



REGENEXX - ADVANCED INTERVENTIONAL ORTHOPEDICS

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OVER THE NEXT TWO DECADES,  
MEDICAL TREATMENTS WILL UNDERGO  
A 21<sup>ST</sup> CENTURY REVAMP EQUIVALENT TO  
THE DISCOVERY OF MODERN ANTIBIOTICS.

#### THE CHAPTER BEGINS

The field of Orthopedics, which focuses on conditions involving the human musculoskeletal system, has seen amazing advances in the recent past, such as the advent of arthroscopic surgery, external fixation of fractures, and a panoply of screws, wires, and devices used to surgically fix broken tendons, bones, ligaments, and muscles. What hasn't happened in orthopedics is the move toward truly minimally invasive treatments. Medical fields such as cardiology have been reengineered, with a shift from big surgeries, such as open heart procedures, to minimally invasive treatments that are conducted through a needle. These advances were the genesis for a new medical field, most commonly known as Interventional Cardiology.

At Regenerative Sciences, the Centeno-Schultz Clinic, and our Regenexx Provider Network, we are bringing the future of non-surgical orthopedic care to patients today. We are pioneering and advancing the new medical field of Interventional Orthopedics by developing the next generation of physical and biologic tools, allowing orthopedic conditions that are commonly treated with invasive surgery to be treated through a needle. This means quicker recovery and less trauma for patients.

Regenerative Sciences is focused on bringing interventional orthopedics to the forefront of orthopedic medical care.

# THE STEM CELL UNIVERSE

## EMBRYONIC STEM CELLS (hESCs)

The center of the Cell Universe, can become all cell types of the body because they are pluripotent.

## ADULT STEM CELLS

The primary roles of adult stem cells in a living organism are to maintain and repair the tissue in which they are found. Their primary functions are to replace cells that die because of injury or disease.

## MESENCHYMAL STEM CELLS

Mesenchymal stem cells are at the heart of Regenxx Procedures. Research has shown these stem cells to be the most effective stem cell for regenerating damaged bone and tissues associated with orthopedic injuries and degenerative conditions, such as osteoarthritis.



## MESENCHYMAL STEM CELLS

Mesenchymal stem cells are multipotent. They can develop into cartilage, bone and ligament, as well as many other tissues. Regenxx Procedures offer non-surgical options for the treatment of various orthopedic disorders, which include loss of cartilage in the knee and hip, non-healing fractures and repair of lumbar disc bulges.



## HEMATOPOIETIC STEM CELLS

A stem cell that gives rise to all red and white blood cells and platelets. They can also help facilitate new blood supply to a damaged area.

Stem Cells are the repairmen of the body. As we age or get injuries, we sometimes cannot get enough of these repair cells to the injured areas. The Regenxx Procedures help solve this problem by amplifying the body's natural repair process. This is accomplished by harvesting cells from areas known to be rich in mesenchymal stem cells and then concentrating those cells in a lab before precisely reinjecting them into the damaged area in need of repair.

## THE REGENEXX PROCEDURES

THE REGENEXX FAMILY OF PROCEDURES OFFER A VIABLE, NON-SURGICAL ALTERNATIVE TO INDIVIDUALS SUFFERING FROM CHRONIC PAIN, OR WHO MAY BE CONSIDERING ELECTIVE SURGERY OR JOINT REPLACEMENT DUE TO INJURY OR ARTHRITIS.



THESE ADVANCED REGENERATIVE STEM CELL AND BLOOD PLATELET PROCEDURES ARE DESIGNED TO PROVIDE OPTIMAL RESULTS BASED ON INDIVIDUAL PATIENT NEEDS AND THE NATURE OF THE INJURY.



### ADVANCED CULTURED STEM CELL PROCEDURE

Regenexx-C was the first cultured, orthopedic stem cell procedure offered in the United States. Every other procedure currently being offered in the United States is a diluted version of this advanced procedure, and none can match the research and care that goes into every Regenexx-C procedure. Regenexx-C starts with harvesting the patient's bone marrow stem cells. Our lab cell biologists then grow these cells over two weeks, using a proprietary platelet lysate lab technique. Once the cells have been grown to between 100–1,000 times more than harvested, they are retested for quality assurance purposes. Once approved, they are precisely reinjected into the injury site using proprietary needle based tools and advanced imaging guidance.



*Regenexx-C was the first cultured, orthopedic stem cell procedure offered in the United States.*

