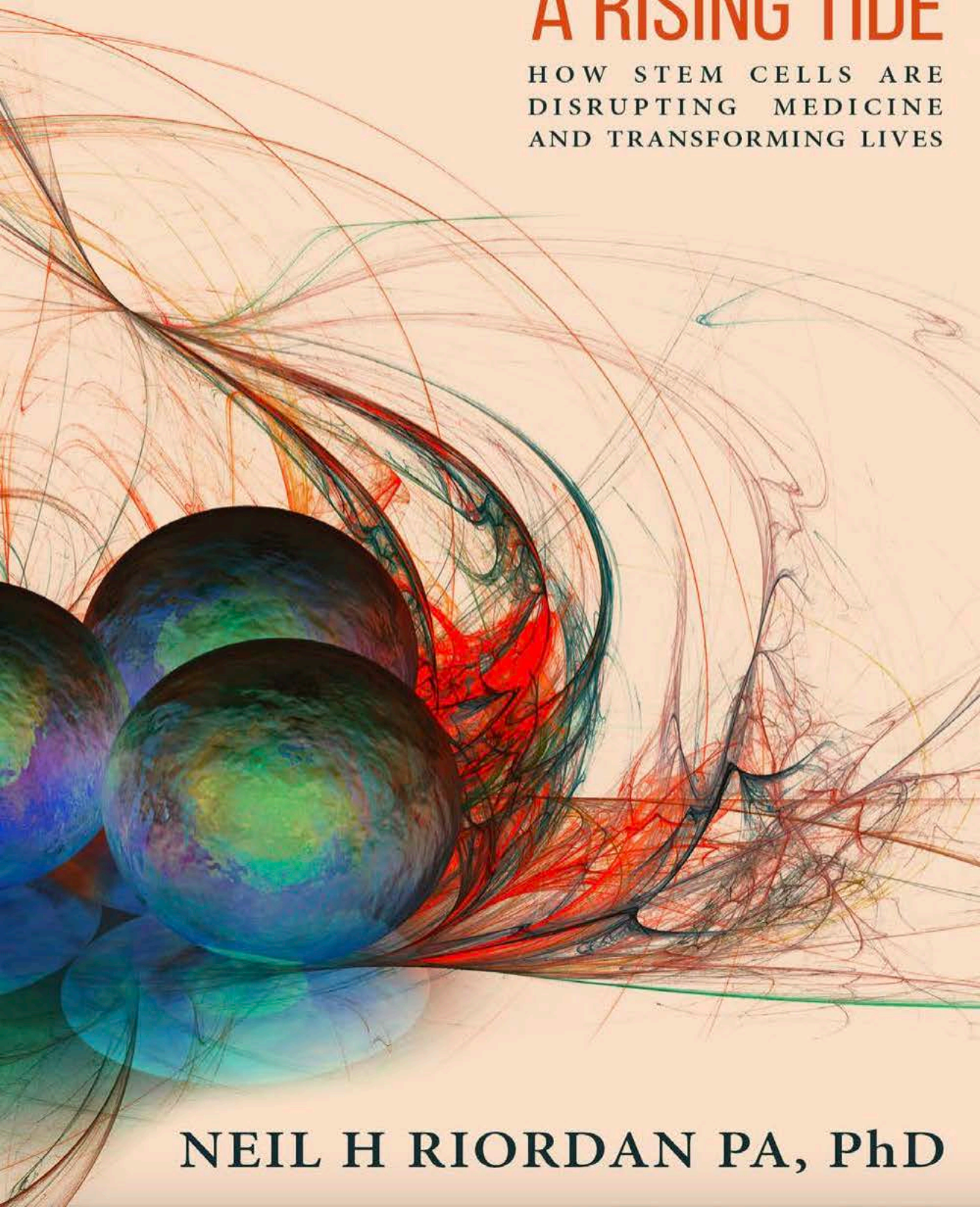
STEM CELL THERAPY

A RISING TIDE

HOW STEM CELLS ARE DISRUPTING MEDICINE AND TRANSFORMING LIVES



NEIL H RIORDAN PA, PhD

"Neil takes readers on a riveting journey through the past, present and future of stem cell therapy. His well-researched, educational and entertaining book could change your life. I highly recommend it."

Tony Robbins, NY Times #1 Bestselling Author

"100 years old will soon become the new 60. Stem cells are a key therapeutic to enable this future. Dr. Riordan's book is your guide to why this is true and how you will benefit. A must read for anyone who cares about extending their healthy lifespan."

Peter H. Diamandis, MD; Founder, XPRIZE & Singularity University; Co-Founder, Human Longevity, Inc.; Author of NY Times Best Sellers *Abundance* and *Bold*

Stem cells are the repair cells of your body. When there aren't enough of them, or they aren't working properly, chronic diseases can manifest and persist.

From industry leaders, sport stars, and Hollywood icons to thousands of everyday, ordinary people, stem cell therapy has helped when standard medicine failed. Many of them had lost hope. These are their stories.

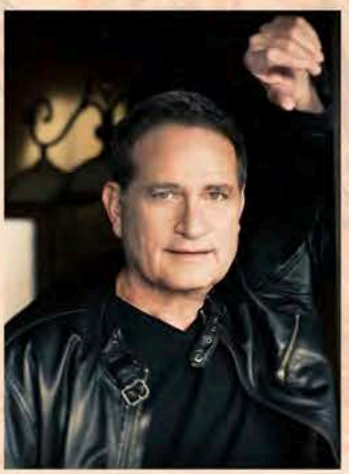
Neil H Riordan, author of *MSC: Clinical Evidence Leading Medicine's Next Frontier*, the definitive textbook on clinical stem cell therapy, brings you an easy-to-read book about how and why stem cells work, and why they're the wave of the future.

"I'm the luckiest guy in the world. Stem cells have given me my life back."

Sam Harrell – Football coach and Multiple Sclerosis patient

"I never want to go back to autism before stem cells."

Marty Kelly – Parent of a child with autism



NEIL H RIORDAN, PA, PhD

Neil H Riordan is an accomplished scientist and developer of regenerative medicine therapeutics, with more than 70 peer reviewed publications and more than 40 patents and patent applications to his credit. He is the author of MSC: Clinical Evidence Leading Medicine's Next Frontier, a groundbreaking compilation of stem cell studies for more than 30 medical conditions, with over 800 references to peer-reviewed articles. Dr. Riordan founded Medistem Panama, a leading stem cell laboratory and research facility that is ISO 9001 certified and fully licensed by the Panamanian Ministry of Health. He also founded the Stem Cell Institute in Panama, where his mesenchymal stem cell technologies continue to be implemented in patients, now numbering in the thousands, with autoimmune and degenerative diseases and injuries.

