LONGER, BETTER LIVES

WITH THE UW INSTITUTE FOR STEM CELL AND REGENERATIVE MEDICINE

Imagine a branch of research that has the potential to take on heart disease, cancer, diabetes, Alzheimer's, vision loss, muscular disorders and other illnesses that rob people of their well-being, even their lives. At the Institute for Stem Cell and Regenerative Medicine (ISCRM) at UW Medicine, we are asking big, difficult-to-answer questions about these complex conditions. And we're discovering answers.

Take, for instance, the recent, world-leading advances we've made in addressing heart disease. It's responsible for one in every four deaths in the U.S., and it costs billions each year. ISCRM researchers are repairing damaged cardiac tissue by regenerating heart muscle and using gene therapy to strengthen heart contractions — and these are just two of the projects that could have a dramatic impact on people's lives.

In heart regeneration and in other areas, advances — even cures — may be just a few years away. We welcome this opportunity to share information on some of our most promising research projects. With you, we can make a brighter future for us, for our children, for our community and for our world.

ISCRM'S "TOP FIVE" WHAT MAKES US UNIQUE?

1. **True collaboration.** We designed ISCRM — from the ground up — to bring researchers together, fostering discoveries and serendipity.
2. **Prime real estate.** Our center of operations is located in the tech-research hub of Seattle's South Lake Union neighborhood, fostering a spirit of entrepreneurship.
3. **Discoveries that work.** We are dedicated to translating discoveries into action: treatments, cures, diagnostics.
4. **Only the best.** ISCRM is one of the University of Washington's prize possessions, and its faculty are global leaders in their fields.
5. **The draw of the cores.** We possess three technological cores that give scientists new opportunities to explore high-tech avenues of research.

THE GRAND EXPERIMENT: FOUNDING ISCRM

Collaboration is a demonstrated key to success. As medicine becomes ever more sophisticated and complex, working together — augmenting knowledge, developing big ideas — has become absolutely necessary. In fact, this collaboration is vital in two essential and complementary pursuits in medical science: understanding the roots of disease and finding new treatments.

When UW Medicine and the University of Washington (UW) created ISCRM in 2006, it was something of a grand experiment. Our goal was to break down walls between stem cell researchers, physicians and other researchers, to have them work together, combining disciplines, expertise and proximity in order to make progress. And to take advantage of UW Medicine's considerable strengths in basic research and its track record of translating science into therapies.

Expertise, proximity, serendipity: the experiment has worked better than we hoped. ISCRM has grown into a world-class institution, one that now includes more than 130 faculty members from 38 UW departments and eight institutions, with its hub located at UW Medicine at South Lake Union. This hub is the site of ISCRM's powerful and productive "cores," suites of technological tools and expertise that catapult science forward.

POWERING MEDICAL RESEARCH: THE CORES

ISCRM's success is founded upon its cores — high-tech equipment, funded by generous, visionary local philanthropists — that speed the work of ISCRM's researchers and their collaborators in the community.

It's an efficient system, one that allows many scientists to share three very important and expensive resources. Investigators also benefit from the expertise of the researchers who manage each core.

THE TOM AND SUE ELLISON STEM CELL CORE LAB

This state-of-the-art facility is the only venue in the region where scientists can collaborate on and receive training in stem cell work, and it is one of the most advanced facilities of its kind in the country. The Ellison core is focused on nurturing scientists, helping them conduct pilot studies that provide excellent preliminary data.

