SPRI NEWS
Steadman Philippon Research Institute

REGENERATIVE MEDICINE SPOTLIGHT

Get to Know SPRI's Healthy Aging Program

SPRING 2019

A SPRI scientist works with a sample of platelet-rich plasma

SPRI Regenerative Medicine Program on Healthy Aging

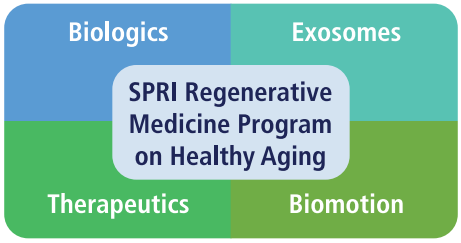
An Innovative Research Program at SPRI is Designed to Help People Age Better and Healthier

The mission of the Steadman Philippon Research Institute (SPRI) Regenerative Medicine Program on Healthy Aging is to understand the influence of age on biologics, develop rejuvenating therapies and translate these discoveries into clinical applications for Healthy Aging.

Everyone ages, and SPRI is committed to finding ways for people to age better and healthier. Built upon the institute's orthopaedic focus, SPRI looks at musculoskeletal disorders—like osteoarthritis—as an age-related disease. This lens allows SPRI's scientists to take a comprehensive approach to their research—instead of looking at something in just one way, SPRI considers multiple perspectives and hypotheses to discover the best treatments.

A FOUR-TIER APPROACH

Under the leadership of Johnny Huard, Ph.D.—SPRI's Chief Scientific Officer and Director of the Center for Regenerative Sports Medicine (CRSM)—the Regenerative Medicine Program on Healthy Aging is focused on four key areas in pursuit of its mission.



BIOLOGICS

Biologic treatments include stem cell therapies, bone marrow concentrate, platelet-rich plasma and adipose tissue-based therapeutics. This tier of the Regenerative Medicine Program on Healthy Aging focuses on the necessary basic science studies to understand the impact of aging at the molecular and cellular level. In performing these studies, SPRI researchers will develop translational approaches to rejuvenating biologics for their best uses.

EXOSOMES

Exosomes are a new and exciting element of SPRI's healthy aging research. Exosomes are microscopic vesicles secreted from stem cells, and SPRI scientists believe they may have the potential to be even more translational than stem cells.

THERAPEUTICS

Therapeutics are an important aspect of SPRI's heathy aging research—our scientists aim to discover whether certain drugs and supplements can improve treatments, delay the effects of aging on cells and tissues and improve cell and tissue function.

BIOMOTION

Evidence suggests that exercise is a force that may be used to rejuvenate cell function. For example, adult stem cells come from blood vessels, and promoting blood vessel formation through exercise could improve stem cell function.

This four-tier methodology enables SPRI to explore different approaches to healthy aging. "In science," said Dr. Huard, "you can't just have one idea and put all of your efforts into that one idea. What if the idea doesn't work? Instead, we're exploring a lot of different ideas about healthy aging, all with one focus: to help people age better."