Stem Cell Therapy
A Rising Tide

How Stem Cells are Disrupting Medicine and Transforming Lives

Neil H. Riordan

Stem Cell Therapy: A Rising Tide
How Stem Cells are Disrupting Medicine and Transforming Lives

www.cellmedicine.com
info@neilriordanbooks.com

This book is not intended as a substitute for the medical advice of physicians. The information provided in this book is designed solely to provide helpful information on the subjects discussed. The reader should regularly consult a physician in matters relating to their health and particularly with respect to any symptoms that may require diagnosis or medical attention. While all the stories in this book are true, some names and identifying details have been changed to protect the privacy of the people involved.

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Foreword

As I read this book, I became very emotional. I had to go back about 28 years ago when my wife and I sat in a doctor's office and listened to a neurologist list in grim detail how our beautiful three-year-old son Ryan would spend his next 20 years. The doctor told us there was nothing that they could do at that time. He suggested that we do everything we could to keep Ryan active in order to maintain the strength he had as long as possible. And hopefully in the next 20 years they might find a cure for muscular dystrophy. The prognosis changed our lives forever. It was a very painful time for all of us.

As I continued to read about all of the patients who have been treated by Dr. Riordan, I realized that we all had one thing in common: traditional medicine had given up on us. There was nothing that could be done. Our own government, founded on the premise of life, liberty, and the pursuit of happiness, had evolved into overreaching bureaucracy that would attempt to prevent us from seeking lifesaving alternative treatments.

But once again, we all had something else in common. We found a man who was willing to do everything in his power to offer us options and give us hope for the future of our loved ones. Dr. Riordan has truly dedicated himself to his profession as a medical pioneer. He has sacrificed everything he has to give those who have been told there are no options a fighting chance and real hope for the future.

Dr. Riordan has never wavered in the face of scrutiny. It takes true courage to stand up to the often judgmental "traditional" medical community—those who act offended when you suggest that there might be a different way.

Fortunately for all of us, Dr. Riordan had the foresight to look beyond the walls of traditional medicine and fight the fight for us. I encourage you to read this book, and not just the chapters related to your condition. As a whole, the book lays out Dr. Riordan's courageous and successful journey through his stories and the stories of his patients.

Thank you, Dr. Riordan, for all that you have done for us and our families. You truly are a hero!

George Benton, Ryan's father

Introduction

BY ARNOLD CAPLAN, PHD

Neil Riordan, PhD, PA is a pioneer of the highest order, in some ways like John Glenn or Neil Armstrong. Neil has ventured where the routes were uncharted and the dangers huge. His rocket of cell therapy was launched on a rickety platform filled with hopes and dreams, and powered by an engine of money. This pioneer has hacked his way through the jungle of naysayers and has produced miracles of enormous proportions. He has taken our scientific dreams and translated them into a high-caliber medical facility that does good by offering exposure to cell therapy treatments that we working scientists only dream about.

Although there are those in my professional realm who would say that Neil is a medical "cowboy" who "experiments" with human subjects, I would say that he is providing access to therapies that are no more experimental than one sees every single day in the surgical suites of major medical centers. In such situations, the surgeon is "forced" to improvise because of the complexity of the wound field. Such improvisation sometimes involves using materials that are not approved but that the surgeon "feels" will work well in the situation he faces. For example, human decellularized skin from dead people was approved for topical applications for ulcerated wounds in diabetic patients. But these "membranes" are fabulous for closing abdominal surgical wounds in hernia repair operations and have changed the way such closures are done. This surgical improvision, originally performed by a "cowboy" surgeon, is now the standard of care. We move forward in medicine by the skill and insightful work of pioneers—some with IRB approval and some not. Riordan's procedures with MSCs currently have IRB approvals.

In a sense of transparency, let me say that I have accepted honoraria from Neil Riordan and gifts of hotel rooms, meals, and, indeed, infusions of MSCs. These all have monetary value, but none influences my opinion. The monetary success of Neil's enterprises evoke jealousy in some entrepreneurs, but Neil's continual reinvestment of money into his next medically successful enterprise displays his true motives—the advancement of a medically necessary science despite great obstacles. The key to his success is in the enormously high quality of his facilities; the people, doctors, nurses, receptionist, PR team, etc. are *all* highly principled and care about the patients they serve. These people care about what they do because Neil recruits them for their skills and attitude. He does not discuss this in this book, but they are present on every page. He talks about Dr. Paz, but he does not tell you of his long medical experience and his reputation in the United States and in Panama for caring and experienced medical judgements. In all of Neil's clinics, quality control labs, hotels for patients, and restaurants where they eat, the staff behind the scenes are dedicated to providing the highest quality medical care possible. Some clinics and hospitals in the United States could take lessons from the Riordan gang. That said, the cell-based therapies Neil's clinics provide have not all been approved and tested by double-blind, placebo control and rigorously monitored clinical trials, although such trials are currently underway. But, like innovative surgeons, these open-label uses have proven effective, as hopefully we will see in published peer-reviewed reports of his studies.

Each chapter of this book recounts the personal stories of how Neil's unwavering confidence that cell-based therapies with MSC preparations from fat, marrow, or umbilical cords can make a medical difference. Neil made medical tourism work, and what he has done is highly laudable, not only because of the patients he has helped, but because of the laws that have been written to support cell-based therapies in Panama. This book is not what I pleaded with Neil to write, however. I have, for many years, begged him to give us outcome reports of his many patients: what they have as clinical problems, what they walk in with, and the longitudinal outcomes after the cell infusions. Hopefully these will be forthcoming, but they are not in this book. What is here in these pages is, none-the-less, amazing.

I first learned about Neil's clinic in Costa Rica and thought his procedures and therapies were brilliant. And these were crude compared to those currently underway in Panama. The Panama GMP-production facilities, his offices and treatment rooms, and the products including MSCs from umbilical tissue are of the highest quality. These are the vehicles and the platform that allow him to write this treatise of the therapies they provide. It is a shame that we have to fly to Panama to have access to these therapies instead of having them available in the United States. How long will it take for such therapies to be available to the patients covered by Medicaid or Medicare instead of those from Beverly Hills or Long Island who can afford to travel to Panama?

Almost daily I receive emails from people who want access to "stem cell" treatments. I tell them that I am just a PhD researcher and cannot suggest an avenue of treatment for medical issues. If you have this book in hand, read the chapters. They are honest, open, and spellbinding. While Neil is not a medical doctor, his clinical experience as a physician assistant along with his research background have prepared him for the serious medical issues for which Neil has organized cell therapy treatments, often with quite significant outcomes. Neil is certainly a student of the medical arts and an expert using innovative treatments. I have talked to patients of Neil's clinics and their family members about their treatments; the stories told in this book are just the tip of the iceberg. This is an interesting book and an interesting and gutsy journey of Neil Riordan. His physician father would be proud to recognize Neil's passion and medical achievements.

