids who defend against bullying may reveal a new avenue toward preventing school-related violence."

Porter surveyed 168 females and 101 males about how they believed their mother, father, best friends and favorite teachers would expect them to respond if they encountered another student being bullied. The offensive behavior included hitting, shoving, name-calling, teasing and ostracizing. Participants attended four middle schools in North Central Florida and were between the ages of 10 and 15.

Peer pressure can be a good thing, the study found. Students said teachers and parents were more likely than best friends to expect them to try to stop a bully, but they were more likely to actually intervene if the message came from a best friend. And more girls than boys reported feeling pressure from friends to come to a victim's aid, Porter said.

Eighty-five percent of girls surveyed said their best friend would expect them to defend or help a bullying victim, compared with only 66 percent of boys, Porter said. In contrast to this 19-point percentage gap, there was only a 1- to 3-percentage point difference in expectations for boys and girls' behavior by teachers, mothers and fathers, he said.

Being female or having more feminine traits as measured by a gender identity scale also increased the likelihood that a student would defend a bully, the survey findings showed.

"Gender stereotypes that girls are more nurturing and boys are more aggressive definitely play out in how we expect boys and girls to behave," he said. "Somehow we communicate these expectations to kids and it can affect their behavior."

Schools may be the ideal place to try to help change those ideas, said Porter, who is now a counselor at Alachua Integrative Medicine in Alachua. "The news sometimes suggests that violence makes schools a hazardous place to be, but schools also are where we can learn how to get along with others and become adults," he said.

Giving a role in bully prevention programs to bystanders who step in to defend the victims on the playground and in the classroom fits in with the recent trend in educational psychology toward positive reinforcement, Porter said.

"There was a time when people were more likely to think of punishing bad behavior," he said. "Now there is a push toward finding and rewarding good behavior."

Porter said he has always been interested in the subject of bullying because he was often beat up as a "new kid" moving from one community to another. "I never understood but always wanted to discover why some students were able to jump in and help others," he said.

Focusing on defenders illustrates dramatic changes in public attitudes, he said.

"There was a time when bullying was not researched because it was considered normal childhood behavior," he said. "It was thought of as being part of growing up — this learning to determine a pecking order, and making people stronger and weeding out the weak."

Bullying expert Drew Nesdale, a psychologist at Griffith University in Queensland, Australia, said this research suggests that a little recognized and under-used source of help might be found in the victims' peers. "Interestingly, the fact that children who help might be responding to the expectations of others is consistent with research that has identified the powerful effect of the norms or expectations of others on their behavior."

Jim Porter, WinningHarmony@gmail.com

Cathy Keen

Growth Industry

A STRANGE-LOOKING SALAMANDER PROVIDES A WINDOW INTO HOW VERTEBRATES REPAIR THEMSELVES

By John Pastor

With flaring red gills that jut out of a milky white body, and round, black eyes that never blink, the axolotl salamander has been trolling tropical pools for 300 million years.

But only in recent years have scientists begun to appreciate the axolotl's amazing ability to repair injuries that would leave humans and other mammals paralyzed — or worse.

"The axolotl is the champion of vertebrate regeneration, with the ability to replace whole limbs and even parts of its central nervous system," says Edward Scott, a professor of molecular genetics and microbiology in the UF College of Medicine and director of the McKnight Brain Institute's Program in Stem Cell Biology and Regenerative Medicine.

While worms, starfish and other invertebrates can perform wondrous feats of regeneration — some starfish can completely regenerate from a single, remaining arm — the axolotl is a vertebrate, with hind limbs and forelimbs — like us. That makes them the closest relative to humans that can regenerate spinal cords, limbs, internal organs and substantial amounts of brain.

The question is why axolotls regenerate so well, while people, by comparison, do not.

The answer is important enough for the National Institutes of Health to invest $2.4 million in a Grand Opportunity grant to Scott and co-investigator Dennis Steindler, executive director of the McKnight Brain Institute. The grant is funded through the American Recovery and Reinvestment Act of 2009.

Working in association with the UF-led Regeneration Project, an international collaboration of life scientists, their objective is to create the genomic tools necessary to compare the extraordinary regenerative abilities of the axolotl with established mouse models of spinal cord injury, stroke, traumatic brain injury and other neural conditions.

One way to do this is to "turn off" the creatures' regenerative abilities, then see if they can be turned back on again.

At the MBI's Stereotactic Radiosurgery Laboratory, three axolotls hover serenely in a water-filled plastic box, only the gentle flutter of their blood-red gills betraying life.

Scott places one of the salamanders in the sights of a linear accelerator, which will deliver precise doses of radiation to the animal's liver and spleen, two organs that seem to be the source of its blood stem cells.

"What we want to accomplish here is something like an axolotl bone marrow transplant," Scott says.

Ray Carson

"Ultimately, what makes the axolotl a great model for regeneration is that the model systems we are most familiar with — mice and humans — do not regenerate very well."
— Ed Scott

The animals' opaque, white body comes in handy. A bright light reveals their internal organs. No sophisticated imaging necessary.

"They're ugly, but in a cute way," Scott says. "You can practically see through them, even when they are adults, and it helps us to do some amazing things."

The idea is to disrupt the axolotl's regenerative ability and then see if it can be restored with transplanted stem cells. Researchers will be able to follow the origin, movement and destination of the cells using green fluorescent proteins. When produced by genetically modified cells, these proteins have the useful quality of glowing vivid green under ultraviolet light.

"Axolotl stem cells look very different than human ones and are concentrated in different areas of the body," Scott says. "You can flush the bone of the axolotyl and get maybe 50 cells. However, the liver and spleen are full of them, which mirrors the embryonic stages of humans and mice. Hopefully we will track stem cell migration from fetal liver to bone marrow through this process."

This experiment is but a single step toward determining whether the axolotyl's regenerative talent is dormant within humans, ready to be revived with new drugs, reagents or treatments. Axolotls and humans share about 90 percent of their genes, and the team has already referenced human and mouse genes with axolotl counterparts.

"Ultimately, what makes the axolotl a great model for regeneration is that the model systems we are most familiar with — mice and humans — do not regenerate very well," Scott says. "By comparing how a mammal and a salamander respond to injuries, we can identify genes or proteins that we can now add back to the mammalian system to make it regenerate better."

The issue of what controls organ regeneration was named among the top 25 major questions facing scientists

in the next quarter century by *Science* magazine in 2005. With medical science adding years to the human lifespan, the importance of rebuilding and restoring old tissue and organs is growing. But science had to enter the 21st century to begin to take advantage of the highly regenerative axolotl as a model for human disease.

