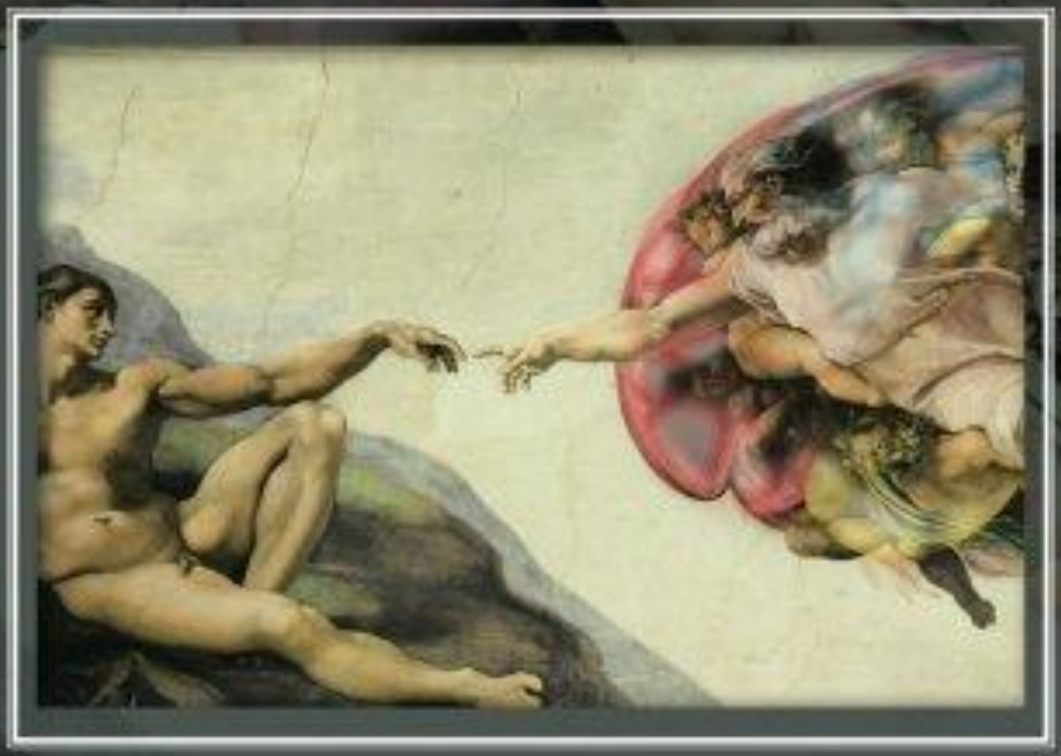
The Stem Cell Revolution



Mark Berman, MD; Elliot Lander, MD

THE STEM CELL REVOLUTION®

ABOUT THE COVER

In 1508, Michaelangelo Buonarroti painted this image of the creation of Adam on the ceiling of the Sistine Chapel. He not only displayed artistic genius but also possessed much knowledge as an anatomist. We now know that Michaelangelo secretly practiced his passion for anatomy at a time when the Church decreed dissection of cadavers punishable by death. He risked his career and his life in his pursuit of anatomic truth and he left us a hidden message in his juxtaposition of God with a cross section of the human brain. The image demonstrates the frontal lobe, the sulci, the hypothalamus, the brainstem, the optic chiasm, and many of the anatomic structures we first learned about in our medical school neuro-anatomy courses. American Neurologist Frank Meshberger first noted this stunning depiction of God as the supreme intelligence during an artistic epiphany while staring at the chapel ceiling nearly 500 years after it was painted. One starts to ponder what other sublime wonders lay hidden in full view. The serendipitous discovery of millions of healing stem cells programed for human repair sitting in plain view just under our skin might just be one of those wonders. We now stand at the inception of a new field of medical

way, it compels the

question: what is one willing to risk for the pursuit of knowledge and truth?

Elliot Lander MD

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STEM CELL REVOLUTION®

BY MARK BERMAN, M.D. AND ELLIOT LANDER, M.D.

FORWARD

In his bestselling 2007 book *The Black Swan*, author Nassim Taleb describes uncertainty and randomness and how we routinely underestimate huge deviations from what we expect to

ves together philosophy, math, history, and business to explain the

The serendipitous finding of high numbers of regenerative stem cells in the fatty tissue just under our skin and the simple use of minor, low-risk surgical procedures and FDA-approved enzymes to release combine to

bio-factory for regenerative medicine. One might call it

How all this will impact the medical world of cell therapy, the academic world of pathways and patents, and the pharmaceutical industry, is still unclear but the effects have already started and

Mark Berman, MD and Elliot Lander, MD

Founders: California Stem Cell Treatment Center and the Cell Surgical Network

PROLOGUE

We have entered the rapidly evolving stem cell age. The media saturates us with stories, hype and promises about stem cell wonders and cures. As clinicians, we witnessed the initial achievements in cell therapy unlocking the potential to for actual organ repair and replacement.

there already exists an alternative clinical industry of stem cell treatment clinics offering cell therapies derived from adult tissues particularly adipose tissue. These centers offer patients

the US, same day surgical procedures permit physicians to transfer tissues rich in stem cells to damaged areas of the body providing patients access to regenerative therapies now. Same day surgical procedures that maintain sterility without risk of disease transmission support the very mission of the current FDA tissue handling rules. Thus, stem cells found in autologous fat, extracted through a safe and near painless procedure afford such clinics the opportunity to help countless patients now.

In 2008, colleagues in Asia provided Dr. Mark Berman, an internationally recognized expert on fat grafting procedures, an improved way to harvest and process fat for grafting. Further, they had developed a method to procure stromal vascular fraction (SVF rich in mesenchymal stem cells) from fat. Once safe enzyme materials were available, we modified the technique to produce a closed sterile surgical method for producing SVF. We quickly realized that we had valuable technology at our disposal but that we would have to use it judiciously. From the start, we created the California Stem Cell Treatment Center®, a multispecialty team necessary for treating conditions beyond our scope of practice such orthopedic, cardio/pulmonary, urologic and other diseases. We set up safety studies for the investigational use of SVF and obtained Institutional Review Board (IRB) approval for them. We built an educational website www.stemcellrevolution.com that explains the nature of this patient funded research. We coined *cell surgery* component thus distinguishing ourselves from the pharmaceutical model. We have now performed over 2000 cases demonstrating extraordinary safety and no serious adverse effects related to SVF deployment. We have seen astonishing results in tissue healing, autoimmune and neurodegenerative disease mitigation, arthritis mitigation and treatment of crippling back pain. The uses and various methods of deploying SVF are continually growing.

Understanding the importance and necessity of teaching our technology to other interested physicians, we formed the Cell Surgical Network® (CSN) in 2012 and started training select physicians in our regenerative medicine techniques. CSN® now includes 79 centers around the world. All Network physicians are performing cell surgery using identical methods and protocols and all are collecting safety and outcomes data in our online database. Our safety study for the first 1000 patients is in manuscript form.

Considered a disruptive technology, point of care production and deployment of SVF allows

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mitigation. The Cell Surgical Network® mission is to accelerate the quality of regenerative medicine and have safe and cost effective cell based therapies available soon to everyone in the world. A vision we get closer to achieving every day.

Elliot Lander MD and Mark Berman MD

Chapter 1

THE SCIENCE OF STEM CELLS

Stem cell: an unspecialized cell that can differentiate (i.e. change into) a specific specialized cell; also has the capability to replicate.

The mention of stem cells raises tremendous controversy, such that the American public tends to presume two things: 1) That the cells in question are embryonic cells, harvested from the tissue of aborted fetuses, or dead fetuses created and altered in a laboratory for scientific purposes, and 2) That actual operations using stem cells derived from human tissue will be a phenomenon of the distant future es for at least another decade. Yet here at the California Stem Cell Treatment Center, our patients have been rec -

the future, how is it possible for us to offer leading-edge treatment right now? And is this even legal?

For starters, the cells that our team works with are non-embryonic cells; CSCTC uses strictly adult (not fetal) tissue and autologous cells, meaning the cells are taken from the person that

receives them donor and recipient are one and the same. Embryonic cells are hailed in the media for their pluripotent property, meaning they can differentiate into any type of cell in the

which is abnormally rapid growth in any context other than a pregnancy, resulting in the formation of teratomas which is a type of uncontrolled neoplastic (cancerous) growth. Such tumor formation has been clinically documented and has severely limited the clinical use of embryonic stem cells which is problematic since most of the basic science stem cell work done in the past 15 years has been using these embryonic cells. The adult cells that we use at CSCTC are not pluripotent, but they are plenty potent for regenerative healing. These adult stem cells (ASCs) derived from fat have been documented to be capable of forming nearly every type of tissue in the human body except placental tissue. We have proof that fat derived stem cells can form nerve tissue and other complex organs. (See addendum- History of Adipose Derived SVF).

Learn to love your body fat loaded with mesenchymal stem cells, a.k.a. multipotent stromal cells, or MSCs, that can differentiate into a variety of cell types. These same cells may also be isolated from several other sources in the body, including bone marrow and the umbilical cord (cord blood cells are adult cells, not embryonic ones). For millennia, the lifeline joining mother and infant was discarded after birth; in recent years, however, growing scientific awareness that the umbilical cord is a rich reserve of stem cells has spurred the development of technology enabling parents to choose the option of having their cord blood preserved and cryobanked (deep frozen at - . However, the focus on the

which are a type of stem cell that is especially intended to form blood products and can be useful in patients that have blood line tumors like leukemia and need therapies that destroy the persons

Bone marrow MSCs have been used for a number of years, particularly for a variety of orthopedic conditions; however, they are found in relatively low numbers, and require FDA

ensure adequate amounts for regenerative purposes. Also, with chronic illness and advanced age the bone marrow is suppressed, and this negatively impacts the quality and quantity of the cells. As cancer patients who have undergone harvesting of their bone marrow appreciate, the removal process is difficult, painful, and invasive. As noted above, the MSCs used at our practice are adipose-

that fat has 2,500 times the number of MSCs as bone marrow; the cells simply lie dormant in the collagen matrix of the fat, but can be made readily available for release and bio-available to our damaged tissue for repair purposes. Scientists abbreviate the term adipose-derived stem cells as ASC, to distinguish them from bone-marrow-derived stem cells, or BSC. While different camps will try to argue that bone marrow cells have advantages over fat-derived cells, studies show that the cells derived from fat are equal if not superior in regenerative potency to the stem cells derived from bone marrow.

- ue to remove the fatty tissue. Liposuction has been the single most popular cosmetic procedure in the United States for several years now. Of course, with basic liposuction the goal is to

lose by normal diet and exercise. Amazingly, while fat frequently finds use in transplantation for facial rejuvenation, breast augmentation, buttock augmentation, and a variety of defect repairs, it is otherwise largely discarded. Today, we know that there are 500,000 to 1 million stem cells

in each milliliter of fat yet during routine cosmetic procedures, surgeons were discarding what amounted to billions of these incredibly important regenerative cells. In most cases, the MSC-rich adipose tissue continues to be discarded. Most liposuction procedures require some type of sedation in addition to local anesthesia;

simple technique for harvesting fa

Even doctors that perform liposuction that have had the procedure done on themselves find it surprisingly pain- ot less painful).

The cosmetic surgeon and the urologist may seem like doctors walk into a

practice despite the mainstream media and medi

the stuff of theory, not practice and to make this therapy available today to people who need it.