Arnold I. Caplan, PhD
Skeletal Research Center
Department of Biology
Case Western Reserve University
10600 Euclid Avenue
Cleveland, Ohio 44106

January 15, 2017

Chapter Nine

FRAILTY OF AGING—REVERSING THE INEVITABLE

Getting old sucks!

As we age our bodies undergo, at varying rates, a series of changes that move us away from homeostasis—or perfect biological balance—and toward a decreased ability to adapt to both internal and external stress, which leaves us more vulnerable to disease. In some people the effects of aging are pronounced, characterizing them as frail—with decreased strength, endurance, physiologic function, and activity, all associated with poor health outcomes. Perhaps you have known people who were dependent on others for their everyday needs—shopping, cooking, and caring for themselves. These are the hallmarks of frailty of aging.

Frailty as a consequence of aging is a major health concern. Rather than an inevitable outcome in the elderly, frailty has recently been considered a medical condition. Frailty is defined as a clinical syndrome with three or more of the following criteria: unintentional weight loss, self-reported exhaustion, weakness, slow walking speed, and low physical activity.[1] There is no specific treatment for frailty,[2] though exercise, nutrition changes, and hormonal therapy have been proposed to delay further deterioration.[3] Loss of skeletal muscle mass (sarcopenia)[4] is driven by inflammation and contributes to

weakness and weight loss associated with frailty. In particular, changes in inflammatory cytokines (chemical "messengers" such as interleukins, tumor necrosis factors, and insulin-like growth factors) are linked with sarcopenia.[5]

One cause for frailty of aging may be the decreased capacity of the body's organ systems to perform under stress, a function known as organ reserve. The body's pool of mesenchymal stem cells (MSCs), as discussed in chapter 5, is depleted in number and robustness with age. Each person is born with a certain number of adult stem cells. This number can be thought of as the amount of money in a bank account. A person "withdraws" money as needed throughout life. As in real life, not all stem cell bank accounts are created equal. Some people are born rich while others are born poor. Most people, however, can be thought of as middle class when it comes to the amount of stem cells they have.

This fact helps to explain why some people are able to enjoy health and longevity despite very unhealthy lifestyles while other people may enjoy neither robust health nor longevity despite healthy lifestyles. In other words, some people are able to "spend" their stem cells more extravagantly than others simply because they have more to spend. Most people fall somewhere in the middle—both the length and the quality of our lives may be influenced to some degree by our choice of lifestyle. Environmental factors also play a key role in determining how rapidly one's bank account of stem cells is depleted.

As an example, you probably know someone who's 80 and looks 60 and someone else who is 40 and looks 60. Think of Dick Clark for the former. I'll let you choose the latter.

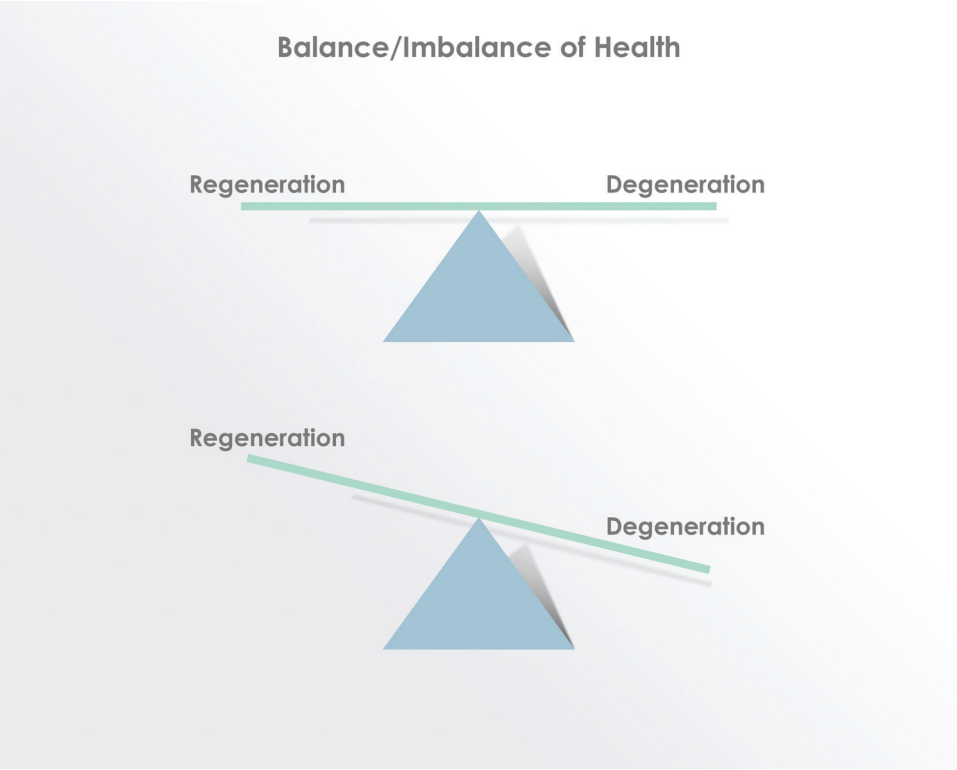
Even under ideal circumstances, stem cells continually diminish with age. Our stem cells exist in every part of the body to repair damage such as broken bones, cuts and bruises, inflammation, radiological and chemical exposure, etc., all of which require stem cells for healing. You may draw on your bank account, like going to an ATM machine, whenever you need to do so until you run out of stem cells. Depending upon how you live your life, and whether you were born with a large or small bank account, after a certain point you may or may not be able to withdraw from your account.

The ATM works quickly and efficiently when someone has a large number of stem cells in the bank. But when the account is almost empty,

which ordinarily happens later in life, the ATM does not distribute the stem cells as readily. In biological terms, this happens for two reasons: 1) the density of capillaries (the home of MSCs) throughout the body diminishes, and 2) the division rate of the stem cells slows considerably. Simply going from a stem cell doubling time of 24 hours to 72 hours can make a 90-day difference in the amount of time required to reach the critical mass of cells required to heal a wound.

As an example, MSCs from a newborn will divide approximately every 24 hours; from a 35-year-old every 48 hours; and from a 65-year-old every 60 hours. If one of those cells were placed in an incubator in growth medium, the yield from that one cell at 30 days would be 1 billion, 32,000, and 200, respectively. If your body needed 10,000 cells to heal, you would be in trouble if you could only produce 200. Not only time and lifestyle affect the overall number of stem cells in your body—if you were to have a massive heart attack or were hit by a truck and broke many bones in your body, there would be a substantial withdrawal from your stem cell ATM as your body tries to repair all of the damage. Below are two graphs—one showing a normal decline in stem cell number over time, the other showing what happens if you have a major heart attack or accident.