"Only now have new genetic, molecular and cellular technologies, as well as scientific knowledge of the salamander, mouse and human genomes and 'regeneromes,' risen to a level where scientists can compare systemwide responses to injury," Steindler says. "I am extremely hopeful with the discoveries being made in comparative regenerative biology that the questions surrounding cell and tissue regeneration in the human following injury or disease are going to be answered."

Steindler founded the Regeneration Project in 2007 as an international effort to overcome barriers that have limited progress in regenerative biology and medicine. Featuring annual think tank-style meetings of stem cell and developmental biologists, biomedical engineers, genomic researchers and clinicians, the initiative promotes information sharing across disparate scientific fields.

It would be unlikely at most symposia, but quite reasonable at a Regeneration Project meeting, for a molecular cell biologist from the Max Planck Institute in Germany, a urological surgeon from Wake Forest University in North Carolina, a tissue engineer from the University of Pittsburgh and a stem cell biologist from the University of Florida to engage in a conversation about their research.

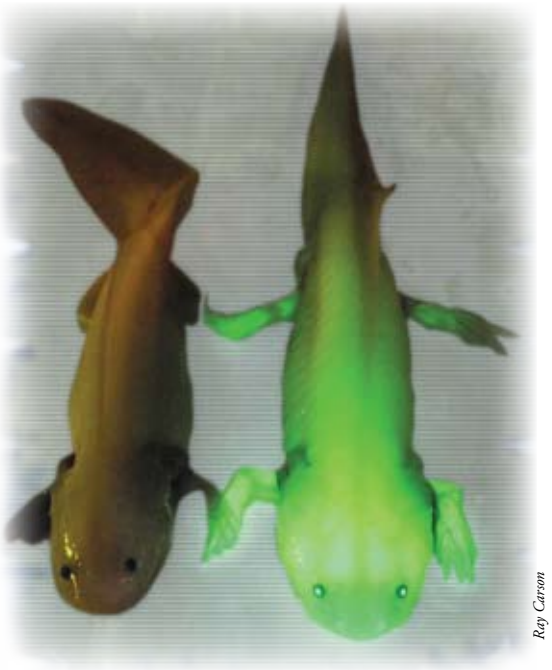
The glue that holds these diverse interests together are research fellows, another Regeneration Project innovation. Introduced as the "experiment within the experiment" by Steindler at the first project meeting, the fellows enhance idea sharing and conduct joint experiments to find answers in the biological systems of simple animals that can be applied to the more complex tissue reconstruction needed in humans.

"It is going to take broad, multidisciplinary collaborations across a number of scientific fields to improve health care, but we are making that happen," Steindler says. "I think the Grand Opportunity (GO) grant shows that these efforts are recognized and valued on a national level."

"We are bringing together the best of the developmental biology world with the best of the stem cell world and starting the conversation, with the focus on how to get regeneration to work in a mammal," adds Scott. "Essentially, our body can heal itself, and that's why many of us live to be 80. But we can't do things like grow an arm or finger as we did in the early stages of our development. We want to learn how to turn those systems back on in people."

GO grants are intended to support research that lays the groundwork for whole new fields of investigation with the promise of advancing biomedical research and improving health care.

"This important model of regeneration is one of several being developed in organisms that can repair themselves, using genetics to find links to mammals," says Naomi Kleitman, repair and plasticity program director at the National Institute of Neurological Disorders and Stroke. "We'll continue to watch the progress of these exciting studies to ensure that discoveries of genes that promote regeneration are one day applied to improving human health."



Ray Carson

Green fluorescent protein allows scientists to track where cells travel in the axolotl's body.

The Regeneration Project is also supported by the Thomas H. Maren Foundation and the Jon L. and Beverly A. Thompson Research Endowment, the UF Office of the Vice President for Research, and an anonymous donor.

Maren, a founder of the UF College of Medicine who died in 1999, was a staunch advocate of using comparative organisms to solve human health problems. His studies of marine life led him to understand the chemistry and biology of an enzyme called carbonic anhydrase, which influences the production and flow of fluid in the eyes, brain, spinal cord and lymph system.

The result was the development of dorzolamide, a top-selling drug for glaucoma that goes by the trade name Trusopt. Royalties from Trusopt support the Maren Foundation and Maren's example helped inspire the Regeneration Project, Steindler says.

Ray Carson

David Blankenship

"I am extremely hopeful with the discoveries being made in comparative regenerative biology that the questions surrounding cell and tissue regeneration in the human following injury or disease are going to be answered."
— Dennis Steindler

"Dr. Maren's wife, Emily, told me her husband valued the strategy of selecting the right organism to answer scientific and medical questions, and that he was familiar with axolotl studies," Steindler says. "He invented Trusopt because of comparative biology, looking at sharks and other marine animals. In that same way, we want to arrive at a technique that can regenerate spinal cord tissue and other tissues of the body."

An authority in adult human brain stem cell biology, Steindler is exploring the potential of what are known as multipotent astrocytic progenitor cells to treat disease and spinal cord injury in humans through their ability to transform into a limited number of needed cell types, such as neurons — the brain's workhorse cells.

Axolotls apparently have the same sort of cells in their brains. The difference is the axolotl cells can repair a vast amount of damage in comparison with their human cousins. Malcolm Maden, a professor of biology at UF and a Regeneration Project member, has shown that axolotls can regenerate up to a third of their brain matter in six weeks, reproducing a structurally sound, functional brain.

Maden has also found hope for recreating some of the axolotl's regenerative capacity in humans through his research on the salamander's limbs.

In a paper last year in the journal *Nature*, Maden and six colleagues found that cells from the salamander's different tissues retain the "memory" of those tissues when they regenerate.

Standard mammal stem cells operate the same way, albeit with far less dramatic results. They can heal wounds or knit bone together, but not regenerate a limb or rebuild a spinal cord. What's exciting about Maden's findings is they suggest that harnessing the salamander's regenerative wonders is at least within the realm of possibility for human medical science.

"I think it's more mammal-like than was ever expected," says Maden. "It gives you more hope for being able to someday regenerate individual tissues in people."

Also, the salamanders heal perfectly, without any scars whatsoever, another ability people would like to learn how to mimic, Maden says.

"If we can figure out why the axolotl does this better than the human and mouse," says Steindler, who has begun cell transplant studies using axolotls and mice, "then we are really going to get somewhere in human regeneration."

As discoveries are made, more researchers will want to use the axolotl as a model for exploring regenerative techniques, which in turn will cause more grant applications to the NIH for axolotl research. In that event, UF and other Regeneration Project scientists will be well positioned to apply for the funding.