Exploring New Uses for Proven Therapeutics

SPRI Scientist Sudheer Ravuri, Ph.D. at Forefront of New Discovery

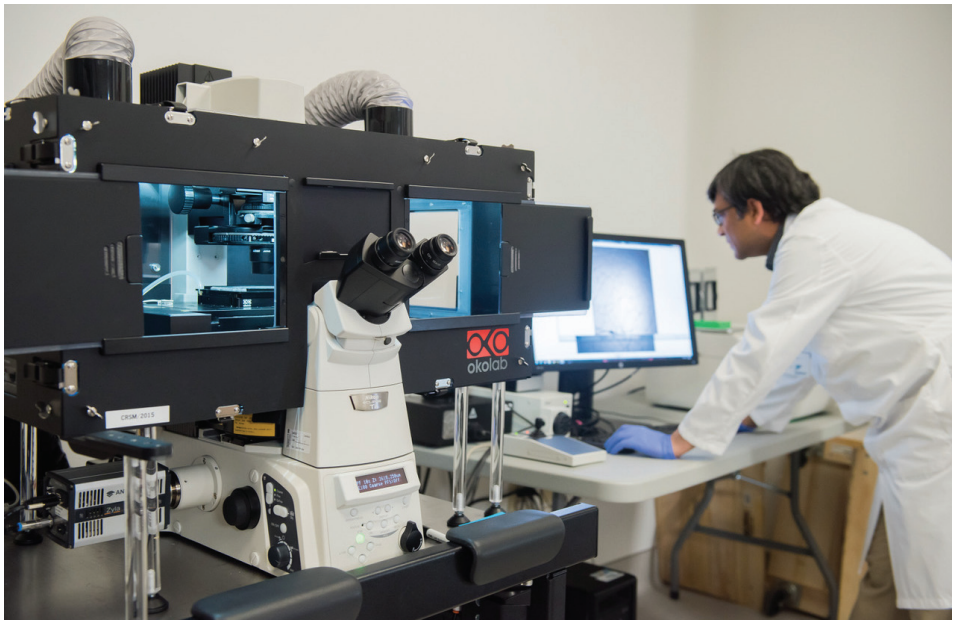
Founded at SPRI in 2015, the Center for Regenerative Sports Medicine (CRSM) has always been committed to bench-to-bedside research, a term scientists at SPRI use to describe studies that begin at the laboratory bench and develop into treatments or therapies that physicians will use for their patients. Also known as clinical translation, it's an important part of SPRI's mission—all of the research performed at SPRI is aimed at finding cures and enhancing lives.

NEW APPROACH TO AN OLD DRUG

When SPRI formally launched its Regenerative Medicine Program on Healthy Aging, it's no surprise that every aspect of the program was designed with a patient focus in mind. Therapeutics, a key tier of the program, isn't only about creating something new—it's also about exploring if existing therapeutics can be used in a new way. That's why SPRI scientist Dr. Sudheer Ravuri explored whether or not an FDA-approved drug for treating worm infestations could have another effect—killing senescent (old or deteriorating) stem cells.

It may seem unlikely that a drug aimed at treating a parasitic infection would be used for treating aged cells in the body, but when you consider senescence in a similar way—senescent cells create more senescent cells, almost like the spread of an infection, the connection seems much clearer. This, coupled with other investigations into this drug, encouraged Dr. Ravuri to investigate further.

"I read about this drug being used in cancer trials, that it showed the potential to inhibit tumors from growing. Knowing about the relationship between senescent cells and cancer (we often think of senescent cells as early cancer, or cells that may turn into cancer cells) I thought that examining the effect of this drug on senescent cells could have major significance."



Dr. Sudheer Ravuri at work in SPRI's laboratory

INVESTIGATING THE IDEA

With this idea in mind, Dr. Ravuri began testing his hypothesis. He used laboratory models to explore the effects of the drug on their senescent cells and discovered that his hypothesis was correct—using this drug demonstrated that senescence could be eliminated in the models.

Dr. Ravuri submitted his results to the International Federation for Adipose Therapeutics and Science (IFATS) and his work was accepted. He gave a talk on his findings, and now plans to pursue additional experiments and eventually, intellectual property for this novel treatment.

"We know senescent cells have a negative effect on aging," said CRSM director Dr. Johnny Huard. "For example, we believe that senescence may hinder the way you heal following an injury or a surgery. Discovering the science that will help us eliminate this condition, like Dr. Ravuri's research, is extremely important."

LOOKING TO THE BEDSIDE

With success in the preliminary studies, the next step is to investigate this drug clinically. The drug could be prescribed to patients or delivered locally—that will be determined by Dr. Ravuri and the physicians with whom he collaborates.

"With this drug being FDA-approved and seeing the results in laboratory experiments, it's exciting to know that the path to the clinic is now shorter," said Dr. Ravuri. "We hope it will make a major difference in how people heal."