If you were fortunate enough to be born with a large amount of stem cells—stem cell rich—then you might be able to smoke, drink, eat unhealthy food, and not exercise, but still live to a ripe old age because you run out of stem cells later than if you had been born stem cell poor. But if you were born on the other end of the spectrum, with a small amount of stem cells, an unhealthy lifestyle will have a more immediate and detrimental impact upon the quality and length of your life. As your bank account approaches zero, physiological healing will become increasingly difficult, until it finally ceases altogether. It's like your own bank account. When you have plenty of money, it's easier to spend. When you are broke, it becomes more difficult to part with each dollar. Likewise, the fewer stem cells that exist in your "account," the stingier the ATM becomes in distributing the contents of that account. Most people are somewhere in the middle. If we think of maintaining health, or homeostasis, as a balance between degeneration and regeneration, we can look at it as a balancing act, much like a teeter-totter with degeneration on one side and regeneration on the other.



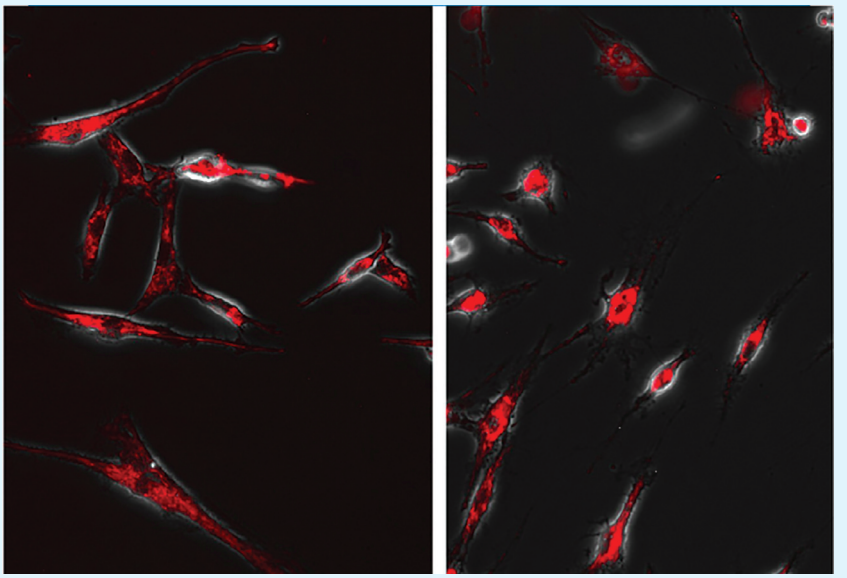
At a certain point in life, which may vary by individual, a disequilibrium between the body's capacity to regenerate and its tendency to degenerate will occur. This imbalance can happen naturally, or it may be accelerated by a health condition or event. When stem cells run low—both those in bone marrow and the MSCs throughout the body—frailty sets in.

When someone has mostly or fully depleted his or her stem cell reserve, the only possible way to get more stem cells is from an alternate source. This is where stem cell therapy comes into play. A fresh supply of regenerative MSCs in someone with a highly depleted reserve may go a long way toward renewing health in that person. MSCs secrete trophic factors and cytokines with a demonstrated anti-inflammatory effect for many conditions. As such, MSCs are positioned as an interesting potential treatment for those affected by frailty or those on the fraily spectrum. I believe the majority of people over the age of 50 are well on their way toward frailty.

Mesenchymal Stem Cells and Aging

Mesenchymal stem cells (MSCs) derived from older individuals lose some of their beneficial characteristics. Cellular environment changes with age,[6] and the amount of circulating cytokines and growth factors is altered, which may affect MSC function and growth.[7,8,9] Younger MSCs are distinctively spindle-shaped, whereas MSCs from older individuals are larger and flatter.[10] The number of MSCs that may be obtained from bone marrow declines with age,[11] and colonies from older MSCs produce a lesser number of viable, newer MSCs.[12] The growth rate of older MSCs as well as the capacity and time to divide are slowed down,[13] and the life span to proliferate is shorter[14,15] than in MSCs derived from younger individuals.

This decline in functionality, or robustness, of older MSCs has critical implications for their participation in the healing process and may be associated with diseases that develop with age.[16] MSCs from an older individual would take much longer to obtain the same regenerative results compared to MSCs derived from younger sources,[17] such as the umbilical cord from healthy, live births. Aside from having faster replication times and a longer life span for proliferation, umbilical cord MSCs secrete abundant cytokines and growth factors necessary for repair and regeneration of the inflamed or injured site and are therefore an attractive source for MSC treatment.



The MSCs in the images above were cultured from the bone marrow of a 65-year-old. The cells on the left were treated with secretions of amnion, a tissue rich in MSCs derived from the amniotic sac of healthy newborns; the cells on the right were cultured with a standard growth medium. Notice the red mitochondria in the cells on the left are evenly distributed throughout the cell body, indicating healthy cells. On the right, the mitochondria are limited mostly to the area surrounding the nucleus, and the morphology of the cells is flattened and more fibroblastic, indicating the cells are near exhaustion, or terminal differentiation. If we measure the trophic factors from the cells on the right, the number and concentration will be much lower than from the cells on the left. This phenomenon highlights the ability of MSCs derived from younger tissue to retrain the MSCs from an older individual to behave like younger MSCs.

The Interdisciplinary Stem Cell Institute at the University of Miami is currently investigating the use of donor MSCs for people aged 60 to 95 with aging frailty in a phase I/II clinical trial.[18] The study aims to demonstrate the safety and effectiveness of donor bone marrow MSCs administered in this population of frail adults. "Allogeneic human MSCs not only help replenish exhausted and/or senescent native stem cells but also have demonstrated systemic anti-inflammatory properties," note the researchers. They are hoping to ameliorate, or even reverse, some of the changes associated with aging. Noting that stem cells can reduce chronic inflammation that erodes the body's repair mechanisms, Goldschmidt, one of the researchers, said,

"In many cases, these seniors can resume walking, cooking, and other daily activities, so they can enjoy a more independent lifestyle."

We have had success at the Stem Cell Institute treating frailty of aging. Mel Gibson's dad Hutton ("Hutt") is a great example. When he was 92, Hutt's health was rapidly deteriorating. His kidneys were backed up and he was in chronic kidney failure due to prostate trouble, his lungs were congested, his heart was failing, and his heartbeat was irregular due to a prolapsed heart valve—Mayo Clinic doctors gave him a grave prognosis. His hips were also in bad shape—one had been replaced and the other had deteriorated badly with severe arthritis, but his current state of health was so fragile that surgery was not an option. On top of all this, his memory was not as sharp as it once was, and he rarely spoke.