As a top cosmetic surgeon in Beverly Hills renowned for face lifts, Mark kept current with scientific studies of adipose tissue all over the world, fascinated by what was becoming

arvested

and repurposed for therapeutic purposes including arthritis and orthopedic injury. Mark felt a professional duty to deploy SVF to help patients with more than just aesthetic medical issues. But, as a cosmetic surgeon, he would beyond his scope of practice if he were to start treating joint conditions. So he convinced a leading Westside orthopedic surgeon, Dr. Thomas Grogan, to consider treating patients with him. After discussing the possibilities, Grogan agreed to evaluate patients sent by Mark. Pretty soon, patients were asking Mark to address their issues with aging joints instead of aging faces.

returned from Japan and was sitting with me talking about how using stem cells for cosmetics was actually a waste of valuable cells when one considers the tremendous therapeutic potential of these cells. It was one of those epiphany moments and I told Mark he was right and not only was he right, but that we were going to do just that. But we both understood that we had to do it correctly. We did not want to get painted with the same broad strokes as those clinics that offered cell therapy but without rigorous protocols, data collection, and standardization of procedures. Mark and I decided to study the investigational use of stem cells found in stromal vascular fraction and offer it to our patients ethically and safely. We understood that we had to charge our patients but we set fair rates and called it patient funded research. After all, who else would fund such a project? Government and private industry had no industry in funding the study of a

- a personal biologic that was not patentable or capable of being manufactured for co

Elliot as a urologist, quickly began thinking about treating so many urologic degenerative diseases, such as erectile dysfunction which afflicts some 65 million Americans. The possibilities were unlimited: if this could be done as a surgical procedure rather than a laboratory based product application, then cell therapy could be made readily available to patients everywhere in the world today without an expensive laboratory or inaccessible university research program.

A well, who else is going to undertake this work? There is no special residency or training for stem cell therapy. B

from Japan to hand you a new recipe with tremendous healing igated to

differentiate

into specialists. Eager to help patients struggling with medical issues that were more than just

cosmetic, and anticipating demand for this exciting new therapy, Mark crossed over into therapeutic practice a rare move for a cosmetic surgeon. Meanwhile Elliot, the urology

liposuction procedure, so he too would be ready to extract and deploy ASC.

The procedure is simple enough that any physician with an MD degree, regardless of his or her

Patients undergo a mini-liposuction that yields the stromal vascular fraction (SVF), a protein-rich segment from processed adipose tissue. SVF contains a mononuclear cell line comprised mainly of autologous mesenchymal stem cells (fat derived and peri-vascular blood vessel derived stem cells), macrophage cells, endothelial cells, red blood cells, immune cells, and growth factors that facilitate the stem cell process and promote their activity. The fat sample is processed in a centrifuge in our treatment room as part of the surgical procedure; our technology enables us to

injected back into their body, either directly into the inflamed area (such as the knee or hip joint) or into the bloodstream, via an intravenous injection. When delivered by IV, the cells travel through the vascular system in search of areas of inflammation; the cells target those areas and then the damaged tissue activates the stem cells to begin the regeneration process.

Confident that we both had sufficient experience with this new method, Elliot came up with the idea to join our two practices

and reincorporate both as branches of the California Stem Cell Treatment Center- dedicated to the investigational study of SVF. We set up our educational website www.Stemcellrevolution.com and in December of 2010, we treated our first patient at CSCTC. The first person to be treated with his own stem cells at the newly renamed facility was a

resolution of his symptoms, and his success is durable to the present time. Like many of our patients, he later offered to invest in our clinic but we continue to remain privately owned in alignment with our philosophy to be physician owned and controlled. Because the service we offer is a totally closed procedure (the entire process is performed without exposure to the environment) ing fat for cosmetic purposes it is absolutely legal to perform since it is a type of lipo-transfer surgery. If it would be a laboratory procedure, it would not be FDA compliant procedure. We modified the technology to make it a surgical procedure instead of a laboratory re one of only groups in the world doing it this way.

Other American facilities working with stem cells are laboratories, and all labs must be overseen by the FDA, to prevent disease transmission. This explains why the science pundits predict that But because we perform closed surgical

- FDA-compliant, completely legal, and available right now

The FDA regulates drugs and medical d As such, our protocol is no different than Mark extracting fat from his aesthetic patients and re-injecting it into their faces ing that for almost 30 years our own on-the-job training, any doctor is able to pick up the technique, no matter how general or specialized the practice s/he operates.

CSCTC is the first American medical practice to offer treatment with adipose derived stem cells

in a methodical, investigative, academic, and organized manner. As the first to do this the way we do, initially we faced a great deal of criticism. We had to fly in the face of some peer issues, as competing clinics were located offshore and their quality was perceived as dodgy. Plus, we e invested thousands of dollars of our own money and substantial time diverted from our own lucrative practices because we believed in what we were doing. Colleagues advised us to wait for peer- charlatans and our treatment is so much snake oil. But we saw no reason to delay putting this proven technology

been doing this for four years now, in a meaningful, controlled wa ve treated more than 2,000 patients.

We turn away as many as 20 percent of people who apply to us for treatment.

What CSCTC definitely does not do is culture cells to increase their strength in numbers. We cannot by law. Although cell culturing is currently par for the course in Spain, Russia, Sweden, Asia, and off-shore, here in the United States, if you grow (i.e. manipulate) cells, then by definition you become a drug manufacturer

FDA. Culturing cells is beyond the scope of minimal manipulation, so growing is, for now, verboten. Hopefully, that restriction will soon change, as the ability to culture cells will permit American doctors to perform life-saving procedures such as generating custom, rejection-proof

tissue-engineered trachea transplant in Barcelona in 2008). Once an organization demonstrates FDA approved Good Manufacturing Practices (GMP) to culture (i.e. replicate and increase the numbers of cells), thus avoiding risk of disease transmission, then your

own cells will eventually be available in even greater numbers. You will eventually bank your cells and get huge returns with interest. This brings possibilities are nearly unlimited such as creating your own individual lines of stem cells that could later be used not only for repair work but also to fight cancers since our stem cells have the ability to bring cancer therapies directly to damaged tissue where malignancies are growing. Many labs around the world are now looking at exploiting the cancer homing and identifying properties of stem cells and this area of stem cell science is attracting a lot of attention and interest today.

we were taught when we took the Hippocratic oath? If we have a treatment that is apparently safe and effective, are we not at least ethically obligated to provide it for our patients? Are we not also obligated to teach it to our fellow physicians?

So, if it was that easy, not to mention legal, to establish an American stem cell clinic, then why

Most likely because specialists from different disciplines rarely

-doctor- and we take that as a compliment. And b

advertised patients find us through word of mouth, physician referral, or by happening upon our Web site I like

shed to see a urologist performing liposuction.

Today, collaborating with our colleagues in different medical specialties, we offer treatment for conditions that are quite different from our original specialties, including heart disease, neurological dise

however, they might not get the news from an endocrinologist, per se, but from a distinguished orthopedic surgeon

who expanded his practice to include stem cell therapy for a range of conditions far outside his

.

Today, the Cell Surgical Network we started in 2012 to teach other physicians has grown into an international organization that not only promotes cell therapy, but also treats actual patients using their own stem cells, harvested from their own fat. The

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doctors currently providing stem cell treatment a service supposedly very complicated and still five or ten years off. While we faced arguments about the limitations of SVF, scientific studies and actual investigational patient treatments have demonstrated far more abilities for cell repair than we originally thought existed. Several of our patients have graciously agreed to share their stories to help illustrate these findings. SVF has provided us with a spectacular journey bridging multiple disciplines, bringing many of us back to the joy of treating a variety of medical problems and often positively impacting our patients when little or no hope existed.

Chapter 2

AESTHETICS TO THERAPEUTICS

issue. But a plastic surgery practice is exactly where many patients suffering from joint degeneration and arthritis experienced an end to months and even years of discomfort and diminished quality of life. Most of these patients had already taken multiple treatments e.g. NSAID (non-steroidal anti-inflammatory) pain medications, steroid injections, hyaluronic acid injections, and even arthroplasty get better. After intra-joint injection of SVF, on the other hand, most showed improvement, with

cosmetic surgery technique liposuction could yield such consistently effective therapeutic results. Today, the majority of our patients and some of our most compelling success stories are people with orthopedic problems who are happy to resume favorite activities many thought

With any new medical technology, the first patients who step forward to try it out are trailblazers

first two patients to undergo our treatment protocol in 2010. The very first was Laurie, who dealt with continual pain in her left knee as a result of a nasty ski accident followed by arthroscopic surgery to try and straighten out her damaged cartilage. A

arthroscopy

keeps Laurie on her feet m

ng fat-derived

just kept it to herself.

understand how badly damaged it had been. The joint felt like a sack of granola. You could practically hear the cartilage particles rubbing together and breaking apart. Laurie became patient

-derived stromal vascular fraction (SVF). But before Mark could perform the procedure on Laurie, it was necessary to have her evaluated by an orthopedic surgeon. Mark turned to Dr. Thomas Grogan of Santa Monica, one of the best, most solid

consider an SVF injection, that would have possibly ended my pursuit of SVF administration for

of adipose- and bone marrow-derived cells for the treatment of a variety of inflammatory and degenerative orthopedic conditions. All I asked is that he evaluate the patients that I referred to

him, and then consider injecting the appropriate joint with cells that I took and prepared from my

injection. Of course, the first time is rarely the charm, as we still needed to work out kinks with the technique of harvesting and producing the SVF from fat. During that first procedure, Mark

SVF while discarding fat lacked the finesse and sophistication of our current techniques call it version 1.0

knee after performing a sterile prep and adding some local anesthesia to prevent pain. Still,

lot of pressure and pain on the injection. This was not a good sign, but the pain rapidly subsided and over the next few days her knee actually started feeling better, with less pain. Laurie started hiking again, and noticed that she could move about with greater ease.

While she seemed to respond very well to SVF, Laurie felt she had overdone it with the hiking,

was done in March 2010. By the end of that year, Mark had made several adjustments to the technique, which improved the procedure significantly. Roche Laboratories was now providing a medical-grade collagenase, and Mark revamped and modified the entire system in order to make it a completely closed, absolutely sterile, surgical procedure. Additionally, he added a filtration procedure that assured that we could not possibly add any debris or particles to the SVF that

ber

2010, we repeated the procedure on Laurie, with Dr. Grogan injecting her knee again. Between

nearly all of them were relatively pain- ion still hurt her a lot. Laurie also

reflex sympathetic

dystrophy. This caused her to experience strange pains in her left arm and hand, especially when subjected to cold conditions. So, to address this, she also received intravenous SVF at the same time as her knee injection.

skiing Montana without pain bending and making turns just as

before her ski injury. As a bonus, the RSD seemed to have disappeared as well. Simply ecstatic,

given her knee a better opportunity to heal without undue force before resuming serious exercise and ski activities. Nearly a year later, her medial (inside part of the knee) seemed to be completely healed, but the lateral (outside) area still had some crepitus (those creaking granola sounds), and some tenderness too. Mark provided Laurie an injection directly into the lateral compartment this time, and within weeks she felt fine. In fact, at her last exam, there was smooth motion and no crepitus at all. Laurie got her knee back and got r

done her last two treatments, we felt we really had the system down

ogous (your own) SVF deployments for a variety of

conditions, primarily to show that it is safe, and secondarily, to gather data to ascertain trends in

but we th

things we have seen since we started this project. Mark and I have been practicing surgeons for 60 years collectively and we both concur that our SVF project has been the most professionally rewarding time in our lives.

There are those among us that enjoy exercise, but this patient loved to run. Of course, even the most avid runners have only a limited amount of running left in their joints after a certain age, and this young lady of 56 had already logged enough miles for someone 100 years old. Three

for trials of various anti-inflammatory medications, as well as a cortisone injection). Nothing seemed to be working, and now the thought of a total hip replacement, although not imminent,

ep into the patient pool to find prospective subjects for SVF trials.

rld,

including a few in the USA? If it did work, we had a unique and simple platform from which to

radiology technician and managed

an orthopedics practice, so she could read X-rays with no problem. Now that she was the

orthopedic patient, she could clearly see the degenerative changes in her own hip. Originally, Dr. Grogan had planned to inject Saralee

scheduling conflict with another surgery, so he referred us to Dr. David Allegra at Resolution Imaging. After doing the mini-liposuction procedure under straight local anesthesia and preparing the cells this time with a better technique, using a medical grade collagenase Mark drove with Saralee a couple miles to the radiology office.