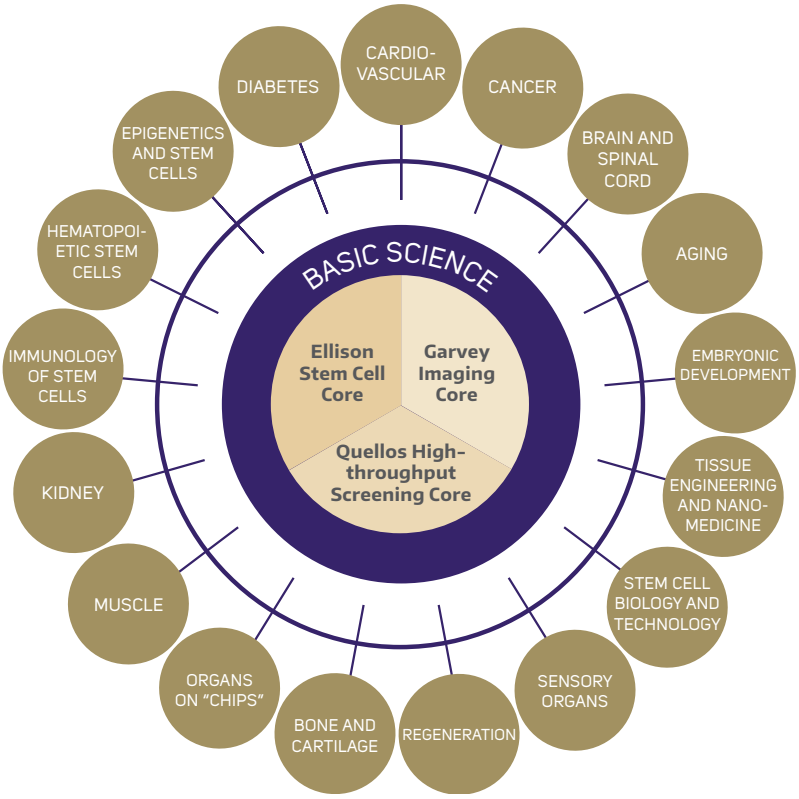
THE QUELLOS HIGH-THROUGHPUT SCREENING FACILITY

This facility allows researchers to use robots to screen for candidate drugs as well as probe the functions of every gene in a cell. It is the only academic facility of its kind in the state and one of only a few on the West Coast.

THE LYNN AND MIKE GARVEY CELL IMAGING CENTER

This center provides leading-edge, advanced microscopy equipment to researchers, which allows them to visualize stem cells both in lab cultures and within living animals.

OUR CORES SUPPORT RESEARCH THAT COVERS ENORMOUS GROUND IN UNDERSTANDING HUMAN HEALTH, INCLUDING:



THE BUILDING BLOCKS: STEM CELLS

Stem cells have the remarkable ability to change — to differentiate — into other types of cells that replenish and repair damaged tissues throughout the body. Researchers at ISCRM work with several types, including:

Pluripotent stem cells: with an unlimited capacity to divide and the ability to become any cell type in the human body, these are the most versatile stem cells. Pluripotent stem cells can be produced at large scale for therapies or research applications like drug screens or genetic testing.

Adult stem cells: unspecialized cells found in low numbers within many adult tissues; responsible for the body's maintenance and repair. Although their ability to differentiate is more limited than pluripotent stem cells, they have been harnessed for the first stem cell therapy, bone marrow transplantation.

PROFOUND DEVELOPMENTS: HEART REPAIR AND OTHER PROJECTS

Since the founding of ISCRM in 2006, our researchers have been making stellar progress in conducting basic science research and working on treatments for specific diseases, including heart disease. Heart failure is the No. 1 cause of death, hospitalization and healthcare costs in the U.S.; in fact, the Centers for Disease Control estimates those costs total approximately $30.7 billion every year.

Much of the disease's impact results from the heart's inability to regenerate after injury. **Charles Murry, M.D., Ph.D.,** and his lab have been investigating stem cell-based approaches to heart repair for nearly 20 years, **leading to a recent, incredible breakthrough:** his lab used human heart cells to create new heart muscle in macaque monkeys; they expect to be in clinical trials in 2019. In a *Seattle Times* article, Harvard stem cell researcher Richard Lee said that this was "a very big deal," noting that Dr. Murry is "an extraordinarily careful and thoughtful investigator." In addition, **Michael Regnier, Ph.D.,** and his colleagues discovered that deoxy-ATP, a building block of DNA and a super fuel for muscle, could be augmented by delivering the RR gene to heart muscle. This **treatment has increased the heart's ability to contract and pump blood,** post-heart attack, in several laboratory models.