The Mayo Clinic was able to stabilize Hutt over the course of ten days, but Mel worried that his father's lack of mobility had been the cause of his declining health. "If only he could get that hip working," Mel wondered. Surgery was out of the question at his age, so when Mel's brother contacted him to tell him about stem cell treatment in Panama City, which he had learned about by searching the Internet, Mel was interested. Mel's good friend Brad Hillstrom, MD, a Mayo trained doctor, was not for it in the beginning, but Mel convinced him to get on the phone with Dr. Paz-Rodriquez, our medical director, and me.

After two lengthy phone calls, a review of studies and papers I had sent him, and consultations with other stem cell researchers who discreetly gave our clinic in Panama—over any other clinic—the green light, Dr. Hillstrom said, "Maybe I'm wrong, but what's your dad got to lose?" They brought him down for treatment. He received IV injections as well as a single injection into his hip. On the plane ride home, Hutt was able to walk without pain. "I have personally taken care of hundreds of patients acutely with hip replacements, and I've never seen anything like it in my life," Dr. Hillstrom told me. "When he went down there he could not sit, walk, stand, or even lay down without pain." Within six weeks, he put on 20 pounds, gained strength, improved mentally, and began walking again with no pain. His kidney and lung function improved, and his prolapsed heart valve even resolved. His eyesight improved and the pigment of his hair darkened. When another set

of Mayo Clinic doctors later followed up with him, they were astounded. He was even taken off several medications.

Hutt has been to Panama three more times and continues to benefit from the stem cell infusions. He has experienced a progressive improvement of health rather than the expected decline people undergo at his age. Hutt is now 98 years old and still going strong. "It was almost like it wound the clock back a few years," Mel said. "He's had six more years of life, and I believe it's a direct result of the stem cells."

About six months after Hutt's treatment, Mel invited me and Dr. Paz out to Beverly Hills to give a lecture to many of his friends who wanted to learn more about stem cells after seeing Hutt's results. After the lecture, which was held at the Beverly Hills Hotel, we went to see Hutt at his house in Agora Hills. When Hutt first came to Panama, he was accompanied by one of his nurses, named Nelly. Nelly's body language the entire time she was in Panama said, "I don't believe in any of this crap." When I walked into the house, she came up to me with open arms, gave me a big hug and said, "Oh, Dr. Riordan! Come over here and look at Mr. Gibson." She showed me his hair and described how it was thicker and some of the white was now black. Then she said to Hutt, "Get out of that chair, old man, and show him what you can do." Hutt proceeded get out of the chair, walked across the room, and then moonwalked back—something I have never been able to do. He was making all sorts jokes the entire time. I was astounded at the turnaround he had achieved. And I was most happy about Nelly thinking differently of me.

"It was almost like it wound the clock back a few years," Mel said. "He's had six more years of life, and I believe it's a direct result of the stem cells."

Because of the amazing recovery Mel and his doctor friend saw in Hutt, Mel, Dr. Hillstrom, and Dr. Hillstrom's wife Tina came down for stem cell treatments themselves. Mel experienced improvement in his shoulders from bone spurs, the doctor experienced relief from knee pain as well as

more stamina and reduced depression, and the doctor's wife experienced improvements in stamina as well as skin and hair health after having suffered through a previous bout of pneumonia. "From an anti-aging standpoint, there is nothing like it," Dr. Hillstrom said.

At the age of 86, Ricardo's health wasn't what it once was. He could no longer drive and opted to stay at home most of the time. He became lost in conversations, and his memory failed him on a regular basis. His energy declined, and he could no longer visit his farm, where he loved to work. Ricardo happens to be the father of Rodolfo Fernandez, laboratory director of Medistem, our clinic's parent company. So when Rodolfo noticed the decline in his father's health, he knew stem cells might help. Ricardo agreed to treatment and received umbilical cord MSCs intravenously. A week later the results were evident. His memory improved, and he regained so much energy that he felt confident to drive again. He even went back to work on his farm. He is now going on 90 and continues to feel well. He is looking forward to another treatment to maintain the benefits he has gained.

Rodolfo's mother, Teresita, has an even better story. Asthmatic since the age of five and later diagnosed with emphysema, Teresita became quite sick when she contracted flu at the age of 80. She was hospitalized, given many medications, and put on oxygen. The pulmonologist told her she would need to stay on oxygen and could no longer travel to her farm, which was at an elevation of 5,000 feet. When Rodolfo saw how successful his father's stem cell treatment had been, he wondered if his mother might qualify to enroll in a clinical trial for asthma that we were undertaking at the clinic. She did qualify, and received her treatment using intravenous MSCs along with intranasal (inhaled) trophic factors. Two months after her first treatment, she called Rodolfo. "I'm feeling different," she said. Her breathing had improved. At that time, her oxygen tank had run out, but she felt so good that she didn't need to use it anymore. That was over two years ago, and she hasn't needed oxygen since. She has traveled to Europe, Costa Rica, the United States, and yes, back to her farm.

The Body's Energy Powerhouses

Within most cells of the body are small yet powerful organelles called mitochondria, responsible for 90 percent of the body's energy production. Remember learning about adenosine triphosphate (ATP) back in science class? ATP is the body's energy currency. Without it, we could not function. Mitochondria produce ATP out of molecules derived from food. The function of our mitochondria is very important to our overall health.

Mitochondria degrade by a process known as oxidation, which essentially means the mitochondria do not get the maintenance they require, so they wear out. Mitochondrial oxidation is inversely related to life span—the more your mitochondria are oxidized, or worn out, the shorter your life span.[19] Oxidation is the biggest predictor of death of an organism.

One risk of frailty in older age is dementia. The brain experiences aging just as the rest of the body does. In some people, this process begins earlier than in others. At the Stem Cell Institute, we generally don't treat Alzheimer's, the most widely recognized form of dementia, largely because it requires frequent treatments that become too costly for most patients. There is one exception, however. A patient whom I will call Wilma has a strong family history of Alzheimer's disease—both her parents and her grandmother had had it. Wilma was tested and discovered that she carried both alleles that strongly predisposed to her the disease. By 2008, when she was 61, they began to notice symptoms, and she was diagnosed with early-onset Alzheimer's disease. While she is not yet considered frail, her condition would put her down an early path to frailty if left to conventional treatment, which does little to help this devastating disease.

Wilma is married to a highly successful businessman—a man with the means to seek out cutting-edge treatments that may be expensive. They learned about stem cell treatment at our clinic from my close friend Dr. Bob Harman, founder and CEO of Vet-Stem, and began visiting regularly, first

Very interesting research in the past few years has discovered that MSCs are the only cells we know of that donate their mitochondria.[20,21] MSCs actually triage cells, just like in the hospital when a nurse triages patients to determine who needs immediate treatment and who can wait a while. When an MSC encounters another cell, if it detects a need for help, it will actually donate its mitochondria via small vesicles (containers) or tubules (tubes), to the cell in an effort to replace the oxidized mitochondria with healthy mitochondria.