While Mark hoped Saralee would be seen and injected right away, there ended up being nearly

whether to keep the solution

cool or at a physiologic temperature

-there. But I knew Mark

Dr. Allegra got Saralee set up on an X-ray table and took a quick shot of her hip. He then numbed her up with a local anesthetic, cleansed the area with a sterile prep, and draped the area off. He skillfully inserted a long needle into the area while checking its position with fluoroscopy (X-ray). He injected a little dye to confirm the proper location, and then Mark handed him the SVF, and Dr. Allegra injected that into the hip joint. And that was that. Saralee walked out of there. She resumed her normal activities the very next day, including light exercise on the stationary bike; the only workout routine she postponed was a return to running. Without remembering exactly when, but within a few weeks after receiving the injection, Saralee noticed

morning upon getting out of bed. A month or so later, Saralee and Mark flew to Boston to visit

s is

-up deployment of SVF a year after that, and today, four years later, she continues to remain pain-free. She avoided running because she

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pain-free now. For two or three years, when traveling, my husband would get way ahead of me at

my hip was that stiff from sitting. Now, ever since that

, no problem. And each time it hits me: . That is huge! On a day-to-day

Encouraged by reasonably successful outcomes with his anesthetist and his wife, Mark began telling patien

n came up time

procedures. Joyce, 68, was anxious to find out how Mark proposed to help her stave off the ravages of facial aging. Several years previously, she had undergone a procedure for which Mark gained popularity or notoriety (depending on whom you talked to and when he had done the

grafting, fat transfer, lipo-transfer

done with good results several years prior, and as time marches on, eventually it needs to be

Mark had an *Aha* moment.

replaced by stem cells that turn into new fat cells, but eventually they run out and our face simply loses volume, so our skin appears to sag. So, even if you put in a permanent filler

or getting hit by a bus, then eventually you simply run out of cells. Your abdomen, hips, and

thighs are simply blessed with so many more fat cells and, consequently, stem cells, that it takes much longer to deplete these cells. Of course, if you live long enough, even these cells become

er 100 with significant fat deposits. All of our organs are made up of cells, and all cells have a life expectancy. Our available reparative stem cells dwindle

ue

well past our eighties most of our body fat remains loaded with stem cells and now, we can actually isolate these cells from fat and not only use them to help improve facial contours, but also for therapeutic applications,

surgeon, on a very preliminary investigative project. If Dr. Grogan found her to be a reasonable candidate, Mark could perform a mini-liposuction procedure under straight local anesthesia and then prepare her cells by separating them from her fat. These cells what we call SVF or stromal vascular fraction could then be injected into the joint to help it regenerate damaged tissue. The one-day procedure would be completed within two hours. Instead of scheduling a fairly lucrative facial cosmetic procedure, Joyce made an appointment with Dr. Grogan, and soon we performed an investigative trial of SVF injections on her knees at mere cost. As she was one of the early

patients in this trial, we just wanted to cover our expenses until we had evidence that this really worked. Well, once again, it did work, just

cleared up fairly quickly, and she became progressively more comfortable moving about. But would it last?

Two years later, Joyce had an appointment with Mark. He walked into the exam room expecting to hear that her knees hurt, her face had aged, or there was some new problem. Instead, she told him that she just wanted to thank him, because her knees continued to be pain-free after all this time. She felt better and simply needed to express her happiness and gratitude for helping her avoid a more invasive and significant operation. So, how did a cosmetic surgeon shift his focus from necks to knees? How did he get involved with SVF rich in stem cells, and start doing therapeutic treatments? And, how did he team with a urologist Dr. Elliot Lander to eventually form a company (California Stem Cell Treatment Center) and a network of doctors the Cell Surgical Network®

be coming out of a university lab or big pharma? And are we really ready for clinical applications? Many of our critics think the answer to those last questions is, undoubtedly yes. They take issue, first and foremost, with the fact that CSCTC got its start in a plast

office. Many people, both within and outside of the medical field, like to put down the specialty. And yet, without plastic surgery and its practitioners, we might never have discovered that adipose tissue fat holds such rich reserves of mesenchymal stem cells.

doctor, Giorgio Fischer, and his father, developed a technique for removing fat through a type of suction and cleaving procedure. Eventually, it caught on in France, where Yves-Gerard Illouz used a strong suction machine alone to remove unwanted fat. Another Frenchman, Pierre Fournier, discovered that you could remove the unwanted fat with a simple syringe harvesting technique. Among the contingency of doctors to have visited was a young man named Michael Elam, who almost jokingly referred to the technique as liposuction. In doing so, he originated the term that Julius Newman would widely popularize.

As a young surgeon, having completed a residency in otolaryngology/head and neck surgery (also commonly referred to as ENT or ear, nose and throat), Mark attended one of the first major U.S. courses on liposuction. This group that toured Europe organized the meeting that they presented in Century City, California, in January 1984. At that time, Mark saw himself as a facial plastic surgeon and intended to apply liposuction to areas around the face, particularly for those with an overly fatty submental (below the chin) area. During this same meeting, two groups of cosmetic physicians agreed to amalgamate their societies and as such, they formed the American Academy of Cosmetic Surgery. In those days, cosmetic procedures were still largely considered something to be learned outside of a traditional residency program. Of course, that made sense as

teaching programs that were essentially subsidized by government and, occasionally, private

up their own resident clinic for cosmetic facial procedures and amassed very significant numbers of cosmetic cases, often with the tutelage of some of the finest ENT and plastic cosmetic surgeons in the Los Angeles area. For just $1,000, a patient could get a face lift and more from

senior residents supervised by the likes of Kurt Wagner or Morey Parkes, two of the giants of the Beverly Hills cosmetic surgery scene.

patients asked if he could also do body liposuction. Having been trained in general surgery prior

procedures into his practice, even though they were below the clavicle. Of course, head and neck surgeons deal with soft tissues, even ones below the clavicle they just mainly fix things above the clavicle even if they harvest tissues from down under. Within a short time, Mark became fairly adept at liposuction and offered it along with his other procedures.

Not long after the advent of liposuction, Mark attended a meeting in Philadelphia in 1986 where Pierre Fournier, one of the fathers of liposuction, declared that he had taken some of his own

performing

or trying to perform fat grafting by injecting fat harvested by liposuction. Even with a host of studies, early attempts were marginal at best and to this day, while it always works, there is a degree of variability from patient to patient. Even

while there may have been a lot of skepticism about fat grafting, there was no doubt that he and his colleagues had mis-diagnosed the main causes of aging and attributed it mostly to gravitational changes on the skin. Thus, all cosmetic procedures had been aimed at lifting. Mark and a number of his colleagues began looking at aging in a three-dimensional way. Ultimately, they came to understand that the appearance of facial aging was largely due to the loss of facial

the true nature of aging namely, that we are made up of dozens of trillions of cells, and that

ls, for example, generally live 7 to 10 years before

preparation process could be performed in a very neat and clean manner. Indeed, the entire process remained a completely closed, sterile, surgical procedure. The fat was optimally harvested and prepared while eliminating dead or broken cells, local anesthesia, blood and any unnecessary debris. Mark bought the machine that day one of the first two machines even sold in the U.S. and soon emerged as a leading practitioner of the fat-grafting technique, with patients seeking him out to rejuvenate their faces and augment their breasts. In the name of surgically enhancing beauty, fat had come to be viewed, not as something to get rid of, but rather, as something valuable to harvest, to combat the aging process. Ultimately, fat would be viewed for what it was all along: a rich source of mesenchymal stem cells.

On a trip to Japan, Mark attended a lecture on stem cells given by Dr. Kotaro Yoshimura, a plastic surgeon and one of the leading researchers working with fat-derived stem cells. Regardless of his or her special -graduate course anywhere in the world, and Mark was blown away. Dr. Yoshimura helped his colleagues to understand how significant these cells were, how they worked, and how doctors could work with them. As a

applications. But the more Mark thought of fat-derived stem cells and their therapeutic potential, the more he wanted to spread the wealth beyond the strictly aesthetic concerns of his chosen surgical discipline. Fat was the missing link: the most natural material with which to correct problems caused by aging in the body, not just the face. The three-dimensional approach to plastic surgery that Mark had espoused now gave him a different approach to the practice of

aging parts notably, the joints -cell-rich fat.

Meanwhile, Elliot was determined to apply the healing potential of fat-derived stem cells for his patients, many of whom struggled with conditions for which there is no cure, only management of pain. Shortly after Mark and Dr. Grogan teamed up to treat orthopedic patients with their own stem cells, we Elliot and Mark partnered to incorporate the multispecialty California Stem Cell Treatment Center, with the goal of further investigating the tremendous potential of SVF for various health issues in addition to orthopedics.

Over the last few yea

but our colleagues rewarded us by effectively recapitulating our findings in their own practices.

As an example, our colleague Dr. Lawrence Schrader, founder of Schrader Orthopedics in Cordova, Tennessee, became an officially trained affiliate of the California Stem Cell Treatment Center in 2012. During his two-day training session, Larry also underwent SVF treatment with

sought-after for his knee pain expertise, but equally impressive are his athletic achievements, and his recovery from an early sports injury.

Larry had been an accomplished athlete and track-and-field star since high school, with a history of heavy weight lifting. As a teenager, he sustained a torn meniscus. The menisci are the two C-shaped cartilages that protect the knee joint

aerobic athletic activity. A meniscus can tear from trauma caused by twisting or hyper-flexing the knee joint. Larry underwent old-fashioned orthopedic surgery to repair the meniscus while still in school (this was back before arthroscopy was a thing). Then, in college, he was on the track team and became a discus thrower; when one particularly motivating coach mentioned that

e for the

hammer throw which happens to be one of the oldest competitions in the Olympic Games but he was determined to master this new athletic challenge. In no time, Larry got so good at the sport that he was competing in national championships by th

tear. Like many collegiate athletes who enter the medical field, Larry decided to practice orthopedi

surgery is very straightforward mechanical engineering. You basically hammered in, or

, get a

bigger hammer

provided a fine example of how, once a joint is subjected to continuous wear and tear, it grows

series of X-

to compete in track and field until age 50, representing at several world championships. In fact, awareness of his vulnerable point fine-tuned his orthopedic practice; Larry became renowned as

but it got to the

if you start learning to snowboard at 50, you fall a lot

yo

practice of routinely counting all of our samples for quality assurance, to check for viability and appearance before deploying (injecting) it into patients. Testing

an abundance of cells in his SVF, so after we finished injecting his shoulders, we asked if there was anything else he might want treated. He mentioned his impending surgery, but said he wanted us to inject the knee anyway.

Larry, wh

Larry experienced the same phenomenon Saralee had described: When chronic joint pain finally

and did some deep knee bends. It surprised me that the pain was gone. But that response has

night, his now pain-free shoulders allowed Larry to enjoy

after returning home, he went ahead with his scheduled partial knee replacement surgery; he

is nothing compared to a twenty-year follow-

-

-up X-rays, four to si

In short order, Larry renamed his Tennessee practice the Schrader Orthopedics and Stem Cell Treatment Center; among his satisfied patients are his wife and two of their three children.

going on that suddenly get better: problems with

after an SVF injection, their speech and balance literally improved. So I tell my prospective stem cell patients there are lots of side effects

Chapter 3

HEART OF THE MATTER

Cardiac disease, as the leading cause of death in the United States, claims the lives of 600,000 people every year and thus represents one of the most important areas of investigational stem cell therapy.

would be tough not to get excited about the applications of stem cell therapy to heart disease. The heart that muscular organ responds very well to treatment with adult stem cells. Stem cells are proving to be very effective in treating cardiomyopathy (congestive heart failure), a chronic weakening of heart muscle function, that historically meant a death sentence for those unlucky enough to receive the diagnosis.

Made up of muscle tissue, the heart works like a pump, stimulated by electrical currents to pump blood through the blood vessels to all parts of the body. In cardiomyopathy patients, the heart muscle weakens and cannot function normally. As the heart loses function, it also enlarges in size. As a result, the heart is increasingly unable to do its job, causing other body parts to lose function too. Ultimately, the patient dies of heart failure but first, he or she experiences a kind of slow, protracted death, with some or all of the terrifying symptoms of heart failure, including

shortness of breath, fatigue, swelling of the ankles, feet, and legs (due to edema, which is buildup of fluid in the tissues), dizziness, light-headedness, fainting, chest pain, heart murmurs, and arrhythmias (irregular heartbeats). With cardiomyopathy, quality of life is comparable to metastatic cancer:

As the final insult, cardiomyopathy also carries an eighty percent mortality rate. And yet, early studies seem to indicate that, after a simple IV infusion of mesenchymal cells, the heart muscle begins to contract and do its job better, growing stronger with each beat.