In the short term, regeneration scientists are working to elevate the axolotl to the level of scientific mainstays such as roundworms known as *Caenorhabditis elegans*, the fruit fly *Drosophila melanogaster*, and, the king of the model organisms — the mouse — as a tool to study biological processes and human disease and injury.

Arlene Chiu, a scientific adviser for the Regeneration Project and director of New Research Initiatives at Beckman Research Institute of the City of Hope in San Francisco, thinks axolotl research could increasingly appeal to the NIH because it touches on many of the institute's priorities, including application of genomics, development of treatments,

Ray Carson

invigoration of the biomedical research community and global health.

Besides that, the model has something special.

"The axolotl is the highest, most complex organism that can still do this clever trick of completely reconstructing a whole body part in adulthood," Chiu says. "I like to think of it in construction terms where we need both the materials such as bricks and beams and the architect's plans. In regenerative medicine, can we learn where the biological blueprint resides, and understand the basis of restoring and reorganizing many different types of lost cells and tissues? Muscles, bones, nerves and blood vessels all have to be reconstructed at the right time and in the right place, all in perfect coordination with the original biological master plan.

"It may sound like science fiction, but the reality is the salamander is able to do all of these things," she says. "We are not so far removed that we can't relate to them, learn from them and try to apply their secrets to improve our capacity to regenerate."

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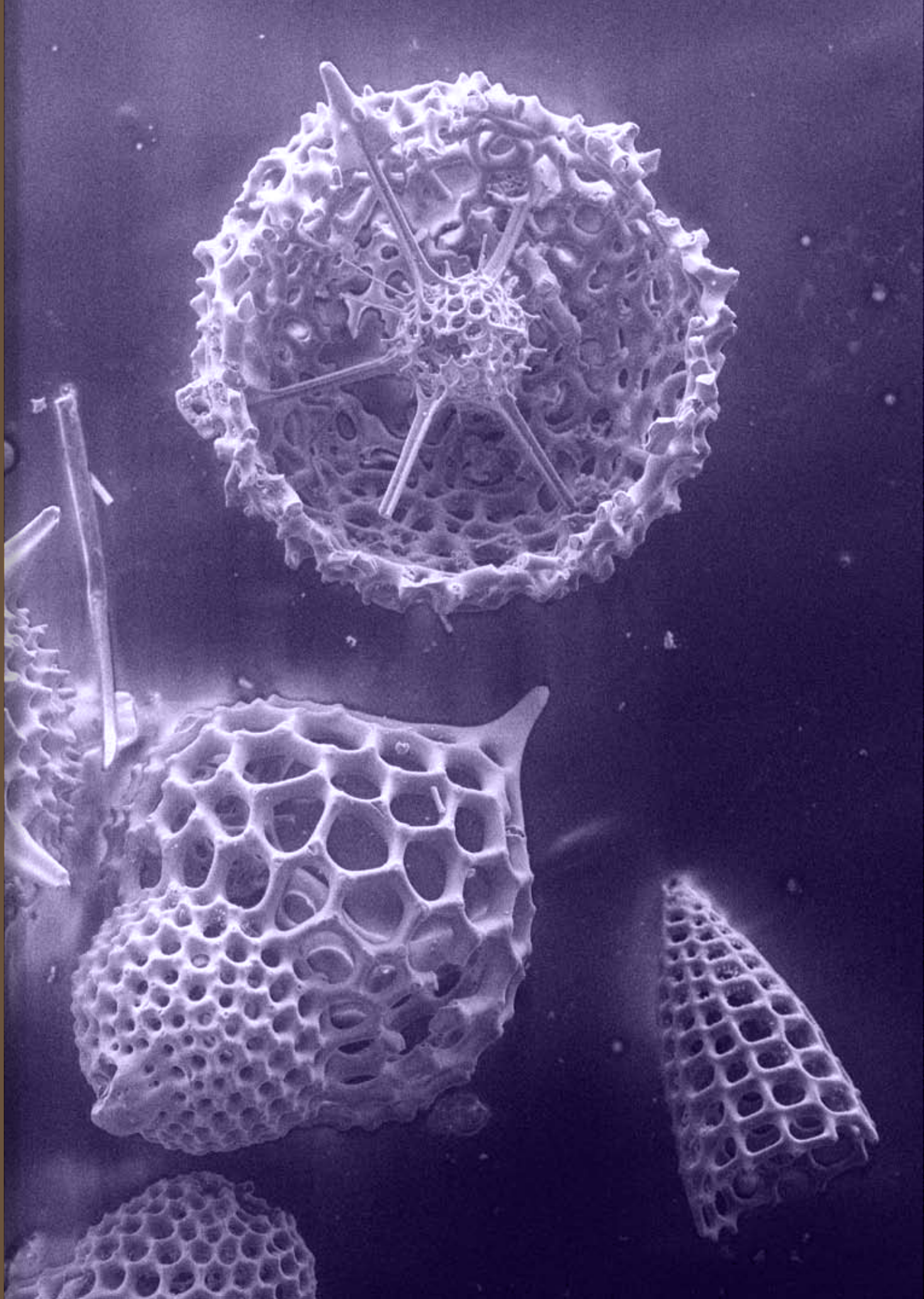

Reading ROCKS

UF geologists travel back in time to understand what made Antarctica cold and what that tells us about climate change today

By Jean Feingold

34 million years ago, Antarctica was covered by a beech forest. 33 million years ago it was covered in ice.

Ellen Martin has spent her career trying to understand what climatic changes occurred all those eons ago and what they can tell us about the future.

"We must look to the past to understand how the climate system works," says Martin, a professor in UF's Department of Geological Sciences. "My research focuses on understanding the complexities of the climate system by looking at the record left behind in the rocks."

Rocks buried thousands of feet beneath the southern oceans.

By studying the chemical composition of microscopic rocks and fossils found in cores drilled from the ocean floor, Martin is getting a clearer picture of the processes that lead to the dramatic climate change in Antarctica.

"Antarctica has a very interesting history," Martin says. "We think of it as a huge, ice-covered continent, but that happened about 33.7 million years ago in roughly 300,000 years, which is very fast in geological time. Before that, it was a green forest."

Martin's research relies on sediment cored from deep beneath the ocean floor by scientists on the research vessel JOIDES Resolution.

The vessel, operated by an international consortium called the Integrated Ocean Drilling Program, travels the world's oceans on two-month expeditions to gather samples from below the sea floor. In addition to the approximately 25 scientists and graduate students on each expedition, hundreds of researchers like Martin utilize the cores.

Over the past decade, Martin has pioneered several innovative techniques for using cores to measure the prehistoric climate.

