Imagine a world without cancer … solving the mysteries of brain diseases like Alzheimer’s … the end of worldwide scourges like HIV …

At The Scripps Research Institute (TSRI), scientists take on the biggest challenges in science and medicine every day.

Millions of Americans are diagnosed each year with diseases like diabetes, Alzheimer’s, and cancer. As federal funding for basic biomedical research declines, many patients and their families are still desperate to find new therapies.

The time to confront the world’s toughest diseases is now.

Researchers need aggressive funding to solve these problems. Building on its proven track record in groundbreaking medical research and drug discovery, TSRI has created six ambitious initiatives, each focusing on areas of excellence and promising pathways for the future:

- The Anti-Cancer Campaign
- The Alzheimer’s and Neurological Diseases Initiative
- The Initiative Against Diabetes and Obesity
- Addiction Science for New Therapies
- The Vaccine and Global Health Initiative
- The Healthy Aging Initiative

These initiatives focus on transforming the future of medicine with breakthroughs that save and restore lives. Philanthropy will play a critical role. Funds raised will be used to further accelerate the institute’s groundbreaking research and discover new treatments for disease by supporting world-renowned researchers and building new state-of-the-art research facilities. This is your opportunity to facilitate life-changing discoveries that will benefit current patients and generations to come.

In the following pages, you can read more about each of the initiatives, some of the scientists conducting groundbreaking work in these areas and ways you can participate. We need your help to support the research that will lead to tomorrow’s treatments and cures.

To learn more, call (800) 788-4931, email philanthropy@scripps.edu or visit www.scripps.edu/philanthropy. We thank you for your participation.
Anti-Cancer Campaign
Finding Answers, Saving Lives

While there have been victories in the war on cancer in the last several decades that have been worth celebrating, there is still much to learn. Overall survival of patients who suffer from several types of cancer has not improved over the last 30 years, despite intensive therapies. Researchers at TSRI believe that we are close to significant breakthroughs … and that new approaches such as personalized treatments and methods for earlier detection are now within our reach.

One in two men and one in three women in the United States will be diagnosed with cancer some time during their lifetimes. More than one million Americans develop cancer each year – a new case is diagnosed every 30 seconds. Cancer is the second leading cause of death after heart disease in the U.S.

Future discoveries will build on a strong record of breakthroughs at TSRI, including, to name only a few:

- Developing and testing the anti-leukemia drug cladribine (Leustatin® by Ortho Biotch), an intravenous medication with remarkably few side effects; cladribine now cures or produces many years of freedom from hairy cell leukemia in almost all those receiving treatment.
- Inventing an advanced blood test for detecting and analyzing circulating tumor cells—breakaway cells from cancer patients’ solid tumors.
- Devising a new technique for connecting drug molecules and antibodies to make highly targeted therapies called “antibody-drug conjugates”—that could be used, for example, to deliver toxic chemotherapy drugs to cancer cells while sparing most healthy cells.
- Identifying a new family of drug candidates with potential for treating breast, brain, skin and other cancers.
- Developing an innovative new method of economically synthesizing ingenol, a highly complex, plant-derived compound of interest to drug developers for its anti-cancer potential.
- Discovering a potentially beneficial use of a once-abandoned compound for the treatment of neuroblastoma, a devastating childhood cancer, and for preventing the progression of colon, prostate, skin and breast cancer—now in clinical trials worldwide.
- Discovering new, safe and highly effective drugs that disable cancer cell metabolism across a broad spectrum of human malignancies.

Half a dozen anti-cancer products based on research at TSRI are currently in various stages of clinical trials.

TSRI scientists, like Associate Professor Brunhilde Felding who is featured in the profile below, are poised to develop new approaches to save lives from this malicious and complex disease.

“I find that at TSRI you really have the freedom to explore ideas and unique opportunities for active collaborations that will improve patient care. This freedom and the diversity of exceptional and world-leading expertise at TSRI... are essential for the development of truly innovative therapies.”