We reckoned that SVF would have a similar effect in getting damaged hearts to pump with greater efficiency and we got compelling validation of our theory after treating several cardiac patients, who have all emerged from treatment to beat the cardiomyopathy odds. One of those patients is Kalani Skinner. For Kalani, yard work is not a chore to be avoided or procrastinated t-healthy workout he looks forward to doing three times a care, who has

manual labor: I use a chain saw to cut down trees and brush, a tree limb saw and a pole saw, a weed whacker to cut down grass, picks and shovels to dig up roots or clean out shrubs that are too big for hand- many of them are imposing redwoods. Where Kalani lives in the mountains outside San Francisco, ten miles from the Big Basin National Park, where forest fires are a sadly common occurrence yard work

upkeep presented

treating patients at his busy chiropractic practice, where his specialty was sports medicine. In addition to helping his athletic patients improve their running game to perform their best, Kalani was quite active himself, logging between 18 and 22 miles of running each week. But one

chest X-

midst of a life-changing cardiac event. The diagnosis: idiopathic cardiomyopathy, or weakened

renowned cardiologist Dr. Jackie See, our colleague and founding member of our treatment

called the ejection fraction, which is the ratio of the

known it for a l

Having worked full-time as a registered nurse in the intensive care cardiac surveillance unit at a nearby hospital, looking after people with tachycardia and lethal arrhythmias, Kalani was familiar with cardiology in general and cardiomyopathy in particular but never expected his own heart would give out on him. Fitted with a pacemaker-

years, from 2000 to

-

diligence as a cardiac patient, staying on a regular exercise program, riding my bicycle because I

gh without risking going into cardiac dysrhythmia

[irregular heartbeat]. Bicycling was a difficult effort, but it was not as traumatic as running. I was also able to do yoga. I got plenty of exercise and sleep, stopped drinking alcohol, and made some dieta

Silicon Valley for office space, which starts at $7.50 a square

full-time as a cardiac cath lab nurse, admitting patients coming into the hospital for angiograms, angioplasties, pacemaker implants, and electrophysiology, as well as teaching cardiac rehab.

In 2008, Kalani developed coronary artery disease, and his first stent was installed. In 2010, his LAD (left anterior descending coronary artery) was found to be blocked by plaque. In 2013, after an episode of shortness of breath, he had another stent installed. In the meantime, Kalani became a patient of our esteemed colleague and founding member of our treatment team, the renowned

ving soul, and his recommendations and alternative therapies helped me recover from my congestive heart failure event. He would examine me every three months, and work with my cardiologist. The fact that I maintained an ejection fraction of 38-40 is amazing, because if you look at the literature, statistically a person with my diagnosis will die within three years. Dr. See had me on branched chain amino acids and other nutritional interventions, including turmeric; he restricted my diet to eliminate sweets and keep

scholarship of regenerative medicine, it was inevitable that Kalani would seek out treatment with

w?

For starters, his ejection fraction went from 38 to a documented 60 percent! But let him tell you

age, the pump has to work harder to

right ventricle, from the original heart failure and cardiomyopathy. My heart has benefited substantially from the autologou

able to do physical work. I can carry a bag of fertilizer up a steep hill, and that was certainly

am today. I felt different within two days of treatment. I can say that the stem cells helped me feel like I was all rested on six hours of sleep, and that my general sense of well-being improved

be able to do tha

John Gregori is another one of our patients who is grateful for increased stamina, both in and out of the yard. John is not as famous as another very well-known cardiac patient, Dick Cheney; in

common: Cardiac disease qualified them both for heart transplantation. For more than ten years, John lived with non-ischemic dilated (congestive) cardiomyopathy, also known as heart muscle

gnosed

correctly until 2008. To look at him, you would never have guessed the gravity of his illness it even escaped his doctors, at first. A bodybuilder all his life, John at age 49 had no problem bench-pressing 250 pounds, twenty times daily, an exercise routine that could easily defeat many men half his age, but one that never left John feeling tired. His lean, muscular physique

six foot two and 185 pounds

-book a

smoke cigar

trouble breathing. When I stopped smoking, the pain would go away, but when I started lighting up again, it would come back. My general practitioner told me I had emphysema, but kept

were so bad that I would spend four hours on the toilet every day. I was also peeing all night, so

hat it was really my heart all along. I

had trouble breathing because my abdomen would fill up with water, crushing my lungs; my

The accurate diagnosis finally came when J

scheduled procedure removal of bone spurs from an old injury sustained during his years working as a bulldozer mechanic had to be performed under anesthesia, so his doctors ordered a routine echocardiogram (EKG) to determine whether or not it was safe to put him under. During an EKG, sound waves are used to show images of the heart and the blood pumping

the hand op

because of a blood clot in my left leg. Then, a blood clot in my right hand turned my ring finger

eceived very bad

John had to get to the emergency hospital without

characteristi

urse were standing

have more than a few years to live, at best. John, whose father had died of the disease at age 63,

a week, and six bad ones. Sometimes, I had two good and fiv

receiving a correct diagnosis, he was able to stop taking prostate medication and using inhalers,

cardioverter defibrillator (ICD). A combination pacemaker-defibrillator, this electronic device is recommended for patients with severe cardiac failure. Inserted under the skin in the upper chest, near the collarbone, the ICD consists of a pulse generator containing a battery and a small computer, connected to specific parts of the heart with one or more lead wires. This device

normal rhythm is restored. John also received low-tech cardiac benefits from the heart-healthy

days when he could barely function

John soon became motivated to research his condition, and possible alternative treatments for it, online on days when he had the energy for it, that is. Even with his name on the waiting list for a heart, John felt hopeless. Statistics show that some 300 people die each year waiting for a

organ transplant, your clock starts ticking even faster than with a failing heart it leaves you

orrectly, a sad reality of organ transplantation: that transplant patients often succumb to cancer, because the immunosuppressive medication -fighting ability. While he awaited a cure that, to him, seemed like just a different kind of death sentence, John t. Shortly after that, in 2011, John came across our Web site, StemCellRevolution.com, and wrote us a letter describing his situation and medical history. In no uncertain terms, he let us know how strong he is, and how fast he heals. After reviewing the application, we reached out to John and at universities that were conducting stem cell trials , his testosterone. During his workup, we noted that his testosterone was low, and testosterone is proven to improve muscle function. The heart is a muscle, so we always advise our cardiomyopathy patients to optimize their testosterone levels.

excellent cardiac resul in November 2012, and all our other cardiac treatments, have been IV only to this day. This makes treatment with stem cells far less

started feeling good again. I felt like I was in my thirties I could go weeks without feeling sick.

bodybuilding routine. He was also eagerly reaching for his axe, and splitting a quarter cord of

two to do a quarter cord

the front door

and go really hard before I needed a nap, so it was pretty amazing. Bodybuilding helped me

s around house work in the

yard, pick up plants, landscape, seed. As a retired mechanic, I can still change tires and work on

my car -rock band;

m done for the day, *I am done* even if that means taking a nap in the early evening, if I

-

t. How did

that happen? Because his ejection fraction went from ten percent to higher than 30 so he no

longer qualified for an urgent organ donation! Today, John experiences, he says, five great days and two bad ones per week a big difference from the

that defined his average week prior to stem cell therapy. He experienced an unfortunate setback when, during a routine device check, a technician mistakenly switched on the rate response feature of his ICD, and his ejection fraction dropped to twenty percent. Although it caused John a great deal of discomfort

he was still no longer sick enough for the heart-transplant waiting list.

myself have pizza once in a while. I still eat a lot of fruit, and I take all kinds of supplements: potassium, L-arginine, L-carnitine, fish

important, the cardiac patient who defied the odds makes a point of getting generous doses of heart-

Chapter 4

JUST BREATHE

In an ideal world, breathing would come naturally to everyone as naturally as pausing to listen

million children who struggle with asthma in America, every single breath is a result of serious effort

I could barely

Children, especially, experience a diminished quality of life as a result of coping with asthma, a

winded real quick, so as a player I was worthless

But after we successfully treated E

accident, Eddie became something of a cheerleader for adult stem cells. Seeing the change

friends and ne

our way.

n the CSCTC Web site that the

body

saying they could treat it

treatment, even the stem cells he champions so vocally, could alleviate (remedy) a lifetime of shallow breathing.

The motivation to be treated came after Eddie who is an avid internet researcher learned that chronic asthma ultimately leads to congestive heart failure. Over time, the lungs cannot take in enough oxygen to keep the heart pumping properly. That information, together with the hope that

he might experience wh

give stem cell therapy a try. We treated him in June 2013. Immediately following the procedure,

the Center

and went to go get lunch around the corner. Maybe half an hour had gone by, when all of a sudden, I took a deep breath

alm Springs. I said,

deep breath

his wife have enjoyed more

The increased stamina Eddie has experienced since treatment enables him to stay in better shape

without getting tired or having any shortness of breath. Nancy and I walk a lot

his breathing and his level of physical fitness: it actually saved his life.

Now, Eddie is even more vocal than ever in hi

people need to be aware, so my job is to tell everybody I meet. Nobody gets past me: every time we meet somebody, we talk about stem cells

an art opening, I will talk about stem cells to anybody and everybody! There should be a channel

brag about it. When I think about my asthma and how long I suffered with it so many people

One of the many patients Eddie referred to us is his friend Sandy Smilovitz. Sometimes, a

nal comedians a run

for their stand- because

it puts more pressure on your kidneys,

obstructive pulmonary disease), a disease of the lungs resulting in poor airflow that worsens over

al

gets to a point where you can kind of fight through the pain and inability to breathe, but at some point you just have to sit down. A friend of mine does biofeedback, and he was teaching me how to breathe deeply t and stop and relax and start thinking about breathing and get

-ish. Just

walking up the driveway to get the mail made my lungs scream there would be a clenching pain, as if somebody had their hands on my lungs and squeezed. So simple things like going to the market and walking around were pretty difficult. On top of that, you can have these panic

As the disease progresses, COPD patients must live with a nose tube attached to an oxygen tank

y much the bottom line for

during his struggle with COPD. Describing his medical history, he sounds more like a seasoned Borscht Belt comic than the retired entrepreneur he is. When he first arrived at our office for a consultation, he was taking two oral medications and using an inhaler twice daily. His

our house without having

quadrant of my lung, and I wheezed a lot. If my blood sugar got too high, my breathing got even

corrected it. Within a week, I was walking up and down my driveway. I could breathe. I threw

knees, my feet, and my back are no good. -

To hear Sandy describe it, his procedure was a great success. Today, he can walk down his

hundred- says

believe it was miraculous; Dr. Lander saved my life. If

Chapter 5

STAYING IN THE GAME

not us, and certainly not our wives. So when patients come to us seeking relief from the physical symptoms of aging that eventually slow

vestigate the applications of adult stem cell therapy. The reason is simple, and as personal as it is professional: We know that, in the not-too-distant future, those patients with old-guy problems could be us, and we want to do whatever we can to stay in the game, for our families and ourselves. We may make every effort to stay in shape, eat right, and adopt only healthy lifestyle choices; but old guy

who promises:

chronological years. But what if the chronology were reversed, and a pers

years say, 38 years young starts experiencing old guy problems? In such a case, that

Keith Warren (changed name as a last minute request to protect identity) played center for the several NFL teams before retiring

the quarterback by tossing it between his legs, in an exchange called

each offensive play. Years of snapping and blocking were bound to exert a great deal of

Keith was

itated hip arthroscopy. Happily, keen intelligence is another occupational hazard of an NFL center, who has the best view of the defensive formation before the snap; he makes the first line call and may also be relied on for play-calling. Charged with so much responsibility, the center is the smartest player on the offensive line, and his career success depends less on brawn than on brains. Keith flexed the latter attribute when he began exploring treatment options for his hip pain, which by April 2013 had become excruciating. In football

and as

fans of the game from way back, we were glad to be under center when Keith passed his hip problem to our office, choosing us to call the play. Incidentally, we have a special interest in helping athletes and former athletes overcome injuries sustained on the playing field, because we have our own in-

on

athletes and former athletes who consult CSCTC about treatment will be able to snap their problems to a physician with experience at play-calling both on the field and in the exam room: Dr. Berman the younger.