## THE REGENEXX PROCEDURES

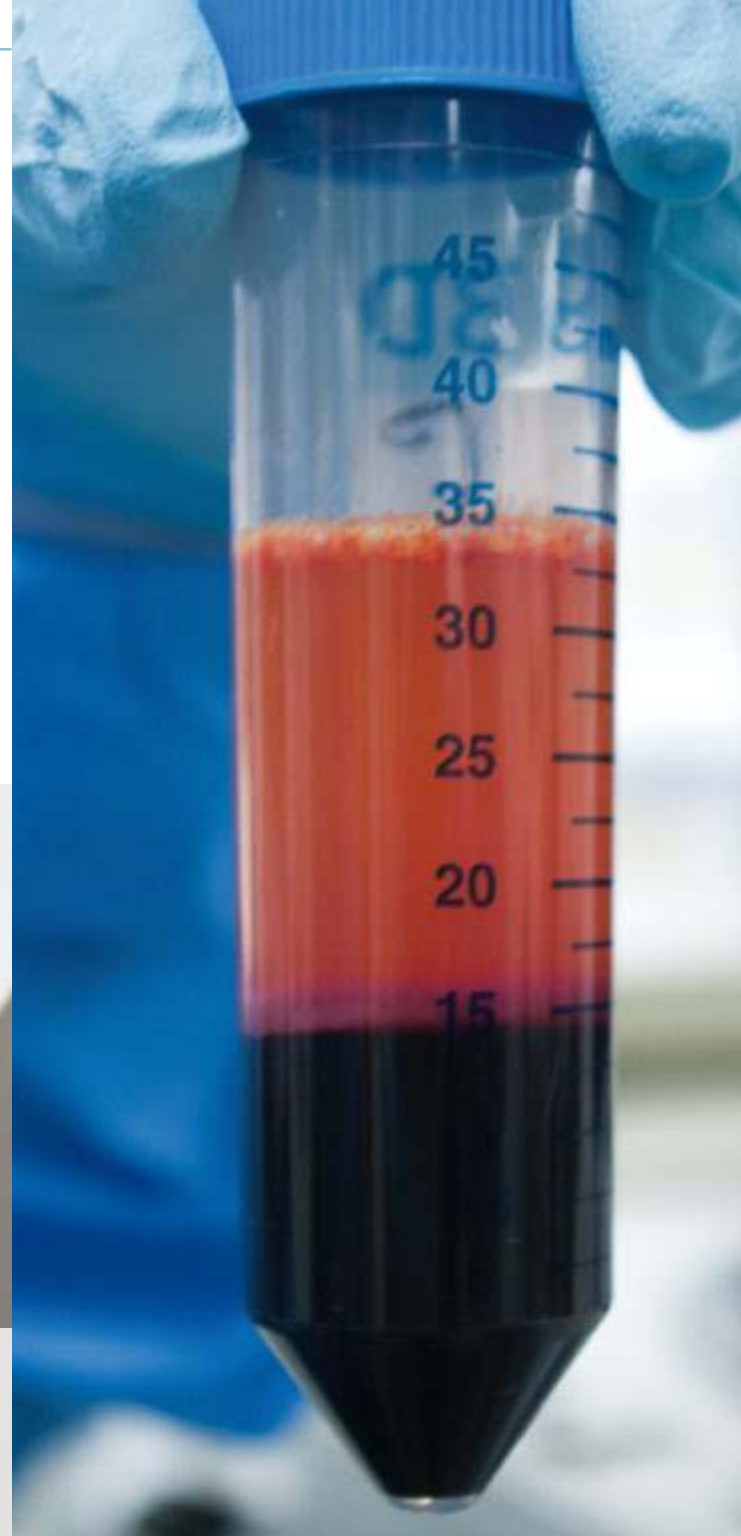


### SAME DAY STEM CELL PROCEDURE

Regenexx-SD is our same day bone marrow based stem cell procedure. Mesenchymal stem cells from the bone marrow are isolated in our lab. By adding a super platelet lab prepared mix of PRP (slow release growth factors) and platelet lysate (immediately available growth factors), we are able to get adult stem cells to grow many times better than with PRP or platelet lysate alone. Lab tests show that we can get more stem cells to grow with Regenexx-SD than any other same day procedure using bone marrow stem cells. The concentrated cell and platelet solution is reinjected into the area of injury using advanced imaging guidance – fluoroscopy and musculoskeletal ultrasound.



After centrifuging the bone marrow derived sample, the middle layer of this sample contains the stem cells that will be used to help heal the patient's injury. Cell concentration is measured in the laboratory prior to reinjection.

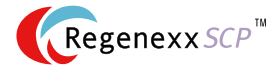


### ADIPOSE DERIVED STEM CELL PROCEDURE

Stem cells derived from fat underperform bone marrow stem cells for most orthopedic procedures. However, there are more mesenchymal stem cells in fat than in bone marrow and in some cases, the mesenchymal stem cells from fat can be beneficial for certain types of tissue regeneration. Regenexx-AD combines our traditional Regenexx-SD procedure with super-platelet mix and adds a structural "fat graft" filled with adipose stem cells. This graft can be used to solve structural problems within the joint.



## THE REGENEXX PROCEDURES



### STEM CELL PLASMA PROCEDURE

Regenexx-SCP is a superior form of today's well known Platelet Rich Plasma, or PRP. Regenexx-SCP contains a higher concentration of platelets than PRP and also contains blood circulating stem cells capable of tissue repair. It is created in a lab, rather than an automated bedside centrifuge, which ensures the mixture is as pure and effective as possible. Regenexx-SCP patients rarely experience post-injection flareups that are frequently seen with standard PRP.



### PLATELET LYSATE PROCEDURE

Platelets slowly release their growth factors in a timed release fashion to help healing. However, there are times when the physician wants all of the growth factors contained in platelets immediately available to the area to prompt healing. In addition, there are areas of the body where using Platelet Rich Plasma (PRP) may cause too much inflammation. Regenexx-PL is created by cracking open the platelets to allow all of the growth factors to be immediately available within the patient's body.