—Associate Professor Brunhilde Felding
Many cancers, including those developing in the breast, prostate, lung, pancreas and the skin, have a propensity to metastasize and when they do, they can be deadly. Metastasis is a dangerous phenomenon in which cancer cells separate from a primary tumor, travel through the lymphatic system and bloodstream, anchor within a distant organ, and begin a satellite tumor that compromises the target organ. Although science and medicine have made tremendous strides in early detection and treatment, cancer still claims hundreds of thousands of lives each year in the U.S. alone – usually the end result of metastasis.

“Too many patients still die from metastatic cancer,” said TSRI Associate Professor Brunhilde Felding. “We are trying to find out what determines whether or not a tumor cell will metastasize. Our goal is to develop new therapies that can eliminate the spread of cancer, especially to the brain.”

Dr. Felding and her group have made progress. “We found antibodies that block the ability of human breast cancer cells to metastasize and help extinguish breast cancer that has already spread,” she said. “Optimizing these antibodies, we might be able to develop powerful anti-cancer drugs that can inhibit cancer spreading. I think we’re moving in the right direction.”

A major challenge that continues to hamper the success of cancer treatment is the development of resistance, especially to cell-killing therapies. This resistance ultimately rekindles the disease and causes relapse, often years later. Working to break this deadly paradigm, the Felding lab focuses on understanding metabolic changes in tumor cells that are critical for the advancement and persistence of the disease. “Based on our findings, we are developing a new strategy aimed at normalizing tumor cell metabolism without generating selective pressure, seeking to halt tumor growth without the emergence of resistant cells,” said Dr. Felding. “Our goal is to render a cancer quiescent and manageable, and to prevent disease progression and recurrence.”

Despite running a busy lab, Dr. Felding finds time for volunteer work with cancer advocates, for example in support of the National Breast Cancer Coalition. She teaches classes in basic cancer biology and lab work to visiting teams of cancer patient advocates. “Academia is great because you can follow a question out of curiosity, but these groups really bring home the message that we need to do research to improve cancer patients’ quality of life and their chances of overcoming the disease,” she said.

Dr. Felding came to TSRI in 1993 after receiving her Ph.D. in Germany. “It has been a labor of love,” she said. “The research has really allowed me to express myself and make a difference. I find that at TSRI you really have the freedom to explore ideas and unique opportunities for active collaborations that will improve patient care. This freedom and the diversity of exceptional and world-leading expertise at TSRI in immunology, chemistry, antibody engineering, and molecular and structural biology are essential for the development of truly innovative therapies.”
Alzheimer’s and Neurological Disease Initiative
Finding Answers, Providing Hope for a Better Future

As our population ages, the future economic impact of Alzheimer’s, Parkinson’s, and other neurodegenerative diseases is projected to greatly increase. But numbers cannot capture the human suffering of patients, families and caregivers caused by these diseases. Unfortunately, more than 200 completed clinical trials for Alzheimer’s have failed, as there is still too little basic information to inform the development of therapies.

Five million Americans currently suffer from Alzheimer’s, and there are no effective treatments and no early diagnostics. More than one million Americans currently suffer from Parkinson’s, with limited treatments for symptoms and no treatments to prevent brain cell death.

Your support of this initiative will enable TSRI scientists to build on a strong track record of breakthroughs in this area, including, to name only a few:

- Discovering the first drug shown to slow the progression of an amyloid disease – research has shown that both Alzheimer’s and Parkinson’s diseases are caused by the misfolding of specific proteins into structures that leads them to cluster together. These microscopic fibrils or plaques are called “amyloid” and form toxic deposits that interfere with organ function.
- Identifying a receptor in neurons that appears to control Parkinson’s damage to brain cells.
- Developing the first of a new class of highly selective compounds that effectively suppresses the severity of Multiple Sclerosis in animal models and offering other new approaches to the disease.
- Unveiling a surprising mechanism that controls brain formation—findings that have implications for understanding some forms of mental retardation, epilepsy, schizophrenia, autism and other diseases.
- Revealing a molecular pathway implicated in motor neuron disease.
- Developing compounds that reactivate the gene responsible for the inherited neurodegenerative disease Friedreich’s ataxia.