When Keith Warren stopped playing in 2009, the pressure to perform as a center was off. But staying in the game on everyday activities, even those us non-athletes take for granted, was

beginning to prove more challenging than play-

Keith ical

challenges no, the abuse

time, was now out of the question for Keith. But of all the

activities he was now sidelined from, horsing around with his children was the one this Dad of

do most of the things I used to be able to do with them. My two

older kids, twins, are real active in sports, so I try to help coach them. Then, it would just really

L,

Keith

so I would ask their opinion on what type of surgery I should have. They all agreed on a total hip

replacement but being in my mid- was of age to get one of those

Keith about CSCTC and our interest in using stem cell

therapy to help pro athletes overcome debilitating pain due to occupational sports injury. He

contacted us and, after a discussion and careful review of his medical records, we evaluated

Keith

[to Ra Keith says.

Keith

hip, the pain was alleviated for almost three months; subsequent injections, however, proved less

l

our star center discovered what our fit and trim patients all commiserate about: a mini-liposuction is not for wimps, and the process of harvesting lipoaspirate from a person without much fat on him can result in significantly more soreness and bruising than a person with, say, a spare tire would feel. For this procedure to have the successful results we aim for, we needed the liposuction to yield at least one to

Keith my

kids were impressed!

in Keith

centrifuge machine, the machine that tallies the viable cells let us know we succeeded in harvesting 121 million cells (a good percentage being stem cells, but technically including WBCs and other cells as well) from Keith

million of those cells intravenously. Then, to ensure that the intra-joint injections would be absolutely precise, we moved him to our interventional radiology department for a CAT-scan-guided deployment of the remaining cells into his hips, under local anesthetic. Seventy-seven million of Keith

factor of doing injections with sophisticated imaging, but Keith

was phenomenal to see the needle go in under the scan looking at X-rays is something I do anyway for my job, but this time I could see for myself when the doctors pointed out that I had

When Keith left our office wearing an elastic-velcro binder around his waist to help reduce swelling, we told him that we estimated it would take between 24 and 48 hours for the initial anti-inflammatory properties of his cells to take effect on his damaged hip. He called to report

sh, my hip has not felt this good for four years! And then, in the back of my mind, the skeptic in me was like, OK, this is just temporary. The doctors instructed me not to exercise or do anything for about eight days after the procedure, which is hard for

ut this time, I waited the whole ei , not even ride the stationary bike. I took

January, when we first started talking about it. On the first day that I could perform physical

So I went on an eight-mile hike up this mountain. Eight days earlier, I literally could not walk, the pain was so debilitating. I ended up hiking and running that first week, maybe sixteen or 20

-Aid type of fix, I thought this might not last either, so I went a little overboard while I could. And it

mesenchymal stem cells

cells bathed in cytokine growth factors (polypeptide signali

is superior to just cells alone. SVF has three main properties, and we try to use each to our

-

rthritis and other inflammatory diseases and can often be effective within 24-

whereby the cells are capable of promoting healing by either directly replacing damaged cells or secreting cytokine growth factors that affect repair using cell-to-cell signaling. This effect takes

- -immune

- n occur, two important events must take place on a cellular level: the first critical aspect of SVF is that the stem cells must be attracted target tissue. This process is called

will preferentially travel to sites that secrete signaling molecules associated with damaged, inflamed, and degenerated tissue. . The other essential event is that stem cells must be

associated with damage, disease, inflammation, or degeneration. The essence of the work we are doing at our treatment and research centers is to attempt to exploit any and all of these three main properties and 2 special events (homing and activation) to optimize clinical outcomes.

SIDEBAR THE 3 PROPERTIES OF SVF after homing and activation

1. Anti-Inflammatory
2. Regenerative
3. Immuno-Modulatory -

In Keith

simultaneously fighting inflammation in his damaged hips, and regenerating the connective tissue, i.e. cartilage, to cushion and promote ease of joint mobility. The third unit of the SVF

army, the Immuno-

Homing and Activating forces did play a role, enabling the stem cells to locate the damaged

We checked in with Keith

three months after the injections and th

and self- Keith

then at three months, it felt really, really good. That ache-y, shooting pain I used to have I

se bone spurs, because nothing

bike, and started going for longer and longer runs; now I try to run at least two miles a day,

-to-twelve-mile

figure out how I was going to walk the next day after a workout, even with pain meds, which I no longer take. When I went skiing in February, I tell you, I was a mess for a week afterward. Now, I cannot wait to get back up on that mountain. I feel like I got it

got back: healthy, competitive play time with his kids. Before his procedure, Keith was playing basketball with the 12-year-

Another one of our patients, Spencer Lehmann was 67 when he first came to CSCTC for a

except his legs were the only part of this dynamic patient you could rig -year-old former NFL player in excellent shape to maintain a competitive edge on his teenage kids after just one cell treatment; now, how about an out-of-shape guy in his sixties getting a leg up on the 38-year-old? After extended time growing increasingly frustrated at being unable to do the activities one is used to doing, one inevitably puts on weight
belly fat, plus the occasional love handle, equals a rich reserve of adult stem cells that may be harvested more than once, for serial treatments that yield impressive results. Spence has 30 years on Keith, but he came through not one but three mini-liposuctions.

Although Spence was never a professional athlete, skiing was one of his passions until back pain conspired with pain in his limbs to make moving down a mountain impossible.

of my neighbors in Palm Springs, Nancy, had been overweight and walking with a cane for a

very bad car accident that smashed up her knees, and was up to nine Vicodins a day. Then, one she looked fantastic. So I asked her about her transformation, and she told me about CSCTC. This was in

he braces he had to wear on his feet and ankles, to cope with the edema that would result from too much time spent on his feet. But uffering from claudication of the calves due to narrowing arteries since 2009.

membered seeing in the mirror freestyle throughout high school and college; the one who still looked youthful when he hit forty. Spence continued skiing as usual, with a normal fighting weight of 160; but the pounds started piling on during his late forties as a result of chronic lower-back pain. A consultation with an orthopedist revealed that the last two discs in his spine had completely degenerated. The

Spence also coped with problems in his first marriage that ultimately led to divorce, so his time sitting behind a desk and not being able to do th y knees; I was taking four salicylate pills check a day 28 each month

much more politely than that, but I really appreciated their honesty. I thought, I like these guys

course; but the extra weight Spence was carrying enabled us to harvest much more than our minimum needed amount of material with ease and that, in turn, let us address several of his issues in one treatment session. With Spence, we easily harvested two full (approximately 100cc) of fat in the same time as it took us to coax just one syringe of fat from young, buff Keith Warren. Guided by the CAT scan, our orthopedic radiology colleague Dr.

into his spine. As for the rest of th e me injections in each calf for the claudication, a shot in each of my knees, and one in my left hip, for a problem I was

improvement; the doctors said I might start noticing something in about six weeks, but for sure

However, we were very happy to hea
imparting body wide relief much more quickly than we could have hoped: he reported feeling

no pain for

after that it was the same thing. After one week, I threw away those braces. Then, three weeks

later we were in Las Vegas at the Wynn Hotel, which as you know is huge figure at least half a mile from the tower to the meeting rooms, and probably longer but I walked that distance to and from every day for a week with no pa

and Elliot Lander and that office did was give me back my life, in every sense of the word. And

dergoing a series of stem-cell treatments for the oldest of old-

strength

the higher the cell count, the more effective the treatment appears to be, regardless of the

Chapter 6

THE HARDER THEY COME

Few disorders are more devastating to think about or discuss let alone experience than Peyronie s Disease, severe inflammation and scarring of the soft tissue of the penis. Just imagine order that affects more than 3% of men in the prime of their sexual life. Imagine if your penis an organ were to suddenly cause terrible pain, both physical and psychological. Peyronie s patients experience all the nightmare scenarios that could

erectile dysfunction. Peyronie s has plagued men for hundreds of years it got its name from the 18th century French surgeon Francois Gigot de la Peyronie yet apart from a few promising pharmaceuticals, most mainstream remedies for it are decades, if not centuries, out-of-date. Some patients are offered surgical repair which often leads to more scarring, shortening or erectile dysfunction.

that part

-

not something to give up on without a

Peyronie s patients and their partners, so we were thrilled to discover that stem cell therapy can help these patients significantly, enabling them to regain a measure of their normal sexual function. Many cases of Peyronie s are caused by trauma to the penis during intercourse, which results in scar tissue formation. Many cases occur for unknown causes and the condition can change spontaneously in curvature and severity until it enters a chronic phase in which scar is so hard it is occasionally calcified.

The full effect of Peyronie s is evident when the penis is erect; while flaccid, it appears normal, but when engo -like it will be and eventually it can make penetration impossible in some cases... (Some beta blocker drugs list Peyronie s as a possible side effect; targeting the beta receptors, this class of drugs is widely prescribed for the management of cardiac arrhythmias, hypertension, and protecting the heart from a second heart attack, but beta blockers are also frequently used by musicians, actors, and public speakers to combat performance anxiety and crippling stage fright.) When cases of Peyronie

The body relies on adequate blood flow to bring stem cells to repair damaged tissue with minimal scar. As scar tissue builds up over time, it interferes with blood flow and erectile dysfunction results. Double ouch. Our patient Ryan had been feeling the pain and humiliation of Peyronie

dismis

o leave me. I was telling this

to my family practice doctor, who showed no sympathy at all. He was looking at his watch the

Happily for the couple, Ryan sought a second opinion, calling us in 2012 after an internet search

s helps you

clarify and reconfirm your priorities, and the top priority for my husband and me was feeling healthy and young and vibr

having intercourse, the hardest part was seeing the emotional damage being done to the man I

l his pain was

a third of the length that I had. I mean, it was terrible

psychologically emasculating as Peyronie s is, the searing physical torture of it is nothing to

on his p when you get an erection,

but this

process was slowed by the numerous lesions on his Tunica (the fibrous core structure of the penis)

painkilling process turned into somewhat of a killer. Stromal Vascular fraction was the injected directly into the plaque (?using multiple penetrations with the deployment needle). After it was

s penis would look like

before he noticed an improvement. Then, about four months later, after his second of three

meaning my ability to keep an erection

I got it all

things are at their worst, there are creative things you can do

-

Today, Ryan is satisfied with his new job and his healthy sex life. As for the frequency, Jane

is the courage Ryan displayed in refusing to let his quality of life be compromised by a condition

courage for

treatment, so it seemed pretty experimental at the time. But instead of feeling humiliated, he

out Peyronie s disease. His outcomes data was included in our original series of five patients who all had spectacular results and were presented at the Western Section American Urologic Association in November, 2013 and at the American Association of cosmetic Surgeons Annual Meeting in January of 2015. We have gone on to treat many more cases of Peyronie s and have improved therapy by adding a series of low intensity shock wave treatments to the Peyronie s tissue to help stem cells home and activate to optimize healing.

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Chapter 7

WALK ON

Muscular Dystrophy (MD) is a group of nine inherited, progressive muscle diseases. All forms of MD cause muscle weakness and muscle loss. Some forms notably, Duchenne MD appear in

within each type of MD, doctors see variations in terms of the muscles affected and the symptoms experienced by individual patients. Some people have mild cases that worsen slowly; severe cases, on the other hand, are disabling. But there is one thing all forms of MD have in

unable to walk. According to virtually every authority on the subject, there is no cure for MD; the standard medical wisdom tells patients and their families that symptoms may be helped by treatments such as physical and speech therapy, as well as orthopedic devices, surgery, and medications.