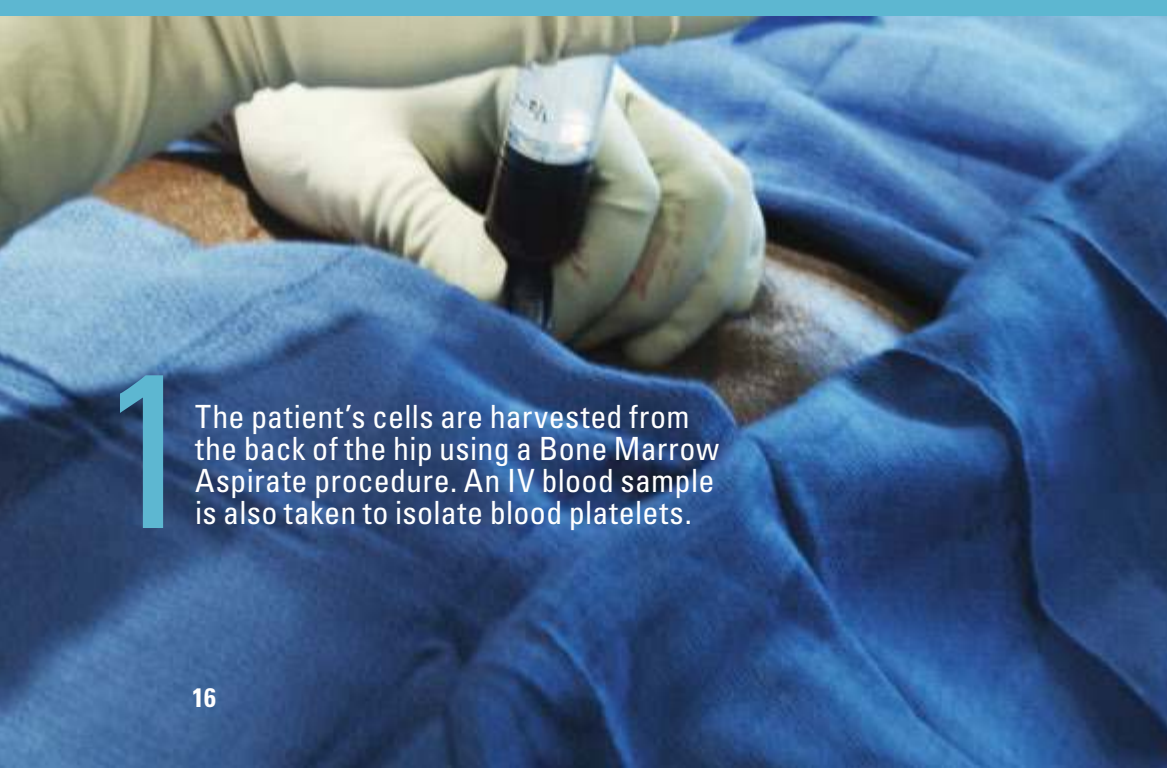


THE REGENEXX-SD (*same day*) PROCEDURE  
CONSISTS OF THREE IMPORTANT PROCESSES.

**1** The patient's cells are harvested from the back of the hip using a Bone Marrow Aspirate procedure. An IV blood sample is also taken to isolate blood platelets.

**2** Mesenchymal Stem Cells are isolated from the bone marrow, while blood platelets are separated from the blood sample.

**3** The concentrated Mesenchymal Stem Cells and Platelet Lysate are reinjected into the target area using real time imaging guidance.

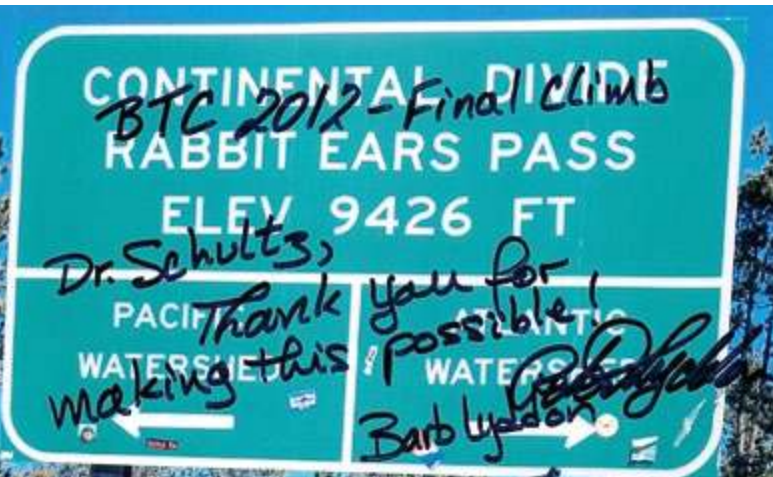




## SUCCESS STORIES

Regenexx Procedures are helping people overcome injuries and achieve their personal goals, whether it's weekend warriors, professional athletes, or individuals who simply want to return to a pain-free lifestyle.

"Both of my knees have behaved exceptionally well since the last injections I received at your clinic. ... I had come to you because every day was a painful experience. I had swelling and when I snow skied (on "black diamond" Western slopes for several hours) I usually took 6 Advil prior and post the ski, I also iced the knees down afterwards. I wore compression and stabilizing braces - usually they still swelled! I was never sure when my knees might simply buckle. After the injections and following the prescribed protocol of easing back into the activities I desired, I have had: no pain, no swelling, no range of movement limitations."