TSRI scientists, like Professor Thomas Kodadek who is featured in the profile below, are poised to develop new approaches to save lives from these devastating diseases of the brain and nervous system.

“Watching my father lose his identity, as he struggled with Alzheimer’s, devastated our family and created a deep fear of memory loss in me. So I sought to support those heroic scientists battling this terrifying disease. And I truly believe we are close to a cure.”

—Tess Gerritsen, best-selling novelist and founder of an online campaign to raise money for Alzheimer’s research at TSRI
Although scientists now understand a lot about the mechanism of Alzheimer’s disease (AD) at a basic level, these insights have yet to be translated into effective therapies.

Scripps Florida’s Tom Kodadek, vice chair of the Department of Chemistry, believes the major stumbling block is the absence of an inexpensive and effective blood test to pick up the disease in its early stages.

“I am often asked why we are so focused on developing an early AD diagnostic,” he said. “Since there is no approved drug for it, why would you want know? But it is extremely difficult to develop an effective drug in the absence of early detection.”

Dr. Kodadek points out several studies have shown the degeneration and death of neurons that eventually leads to AD is under way for at least 20 years before symptoms appear, at which point the patient’s brain has sustained massive damage.

“The irony is we may already have in hand potential drugs capable of reducing neurological damage,” said Dr. Kodadek. “But clinical trials are doomed to fail because these drugs are designed to slow the rate of neurodegeneration. With a test to identify patients early on, a clinical trial could determine the efficacy of such a drug in slowing or stopping progression of the disease.”

The snag in early detection to date has been that researchers have failed to identify molecules in the blood tightly linked to AD progression.

Dr. Kodadek and his colleagues, however, have hypothesized the immune system reacts to AD and, as part of that response, produces unique antibodies (antigens) directed against AD-specific molecules not present in a healthy person. If true, then a blood test monitoring these molecules would allow detection at a presymptomatic stage.

“When we first suggested this, many people thought we were a little nuts because of two big problems,” he said. “One is that there was no hard evidence that there is an immune reaction to AD. The second is that, even if there were, we have no idea what the antigens might be to measure their levels.”

To address these questions, Kodadek and colleagues developed a radical new approach. They created a collection of millions of different chemical compounds of varying shapes, sizes and properties and then exposed them to the circulating antibodies in healthy individuals or people with AD. By comparing the results, they were able to identify chemicals that bound to antibodies present in the blood of AD patients, but not healthy volunteers. These promising preliminary results were published in 2011.

Since then, the scientists have found in larger-scale trials that more work will be needed for their findings to become a clinically useful tool.

“We are going to have to put in more effort to either optimizing the antibody-binding chemicals and/or discovering improved probes,” said Dr. Kodadek. “We are exploring both of these avenues now. I am optimistic that this approach will eventually provide us with a good diagnostic for AD. Moreover, the work opens up a raft of possibilities in other areas, especially the early diagnosis of cancers and autoimmune diseases, which could have a huge clinical impact.”

Professor Tom Kodadek is working on early detection of Alzheimer’s, which he hopes will open the door to a host of new therapies.

Research Brief

Finding Clues to the Cause of a Mentally Debilitating Childhood Disorder

TSRI scientists led by Professor Jerold Chun have found what may be a major cause of congenital hydrocephalus, one of the most common neurological disorders of childhood that produces mental debilitation and sometimes death in premature and newborn children. The study in mice suggests that hydrocephalus can be triggered by abnormal levels of lysophosphatidic acid (LPA). LPA is a blood-borne lipid that can enter the brain in high concentrations during bleeding events, with profound effects on developing brain cells.