Clinical Trials: A Vital Component of Translational Research

SPRI Launched More Clinical Trials in 2018 than Ever Before; More Clinical Trials Planned for 2019

When considering bench-to-bedside or translational research, clinical trials are an imperative step—they are the method by which scientists and physicians validate treatments before they reach a wider patient audience. Clinical trials give credibility to research, because they show evidence of how a treatment works in patients.

BUILDING FROM HISTORY

SPRI has been conducting retrospective clinical trials since the organization was founded in 1988—these types of clinical trials involve looking at patient outcomes. Both Dr. Steadman and Dr. Philippon—SPRI's Co-Chairs—have recently published 20- and 10-year outcomes studies for their innovative surgical treatments. In the case of both physicians, these surgical treatments have become the gold standard of care in well-selected patients; their retrospective outcomes studies further validated their techniques.

Prospective clinical trials are relatively new for SPRI; these trials watch for outcomes—like the success of a treatment—during a study period. These clinical trials are the way in which SPRI validates its new treatments and therapies, and with the launch of ProofPoint Biologics, SPRI and The Steadman Clinic started more prospective clinical trials in 2018 than ever before. In 2018, ProofPoint Biologics processed 918 patient samples, helping SPRI to run 6 clinical trials on biologic treatments like platelet-rich plasma (PRP) and bone marrow concentrate. The institute also launched a clinical trial on a knee brace designed for stabilizing the ACL in the Department of Biomedical Engineering. New clinical trials are already underway in 2019, with more under review and planned. SPRI will likely have 10 active clinical trials up and running by the end of the year.

CLINICAL TRIALS AND THE HEALTHY AGING PROGRAM

In addition to its robust work in biologics trials, which represent a significant aspect of the Regenerative Medicine Program on Healthy Aging, SPRI is currently engaged in several therapeutic clinical trials that look at new uses for FDA-approved therapies. They include a hypertension drug that reduces fibrosis following surgery and a cancer drug shown to improve joint healing, amongst other therapeutics.

"Age effects the way we heal," said SPRI scientist Dr. Chelsea Bahney. "When you look at how a child, adult, or elderly person recovers from injury or a surgery, the differences in timeframe is remarkable. The older a person is, the longer it may take for them to heal."

This makes these clinical trials especially impactful. Improving healing for all patients is important, and it can be even more significant in older populations facing other aging-related challenges.

A GLOBAL FOCUS

With a passion for evidence-based medicine, SPRI looks to perform more clinical trials to test their ideas for new therapies. Once new treatments and techniques are validated in clinical trials, they can be shared with a wider audience. According to Dr. Huard, "the ultimate goal here is a global one. We're not just looking to help patients locally; we want to discover treatments that will help people all over the world."

The Steadman Clinic physician and SPRI researcher Dr. Thos Evans extracts bone marrow from a patient as part of a clinical trial

Chelsea S. Bahney, Ph.D. Joins Center for Regenerative Sports Medicine

Former patient of The Steadman Clinic returns to Vail as Top Scientist

SPRI welcomed scientist Dr. Chelsea Bahney in August 2018 to launch the Bone Repair and Skeletal Engineering Program in SPRI's Center for Regenerative Sports Medicine (CRSM). Most recently faculty at the University of California, San Francisco (UCSF), Dr. Bahney has dedicated her career to harnessing regenerative medicine to find solutions to bone and cartilage injuries.

Although Dr. Bahney is new to SPRI, she's no stranger to the community here. Nearly two decades ago, Dr. Bahney suffered a serious knee injury while she competed for the University of Colorado's Freestyle Ski Team. Her surgeon was none other than Dr. J. Richard Steadman, founder of The Steadman Clinic and SPRI.