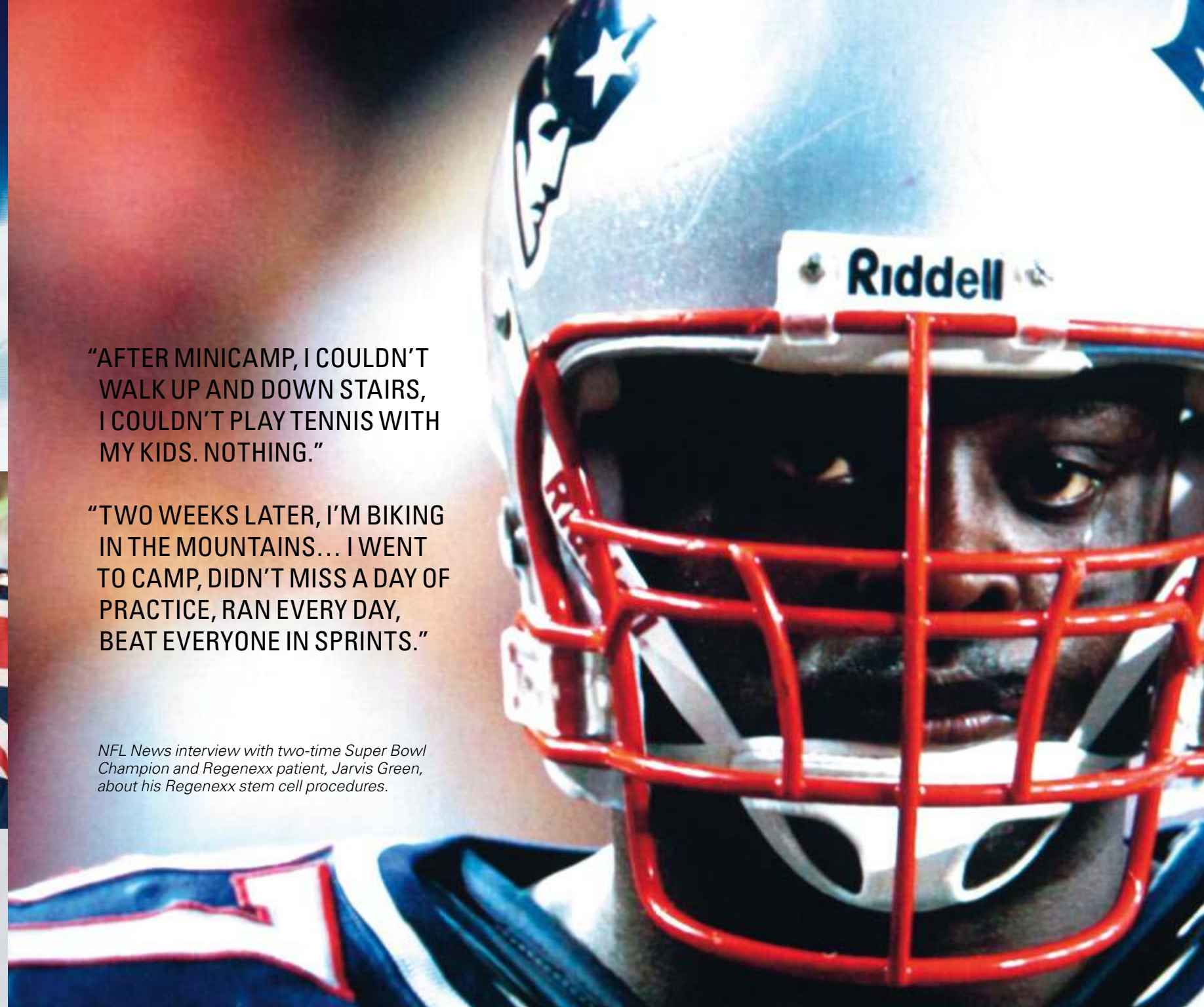


Cydonie Mothersill is an elite track athlete and gold medalist at the 2010 Commonwealth games, 2010 Mayaguez, and CARIFTA games. Regenexx Procedures were used to treat a non-healing tibial stress fracture, achilles tendonitis, and a hip labrum tear. At age 32, with her fifth Olympic Games looming, a lengthy surgical recovery was simply not an option. Regenexx Procedures allowed her to continue training during her treatment period and she subsequently won the 200M at the Cayman Invitational. Cydonie will represent the Cayman Islands in the London Olympic Games in 2012.

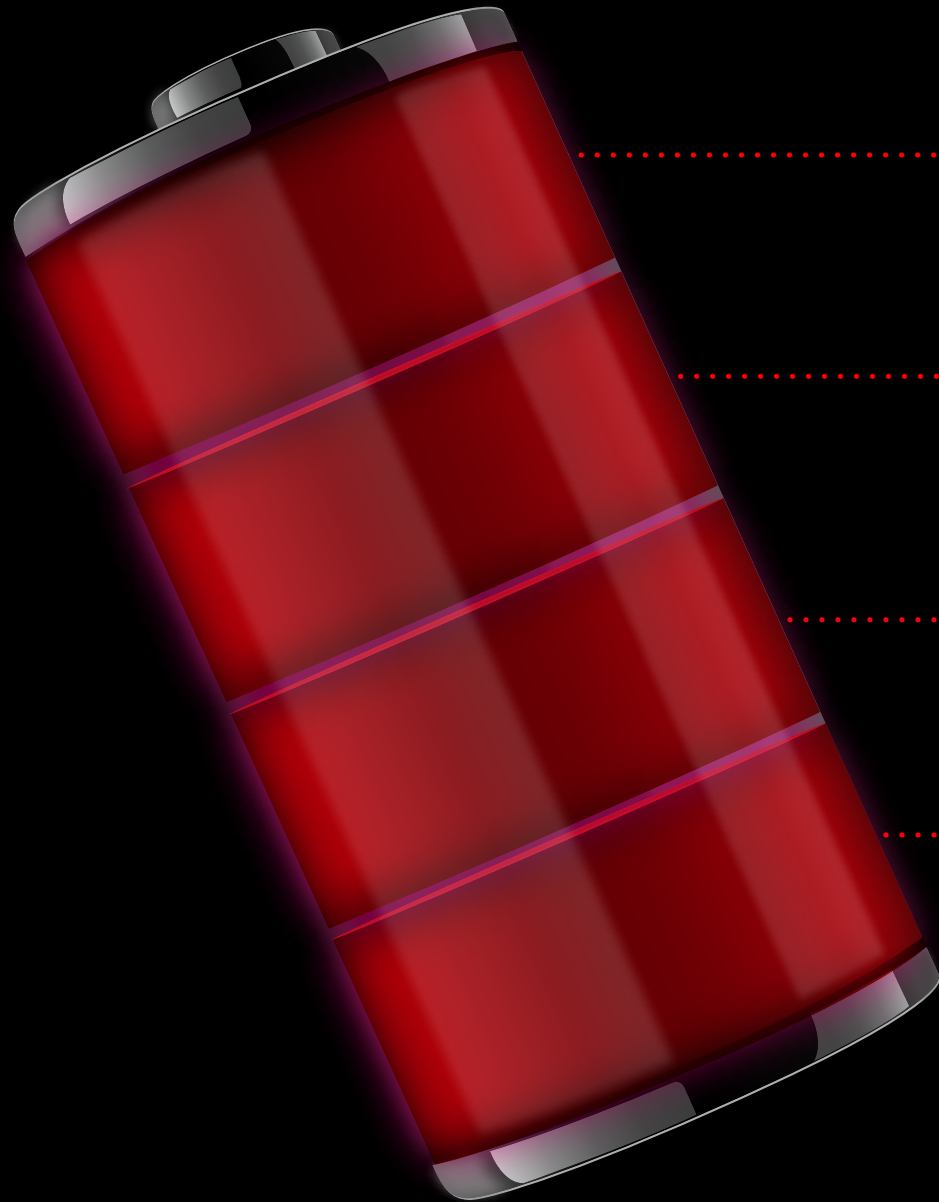
"AFTER MINICAMP, I COULDN'T WALK UP AND DOWN STAIRS, I COULDN'T PLAY TENNIS WITH MY KIDS. NOTHING."