“This provides proof of concept for the medical treatment of this disease,” said Professor Jerold Chun (back), shown here with Research Associate Yun Yung.
**Initiative Against Diabetes and Obesity**

Combating the Epidemic, Diminishing Suffering

The national epidemic of diabetes, obesity and related conditions is alarming. While diet and inactivity have contributed to this situation, a lack of fundamental understanding of the complexities of how humans use and store the energy that our cells need to survive has hampered the development of life-changing therapies. Scientists at TSRI are focusing on uncovering this mystery and much more – how aging affects our metabolic rate, how junk food can become an addiction, and how current therapies work in our body – this information is critical to the development of safer and more effective medicines to combat diabetes and obesity.

Diabetes is a contributing factor in a range of health problems, including heart disease, stroke, hypertension, blindness and eye problems, kidney disease, nervous system damage, and amputations. A staggering 79 million Americans today are considered prediabetic. Obesity is affecting an increasing number of Americans – now over one third of adults and 17% of children are obese.

You can help make the next breakthrough a reality with your support. Future discoveries will build on a strong track record of breakthroughs at TSRI, including, to name only a few:

- Establishing a new class of an anti-diabetic compound targeting a unique molecular switch.
- Pioneering an anti-obesity vaccine that significantly slowed weight gain and reduced body fat in animal models.
- Discovering a catalytic antibody that degrades a known appetite stimulant, a potential treatment for obesity.
- Identifying a key regulator of fat cell development that may provide a target for obesity and diabetes drugs.

TSRI scientists, like Assistant Professor Michael Conkright, who is featured in the article below, are poised to develop new approaches to improve health and save lives.

“I like supporting a new medical innovation with mass application that could potentially help millions of people. There is no better place to make a philanthropic investment in medical research and human health than The Scripps Research Institute. All of us in the community are very lucky to have such a world class institution in our own backyard.”

—Rick Stone, donor to diabetes research at TSRI
Michael Conkright: Revealing the Molecular Secrets of Short, Intense Workouts

In the last few years, the benefits of short, intense workouts have been extolled by both researchers and exercise fans as something of a metabolic panacea capable of providing greater overall fitness, better blood sugar control, and weight reduction—all of it in periods as short as seven minutes a few times a week.

In research featured recently in The New York Times, a team led by Scripps Florida biologist Michael Conkright have confirmed that there is something molecularly unique about intense exercise: the activation of a single protein. That protein is known as CRTC2.

The scientists showed that following high-intensity exercise, which enlists the sympathetic nervous system’s “fight or flight” response, CRTC2 integrates signals from two different pathways—the adrenaline pathway and the calcium pathway, to direct muscle adaptation and growth only in the contracting muscle.

Using mice genetically modified to conditionally express CRTC2, the scientists showed that molecular changes occurred that emulated exercised muscles in the absence of exercise.

“The sympathetic nervous system gets turned on during intense exercise, but many had believed it wasn’t specific enough to drive specific adaptations in exercised muscle,” said Dr. Conkright. “Our findings show that not only does it target those specific muscles, but it improves them—the long-term benefits correlate with the intensity of the workout.”

In the genetically altered animal models, this resulted in a muscle size increase of approximately 15 percent. Metabolic parameters, indicating the amount of fuel available to the muscles, also increased substantially—triglycerides went up 48 percent, while glycogen supplies rose by a startling 121 percent.

In an exercise stress test, the genetically altered animals improved 103 percent after the gene was activated, compared to an 8.5 percent improvement in normal animals.

“If you think of the adrenaline system as something that mobilizes resources when you encounter, say, a bear on your way to work, what we found is that the system also gets you ready for your next bear encounter,” Conkright said.

The new findings open the door to a range of potential exercise enhancements.

The team is now exploring ways to activate CRTC2 so that even an average exercise routine might be made more beneficial.