MD has become almost as politically charged as the topic of stem cells. For forty-four years, this

-running

annual Labor Day telethon hosted by actor-comedian Jerry Lewis. Celebrities ranging from Joan Crawford to John Lennon and Yoko Ono made appearances, urging TV viewers to donate money to the cause, which collected more than two billion dollars. But the telethon came under fire in recent years for using disabled people in wheelchairs particularly children as fundraising

to provide them with basic civil rights, such as employment opportunities and accessible transportation and housing. They argue that Jerry Lewis merely preached pity for people with MD, when what they really deserve is respect. (The Muscular Dystrophy Association phased out the telethon, and Lewis as its spokesperson, replacing it in 2012 with an annual Labor Day TV

raid of the dark

At the end of the storm is a golden sky and the sweet silver song of a lark

Walk on through the wind, walk on through the rain, though your dreams be tossed and blown

-the-

patient culture is himself a former telethon poster child who once appeared on TV with Lewis.

tle of his blog), the wheelchair-

all due respect to Ervin and many other vocal critics of the Jerry Lewis approach, is it wrong for

rrect, many did continue to hope but perhaps none more

-Girdle Muscular Dystrophy (LGMD)

and, although wheelchair-bound, remained determined that one day she would enjoy life without

be a

the age of thirteen, her heel cords the Achilles tendon

-Girdle Muscular

Dystrophy. My condition kept declining, and by the time I was fifteen, I was using the wall to help myself walk I had no balance, I was losing muscle mass and strength. By the age of 29, it

in the words of the old MDA song

walk on.

negatively impacted by the disease. Although a beautiful, vibrant young woman, Regina felt self-conscious about dating. With LGMD, it becomes increasingly difficult to lift the front part of the foot, and this causes one to trip. Regina often worried what would happen if she were out on a

or

fully believed would be the day doctors would find a cure for MD, Regina bravely prepared herself like a dedicated athlete gearing up to compete in an Ironman Triathlon. Regina contacted us after she heard about another woman in her home town in Louisiana who had a successful treatment at our center for interstitial cystitis which is a very painful bladder condition that has no effective treatments and is known to make people feel like they have a urinary . The first thing we explained to Regina is

her condition. However, we did relay to her that we had treated several MD patients with excellent results in terms of mitigating their muscle damage and stiffness. We explained to her that she may be able to achieve similar results, with the possibility that she may require multiple

On Ice itions

like Muscular Dystrophy.

the clinic in a push chair, and right after my cells were injected, I remember walking out of the treatment room with assistance from the nurse. I was really tired, maybe because of traveling from Louisiana to California. I think I slept sixteen hours straight in California! The next day after coming home, Saturday morning, I felt some of my muscles getting stronger. I felt it first in

y of us take for

grab a piece of clothing, or a towel on the floor, I would have had a really hard time coming back up to the sitting position, much less carryin

percent of my muscles are working again it almost feels like I have the muscles of a newborn

nobody is here to help me; but I get on my feet and walk around the house and do things I

happy to do if only you had the strength to load the washer, then empty it and place its contents

heets,

take them out of washer, and put them in dryer. Before, just bending down and getting laundry out of the machine was a challenge

d of tight. But for the most part, I can

more, the symptom that first marked the onset of her MD tightened heel cords showed major

negative 38. As of my last Active Release session, the right one measured negative 20 and the left negative 5

-conscious patients with orthopedic issues

complain that they cannot wear their beloved heels, and many are thrilled to be able to return to gravity-defying footwear post-

collection of stilettos). Regina was the opposite: She longed to wear flats, but needed the support

my favorite pair of flip-flops and my tennis shoes which

Regina has a strong character; that inner fortitude reveals itself in her physical endurance and high tolerance of pain. Her commitment to exercise would be an integral part of her success. Immediately after treatment, we had her see Michael Butler, an elite trainer and expert in active release techniques in Palm Desert, California, and he started Regina on an aggressive regimen of physical therapy. Active release is a movement based massage technique that treats problems with muscles, tendons, ligaments, fascia, and nerves. It works by relieving tension throughout the

massage is relaxing, deep muscle therapy can be quite uncomfortable and even painful at times,

Before going to bed, Regina downs a protein shake, a mix of whey and time-

nutritional supplement favored by bodybuilders (its active ingredient is creatine). She also takes several supplements for optimum cellular health, including vitamin D3, nitric oxide, and L-Arginine. Many of our patients take nitric oxide after their procedures, since it improves vascularity and blood flow, and has been shown to help stem cells differentiate. It is a simple remedy made of beets and hawthorn; Neo40 makes the best quality nitric oxide that actually provides you with the enzyme your body needs to turn nitrates into nitric oxide. (On a side note, we were surprised when Regina told us of her scientific interest in cannabis, and that she smokes marijuana every day as an adjunct therapy. Wherever you stand on the controversial topic of

ty to differentiate.)

Her avid interest in a healthy diet and exercise routine is partly the influence of her boyfriend, a

that really got me on those supplements, and he helps with

fear of what might happen to me, would my condition get worse, and how would they take care of me I think all this was in the back of their minds, plus my not being able to work a full-time

job, and the pressure of having to support a disabled person. That hurt my previous

Since her treatment, Regina has been walking tall in many aspects of her life, professionally as

perfect

-time

experience with stem cells and her sincere wish to help raise awareness so that more patients might be helped is encouraging her to explore politics as a possible future career path. As part

years old

her running shoes will see serious action for the first time since her high-speed, high school days. When she can finally strap them on, stretch her legs, and let rip, where would Regina like to go?

with weight training and putting on her own show of strength for the delight of her friends and

something doctors had alw

Chapter 8

VISION QUEST

As practicing MDs with a combined fifty years of experience, we are acutely aware of the need for prescription medications. We would never argue, as some of our detractors suggest, that stem cells could ever replace doctor-prescribed pharmaceuticals. However, there are cases in which prescription meds simply cannot be a long-term answer for certain patients cases for which stem cells offer a life-changing alternative to drugs that, taken over an extended period of time, carry more risks than benefits. One of these medications is Prednisone, in the category of corticosteroids. These synthetic drugs are widely prescribed because they work extremely well as immune-suppressants i.e. they slow down the immune system when it becomes abnormally overactive, as in cases of autoimmune disease (when the body literally attacks itself), or organ transplant, or cancer. But the limitations of corticosteroids and the urgent need for a therapeutic alternative became dramatically apparent when ophthalmologist Larry Geisse, MD contacted us about one of his patients in 2011.

One year earlier, in November 2010, Julia Matsumoto went to see Dr. Geisse, complaining of sudden vision loss. The 31-year-old was a fit, active wife and mom of two who had had no prior health prob

-drop, and eventually,

The diagnosis was optic neuritis, an autoimmune swelling of the nerve connecting the brain to

patients experience optic neuritis in one eye, and it takes just a few hours for the vision in that eye to darken; then, inexplicably, the vision might return later. Other patients experience optic neuritis in both eyes, and it takes a period of weeks before their diminishing sight is almost entirely gone.

Typical optic neuritis, as with MS, is rapid in onset, but usually recovers over time with treatment, and usually [involves] one episode, or another episode years later. This type of optic neuritis, on the other hand, runs a progressive, downhill course with no recovery, with each episode resulting in further loss of vision that is not recoverable. This occurs over a very short time, and is usually somewhat

reason,

proven effective at slowing vision loss in optic neuritis cases. So, Dr. Geisse prescribed

needed to prevent further vision loss was 100 milligrams per day in addition to weekly intravenous delivery of methylprednisolone (Solu-Medrol).

quality of life suffered significantly. The steroids caused her to experience dramatic weight gain;

within three months, she was 100 pounds overweight and morbi

five days a week I used to take spin class, do weight lifting and crunches, go running but with the Prednisone, it was as if someone put a tire pressure monitor on me: I was literally just

that was the scary part.

were unable to cover her rapidly expanding body mass was stretched to the breaking point. The combination of weight gain and vision loss resulted in an inability to exercise. Another side effect of Prednisone is severe joint pain, which Julia felt with every movement. While her body would not stop expanding, her bones were becoming dangerously thinner, weaker, and more fragile another adverse effect of long-term steroids that results in osteoporosis, which makes exercise risky due to the increased likelihood

welling with

the high steroid doses, her vision rapidly vanished.

stretched so tight that it was splitting in areas. She could hardly move her joints. She had tremendous joint pain and back pain; she was very weak and could not walk. Her stomach hurt all the time despite the use of Proton Pump Inhibitors to protect the stomach. She was sick all the time with colds, since the Prednisone was suppressing her immune system. Her bones became

h steroids? Basically, to save her life, we had to stop the medication

ut it was the only choice for me at the time. I told my daughter that I

.

Under the weight of that triple setback, she began the difficult process of recovering mobility

lly was running into everything. I would constantly hit the kitchen counter with my hip in the same spot I could never learn that stupid corner, and it would make me so mad I cannot even express it! I would count the steps,

Dr. Geisse

stigating stem cell

one of them had a sales person call me to discuss the treatment protocol and then try and sign

rman and Dr. Lander called me back as physicians to discuss the case, and only they said that there was a small chance this might help her, and that they had not treated anyone for this problem before. The other centers all said Julia would

respond well with the treatment and virtually guaranteed that she would be cured that was

to be really trying to help patients and not just make money. So, we went with

so we scheduled an appointment for her at our Beverly Hills location. We then learned that

b and her health coverage, and that

carrier] just booted her out

treat Julia at no cost. Mark gave Julia her first treatment in November 2011. Julia remembers

not Julia, her ophthalmologist,

nor any of us at CSCTC could have predicted the tremendous gains that started accruing after that initial treatment.

can keep her vision and keep her off the steroids

completely

color markings on these tiny, fast-

oticed was

something red

crimson plumage

Today, Julia sees different stripes and colors notably, the ones marking the traffic lanes and signs near her home. Seven months after folding up her white cane,
with her current vision, and is able to operate her vehicle to access the shopping mall across the

herself to a life without sight.

As doctors applying stem cells to vision loss, we still have a long road ahead of us. It would be

are definitely reversing it, and maybe stabilizing it. Part of the challenge is that her condition may be a variant of MS, and there is a circle of thought that suggests you need to knock out the autoimmune cells that are attacking the optic nerve, and then restore the nerve function with the SVF. Actually, there are some MS studies in which the SVF first attacks the autoimmune cells to wipe them out before trying to repair the damage with fresh stem cells. This may indeed become

tocols.

as she needs us to. Mark saw the ultimate validation of that decision when he received a holiday

heartwarming Christmas cards I ever received in

-drawn and

Julia every two months since her first procedure. Yes, that is a lot of

produces more fat, but also more stem cells. Our future plans to cryo-preserve cells through our

far less cost and far greater convenience. At one recent treatment, we harvested 80 million viable cells. Because the local anesthesia, when done well, is nearly painless, the liposuction is painless and the only pain is the discomfort around the liposuction site as it i

patient

*

Often, when people spot someone with a visual disability, the first instinct is to want to grab the

he is, in fact,

legally blind he rarely elicits that type of re

also snowboards and exercises his passion for the martial arts both activities that he undertook for the first time, amazingly enough, *after* his vision became impaired.

also

spy him running confidently alongside vehicular traffic in shorts and flip-flops, on his way to an appointment. Watching him in motion, your first instinct is admiration, not pity. Looking much younger than his 47 years, Chad makes you think of a Japanese anime character, or perhaps one of the X-men, come to life

super-cool Moya Brand gi (the kimono-style apparel worn by martial artists). He gets around town on foot or on his bicy

way before I lost

high-walled skate park, or perfecting his jiu jitsu moves, Chad simply does not move through life like someone who cannot see.

responds more quickly to texts than many people we know who have no visual impairment! In fact, hi

Tiffany parks in a space reserved for people with disabilities. Hopping out of their car, both looking fit and active, Chad and Tiffany are frequently confronted by other motorists chiding

smiling and shaking his head.

surprised at what you can do when you have a memory of sight, even 25 years later. My world is

for his father, who grew grapes in the Coachella Valley, and soon after that, met the love of his

like, whatever

let my Mom

ganglion cells and their axons leads to acute or sub acute loss of central vision. LHON affects

ted i.e., transmitted from mother to

child (men cannot pass the disease to their kids). The toughest part for Chad after learning that his mystery ailment was permanent, not lens-corrective, and not responsive to any medication was getting used to se

anger that made me passively suicidal

was always the good-time guy, the one that would pick up and go on the spur of the moment

because I figured, at this point, I was defective. Thankfully, as hard as I tried to push her away, she saw enough in me to stick around, and we ended up developing a more serious relationship,

up skat including

changing diapers himself, swiftly administering CPR when one of the boys almost choked on a piece of candy, and, later, experiencing their first baby skateboarding steps motivated Chad to

him *not* bowl-riding. One thing Chad never gave up was the hope that his vision might improve.

followed every possible therapeutic lead,

however bogus-sounding and as doctors, we confess that some of the snake-

-

in his typical bring-it

pepper drops prescribed by a Cuban faith healer. One year, I traveled to Tijuana every three weeks with a pocket full of cash, for shark-

The life-chang

suggestion. Today, he holds a brown belt in judo *and* jiu jitsu. As he improved his moves, he also adopted a healthier lifestyle, juicing his share of carrots and spinach.

treat Chad with his own stem cells, and to find out how a condition like his would respond, was an even bigger opportunity for us. The prevalence rate of LHON is approximately one in 30,000

even rarer still. Chad was referred to us in 2013 by one of our MD colleagues at Eisenhower Medical Center in Rancho Mirage, California (where Elliot has been on staff for seventeen years and served as past Chief of Urology). We treated Chad in March 2013. After we extracted fat

ect the cells

directly into his eyes, because at that time we were still awaiting approval from our IRB Institutional Review Board to perform intra-ocular injections.

o work to

extract what fatty tissue he did have. Still, we managed to harvest an impressive number of cells

of more viable cells than those with, say, a spare

-adipocytes,

which have very potent regenerative properties. When we first started treating patients with their own fat-derived cells, we thought heavier people would have the advantage of more cells, but that was a misconception. With leaner patients, most of the cells come in the form of these potent pre-adipocytes, which helps us get a good result.