"TWO WEEKS LATER, I'M BIKING IN THE MOUNTAINS... I WENT TO CAMP, DIDN'T MISS A DAY OF PRACTICE, RAN EVERY DAY, BEAT EVERYONE IN SPRINTS."

*NFL News interview with two-time Super Bowl Champion and Regenexx patient, Jarvis Green, about his Regenexx stem cell procedures.*



POWERED BY A SHARP FOCUS ON FOUR KEY AREAS



### CLINICAL RESEARCH

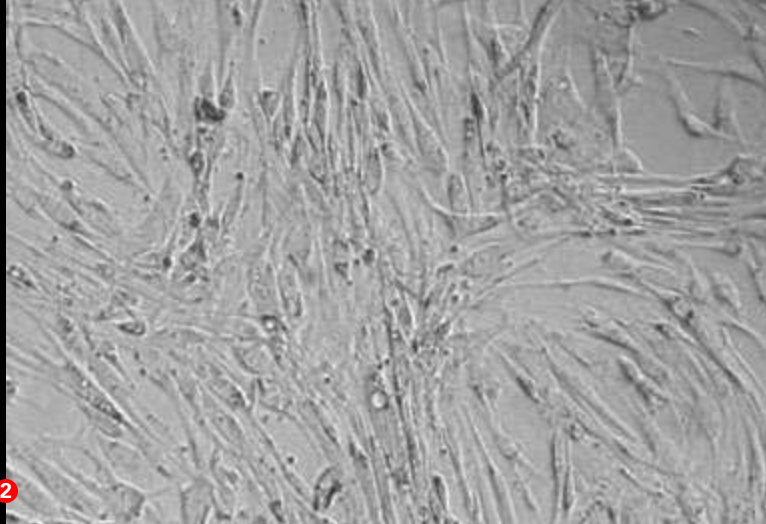
**In Vivo Partial Repair of a Human Femoral Chondral Lesion using Percutaneously Implanted, Autologous Mesenchymal Stem Cells**  
 Christopher J. Centeno, M.D., Dan Busse, M.D., John Koshy, Ph.D., Cristin Keohan, Michael Freeman, Ph.D., D.C.

**Regeneration of meniscus cartilage in a knee treated with percutaneously implanted autologous mesenchymal stem cells**  
 Christopher J. Centeno<sup>1</sup>, Dan Busse<sup>2</sup>, John Koshy<sup>3,4</sup>, Cristin Keohan<sup>5</sup>, Michael Freeman<sup>6</sup>, David Kati<sup>7</sup>

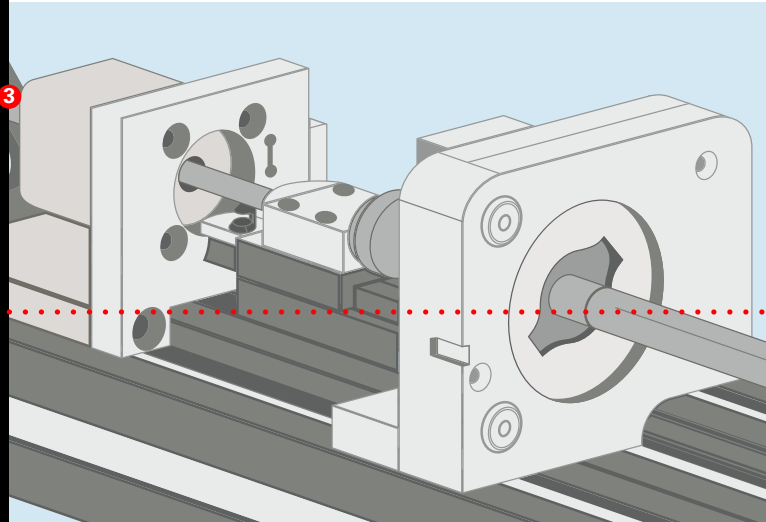
**Increased knee cartilage volume in degenerative joint disease using percutaneously implanted, autologous mesenchymal stem cells, platelet lysate and dexamethasone**  
 Christopher J. Centeno<sup>1</sup>, Dan Busse<sup>2</sup>, John Koshy<sup>3,4</sup>, Cristin Keohan<sup>5</sup>