Research Brief

Mapping a Way to Better Diabetes Drugs

A team led by William E. Balch, professor and member of the Skaggs Institute for Chemical Biology at TSRI, has created the first comprehensive roadmap of the protein interactions that enable cells in the pancreas to produce, store and secrete the hormone insulin. The research findings, reported recently in the journal Cell Reports, make possible a deeper scientific understanding of the insulin secretion process—and how it fails in insulin disorders such as type 2 diabetes.
Addiction Science for New Therapies
Saving Lives Through Science

Addiction touches so many lives. One in every 10 Americans is addicted to alcohol or drugs. Yet only about 10 percent of those who suffer from addiction receive medication to treat it. Science can help change this picture. Understanding the biological, environmental and genetic factors that contribute to addiction is absolutely critical to overcoming this heartbreaking epidemic and saving lives.

Alcohol abuse leads to 88,000 deaths in the U.S. each year and an estimated 76 million Americans have been exposed to alcoholism in the family. Overdoses from illicit drugs – including cocaine, methamphetamine, heroin, “bath salts” and other drugs of abuse – kill nearly 40,000 each year.

Future discoveries will build on a strong track record of breakthroughs at TSRI, including, to name only a few:

- Facilitating the approval of two drugs to treat alcohol dependence.
- Developing an antidote for cocaine overdose in a preclinical study.
- Creating preliminary vaccines against the effects of nicotine, heroin, cocaine and methamphetamine – potential treatments that could support addicts committed to recovery by preventing these substances from ever reaching the brain.
- Conducting the first randomized, controlled clinical trial showing that gabapentin, an FDA-approved drug used for seizures and some types of pain, is safe and effective for treating alcohol dependence while diminishing mood and sleep disturbances.
- Showing a combination of two existing medications (naltrexone and buprenorphine) has potential for people addicted to cocaine, offering a therapy that would reduce their craving for the drug and blunt their symptoms of withdrawal.
- Identifying a pathway in the brain that regulates an individual’s vulnerability to the addictive properties of nicotine, suggesting a new target for anti-smoking therapies.

TSRI scientists, like Professor Kim Janda who is featured in the profile below, have long been leaders in the field of addiction studies, conducting groundbreaking research that has changed the way we think about addiction and the tools we have available to treat it. Yet there is much more to do.

“Many people fail to realize what a powerful, costly, and deadly disease alcoholism is, and how many lives are affected by it. I believe that with increased funding by the government and dedicated individuals, we can make advances similar to those that have been made for cancer, heart disease, and other major medical conditions in the area of alcoholism and addiction research. I’m pleased with my decision to give to The Scripps Research Institute and I plan to make additional financial commitments in this area of research in both the private and institutional sectors in the years to come.”

—Mark Pearson, TSRI trustee and donor
Kim Janda: Hope in the Battle Against Drug Addiction

Heroin, meth, cocaine – it’s easy to get hooked on them, but hard to kick the habit. Hope in the form of a new way to battle addiction could be coming from the laboratory of Kim Janda, Ely R. Callaway, Jr. Professor of Chemistry, director of the Worm Institute for Research and Medicine, and member of The Skaggs Institute for Chemical Biology at TSRI, who is in the vanguard of addiction science.

Worldwide, an estimated 12 to 14 million people use the illicit drug heroin. Recognizing this, Dr. Janda has developed a heroin-blocking vaccine that is ready for human clinical trials. The new vaccine stops heroin from reaching the pleasure centers in the brain, preventing a “high.” Vaccinated rats that went through withdrawal and then had access to heroin again did not seek out the drug.

Addiction researchers have been trying for decades to concoct a vaccine that neutralizes the effects of heroin, with various degrees of success. But Dr. Janda took a different approach, based on his insights into chemistry.

“The vaccine causes the body to produce antibodies against not only heroin, but importantly its psychoactive metabolites and that is the key to the success of our vaccine that others missed,” said Dr. Janda. “These antibodies circulate in the bloodstream, and neutralize any of these substances they encounter before they reach the brain. It’s like the old ’80s game Pac-Man … seek and destroy the drug.”