But at the end of the day,

vision is still poor, but I did notice a little bit of change: colors definitely appear richer now.

been more than half of my life, it

e the first to crack a joke about it. I still have my moments, but every day is healing, so as

on his current athletic path: Working toward his black belt in t

came on

r the direct injection to

assist his cells in locating their target, resulting in even more vision improvement. A goal we can now attain since we have IRB approval for eye injections since October 2014. Chad returned for a second liposuction and IV injection in September 2013. We were so glad to see that he needed no help walking down the hall of our office; he was also identifying colors better. His extreme-athletic lifestyle can be rough on the extremities, so we were happy to hear that his follow-up trea

like I just drank coffee. Training with professional athletes in their early 20s, I was able to keep up. Some repetitive-stress injuries throughout my body were kind of disappearing too. I felt

rejuvenated especially my feet, which are always in pain because of all the physical activity I

rtive shoes. One foot had been hurting really bad but then,

by alleviating repetitive-stress discomfort in his joints ty of

As for his vision after that second treatment, Chad told us he could see the edge of the skate

n had improved slightly.

never afraid to take that turn down that

recently on Faceboo

a Zacuto Z-Finder attached to his Canon 7D camera, Chad now confidently captures still images

-

Chapter 9

GO WITH YOUR GUT

When we opened the California Stem Cell Treatment Center, we made a conscious decision not to advertise our new practice. Our reasoning was that we were doing investigational work and if we were successful in treating our patients, then the results would speak for themselves. Besides, many people patients as well as fellow physicians
fortunate that word-of-mouth helped build our reputation in Rancho Mirage and in Beverly Hills where our patients became walking advertisements for CSCTC, telling their neighbors and friends about what we do. But word-of-mouth only reaches so far, and there were many patients located far from California who were actively seeking exactly what we had to offer, yet had a tough time finding us. One of those patients is Julia Szabo, a determined New York journalist who spent several years diligently searching the Internet, trying to locate doctors with a treatment protocol exactly like ours.

Even a year after her successful treatment at CSCTC, Julia still shakes her head to think that she

about CSCTC faster and found relief from years of discomfort
the existence of the Center in 2010, the year it opened, I could have also avoided getting myself into some very unpleasant situations in my quest to be treated with my own stem cells! But they

and misadventures of her medical odyssey in a

memoir titled *Medicine Dog: The Miraculous Cure That Healed My Best Friend and Saved My Life* (Lyons Press, 2014). The book chronicles her four-year journey to receive treatment with her own stem cells, which ended positively at our Rancho Mirage office. But before she found us, Julia was obliged first to travel as far away as Panama and Spain in the hope of finding a viable cure for the perirectal fistula which is an aberrant connection between the rectum and the skin that had plagued her since 1999.

By the time she finally did find us, in 2013, Julia had suffered for fourteen years with this lifestyle-hampering condition, which regularly leaked fecal matter into her bloodstream. A fistula is an abnormal passageway, like a tunnel (fistula is Latin for pipe) connecting the inside of the anal canal to the skin around the anus or buttock. The abnormal opening can arise between

dangerously low blood pressure; she was septic as a result of a perirectal abscess. Sepsis also known as systemic inflammatory response syndrome, or blood poisoning is very often a fatal condition, so Julia was fortunate that she was taken to the ER in time.

As her perirectal fistula had leaked infectious matter into her bloodstream, a red, inflamed boil appeared on her right buttock. It was the outer manifestation of what was going on inside: 30 cubic centimeters of pus had collected from the perirectal leakage, and was displacing the tissue of her buttock to create a container for itself. Her body was reacting dramatically to the presence of that pus, which was basically trying to poison her. The ER doctors performed an incision and drainage (I&D for short) to drain the pus; the location of the incision, so near to both the anus

and genitalia, made it very difficult to heal. The incision actually never did heal, so Julia was left with not one but two fistulas: the perirectal one, and the one on the inner edge of her right butt-cheek. Julia was also left with many of the symptoms people describe when they have an IBD (inflammatory bowel disease).

collectively termed IBD, for inflammatory bowel disease. Patients with IBD in America number 1.4 million. And yet, surprisingly, too little is written about the day-to-day logistics of struggling with IBD. For patients like Julia, the basic bodily function of defecation is often an excruciating ordeal inste

times. Accidentally ingesting one rogue bacterium could result in an unexpected bout of

no way to prevent bacteria from entering the GI tract, so continuous leakage from her rectum into her bloodstream caused Julia to experience the beginnings of sepsis every few months.

A body struggling with sepsis is reacting to bacterial infection that runs rampant through the bloodstream. The system is basically coping with continuous inflammation. Th
way to live. Julia knew that something had to be done to stop the cycle of infection and re-infection, or she could encounter further health problems as her immune system got tired of battling continuous inflammation. Considering that more than one million Americans live with IBD, one would think that gastrointestinal specialists would be motivated to develop a high-tech

-fashioned

procedure: a fistulotomy, in which the intestine is tied off with a silk cord (seton) immediately above the abnormal opening that permits infectious matter to breach the bloodstream. This closes off the abnormal opening to prevent further re-infection. The damaged part of the intestine is left to atrophy away, and the patient is left anally incontinent for a period of weeks during healing time.

his joint strength. Upon realizing that people could not receive stem cell therapy in America at that time, but companion animals could, Julia deduced that, in the United States, veterinary medicine was ahead of human medicine. Her dog could receive treatment with his own stem cells, but she could not. When, a few months later, Time magazine covered Vet-Stem in its July

Word-of-

finally led her to our doorstep. The founder of Vet-Stem, Dr. Bob Harman, was one of our

the intrepid Pet Reporter finally achieved her goal

so we took that as a compliment. After studying Dr. Garcia- on PubMed.com, we decided to put our own stamp on his procedure by adding an IV injection to approach the

an almost exact replica of the Vet-Stem procedure, which is what her dogs had undergone and what she wanted for herself from the beginning.

enced a

relapse, which was often. Every few months or so, she would endure the beginnings of septicemia, complete with extreme exhaustion and abdominal cramping. Our plan was to inject

Julia both intravenously and directly into her unhealed surgical wound with the goal being for the cells to get to work closing the inner fistula first. If the outer fistula were to close up first, infectious matter would have no way to drain away from her body. So, on the day of her treatment, Julia would receive two injections: the first would be delivered intravenously into

-cheek.

The procedure we performed on Julia was not an exact replica of the one pioneered by Dr. Garcia-Olmo

cells. So we performed our own version of the Madrid procedure. Instead of using fibrin glue, as

-

own blood. It is rich in growth factors and sticky platelets, so we figured it would help her stem

cells, but here at CSCTC, we believe that the vascular delivery of cells is, in many cases, the

also gave her an IV infusion of her stromal vascular fraction which we carefully filter to prevent any clots from forming inside the body.

The success of any stem cell procedure depends on the number of cells extracted from the

work with. In fact, when Elliot first met her on the morning of her procedure, he was dismayed

and he was only half

mini-liposuction yielded 42

bloodstream by IV injection. As for the second 21 million, those we injected directly into her exterior fistula.

o expect from our two-pronged approach, since we had not treated a

better off for having the procedure done. She has frequently described her experience with stem

sed that she felt immediately better.

If I told you that, upon receiving the second injection, I announced that I felt better already, would you believe me? I hardly believed it myself ical reporter

particularly un-

I did upon waking the next morning was drum roll, please produce a perfect, pain-free poop.

We typically tell people to expect healing results anywhere from a few hours to several months after treatment. This is because different cells in the body divide at different rates, so every patient will experience a different result, depending on the condition for which he or she is being

inflammation the area the stem cells would target for healing was her gut. It so happens that gut stem cells divide faster than almost any other cell in the body about every sixteen hours. So, miracles aside, it makes scientific sense that she would feel an improvement almost immediately, and that twelve hours later, she wou

bowels were complying with her for the first time in almost fifteen years. That first post-treatment bowel movement was so epic for Julia that she took a photograph of it with her iPhone and emailed the pict

our careers. To this day, Julia has enjoyed normal bowel function.

wrong: Usually it was word-of-mouth that would lead our patients to us. We just never imagined that word could spread so efficiently from the non-speaking mouth of a loyal dog! The moral? Always go with your gut.

Chapter 10

CONFRONTING OUR CRITICS

Atlas Shrugged, the central protagonists are characters who all share a strong sense of self-esteem, self-worth, and the kind of selfishness that is widely misunderstood. Their names are Francisco, Ragnar, and Hank. (Of course, the elusive John Galt is the

is the very first line of the book and an oft-

So, what are we getting at? Any time someone whether in an Ayn Rand

puts forward an effort that flies in the face of conformity, the critics will object. And worse, if the non-conformist is successful, others will claim that his or her success belongs, not to the individualist, but to the majority. Rand herself experienced this, and although she died in 1982, she and her work continue to draw heated criticism. We can relate: From the start of our venture into the deployment of adipose derived stromal vascular fraction (SVF), we have been treated to an uninterrupted stream of criticism. After all, what right do we have to use these adipose cells to investigate therapeutic applications, and to charge for our services before the protocol has been proven (by whom?) to be successful?

Early criticisms c

if SVF deployment was safe or any better than a placebo. While we cared that treatments were effective, we focused our initial study on safety by looking at adverse events. If it

why would we venture into this area? Of course, a plethora of empirical and anecdotal data existed suggesting safety would not be an issue. Nonetheless, stories of calamities related to

, make it into the press or the online chat sites and get disseminated throughout the medical community and general public. People could be easily scared. Nonetheless, our first study focused on any adverse events. While there were the occasional complaints about the liposuction (mainly that there was some pain at the site after surgery), there were no significant adverse events (complications) directly related to the administration of SVF. Of course, we expected this. These cells came from the same person, were just released in larger numbers, procured in a completely sterile manner, filtered through a

100 micron filter, and if administered intravenously they passed through an intravenous filter for blood (170 micron). Thus, there was no chance of infection or clotting from an embolus.

The second predominant line of criticism came from doctors who admonished us for not performing evidence-

controlled studies; we just wanted to see if SVF really worked in any consistent manner. We wanted to see if some of the claims and testimonials made throughout scattered clinics around the world had any merit while validating the safety of the procedure. If all went well, then we

As you may recall, we started by looking at orthopedic cases. Most of our patients that suffered from joint degeneration had already had multiple treatments e.g. NSAID (non-steroidal anti-inflammatory) pain medicines, steroid injections, hyaluronic acid injections, and even arthroplasty

possibly occurred from a proposed therapy. However, early on we found that these same patients responded positively to SVF. It would be highly unlikely that SVF has any better of a placebo effect than any other received therapy. Thus, it would be illogical to suggest that improvement following

to support these findings. In the meantime, patients are seeking relief from years of pain and

therapy and optimization

of therapy.