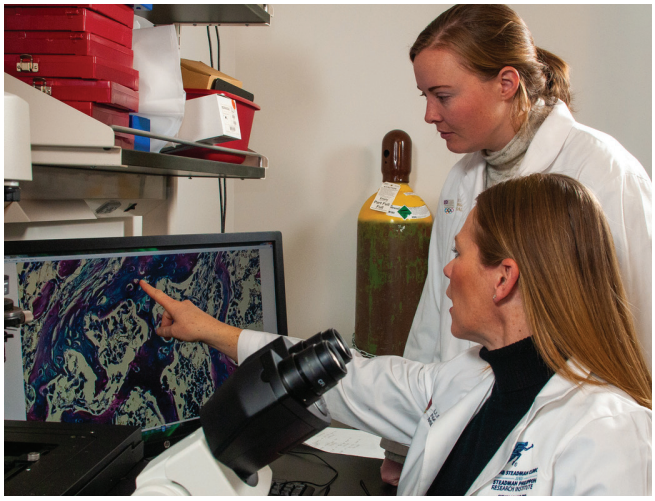
Now a top scientist in her field, Dr. Bahney's own experience as a patient influenced her career interests. "My passion, which I discovered in my undergraduate years, was tissue engineering, partially motivated by all of my injuries when I was racing in college and from my time as a patient at The Steadman Clinic. I must admit that my professional goals were driven by a little bit of selfishness to find better ways to keep myself active."

FOCUSING ON FRACTURES

With a focus on bone repair and skeletal engineering, much of Dr. Bahney's scientific focus currently revolves around fracture healing. And while it may seem like a distinct research focus from other healthy aging projects, Dr. Bahney sees this research as an imperative piece of the program.

"Fractures are intrinsically connected with aging," she explained. "One in three women and one in five men will suffer from an osteoporotic—brittle bone—fracture as they age. A young child might heal from their fracture in six weeks; in people over 65 it may take six to nine months or fail to heal at all. Poor healing as we age is associated with decreased activity of your stem cells, blood circulation and increased inflammation."

To solve this problem, Dr. Bahney is taking a step-by-step approach to understanding the molecular and cellular processes of fracture healing. "We know the long-term goal is to develop novel strategies to stimulate fracture repair," explained Dr. Bahney, "but first we need to understand the biological processes that contribute to poor bone regeneration in the elderly skeleton to ensure our therapy is effective."



Dr. Chelsea Bahney and Research Technician Lizzie Morris review findings in the lab

INITIATING NEW RESEARCH

The research will begin with characterizing the function of stem cells during fracture healing in old and young populations. Next, researchers will use a novel biomarker—recently validated by Dr. Bahney's team in a clinical trial—to quantify how healing differs in old and young fractures and finally, Dr. Bahney and SPRI scientists will work to therapeutically activate the stem cell gene Sox2 to accelerate fracture healing in elderly patients.

Dr. Bahney is excited to begin this project in the Regenerative Medicine Program on Healthy Aging. "To our knowledge, we are the first scientists to propose the concept of rejuvenating native stem cells by therapeutically activating the Sox2 gene to promote repair following injury," she said. "This research has tremendous promise and could greatly impact how people recover from fractures—which are so common in older patients. Importantly, this research has a broader implication in regenerative medicine since we know Sox2 is a marker of stem cells in the adult brain, gut and salivary gland."

COLLABORATION IS KEY

Now in the second half of her first year at SPRI, Dr. Bahney is enthusiastic about the science being performed across the institute. "One of the many things that drew me to SPRI was the way the different departments collaborate and work together. We're talking about the Regenerative Medicine Program on Healthy Aging, but it's not just the Center for Regenerative Sports Medicine that's involved in the research—we've got Biomedical Engineering working on exercise and Biomotion studies, Imaging Research using advanced imaging to look at blood vessel formation and tissue regeneration, our Outcomes Research tracking our patients—even our Education department teaching the fellows and scholars about our new treatments and sharing our discoveries with the public. And of course, our connection with The Steadman Clinic lets us translate our discoveries directly to patients. The entire Institute is working together in the Healthy Aging program, and that's just one reason why this place is so special."