**Partial Regeneration of the Human Hip Via Auto-Marrow Nucleated Cell Transfer: A Case Report**

### LABORATORY RESEARCH



### BIOENGINEERING



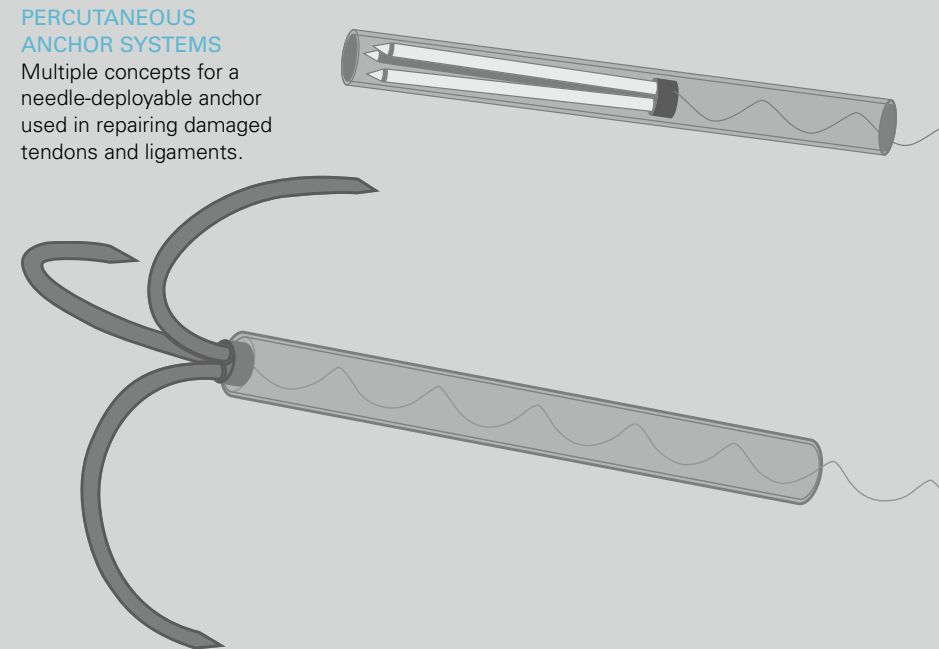
### REGENERATIVE MEDICINE



## INVENTING THE TOOLS OF A NEW MEDICAL SPECIALTY

As we move orthopedics into the future towards true “through a needle” treatments, the tools of the past often need reinvention. Our daily real world clinical experience treating patients provides feedback into the research loop, allowing us to rethink today’s medical devices and create the Interventional Orthopedic tools of the future. These devices will enhance the ability of stem cells to do their work, by administering them more accurately, effectively and in less invasive ways, allowing us to reach areas in the body that cannot be reached with traditional needles.

Regenerative Sciences employs a full time bio-engineering staff, lab research staff, and clinical research staff to advance the development of next generation devices and procedures.

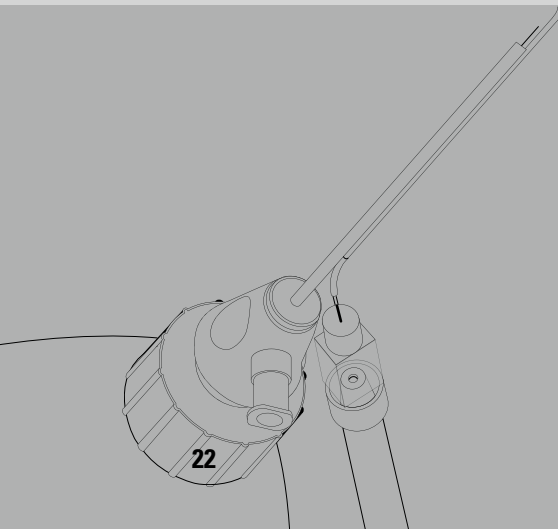


### PERCUTANEOUS ANCHOR SYSTEMS

Multiple concepts for a needle-deployable anchor used in repairing damaged tendons and ligaments.

### ARTHROSCOPE-BASED CELL DELIVERY

A device to allow a needle to be deployed directly in the field of view of an existing arthroscopic visualization system.