This scientific discovery deserves a Nobel Prize in my opinion. In the future, I believe we will be able to bioreact MSCs, optimizing them to produce these microvesicles and microtubules of mitochondria that will perhaps allow people to live a healthy life span of 200 years. MSCs as mitochondrial factories may one day be one of the most important science breakthroughs of our time.

to our clinic in Costa Rica and then to Panama. As a matter of fact, Wilma has been down for 10 treatments in Panama and has received a total of 52 injections—796 million cells since August 2010. "She never feels any type of side effect with intravenous stem cell treatment," her husband said. She has received more intravenous stem cells than any other patient we have treated. The only other treatment she receives for Alzheimer's disease is gamma globulin infusions biweekly, which was added in 2014.

While her disease has progressed some, Wilma and her husband believe that it is progressing at a much slower rate than it would without stem cell treatment. She is still fully functional. She can drive and is independent. She still goes to the grocery store and shopping with her friends. Only her short-term memory is somewhat challenged. I had dinner with Wilma and her husband a few months ago with several other patients—no one could tell she had that diagnosis. Given that the average time to death is seven years for people with her diagnosis, I find it incredible that she is doing so well eight years later. "The stem cells,

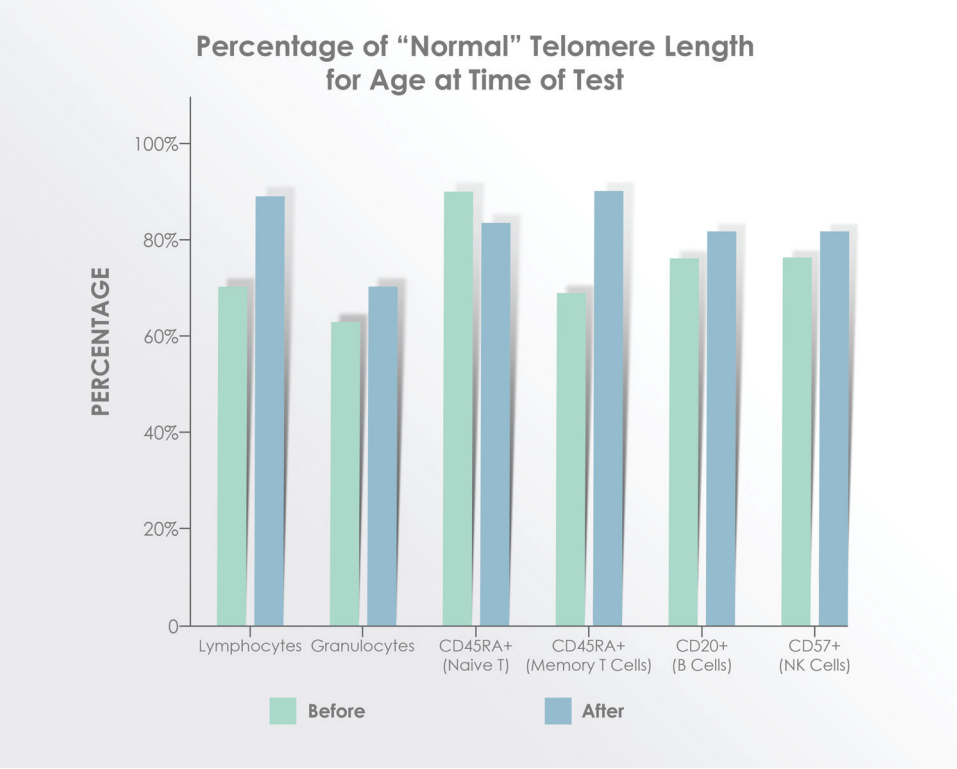
"The stem cells, I think, are the key," said her husband. "She can tell after receiving the cells that her memory improves for a period of time."

I think, are the key," said her husband. "She can tell after receiving the cells that her memory improves for a period of time. Sometimes her memory starts getting "iffy" and she says, 'When are we going to Panama?'"

Hendrikje van Andel-Schipper was once the oldest woman in the world. She died in 2005 at the age of 115, at which point her body was donated to science at her request. Interestingly, scientists studying her body found that all the white blood cells in her blood were derived from just two stem cells, suggesting that her stem cells had all but run out by the time she died.[22] The telomeres, or DNA tips, of her white blood cells were greatly worn down, a sign of cell aging and deterioration. This research begs the questions, as the scientists put it, "Is there a limit to the number of stem cell divisions, and does that imply that there's a limit to human life? Or can you get around that replenishment with cells saved from earlier in your life?" Did this woman live to such an old age because her stem cell supply was abundant? Could she—or anyone for that matter—extend life by increasing her supply of stem cells? These are the questions that we will be faced with as this field moves forward.

A colleague recently sent me the test results of a 79-year-old man with pulmonary fibrosis who had undergone three treatments with IV umbilical cord MSCs. The telomeres in five of six different cells—lymphocytes, granulocytes, naïve T cells, memory T cells, B cells, and NK cells—increased in length over the course of a year. His cells now have a much "younger" telomere length than prior to treatment. Idiopathic pulmonary fibrosis patients have shorter than normal telomeres, which is thought to be, at least in part, the etiology of the disease. Once telomeres become too short, the cell cannot divide and therefore senesces, or deteriorates. Senescent cells are the root of all evil in aging and lack of repair. In fact, they not only do not contribute to repair and remodeling, but they also actively inhibit those activities in neighboring cells. There is active research on how to selectively remove senescent cells to increase health, decrease disease, and increase lifespan.

This is the first time I've seen a human's telomeres increase in length. They increased after stem cell therapy, a completely nontoxic treatment that is also improving his health. Scientists have been searching for a way to increase telomere length for many years, believing it to be the key to the "Fountain of Youth."



Telomere Length in Various Immune Cells Before Stem Cell Treatment

Sample Dates (mm/dd/yy) **Draw:** 12/02/15 **Received:**12/03/15 **Resulted:** 12/16/15

Lymphocytes			Granulocytes			CD45RA+ (Naïve T)			CD45RA+ (Memory T)			CD20+ (B Cells)			CD57+(NK Cells)		
MTL	MTLN	INT	MTL	MTLN	INT	MTL	MTLN	INT	MTL	MTLN	INT	MTL	MTLN	INT	MTL	MTLN	INT
(kb)	(kb)		(kb)	(kb)		(kb)	(kb)		(kb)	(kb)		(kb)	(kb)		(kb)	(kb)	
3.8	5.4	L	4.7	7.4	VL	5.1	5.7	N	3.5	5.1	L	5.7	7.2	L	4.0	5.2	N

MTL = Patient Median Telomere Length

MTLN = Normal MTL at age (50th percentile)