The vaccine isn’t intended to provide a one-stop solution for heroin addicts. It’s meant to help addicts struggling to overcome the addiction to the drug by eliminating the damaging effect of a drug relapse.

Money is the main obstacle to beginning human testing. Dr. Janda and his colleagues are looking for a philanthropist to fund the clinical trials.

Dr. Janda has also been developing other anti-drug vaccines since the 1990s, such as a cocaine vaccine now in Phase 2 clinical trials. His team’s vaccine against methamphetamine, an addiction for an estimated 25 million people worldwide, is also nearing readiness for such tests.

“We view our drug-abuse vaccines to be most useful with addicts who are prepared to quit, but have problems with abstinence,” said Dr. Janda. “Addiction is devastating to not only the addicts, but their families, friends, and society in general. It’s heartbreaking when you see the results of addiction. Our vaccines provide hope to those prepared to overcome the challenges of the addiction cycle.”

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Research Brief

Stopping the Addictive Cycle

Scientists from TSRI’s Florida campus, led by Associate Professor Laura Bohn, have described findings that could enable the development of more effective drugs for addiction with fewer side effects. The study showed in a combination of cell and animal studies that one active compound known as 6’- guanidinonaltrindole (6’-GNTI), maintains a strong bias towards a single biological pathway, providing insight into what future drugs could look like.

“Essentially, we have shown an important link between cell-based screening assays and what occurs naturally in animal models,” said Associate Professor Laura Bohn.
A myriad of viruses and bacteria are responsible for human diseases worldwide. These organisms are constantly mutating, greatly complicating efforts to counteract them. The need for new defenses against these diseases is pressing. Vaccines, which currently save an estimated 2.5 million lives every year, in particular continue to hold promise for protecting against current and emerging threats.

The influenza virus harbors the potential for causing global pandemics such as the four that have struck in the last 100 years. An estimated 1.1 million people in the U.S. and 34 million people worldwide currently live with HIV. Ebola hemorrhagic fever, caused by the Ebola virus, is one of the most virulent diseases known to humans; the fatality rate can be up to 90 percent depending on which strain is involved. One third of the world’s population is infected with tuberculosis.

Your support of this initiative will enable TSRI scientists to build on a strong record of breakthroughs, including, to name only a few:

- Discovering and characterizing antibodies that target critical sites of vulnerability on a variety of viruses—including HIV, influenza and hepatitis C.
- Describing the mechanisms of action of important Ebola virus proteins, providing potential new targets for drugs.
- Developing the first screening method that rapidly identifies individuals with active river blindness, a parasitic disease that afflicts an estimated 37 million people.
- Discovering a promising new compound that attacks tuberculosis in two different ways.

Scientists, like Professor Erica Ollmann Saphire who is featured in the profile below, are poised to develop new vaccines and other interventions to save lives.

“Private philanthropic support has provided us with the seed money for risky projects. With these funds, we’ve been able to do the big initial work and make discoveries that then set up the next 10 years of federal funding.”

—Professor Erica Ollmann Saphire

The Ebola virus, pictured above, causes a disease with a fatality rate of up to 90 percent.
Biomedical researchers in search of knowledge about viruses and diseases typically make their discoveries in labs. But for TSRI Professor Erica Ollmann Saphire, the key to understanding deadly viruses also lies in meeting them in their den – the deep reaches of the African jungle.

Dr. Saphire has several times traded her climate-controlled La Jolla lab for the 95-degree humidity of the West African jungle, where she has tracked the Ebola virus, Lassa hemorrhagic fever, and related pathogens, such as Marburg virus – the subjects of her research for the past 10 years.