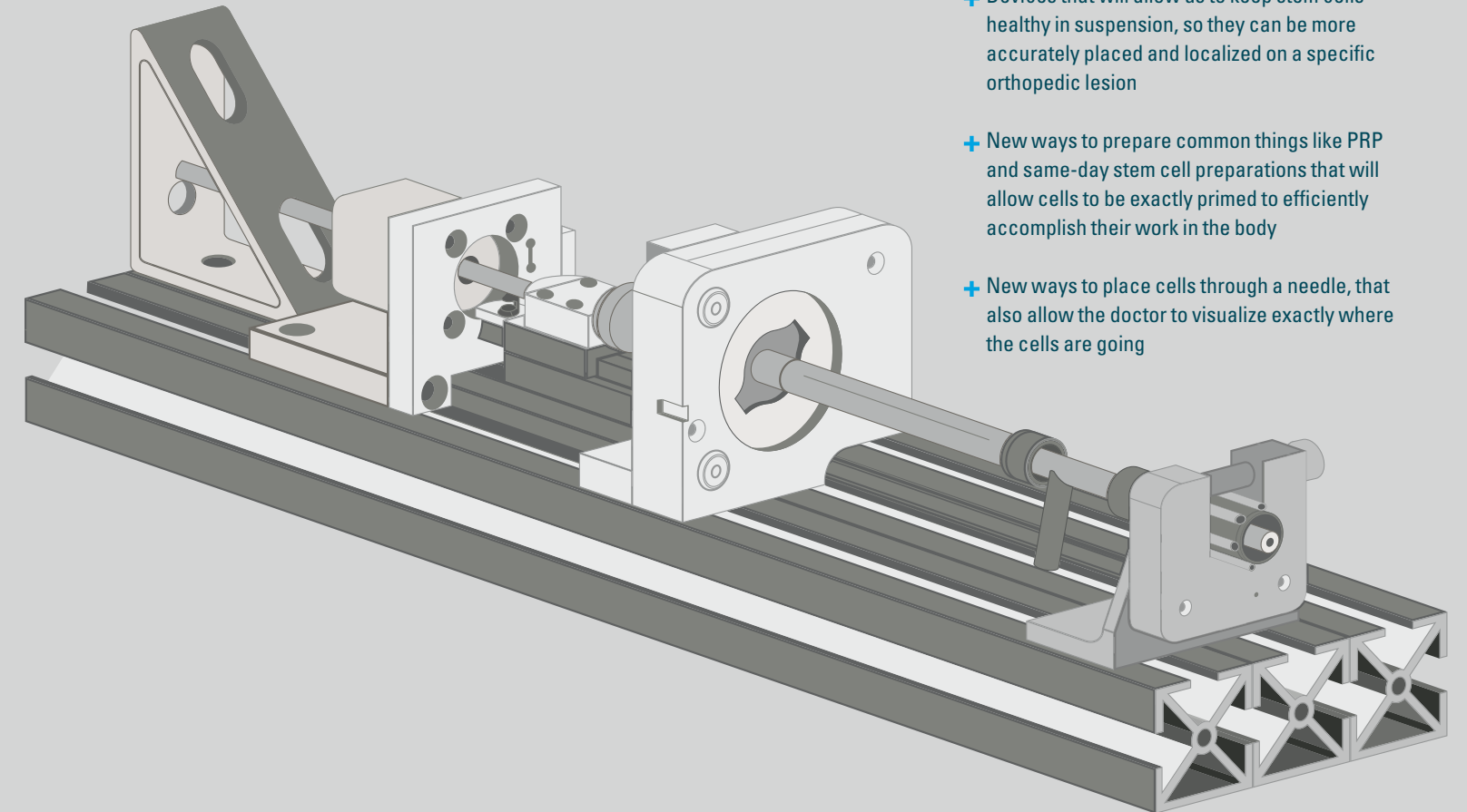


## INTERVENTIONAL ORTHOPEDIC MEDICAL DEVICES OF THE FUTURE

- + New types of needles and catheters designed to place cells in very specific areas where traditional and existing needles can't reach
- + New bio-scaffolds to allow stem cells to do their work better and faster
- + Devices that will allow us to keep stem cells healthy in suspension, so they can be more accurately placed and localized on a specific orthopedic lesion
- + New ways to prepare common things like PRP and same-day stem cell preparations that will allow cells to be exactly primed to efficiently accomplish their work in the body
- + New ways to place cells through a needle, that also allow the doctor to visualize exactly where the cells are going

### NOVEL SYRINGE PUMP

A syringe pump designed to improve the cultured cellular environment during delivery.