INT = Telomere length interpretation

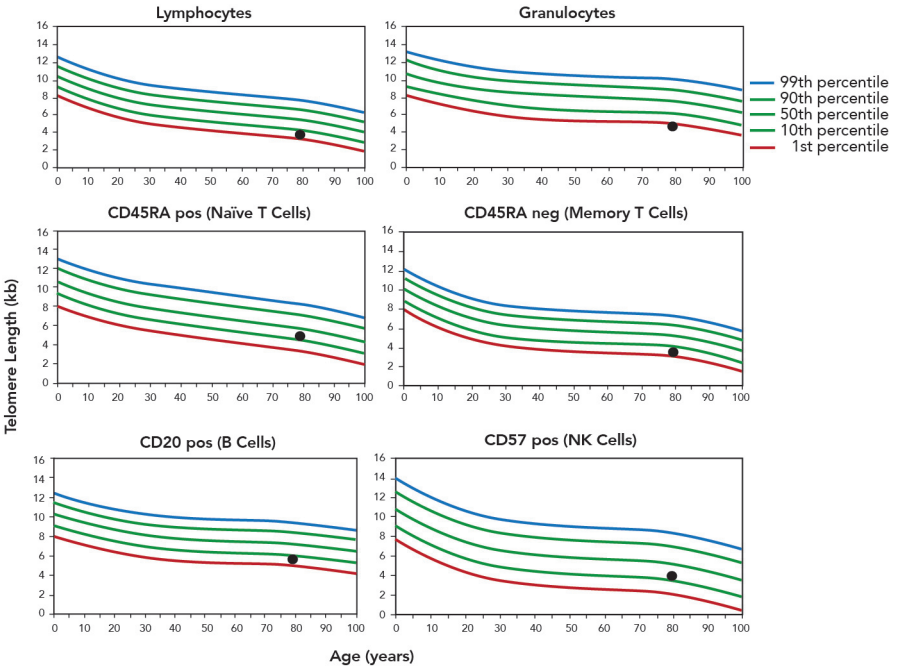
VH = Very High (≥ 99 percentile)

H = High (≥ 90 and < 99 percentile)

N = Normal (≥ 10 and < 90 percentile)

L = Low (≥ 1 and < 10 percentile)

VL = Very Low (1 percentile)



Telomere Length in Various Immune Cells After Stem Cell Treatment

Sample Dates (mm/dd/yy) **Draw:** 11/16/16 **Received:**11/18/16 **Resulted:** 11/30/16

Lymphocytes			Granulocytes			CD45RA+ (Naïve T)			CD45RA+ (Memory T)			CD20+ (B Cells)			CD57+(NK Cells)		
MTL	MTLN	INT	MTL	MTLN	INT	MTL	MTLN	INT	MTL	MTLN	INT	MTL	MTLN	INT	MTL	MTLN	INT
(kb)	(kb)		(kb)	(kb)		(kb)	(kb)		(kb)	(kb)		(kb)	(kb)		(kb)	(kb)	
4.8	5.4	N	5.2	7.4	L	4.8	5.6	N	4.6	5.1	N	6.4	7.2	N	4.3	5.1	N

MTL = Patient Median Telomere Length

MTLN = Normal MTL at age (50th percentile)

INT = Telomere length interpretation

VH = Very High (≥ 99 percentile)

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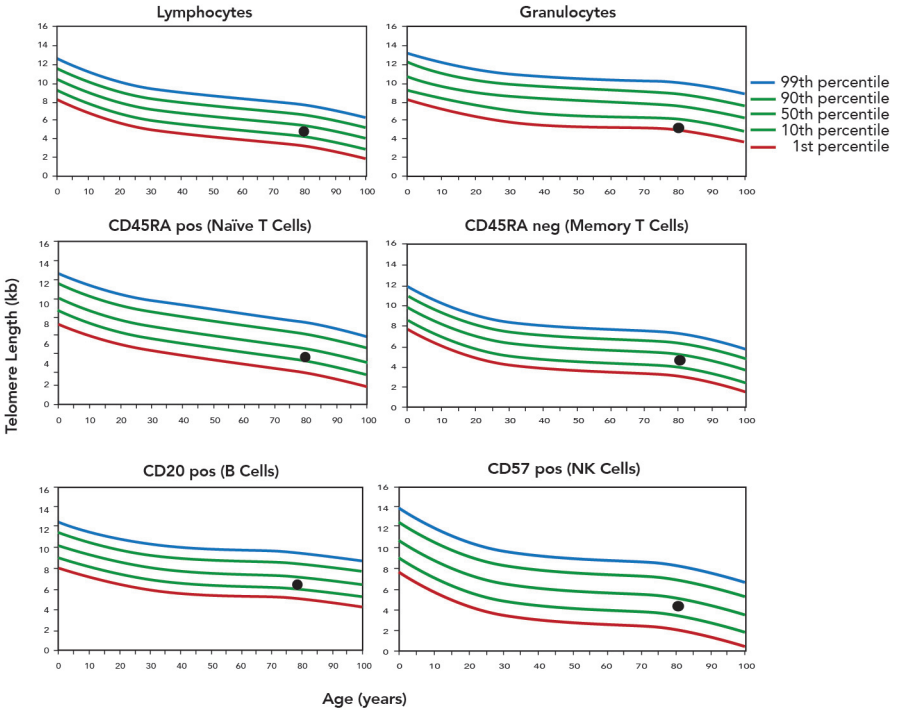

21. Liao W, Xie J, Zhong J, et al. Therapeutic effect of human Umbilical cord Multipotent Mesenchymal Stromal cells in a rat model of stroke. Transplantation. 2009;87(3):350–359.doi: 10.1097/TP.0b013e318195742e.

22. Mathiasen AB, Qayyum AA, Jørgensen E, et al. Bone marrow-derived mesenchymal stromal cell treatment in patients with severe ischaemic heart failure: A randomized placebo-controlled trial (MSC-HF trial). Eur Heart J. 2015;36(27):1744–1753.doi: 10.1093/eurheartj/ehv136.

23. Perin EC, Borow KM, Silva GV, et al. A phase II dose-escalation study of allogeneic mesenchymal precursor cells in patients with ischemic or nonischemic heart failure. Circ Res. 2015;117(6):576–584.doi: 10.1161/CIRCRESAHA.115.306332.

24. Perin EC, Dohmann HF, Borojevic, et al. Transendocardial, autologous bone marrow cell transplantation for severe, chronic Ischemic heart failure. Circulation. 2003;107(18):2294–2302.

25. Fisher SA, Brunskill SJ, Doree C, Mathur A, Taggart DP, Martin-Rendon E. Stem cell therapy for chronic ischaemic heart disease and congestive heart failure. Cochrane Database Syst Rev. 2014;(4):CD007888. doi: 10.1002/14651858.CD007888.pub2.

26. Fisher SA, Doree C, Mathur A, Martin-Rendon E. Meta-Analysis of cell therapy trials for patients with heart failure. Circ Res. 2015;116(8):1361–1377.doi: 10.1161/CIRCRESAHA.116.304386.