In a paper in the journal *Science* in 2006, Martin and a graduate student described how they used a rare element found in tiny fish teeth to date the opening of the Drake Passage between the Atlantic and Pacific at the southern tip of South America. The passage created a circular current around the pole and scientists wondered if it contributed to Antarctica's sudden cooling.

Scientists have long puzzled over this rapid cooling because it occurred in a very warm era when levels of carbon dioxide were three to four times current levels.

Theorists had suggested the plummeting temperatures could be related to the opening of the Drake Passage, but before Martin's research it was unclear whether the opening and development of the circumpolar current occurred before or after the cooling.

Scanning Electron Microscope image of mineral skeletons of radiolarians, tiny zooplankton that live in the surface waters of the ocean. When these organisms die, their skeletons contribute to the underlying ocean sediment. Image courtesy of Ann Heatherington, UF Department of Geological Sciences.

Climate vs. Weather

Geologist Ellen Martin may have been one of the few people walking across a frigid University of Florida campus this winter who wasn't wondering whether all the talk about "global warming" was just hot air.

But for someone who's looking at global climate 34 million years ago, a change in the local weather is no big deal.

"Weather is a daily atmospheric state, whether it's raining, windy, what the temperature is," she says. "Climate is defined as a 30-year average of weather. It is 'expected' weather."

Martin points out that the mean annual global temperature, averaging readings for every part of the whole world, has increased by 0.7 degrees Centigrade over the past century.

"Florida's cold winter was balanced by, for example, how hot it was in Vancouver during the Olympics," Martin says. "So you can't just look at one place or one short time period and talk about global climate. Global warming is a climate phenomenon. Local cold temperatures are a weather phenomenon. The two should not be confused."

Martin's approach was to analyze isotopes of the metal neodymium, which is absorbed by fish teeth the size of grains of sand lying on the ocean floor.

Because neodymium has a chemical signature that varies depending on whether it came from the Atlantic or Pacific, Martin was able to show that water was moving between the two oceans at least 40 million years ago.

"Before that current developed," Martin says, "water traveled from the equatorial region to Antarctica and back, carrying heat from the subtropics to Antarctica."

While the opening of the Drake Passage could have precipitated the plunge in temperatures because it isolated Antarctica from that warm water, the timing wasn't quite right.

"Our research suggested the ice could not be strictly a consequence of cold water circulating around Antarctica," Martin says.

So she started thinking about other ways of looking at the climate, especially the CO_2 levels, around the time of the cold shift.

"The alternative explanation is that global concentrations of greenhouse gases in the atmosphere, such as CO_2, became low enough to let Antarctica freeze, which is the focus of my current research," Martin says. "Once it started to get cold enough, the ice reflected sunlight away, so it got colder and more ice formed."

Martin applied to the National Science Foundation's Marine Geology and Geophysics Program for funding to continue her studies and was awarded a three-year, $295,000 grant through the American Recovery and Reinvestment Act of 2009. In all, Department of Geological Sciences faculty have been awarded $1.87 million in federal stimulus money to date.

The new research uses lead isotopes found in ocean sediment to understand the kind of rock weathering occurring on Antarctica during the big climate transition.

"When rocks are weathered on a continent, it can happen two different ways," explains Martin. "There's physical weathering from wind or rain or glaciers, which breaks big rocks into little rocks. And then there's chemical weathering when water and CO_2 from the atmosphere combine to form carbonic acid, which dissolves rock."

"The best way to understand the complexities of the climate system is by looking at the record left behind in the rocks."
— Ellen Martin

Ray Carson

Only chemical weathering removes CO_2 from the atmosphere, so significant chemical weathering at the time of the great cooling could indicate CO_2 levels were changing.

The challenge was that there was no reliable way to differentiate chemical and physical weathering in the geologic record.

"One goal of this research is to develop a new technique to determine the chemical and physical weathering history on Antarctica during this big climate transition," she says. "In geology, we are constantly looking for something we can read in the rock record that can tell us about a fundamental process like this. We don't currently have a good proxy for determining the weathering regime, to determine whether it's chemical or physical."

So Martin and doctoral student Chandranath Basak are developing one.

They are processing 370 small core samples, each just 3 inches long, collected by the JOIDES Resolution in the 1990s from five different sites in the extreme southern Atlantic and Indian oceans.

Each sample is analyzed in two ways. First, microscopic fossils provide information about the composition of the ancient seawater. Then, silicate rock fragments are analyzed to learn about the chemical composition of ancient Antarctic rocks.

"We then compare lead isotopes from the seawater and rock records," explains Martin. "When they are the same, it indicates Antarctica was experiencing chemical weathering. When they are different, it implies Antarctica was subject to more physical weathering."

Preliminary analysis of sediments from one site found that the lead isotopes from the seawater and rocks were similar when CO_2 was high and Antarctica was green, indicating there was much more chemical weathering which helped reduce CO_2, leading to the buildup of ice. Analysis of samples after ice had formed showed distinct isotopes for the two fractions, suggesting much more physical weathering. In between, the signals were mixed.

"The point is to expand this to other places and times where we don't know what to expect," she notes. "It will help develop a tool for future studies that can be used to learn more about changes in atmospheric CO_2 concentrations."

Martin says climate is an extremely complex system that is hard to decipher based on human time-span observations.

"The CO_2 we put into the atmosphere today will be there for 100 years. It will take a million years for all of the CO_2 humans have generated already to go away," Martin says. "We must look to the past to understand how the climate system works. The best way to understand the complexities of the climate system is by looking at the record left behind in the rocks."