RESEARCH ACCOLADES

Harvard stem cell researcher Richard Lee said that a recent regeneration breakthrough in the Murry Lab was "a very big deal," noting that Dr. Murry is "an extraordinarily careful and thoughtful investigator."

In addition to making major inroads in defeating heart disease, ISCRM has also made progress in these promising projects:

KILLING CANCER

Each cancer is unique, and many are highly adaptable, making cancers difficult to treat. The new, bright hope in cancer care is called precision medicine, a process that determines what drug works best for an individual patient based on his or her biological profile: DNA sequence, gene and protein expression, and cellular metabolism. **Pamela Becker, M.D., Ph.D.,** and her team are using precision medicine to take on a rapid-progression, often fatal disease called acute myeloid leukemia. **Her lab is one of only two groups in the world taking on this challenge.** With the help of ISCRM's cores, Dr. Becker and her colleagues are bombarding leukemia cells with multiple cancer drugs and other compounds. The results are promising: each cancer they're testing seems to have an Achilles' heel that can be targeted by drug treatment. They are now using the technology to address other cancers.

MAKING THE LEAP TO MOBILITY

Muscular dystrophies typically affect boys in infancy or early childhood, rendering them unable to walk and markedly shortening their lives. These conditions result from mutations in genes essential for normal muscle function. The laboratory of **Casey Childers, D.O., Ph.D.,** recently made a breakthrough in the treatment of one of the deadliest forms of muscular dystrophy, myotubular myopathy, by developing a gene replacement therapy. The therapy produced the missing gene product in muscle cells in a family of dogs who had a naturally occurring form of the disease.
In an amazing reversal, the dogs treated with the therapy — whose disease had progressed so far that they could not stand or eat — **were able to walk normally and play again in a matter of weeks.**
A clinical trial to test this approach in young boys is planned for 2017.

STEM CELLS, MEET ENGINEERING: ORGANS ON A CHIP

Drug development is founded on a path: first, a discovery is made, then layers of testing take place — in petri dishes, in animal models, and then in humans (if all goes well). Organs on a chip, also known as organoids, are improving on that model. Tissue engineers use microfabrication techniques to produce three-dimensional models, then **stem cell experts at UW Medicine populate the scaffolds with specific, living cells:** heart cells, liver cells, pancreatic cells, and, in the case of **Benjamin Freedman, Ph.D.,** kidney cells. These organs on a chip can be used to conduct medical testing, giving researchers a better idea, earlier, if a drug might work in humans. They can also lead to the invention of artificial organs.

UNTANGLING ALZHEIMER'S DISEASE

Alzheimer's disease and other dementias affect an estimated 46.8 million people worldwide. Patients with Alzheimer's follow an age-linked progression involving failing memory, loss of basic functions such as walking and swallowing, and, eventually, death. Researchers think the disease is caused by a combination of factors: environmental, genetic and lifestyle. **Jessica Young, Ph.D., is determining how genetic factors either predispose people to Alzheimer's or protect them from it,** and she's using ISCRM-based technology to help determine what compounds, drugs or therapies might work best for individual patients.

JOIN OUR CAMPAIGN

Founded approximately a decade ago, the Institute for Stem Cell and Regenerative Medicine was indeed a grand experiment. By bringing scientists together, by focusing both on basic and applied research and by working on projects of great import to human health, we thought we could make real inroads into medicine. We were right.

We are making these inroads, and leveraging the enormous potential of stem cells, gene therapy and other techniques is a key priority for our Campaign. To fully leverage this potential, we are seeking additional philanthropic investment from our friends and partners: from you. **With funding, we will be able to underwrite our research projects, retain and recruit superb scientific personnel, promote the work and careers of junior investigators, and sustain and build capacity in our three core facilities, which are the heart of our program.**

If you would like to support ISCRM's ground-breaking research or learn more about any of these projects, please contact Jim Boyle, senior director for philanthropy, at 206.543.7252 or boyleje@uw.edu, or visit depts.washington.edu/iscrm/. Thank you for your interest in our work.

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