## CLINICAL LABORATORY

CELL BIOLOGISTS IN OUR CLINICAL LABORATORY  
ENSURE SUPERIOR PROCEDURE RESULTS



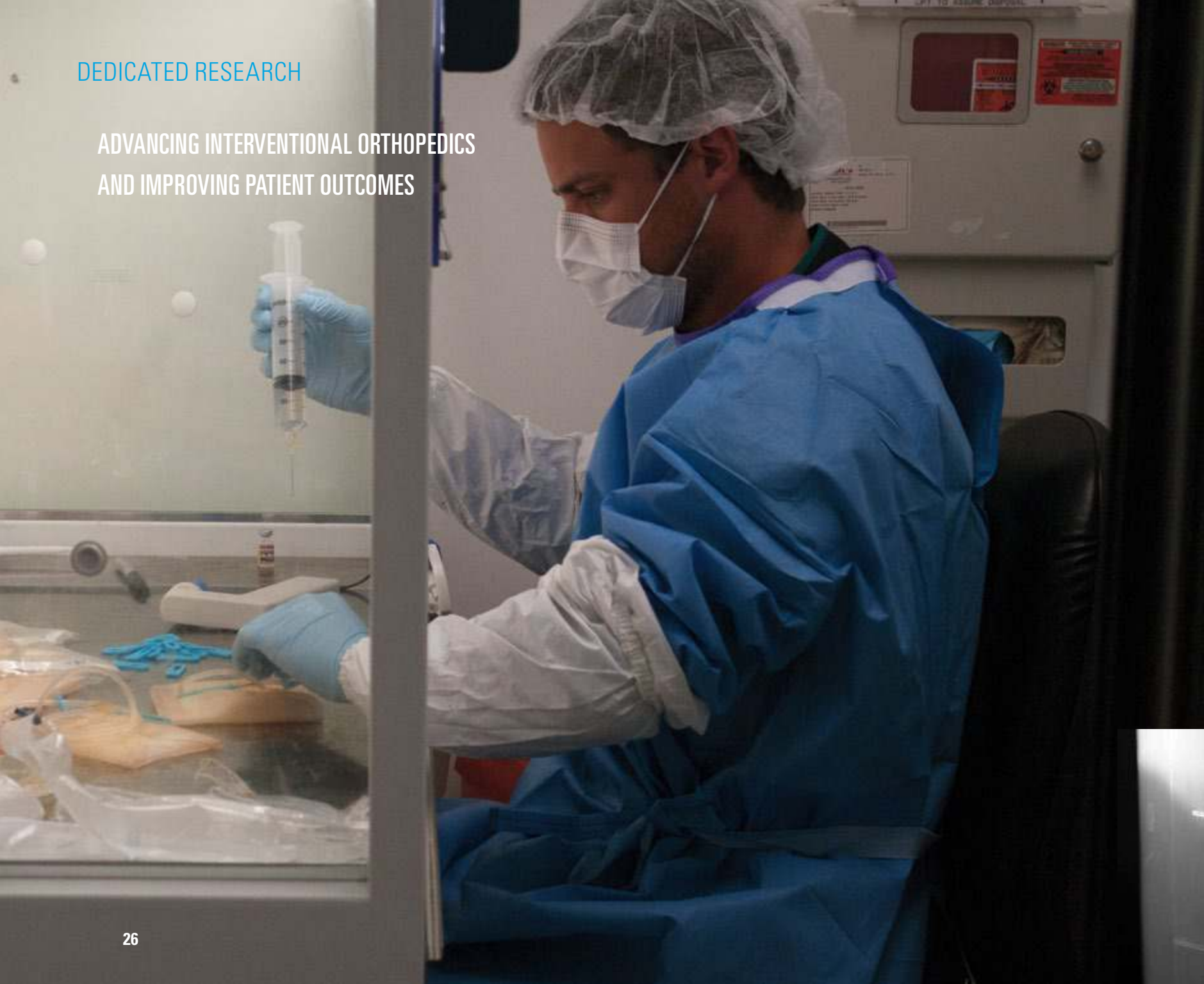
### DEDICATED CELL BIOLOGISTS AT REGENERATIVE SCIENCES

The advanced labs at the Centeno-Schultz Clinic and the Regenexx Cayman facility provide advanced capabilities, including cell culture, flow cytometry, phase contrast and fluorescent microscopy (the ability to see and count cells without harming them by staining), cryo-preservation (the ability to bank cells and save quality assurance samples) and more.

The Centeno-Schultz clinic has always used dedicated cell biologists to process our patient's bone marrow and blood derived samples, rather than bedside centrifuges or in-office hoods with cross-trained medical assistants or nurses. This allows us to ensure cell viability and produce the best possible outcomes for our patients, including the ability to adjust a patient's cell samples to address their exact needs.

## DEDICATED RESEARCH

ADVANCING INTERVENTIONAL ORTHOPEDICS  
AND IMPROVING PATIENT OUTCOMES



## DEDICATED RESEARCHERS AT REGENERATIVE SCIENCES

At Regenerative Sciences and the Centeno-Schultz Clinic, we are physician leaders in research presentations, publications, and academic achievements relating to stem cell therapy for orthopedic injuries.

As a leader in the field of Interventional Orthopedics, research is a critical component of our business. Regenerative Sciences strives to provide patients with the most effective treatments possible. As practitioners of our trade, the Centeno-Schultz Clinic is the original stem cell based musculoskeletal practice in the United States, with more stem cell orthopedics experience than any other clinic.



## THE TEAM

THE DIVERSE AND RAPIDLY EXPANDING TEAM at Regenerative Sciences and the Centeno Schultz Clinic drives the success, innovation and patient satisfaction we are known for. Our team includes staff within our four key areas of focus, as well as administrative and support teams.

**RESEARCH LAB:** Our lab has full research capabilities, so our physicians test in-vitro what they believe may work better for patients. In addition, our lab is constantly working on better and more efficient ways to isolate and grow stem cells.

**CLINICAL RESEARCH:** We have created a proprietary suite of software that allows us to data mine millions of pieces of clinical data generated by our provider group through a registry. This allows us to quickly decide what's working and to predict which therapies deserve more intense study. We call this approach "Long-tail Medicine" which follows the basic concepts behind the successful "Long-tail" business practices currently in use on the Internet.



**REGENERATIVE MEDICINE / MEDICAL STAFF:** Along with our Colorado medical doctors and staff, our Regenxx Network is a hand-picked group of qualified providers dedicated to helping us create this new field of Interventional Orthopedics. The data they generate through our registry forms the basis of our long-tail research approach.



**BIOENGINEERING TEAM:** Interventional Orthopedics requires a brand new set of tools that can be delivered through a needle and that can place cells accurately, anywhere in the musculoskeletal system. Our physicians work closely with our bioengineering department to ensure that the tools we create are immediately useful for patients.



*Broomfield, Colorado is ground zero for the development of Regenexx Procedures. In October of 2011, Regenerative Sciences licensed the first doctor outside of the Centeno-Schultz Clinic to perform Regenexx Procedures. The rapidly growing physician network will consist of doctors in all regions of the mainland United States by the end of 2012. All doctors within the Regenexx Procedure Network are hand-picked and trained at our Colorado location.*



## OUR VISION

We envision a future where 90% of what's currently done through surgery will be accomplished through an injection. Where regenerative procedures are the norm, rather than the exception. Where patients walk-in and walk-out from their orthopedic procedures with minimal, if any, downtime.

***Where everyone has access to the safest and most effective treatments available.***

**OUR GOAL AT REGENERATIVE SCIENCES IS NOTHING LESS THAN THE REINVENTION OF ORTHOPEDICS FROM THE GROUND UP.**

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