27. Ichim TE, Solano F, Lara F, et al. Combination stem cell therapy for heart failure. Int Arch Med. 2010;3(1):5.doi: 10.1186/1755-7682-3-5.

28. Tuma J, Carrasco A, Castillo J, et al. RESCUE-HF trial: Retrograde delivery of Allogeneic Umbilical cord lining Sub-Epithelial cells in patients with heart failure. Cell Transplant. 2016; January. [Epub ahead of print]

29. Silvestre JS, Menasché P. The evolution of the stem cell theory for heart failure. EBioMedicine. 2015;2(12):1871–1879. doi: 10.1016/j.ebiom.2015.11.010.

30. Menasché P. Stem cells for the treatment of heart failure. Philos Trans R Soc Lond B Biol Sci. 2015;370(1680):20140373. doi: 10.1098/rstb.2014.0373.

31. Poglajen G, Vrtovec B. Stem cell therapy for chronic heart failure. Curr Opin Cardiol. 2015;30(3):301–310.doi: 10.1097/HCO.0000000000000167.

32. Winters AA, Bou-Ghannam S, Thorp H, et al. Evaluation of multiple biological therapies for ischemic cardiac disease. Cell Transplant. 2016;25(9):1591-1607.

33. Wang J, Zhang S, Rabinovich B, et al. Human CD34+ cells in experimental myocardial infarction: long-term survival, sustained functional improvement, and mechanism of action. Circ Res. 2010;106(12):1904-11.oi: 10.1161/CIRCRESAHA.110.221762.

34. Zhang S, Shpall E, Willerson JT, Yeh ET. Fusion of human hematopoietic progenitor cells and murine cardiomyocytes is mediated by alpha 4 beta 1 integrin/vascular cell adhesion molecule-1 interaction. Circ Res. 2007;100(5):693-702.

35. Shabbir A, Zisa D, Suzuki G, Lee T. Heart failure therapy mediated by the trophic activities of bone marrow mesenchymal stem cells: a noninvasive therapeutic regimen. Am J Physiol Heart Circ Physiol. 2009;296(6):H1888-97. doi: 10.1152/ajpheart.00186.2009.

Chapter Nine

1. Fried LP, Tangen CM, Watson J, et al. Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56(3):M146-56.

2. Lally F, Crome P. Understanding frailty. Postgrad Med J. 2007;83(975):16-20. doi: 10.1136/pgmj.2006.048587.

3. Espinoza S, Walston JD. Frailty in older adults: insights and interventions. Cleve Clin J Med. 2005;72(12):1105-12.
4. Marcell TJ. Sarcopenia: causes, consequences, and preventions. J Gerontol A Biol Sci Med Sci. 2003;58(10):M911-M916.
5. Jensen GL. Inflammation: roles in aging and sarcopenia. JPEN J Parenter Enteral Nutr. 2008;32(6):656-9.
6. de Gonzalo-Calvo D, Neitzert K, Fernández M, et al. Differential inflammatory responses in aging and disease: TNF-alpha and IL-6 as possible biomarkers. Free Radic Biol Med. 2010;49(5):733-737. doi: 10.1016/j.freeradbiomed.2010.05.019.
7. Lepperdinger G. Inflammation and mesenchymal stem cell aging. Curr Op Immunol. 2011;23(4):518-524.doi: 10.1016/j.coi.2011.05.007.
8. Boyette LB, Tuan RS. Adult Stem Cells and Diseases of Aging. J Clin Med.2014;3(1):88-134.doi: 10.3390/jcm3010088.
9. Wong TY, Solis MA, Chen YH, Huang LL. Molecular mechanism of extrinsic factors affecting anti-aging of stem cells. World JStem Cells.2015;7(2):512-520.doi: 10.4252/wjsc.v7.i2.512.
10. Baxter MA, Wynn RF, Jowitt SN, Wraith JE, Fairbairn LJ, Bellantuono I. Study of telomere length reveals rapid aging of human marrow stromal cells following in vitro expansion. Stem Cells.2004;22(5):675-682.
11. Caplan AI. Adult mesenchymal stem cells for tissue engineering versus regenerative medicine. J Cell Physiol.2007;213(2):341-347.
12. Sethe S, Scutt A, Stolzing A. Aging of mesenchymal stem cells. Ageing Res Rev. 2006;5(1):91-116.
13. Sethe S, Scutt A, Stolzing A. Aging of mesenchymal stem cells. Ageing Res Rev. 2006;5(1):91-116.
14. Zhou S, Greenberger JS, Epperly MW, et al. Age-related intrinsic changes in human bone-marrow-derived mesenchymal stem cells and their differentiation to osteoblasts. Aging Cell.2008;7(3):335-343.
15. Stenderup K, Justesen J, Clausen C, Kassem M. Aging is associated with decreased maximal life span and accelerated senescence of bone marrow stromal cells. Bone.2003;33(6):919-926.
16. Sharpless NE, DePinho RA. How stem cells age and why this makes us grow old. Nat Rev Mol Cell Biol.2007;8(9):703-713.
17. Fan M, Chen W, Liu W, et al. The effect of age on the efficacy of human mesenchymal stem cell transplantation after a myocardial infarction. Rejuv Res.2010;13(4):429-438.doi: 10.1089/rej.2009.0986.
18. Golpanian S, DiFede DL, Pujol MV, et al. Rationale and design of the allogeneiC human mesenchymal stem cells (hMSC) in patients with aging fRAilTy via intravenoUS delivery (CRATUS) study: A phase I/II, randomized, blinded and placebo controlled trial to evaluate the safety and potential efficacy of allogeneic human mesenchymal stem cell infusion in patients with aging frailty. Oncotarget. 2016;7(11):11899-912. doi: 10.18632/oncotarget.7727.
19. Barja G, Herrero A. Oxidative damage to mitochondrial DNA is inversely related to maximum life span in the heart and brain of mammals. FASEB J. 2000;14(2):312-8.
20. Islam MN, Das SR, Emin MT, et al. Mitochondrial transfer from bone-marrow-derived stromal cells to pulmonary alveoli protects against acute lung injury. Nat Med. 2012;18(5):759-65. doi: 10.1038/nm.2736.
21. Sinha P, Islam MN, Bhattacharya S, Bhattacharya J. Intercellular mitochondrial transfer: bioenergetic crosstalk between cells. Curr Opin Genet Dev. 2016;38:97-101. doi: 10.1016/j.gde.2016.05.002.
22. Holstege H, Pfeiffer W, Sie D, et al. Somatic mutations found in the healthy blood compartment of a 115-yr-old woman demonstrate oligoclonal hematopoiesis. Genome Res. 2014 May;24(5):733-42. doi: 10.1101/gr.162131.113.

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