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Related website:
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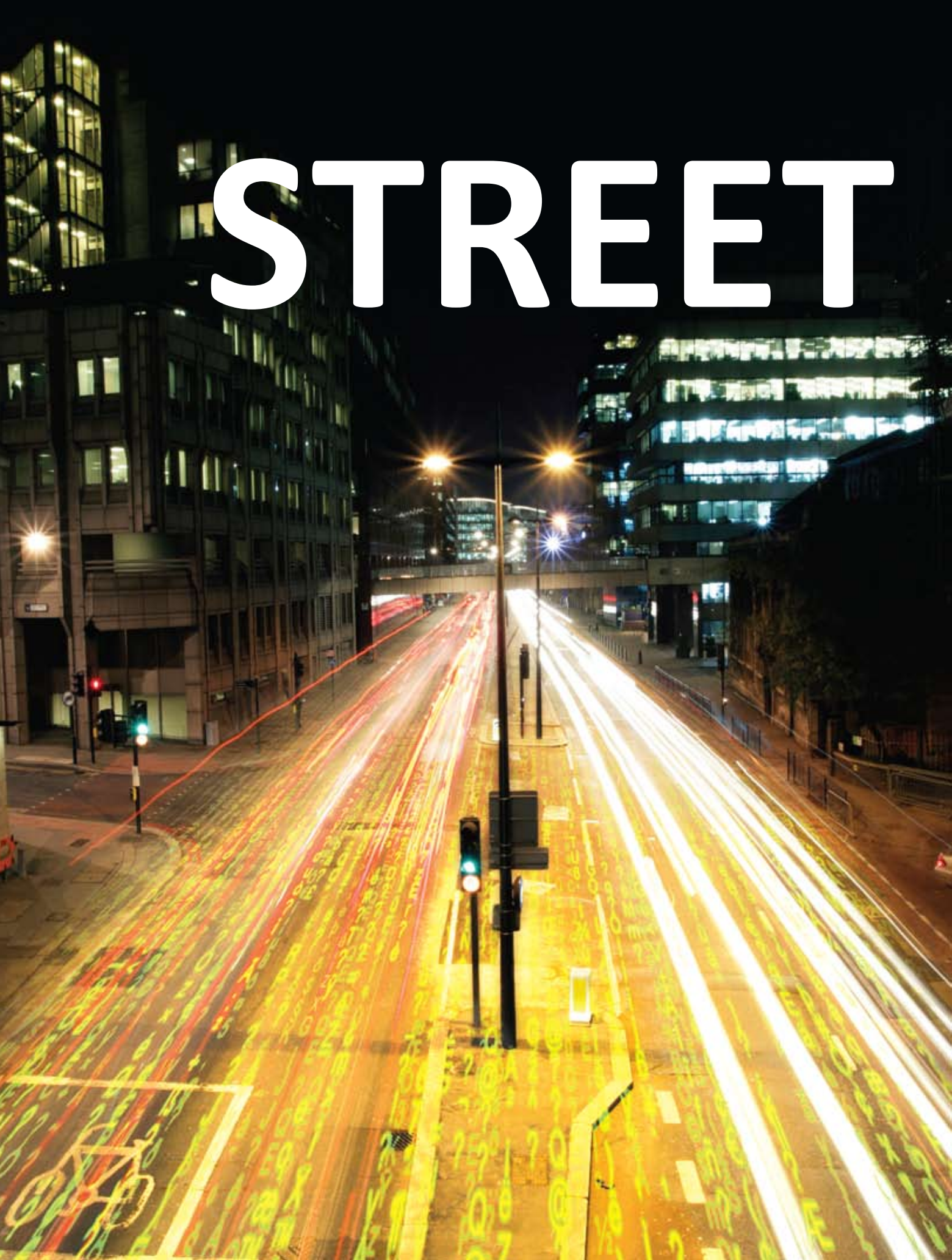
STREET



SMARTS

UF COMPUTER ENGINEERS ARE DEVELOPING WAYS FOR ROADS AND CARS TO TALK TO EACH OTHER

By Megan E. Gales

Red means stop. Green means go. Yellow ... well, yellow might be out of a job.

Imagine a system of roads connected to each other through a wireless network. With sensors at every intersection, on road signs and — potentially — in cars themselves, information flowing freely among them all.

With a grant of more than half a million dollars from the National Science Foundation and funded by the American Recovery and Reinvestment Act of 2009, computer engineer Shigang Chen and transportation engineer Yafeng Yin hope to develop a system that's part transportation, part communication, and spans entire cities.

The idea is to turn a city's existing pervasive traffic infrastructure into a pervasive communications infrastructure, Chen says. The sensors and wireless nodes would need power. Traffic lights and telephone poles carry power.

"So if we can install wireless devices at these places, we have the power supply," Chen says. "And these wireless devices would be able to communicate among themselves or with other nearby wireless devices to form a wireless network."

And because the wireless nodes would be right there with the sensors, they could easily share the information the sensors collect. Applications become virtually limitless because the Intelligent Road's communication network would be a two-way street.

Chen, an associate professor at the University of Florida, says the network would create a real-time traffic map, from which congestion could easily be monitored. If a wireless device — maybe a souped-up GPS unit — in a vehicle tapped into the map, the driver could pick a route based on distance and traffic conditions, and avoid what could have been an unpleasant commute.

Cameras and other sensors could help dispatchers send the right kind of emergency personnel because accidents could be assessed remotely. The architecture of the network would not require the video to be sent back to a central location only; video feeds could be accessed from anywhere in the city.

Gone would be the yellow-light dilemma zone, where a driver must quickly decide between a difficult stop or the risk of running a red light, says Yin, a civil engineer who brings transportation systems expertise to the iRoad project. Because sensors would communicate with each other, the traffic light would realize a car was approaching, and could postpone the yellow light slightly to give the driver a chance to make it through the intersection without feeling the need to slam on the brakes.

By sending a signal to a wireless device in a vehicle, sensors on road signs could warn a driver of impending danger — such as a sharp curve in the road for a car traveling at a high speed, or a car approaching too quickly from the other direction when making an unprotected left turn.

ONE-WAY STREET

Many modern roads already have sensors in the pavement at intersections. When vehicles travel across them, the magnetic field of the vehicles triggers the sensor and sends a signal to a control box on the side of the road. The controller in turn assigns green light times for the signal accordingly. These sensors measure traffic volume, density and flow, but they have no way of communicating with each other.

Lily Elefteriadou is director of UF's Transportation Research Center, a nearly 40-year-old highly respected

interdisciplinary research center sought out for its ability to analyze and solve transportation issues.

"New technologies help us predict traffic flows better — better than the flow that's at the intersection, and help us coordinate better because you can anticipate the amount of traffic that you're going to have much better," Elefteriadou says.

She says there is a lot of research being done in transportation technology right now, either to provide additional information about traffic in order to more effectively optimize the system, or to provide drivers with more information so they can manage their travel more efficiently. TRC studies show people are generally not bothered if they know how long their trip will take and can plan accordingly.

"People get frustrated when they think that their trip is going to take half an hour, and it takes an hour and a half," Elefteriadou says. "That's the most frustrating part."

The 95 Express project in Miami is an example of one way technology can be used to ease congestion on crowded roads. The first phase of the project was launched in January, and the second phase is expected to follow in a couple of years. It uses a variable pricing strategy, where express lanes on Interstate 95 are reserved for those willing to pay a toll to use the lanes. Mass transit vehicles and registered carpoolers can use the express lanes for free. Drivers who don't want to pay and aren't carpooling or driving a city bus can use the general purpose lanes for free.

"But if you're in a hurry and you're willing to pay, then you can use the managed lanes," Elefteriadou says. "And the worse the congestion, the higher the price."

Right now, tolls range between 25 cents and $2.65, but may go as high as $6.20 in extreme conditions.