“It is an opportunity to see where these viruses live,” said Dr. Saphire. “In the lab, we use biochemistry and biophysics to visualize and understand their component molecules. But these molecules are made this way so they can function not in a lab, but in a rainforest, cave, or hut … In Africa, you also see the people affected, and that provides inspiration to keep working on the problem. Our goal is a roadmap for understanding and conquering these viruses, which have been largely undefeatable.”

The Ebola virus is among the more horrific known to humankind, and there is currently no cure for Ebola hemorrhagic fever, which inflicts a death rate as high as 90 percent. It spreads when people come into contact with the bodily fluids of an infected individual. Symptoms first include a fever, headache, and sore throat, then progress to vomiting, diarrhea, rash, and kidney and liver failure. In the final stages, massive hemorrhaging causes heavy bleeding from body openings and internal organs.

Dr. Saphire has made headlines as the woman who broke open the secrets of the Ebola virus. Her breakthrough study on Ebola appeared on the cover of the journal Nature, lifting the veil from the virus’s spike-shaped protein and finding a weak spot, a critical step in understanding how Ebola works and developing any potential treatment or a vaccine.

Her latest project focuses on finding the best antibody “cocktail” to fight the Ebola virus. With a five-year grant of up to $28 million from the National Institutes of Health, Dr. Saphire will lead a new multi-institutional center dedicated to identifying the most effective antibody treatment. The funds funnel out to 20 labs in seven countries, bringing those in the field together in a singular effort towards a definitive treatment. Dr. Saphire and her team are also working to develop a diagnostic.

The chief of the village of Yawei in Sierra Leone was so grateful for the team’s work, which included trapping rodents that helped rid the village of Lassa, that he gave them a goat, a prized possession that normally costs a year’s salary, as a gift in gratitude.

Dr. Saphire’s colleagues describe her as a brilliant, tenacious star in the world of virus fighters – she is committed to defeating the worst viruses and never gives up – ever.

Research Brief

A Natural Compound that Virtually Eliminates HIV

A study by biologist Susana Valente and her colleagues on TSRI’s Florida campus shows a natural compound can virtually eliminate human immunodeficiency virus (HIV) in infected cells. The compound defines a novel class of HIV anti-viral drugs endowed with the capacity to repress viral replication in acutely and chronically infected cells. The medically promising compound is known as Cortistatin A. This natural product was isolated in 2006 from a marine sponge, Corticium simplex, discovered more than 100 years ago.

The compound under study virtually eliminates all viral replication from already-infected cells where HIV hides.
Healthy Aging Initiative
Better Health as We Age, Within Our Grasp

Aging affects everyone, and few questions are more important than how we can age more healthfully. Researchers at TSRI are working to find ways to make healthy aging a possibility within the grasp of us all. TSRI has a department dedicated to research on aging—one of only a few in the nation focused on age-related metabolic changes.

Aging results in impaired function of all organs and tissues. Currently those over the age of 65 comprise the fastest-growing segment of the world’s population. It is estimated that by 2030, there will be about 72.1 million people 65 or older in the U.S., more than twice their number in 2000. Aging is associated with a range of diseases and conditions, including coronary heart disease, stroke, cancer, Alzheimer’s, Parkinson’s, vision and hearing loss, osteoarthritis, osteoporosis and type 2 diabetes.

You can help make the next breakthrough a reality with your support. Future discoveries will build on a strong track record of breakthroughs at TSRI, including, to name only a few:

- Identifying signaling pathways activated with aging that represent novel therapeutic targets.
- Finding therapeutic targets to prevent onset of metabolic syndrome—which raises the risk for heart disease, diabetes and stroke—during aging.
- Pioneering approaches for the treatment and prevention of osteoarthritis.
- Developing the use of adult stem cells for treating age-related diseases, including vision loss.

TSRI scientists, like Professor Paul Robbins who is featured in the profile below, are poised to develop new approaches to staying healthy as we age.