Elefteriadou says the project is an attempt to minimize congestion, as well as to encourage people to use mass transit. TRC is currently working on a project to analyze the impact of 95 Express, but she says generally speaking it seems successful.

Another approach is Orlando's new variable speed limit project on Interstate 4. In this case, transportation authorities attempt to manage congestion as well as safety by managing speeds.

"When they detect that there's congestion at one point, they're trying to lower the speeds upstream so that you don't have rear-end collisions as people are approaching the congested area," Elefteriadou says.

It's like a crowd trying to leave a packed stadium after a game. When everyone is doing their own thing, it takes a long time. Get people to follow an established order, and everyone gets out of the stadium faster. Follow the order, increase the throughput.

"If everyone follows the speed limit, you actually end up traveling faster," says Yin, an assistant professor at UF.

Practically speaking, though, getting drivers to comply with the variable speed limit can be difficult, he says.

But what if the variable speed limit was also connected to sensors in vehicles that physically limited the maximum speed? It's this kind of question that keeps Yin awake at night. The network he and Chen propose would be capable of imposing such restrictions, if auto manufacturers equipped vehicles with the right sensors. It's a touchy subject at best, though.

"On the one hand, I think people don't like to have their vehicles being controlled," Elefteriadou says. "However, from a traffic and a systems perspective, you can optimize operations much better if you have that kind of control over vehicles."

There would be no bottlenecks, there would be no congestion. Think of how a large crowd of people moves slowly up a staircase, but quickly on an escalator — as long as no one treats the escalator like stairs.

SPEED BUMPS

Words like bandwidth, protocol and frequency roll off Chen's tongue like water, and he explains how wireless networks work with elementary ease. But setting up a citywide wireless communications network isn't as simple as Chen's explanation makes it sound. It takes a lot more digital oomph to keep a network of this kind of caliber going. So much so that wireless network's capacity for data transfer — its bandwidth — becomes an issue. Bandwidth is fundamentally limited by the frequency range made available for wireless communication. It's easy to increase a non-wireless network's bandwidth: just run more cables. But adding more wires isn't exactly an option for wireless systems.

Wireless networks transmit information using radio waves of a certain frequency. A wireless device, whether it's a laptop in the living room or a piece of hardware on top of a traffic light, encodes information as radio signals and sends it to a router. The router receives the information, decodes it and sends it through a wired connection to the Internet. Because information flows both ways, the process works in reverse, too.

Similarly, devices like radios, televisions, cell phones and even garage door openers rely on certain radio frequencies to send and receive information. The trick is that technology in all of its forms must share the air. If they all tried to

Ray Carson

Shigang Chen believes integrated transportation and communication systems will help speed traffic through busy intersections like this one in Gainesville.

use the same frequency, they would block each other's signal and none would work. In the United States, the Federal Communications Commission regulates the use of frequencies and allocates to wireless networks a specific, finite frequency range. And just as the amount of cable in a wired network determines its capacity, so the frequency spectrum dictates a wireless network's bandwidth. The Average Joe's wireless home network transmits at a frequency of 2.4 GHz and uses a networking standard called the 802.11 protocol. Most wireless technology, in fact, is geared toward this kind of wireless networking, Chen says.

But trying to use this kind of protocol for a system as robust as the one the researchers envision is like trying to use a garden hose to extinguish a house fire.

Therein lies Chen's challenge: to establish a new theory in protocols for the sophisticated management of wireless communication bandwidth.

"Even though a lot of research has been done," Chen says, "not many large-scale wireless network systems like this have been deployed."

The trick, Chen says, is to manage the traffic on the network in order to make better use of the bandwidth. Various kinds of traffic — still on the network, not the road — will need to be prioritized, also. For example, emergency services would always need to be able to send and receive the information it needs. If digital congestion slows the network, the system must be able to detect the bottleneck and reroute network traffic around it in order to recover.

Another red flag the system must be able to detect is compromised nodes. Chen says his team will develop secure protocols to protect the system, study all possible attacks they can think of and program it accordingly. But to truly ensure the security of the system, there must be a way to detect and isolate any node featuring the fingerprints of a hacker.

Programmers with good intentions will be encouraged to develop applications. Chen says the researchers plan to develop an engineering framework that will allow efficient leverage of the system.

Chen hopes to take iRoad to prototype stage in about three years. In many ways, the implementation of this kind of technology depends on government, auto makers and consumers. Yin calls it a chicken-and-egg problem: who will come first? Toward that end, the U.S. Department of Transportation created a program called IntelliDrive. The program brings together the three groups in an effort to connect vehicles and roadway infrastructure and make transportation in the U.S. easier and safer — and perhaps even crashless. IntelliDrive resonates with the iRoad researchers.

"That's the vision we have," Yin says. "We think the next generation of transportation should be this way."

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Fit for LIFE

UF's Institute on Aging is leading efforts to keep older Americans moving longer

By Czerne M. Reid

Shortly after moving from Rome, Italy to Memphis, Tennessee, Marco Pahor was walking to work as he had done every day for years when a police officer asked if his car had broken down.

While living in Europe, Pahor typically got several hours of exercise daily by walking to and from public transportation, taking stairs and bicycling in the course of his daily activities.

"In Italy, you exercise to live," he says. "When I moved to Memphis I realized that you have to exercise to exercise."

Now at the University of Florida, Pahor runs most mornings and weight trains at the gym a few times a week.

Being physically active is not just a way of life for the 53-year-old Pahor, who has been director of the UF Institute on Aging since 2005. It is a major focus of the research program he leads. His mission, and that of the institute, is to use multidisciplinary basic, clinical and translational research and training programs to help older adults maintain their health and physical independence.

The institute builds on a long tradition of aging research at the University of Florida, where geriatric studies have been conducted in various disciplines since 1951, when the first baby boomers were entering kindergarten.

As the boomers advanced in age, UF also advanced in its studies of how to help them enjoy good health in their golden years.

Today, UF is well-positioned to be an authoritative voice on aging and geriatrics. Florida is the nation's "oldest" state, with nearly 19 percent of its 18 million residents older than 65. As the retiree population of the state grows, Florida has the opportunity to lead the nation in the science of aging.

UF has embraced that challenge through the Institute on Aging. In recent years the institute has blossomed, recruiting top researchers, conducting leading-edge research and winning multi-million-dollar grants from the National Institutes of Health and other agencies.

They include the largest grant ever to the university — $64 million from the National Institute on Aging to pursue a conclusive answer about whether physical activity can help older adults retain their mobility longer. The first two years of the Lifestyle Interventions and Independence for Elders, or LIFE, study is covered by $29.5 million through the American Recovery and Reinvestment Act of 2009.

The six-year LIFE study will compare the long-term effectiveness and practicality of a physical activity program and a successful aging health education program among seniors.

Many studies have shown that regular exercise improves physical performance, and the U.S. Department of Health and Human Services recommends that adults engage in at least 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity aerobic activity each week, as well as muscle-strengthening activities.

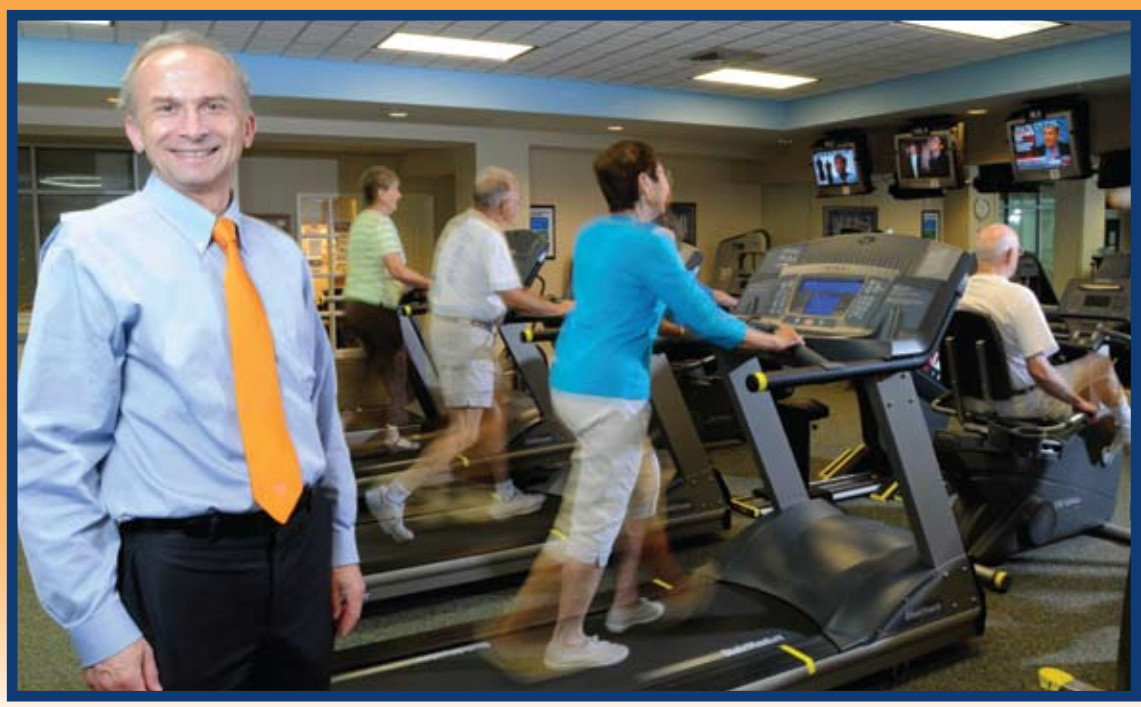
Still, little is known about whether exercise actually helps prevent major movement disability, defined as the inability to walk a quarter of a mile, or four blocks.

"We all know that physical activity is good for our health, but the definitive evidence of whether it can prevent

Ray Carson

"Over time, muscle shrinks as fat expands. We are looking for novel ways to slow this process, but right now nothing beats the benefits of physical activity."

— Marco Pahor



UF's Oak Hammock retirement community is a natural laboratory for Marco Pahor's research.

disability in older people — whether you can prevent them from being unable to walk — is lacking," Pahor says.

Ultimately, about 1,600 participants will be randomly assigned to take part in either a structured physical activity program that includes moderate-intensity physical activity such as walking and exercises to improve strength, balance and flexibility, or in a successful aging program that includes health education workshops and supervised stretching. Individuals will be followed for about four years.

The study is being conducted at UF and seven other institutions around the country: Northwestern University, the LSU Pennington Biomedical Research Center, Stanford University, Tufts University, the University of Pittsburgh, Wake Forest University Health Sciences and Yale University.

The results of this study have important implications for public health in a rapidly aging society and will fill an important gap in knowledge in geriatric medicine, Pahor and a colleague wrote in a January commentary in the journal *Archives of Internal Medicine*.

The study will also provide valuable information about the impact of physical activity on a range of health conditions, and make a mark on clinical practice and public health policy. In the end, that means a benefit to individuals as well as to the wider society, the researchers say.

In January, the National Institutes of Health awarded the institute another $15 million in recovery act funds for the construction of a 40,000-square-foot building to house its programs. The one-stop facility — which includes clinical research suites, laboratories, and lifestyle intervention amenities such as an indoor walking track and demonstration kitchen — will make it easier for older adults to take part in clinical trials, and strengthen connections among existing UF research centers. Those include the Claude D. Pepper Older Americans Independence Center, the Clinical and Translational Science Institute and the newly established Cognitive Aging and Memory Clinical Translational Research Program.

The building project will create or retain an estimated 376 jobs, three quarters of which will be construction-related. The others include 30 faculty positions as well as graduate assistants and support and administrative staff.

Scheduled to open in 2015, the four-story building is being designed according to LEED Platinum certification standards of the United States Green Building Council. Platinum is the highest of a four-level rating system aimed at responding to environmental challenges such as responsible use of resources, reduction of pollution and making indoor spaces conducive to good health and well being. The new building incorporates features to improve indoor air quality through the use of low-emission building materials, efficient energy production and use through photovoltaic cells, and light sensor technologies and water conservation technologies. The project also calls for prevention of construction activity pollution and reduction of light pollution from the completed building.

With more than 90 active NIH and other grants totaling more than $160 million, the new Institute on Aging building promises to be a busy place.

"The Institute on Aging initiative is very important to the state and the nation," says Win Phillips, UF's vice president for research. "Major support from the National Institutes of Health enables the University of Florida to take a national leadership position in this important endeavor."

Ray Carson

One of the early successes under Pahor's tenure was a winning bid to establish a coveted Claude D. Pepper Center at UF, one of only 11 around the country. UF's Pepper Center is focused on addressing the problem of muscle loss during aging, a condition called sarcopenia.

"Over time, muscle shrinks as fat expands," Pahor says. "We are looking for novel ways to slow this process, but right now nothing beats the benefits of physical activity."

Pahor began his commitment to aging at the bedside, for 16 years practicing geriatric medicine in Italy and conducting research on arrhythmia and damage to the aging heart.

In 1990, his interest in conducting large population studies on cardiovascular disease led to a career-defining meeting with Jack Guralnik, chief of the Laboratory of Epidemiology, Demography, and Biometry at the National Institute on Aging, who was in Italy teaching a three-week course on the epidemiology of aging.