“A medical research is extremely important to me. I contribute to research at TSRI because I feel it’s the building block for improved health and saving lives. Medical research is often serendipitous—the most significant research usually comes about when people are looking for something else entirely. Many diseases in our lifetime would not have been cured without multi-disciplinary science. What I like about TSRI is that it furthers science by integrating various disciplines like biology, chemistry, physics, and molecular biology.”
—Eleanor Mosca, donor

Aging affects all cells in the body, including endocrine cells called islets (as shown above).
In the next 20 years, the number of individuals in the United States over the age of 65 is projected to double, reaching more than 70 million. More than 90 percent of Americans over 65 have at least one chronic disease, while more than 70 percent have at least two.

While aging may be one of the most familiar (and certainly one of the most discussed) aspects of human biology, it remains one of the least understood. We age but no one really knows precisely how we get there.

Thanks to a new $10.6 million National Institute on Aging grant to a team led by Professor Paul Robbins on the Scripps Florida campus, the puzzling questions of human aging may soon receive answers.

The study will focus on identifying just how damage that accumulates over time drives the human aging process. The scientists will focus their research on stress caused by DNA damage, specifically by looking at the effects of taking away a cell’s ability to repair this damage.

Dr. Robbins is also looking at compounds and even stem cells that could affect stress response pathways in a therapeutic way. “It’s something that our research and the TSRI research environment lend themselves to – identifying pathways as potential therapeutic targets and screening potential drug candidates,” he said. “The ultimate goal isn’t to allow people to live longer, but to help them maintain good health as they age.”

Budget cuts at the National Institutes of Health (NIH), have wiped out more than 25 percent of overall funding for research and development since 2003, increasing the need for private giving and creating a challenge for scientists. Dr. Robbins’s $10.6 million grant actually constitutes an 18-percent cut from the funds that he and his team proposed to optimally perform the research.

In his research program, Dr. Robbins focuses on various biological approaches to understanding and treating age-related degenerative diseases, including cancer and diabetes. He has developed a gene therapy approach for treating arthritis and is participating in a clinical trial for osteoarthritis. His laboratory is also studying a novel peptide for bone healing.

“The quality of the research at TSRI is spectacular, not to mention the collaborative atmosphere and the outstanding facilities,” said Dr. Robbins.

Dr. Robbins recently was one of the organizers of the first Scripps Florida Spring Workshop on Biology and Aging, a four-day event devoted to figuring out what might be the best therapeutic approaches to extend human “healthspan” over the next decade. Dozens of scientists from around the country came to Jupiter, Florida to take part in the event.

“The symposium was an unqualified success,” said Dr. Robbins. “It was a remarkable commentary on the growing interest of aging research and a good sign we’re moving in the right direction to develop drugs able to extend human healthspan.”

Professor Paul Robbins is investigating just how damage that accumulates over time drives the human aging process.

Research Brief

Team Finds ‘Weakest Link’ in the Aging Proteome

Proteins are the chief actors in cells, carrying out the duties specified by information encoded in our genes. Most proteins live only two days or less, ensuring that those damaged by inevitable chemical modifications are replaced with new functional copies. A team led by researchers including TSRI Professor John Yates have identified a small subset of proteins in the brain that persist for longer, even more than a year, without being replaced. These long-lived proteins have lifespans significantly longer than the typical protein, and their identification may be relevant to understanding the molecular basis of aging.

Research Brief

Team Finds ‘Weakest Link’ in the Aging Proteome

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The study led by Professor Yates was featured on the cover of the journal Cell.
Become a Partner in TSRI’s Initiatives to Find Answers, Provide Hope, and Save Lives

There are many ways you can support TSRI’s new initiatives and every dollar raised makes a difference in the lives of millions of people who have devastating diseases around the world. Most donors make gifts and pledge payments by check, credit card, or automatic bank drafts. Others take advantage of tax savings that come from giving appreciated stocks, shares of mutual funds, or real estate. Gifts can be designated to any of the initiatives. For your convenience, we offer a variety of ways for you to make a donation.

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—Doug Dawson, Ellen Browning Scripps Foundation