"He was clearly one of the star students in the class — he was very knowledgeable and highly motivated to do good work," Guralnik says. "It was just obvious to me then that he was really dedicated to doing really good science in aging."

When Guralnik invited Pahor to become a visiting scientist at NIH, Pahor seized the opportunity. For three years, he traveled from Italy several times a year to participate in large epidemiological projects at NIH and at the Johns Hopkins University.

The NIH experience convinced Pahor he should relocate permanently.

"I realized that if I wanted to continue in this area I'd be more likely to succeed on this side of the Atlantic Ocean than the other," he says.

Pahor spent three years at the University of Tennessee Health Science Center in Memphis studying aging and hypertension. He then moved to Wake Forest University in North Carolina to head the prestigious Sticht Center on Aging and Rehabilitation, and became engaged in physical activity research. He led Wake Forest's successful effort to renew its Pepper Center and restructured the center to expand its focus from behavioral science to include translational science, integrating biological sciences and genetics.

It was during this period that the seeds of the LIFE study began to germinate, when a pilot study found that the rate of onset of mobility disability was lower among a group of older adults who engaged in a structured exercise program for a year, compared with a group of seniors who took part in a health education program for the same length of time.

That and later, larger studies have contributed to what Pahor called in his *Archives of Internal Medicine* commentary "a growing body of evidence that has given legs to the hypothesis that the promotion of physical activity may be the most effective prescription that physicians can dispense for the purposes of promoting successful aging."

In late 2004 the UF College of Medicine was looking to reinvigorate its aging research program and Pahor was ready for a new challenge.

"When I looked at his CV my first reaction was, why would he want to move," says Craig Tisher, then dean of the College of Medicine. "He had a very strong program at Wake Forest."

But Pahor saw an opportunity at UF to create and shape a program that would bring together researchers from around the campus as part of the same multidisciplinary team.

In addition to assuming leadership of the Institute on Aging, Pahor was named chair of a new Department of Aging and Geriatric Research, which focuses on finding ways to prevent disabilities that keep people from performing basic activities of daily living, such as walking, eating, taking care of personal hygiene or just getting out of bed.

The institute employs a multidisciplinary approach, incorporating basic laboratory science as well as human trials to identify potential areas in which to intervene.

Today the institute's talented epidemiologists, exercise physiologists, geneticists, physicians and other experts work under one umbrella toward a common goal. The institute has recruited talented senior and junior faculty over the years who are taking innovative approaches to the science of aging.

Professor Christiaan Leeuwenburgh, chief of the biology of aging division, leads a team that is working to identify cellular processes that lead to the loss of various functions such as sight and hearing in the elderly. The group is also investigating the molecular mechanisms by which processes such as programmed cell death influence loss of muscle mass in the elderly.

Junior faculty members, such as assistant professors Todd Manini and Stephen Anton, also are actively engaged in a number of studies, including a clinical trial of whether resveratrol, a compound found in red wine and dark-skinned grapes, can help improve memory and physical functioning in older adults.

And leading the team forward is Pahor, who still takes the stairs every time.

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INNOVATION HUB

FLORIDA INNOVATION HUB AT UF

Florida Innovation Hub at UF Expected To Lead Downtown Gainesville Job Growth

Construction began in June on the Florida Innovation Hub at UF, a "super incubator" at the newly designated Innovation Square site between the university and downtown Gainesville that is designed to promote the development of new high-tech companies.

The project is being funded through an $8.2 million grant from the federal Economic Development Administration and $5 million from the university.

The 45,000-square-foot facility will nurture start-up companies in much the same way as the Sid Martin Biotech Incubator in Alachua. But the Florida Innovation Hub will also become home to the university's main commercialization efforts. The building is scheduled for completion by December 2011.

The hub will provide technology start-up companies connected with the university with office space, laboratories, conference rooms and other capabilities. In addition, it will house UF's Office of Technology Licensing and UF Tech Connect, the main commercialization offices for the university.

"The hub will serve as a catalyst to get innovation from university laboratories into the marketplace, where it can have an impact on the world while creating jobs in Florida," said UF President Bernie Machen.

Programs and activities at the hub will bring together entrepreneurs, investors, students and service providers to maximize the university's ability to create technology-based companies for purposes of commercializing more of the research conducted at UF.

"The economic downturn showed us how important it is for Florida to diversify its economy beyond tourism and agriculture," said Win Phillips, UF's vice president for research. "Creating this Florida Innovation Hub allows Florida to leverage UF's massive research base for the benefit of the state as it transitions to a more innovation-based economy."

The grant is one of the largest of its kind ever awarded by the Economic Development Administration's Atlanta regional office, said EDA regional representative Philip T. Trader.

"We are pleased to partner on this project with the University of Florida," Trader said. "It is exactly the type of project EDA likes to fund because of the impact it can have on helping to create jobs for the state of Florida, particularly in emerging, technology-driven sectors of the economy."

UF is nationally recognized for its efforts to commercialize research and averages about 10 new technology-based companies each year, said Jane Muir, associate director of UF's Office of Technology Licensing and principal author of the EDA grant proposal.

While companies located in an incubator are four times more likely to succeed than those that are not, according to the National Business Incubator Association, enhancing the incubator concept by co-locating it with the university's main commercialization offices is a new model the university believes will yield even better results, Muir said.

"This is a super incubator," Muir said. "By putting all the players in the same building, we expect the synergy that's created to accelerate our ability to create companies."

Muir added that as these companies mature in this facility and graduate into their own space nearby, they will create demand for restaurants, hotels and other businesses to serve the growing workforce.

UF's proposal to EDA emphasized the statewide impact of the project, given the university's strong ties to tech-transfer efforts throughout the state, including partnerships with the Florida High Tech Corridor Council and Enterprise Florida.

"The Florida Innovation Hub is more than a bricks-and-mortar undertaking," said David Day, director of the Office of Technology Licensing. "We envision this project will enable us to create numerous start-up companies that will locate in the Gainesville area as well as throughout the state."

The project is also the anchor for Innovation Square, an ambitious plan to develop the rest of the property over the next decade. Likewise, Innovation Square is viewed as an important component of the City of Gainesville's plans for the Southwest Second Avenue corridor that connects the university with downtown.

Officials foresee mixed use for the remaining acreage, possibly including both public and commercial spaces. Plans for the new site will continue to develop over the next year, Machen said. Funding for the property's long-term development likely will come from a variety of sources, public and private, depending on the nature of the project at hand.

Looking beyond the Innovation Hub and the surrounding property, community leaders believe the Second Avenue corridor will add a vital element to the community by creating an unbroken bridge between the UF campus and downtown Gainesville.