As we started to grow the Cell Surgical Network®, we started to garner more attention. Although

colleagues that knew us or heard us speak became interested in joining up with our team. We slowly and organically started forming a network of doctors dedicated to investigational deployments of SVF. Unfortunately, our colleagues, while attending various stem cell conferences, have reported that some of the speakers had lumped us in with other organizations doing stem cell work and then proceeded to vilify us. A well-known bioethicist declared that we

hed a

professional dialogue with this bioethicist, and tried to explain our position both as surgeons and

We stand by the premise of our practice: The protocol of the Cell Surgical Network® investigational deployments of SVF for therapeutic purposes is not FDA-approved, but it is FDA-compliant, and hence, entirely ethical.

While this dialogue occurred in a very polite email environment, we could never get the abovementioned bioethicist to understand or agree with our position. And, it turns out, without having mentioned it, this bioethicist had actually reported us to the FDA as an organization that needed to be looked into and potentially shut down. Ironically, he had sent this letter in January

2013, at least 10 months prior to our conversation, yet never mentioned it to us during our conversations. We tried to explain that we perform a surgical procedure and the FDA has no jurisdiction over the practice of surgery. The FDA has jurisdiction over drugs and devices. Once a device or drug has been approved for any claim, a surgeon may use said drug or device in any manner they see fit. Momentarily, we will go into detail about the FDA is

understood even though there will doubtless be criticism even of this explanation.

After doing an interview with a noted PhD stem cell blogger, we were summarily dismissed for

king advantage of our patients for monetary gain. Simply, we were noted to be greedy doctors preying upon desperate patients.

The FDA continues to effectively and ethically do exactly what Congress mandated them to do, which is protect society from the transmission of disease by regulating our food and medicine supply. The vocal PhD critics, on the other hand, are using their prestigious credentials and titles

This is, we believe, the opposite of ethical. For decades, physician practices, research, and overall behavior have been closely regulated and controlled by medical boards, peer review, insurance companies, local laws, malpractice attorneys, patient groups, hospitals, and various other regulators. It is only very recently that grant-receiving biologists have suddenly stepped up

qualified nor entitled to regulate physicians. They should engage primarily in peer review and

the NIH that have not been cleared for sterility (

Stem Cell Registry and FDA approval render most federally funded hESC lines unsuitable for

Cell Stem Cell, 14:139-40, 2014), but have been used in research for

commercialization for more than twelve years. Such endeavors are the most appropriate for these

negative press. Why? Understanding the FDA rules and regulations, and how they have been manipulated by self-interested individuals and groups, is only part of the reason why we comfortably confront our critics. The main reason we can comfortably stand up for our position is our commitment to carrying out our duties as physicians. Our responsibility is a substantial one: to come to the aid of our patients whenever possible. It is, or should be, a fundamental responsibility of all practicing physicians. If you can help them, then you should provide the effort.

So, how is it that the FDA regulations have been cited to suggest that we are out of bounds in providing investigational deployment of SVF? For this we need a little history lesson, as well as an understanding of FDA responsibilities. First, to be clear, the FDA, with respect to medicine, has always been responsible for two things: drugs and devices. In order for a drug or device to be approved, it must go through FDA-approved tests that ultimately show a reasonable degree of safety and efficacy (effectiveness). Indeed, there are many very useful drugs that can help a large

may

experience an allergic response or sustain some other serious harm as a result of taking the drug. Further, drugs that help most people might not actually be effective for a select group of patients.

they can be FDA approved. Nearly every medication and device carries certain known risks, even though FDA-approved disclosures about these risks must be made. Once a drug or device has been approved for any claim, medical doctors surgeons as well as physicians can use those products in any capacity they see fit.

- And the FDA does not limit doctors as to how we may use an approved drug or device. The only limit on drugs and devices relates to how a company may fairly advertise their product to physicians and to the public.

For example, the uber-popular drug Botox has long been used to wipe out a large variety of facial wrinkles. The product was originally developed and approved for use in blepharospasm (uncontrolled eyelid twitching). Eventually, while Botox was used for several different facial wrinkles, the company eventually got FDA clearance for the correction or softening of the glabellar wrinkle (the frown lines between your eyes). Of course, the drug is used for multiple

other wrinkles. The Federal Trade Commission and Federal Communications Commission

ertisements that seemed to promote Botox without specifying its actual claims, and suggested it could simply support any kind of cosmetic enhancement. The ads were eventually pulled, but still medical doctors are free to use Botox any way they see fit.

This actually makes a lot of sense. It would be overwhelming for a drug or device manufacturer to satisfy every possible claim that could arise from any of its products. Aspirin, for example,

may have been approved as a headache remedy, but as a blood thinner, it has become an important medication for heart and stroke patients, and patients at potential risk from clotting. Some studies suggest there are other benefits beyond these, but what aspirin manufacturer wants to pursue every claim? Scientists and doctors may see empirical evidence of the value of aspirin, and may thus set up a variety of studies to support or reject such hypothesis, but the companies

then th

drive sales of their product.

In 2001, the U.S. Congress passed a law that mandated the FDA to set up regulations for the purpose of preventing disease transmission in the exchange of body parts. In particular, there existed concern over organ donations, whereby a number of recipients had succumbed to HIV, hepatitis, and other serious infections after successful transplantation of donated organs. Congress wanted someone to police or regulate such tissue transfers, to minimize or eliminate risks of disease transmission. 21 Code of Federal Regulations part 1271 emerged in 2005, providing a set of guidelines for which the FDA could claim jurisdiction over human body parts. It may seem strange that in America, a government body could establish any regulations as to how its citizens may use their own body parts; however, Congress asked the FDA to do just that. If you read the first page of this regulation, you actually learn that the purpose of this rule is to

when they have jurisdiction over your tissues i.e. they must meet the definition of a drug or device.

The FDA came up with a list of exemptions that would allow doctors to circumvent the need for formal FDA approval through filing an Investigational New Drug application. If all of the following criteria were met, then a doctor or medical organization would be free to treat a patient with an HCT/P (Human Cells, Tissues, and Cellular and Tissue-Based Products). These exemptions include: 1) the parts must be autologous (from the same person); 2) for homologous use (used as the same tissue); 3) done during the same surgical setting; 4) minimally

relative, or c) used for reproductive purposes.

Now, what our critics fail to understand is that if there is any risk of disease transmission, then the FDA must invoke its jurisdiction, and it must support its position by showing that the process in question comes under its jurisdiction. To date, the FDA has shut down several clinics and laboratories. In all cases, they visited the site and found violations of GMP (Good Manufacturing Practices): manufacturing that could jeopardize sterility. As such, these organizations were told

nd close their doors until they were in compliance. One well-known group from Colorado that was using a laboratory for their technology decided to sue the FDA because they believed that the FDA had no jurisdiction over the practice of medicine. However, the FDA, by virtue of the Congressional law, was given the responsibility to prevent disease transmission, and when a laboratory gets involved, the FDA exerts its jurisdiction over the production process.

The lawsuit against the FDA failed in part because the FDA simply argued that it had jurisdiction over these organizations that violated GMP procedures. To cite its jurisdiction, it showed a list of

plus, the same company provided testimonials and made

then the FDA had jurisdiction. The courts upheld the FDA position. The courts agreed that this particular medical group could harvest cells from patients and provide them back to the same patients

delivery, the laboratory expansion (culturing to grow more cells) came under the FDA jurisdiction, and thus had to prove there was no risk of disease transmission.

For a variety of reasons that we can imagine, but in this context will not speculate upon, the same organization in conflict with the FDA had colleagues send correspondence to the FDA asking if

process autologous lipo-aspirate (the fat

respond to these requests. They evaluate these notes in a committee referred to as a Tissue Reference Group (TRG). They are not legal documents, but do represent the opinion of the FDA. We can tell you that if we worked at the FDA we would not approve any such note, and we use collagenase to process our cells. Why? Such open-ended letters are rather deceptive. While they may sound fairly clear, too much is missing in order to provide an affirmative response. If the

calamity later occurred, then these physicians could claim that they had been vetted and essentially approved by the FDA.

One such TRG letter that cast false aspersions on the use of collagenase was written by a physician related to the abovementioned Colorado group, which focuses exclusively on the use of bone marrow as a source of stem cells. Using bone marrow cells does not include the use of collagenase, which is only used to procure fat-derived stem cells and subsequently, that TRG letter which was well-circulated by the marketing department of the Colorado organization undermined the efforts of those using fat, creating an unfair marketing advantage. The abuse of the regulatory process for economic benefit is prevalent in many new scientific fields and the

prevent transmissible spongiform encephalopathies (TSEs), more commonly known as the cause

the collagenase, could safely give permission for such manipulation. The type of collagenase that we use is prepared by Roche Laboratories from a specially cultured bacterium by GMP standards and carries no risk of disease transmission.

Clearly, in such a case as described, the FDA has too much to risk and virtually nothing to gain.

e caught up in such potential legal battles.

has been adulterated to suggest that the FDA can stop anyone that deviates from any of the above

d by

the FDA. However, in surgery, we frequently use tissues that are more than minimally manipulated, and we use them in non-homologous areas. For example, a burn might be covered by a skin graft that has been run through a device that cuts into it so severely that it can be

FDA would never interfere in their use.

Collagenase, the drug in the middle of this controversy, only affects the collagen tissue that binds

manipulation of the cells, just the non-cellular collagen. Yet our critics will suggest we are more than minimally manipulating the tissue, because the FDA suggested such in their TRG response.

as an FDA-approved drug for use in a couple of well-known medical conditions. The drug can

When we use it, we completely wash it out from our final product, yet there are those concerned that some collagenase could get into the body and be harmful. Are they serious? Our studies with Roche show no significantly measurable collagenase left in the SVF; our critics countered that some residual collagenase could be getting into the body already allowed to inject

arguments. Recall that, as surgeons, we are allowed to use any approved drug or device any way we deem necessary, regardless of the exact claims approved. Recent FDA draft guidance

having jurisdiction over any type of fat digestion IF there was a risk of transmissible disease.

Our critics also like to point out that we are not using the SVF cells for homologous purposes.

y

new cartilage or restore vascular or nerve function it seems pretty obvious that they are being

namely, differentiate into the needed cells or tissues.

Nonetheless, as surgeons, we routinely use cells or tissues for non-

give you some simple examples. Start with a very popular procedure: coronary artery bypass grafting. This procedure is freque -

mostly use fat to help repair fat loss from aging in the face, it has also been used for non-homologous purposes, such as filling in defects from muscle tissue losses or filling in breast defects after resection or radiation damage to breast tissue. A bladder removed because of cancer or some other damage can be reconstructed with a section of ileum (small intestine). These are all non-homologous surgical procedures, over which the FDA has no jurisdiction.

and devices without any risk of disease transmission yet our critics remain adamant that we are somehow in violation of 21 CFR part 1271, and the FDA should shut us down. In fact, some of these critics have even written to the FDA as far back as January 2013, yet the FDA has not taken any action against us. Still, t

rsuing FDA approval

system. As such, we planned some straightforward investigations to test the safety and efficacy (effectiveness) of our system. Through conversations and our pre-IDE meetings with the FDA, they provided us guidance on how to best achieve our approval for the TimeMachine® (the SVF devices we trademarked from Korea). We are not flying under FDA radar, and we run absolutely no risk of disease t
multiple tissue samples of SVF out for evaluation, and have never had a positive response (i.e. any contamination with bacteria). Thus, we have no real issues with the FDA in spite of the critics.

interest groups that have used the FDA to falsely support their position, keep out competition, and prevent doctors like us from simply caring for our patients. Indeed, as physicians, we appreciate that the Hippocratic oath, (and the AMA code of ethics), are pretty clear about a

knowledge to support the use of SVF, all of our patients and affiliates recognize that, during this

empirical data that will help us improve delivery of cell therapy to a variety of conditions and

learn about SVF and its ability to correct (or not correct) a variety of inflammatory and degenerative conditions.

Another criticism we frequently get is that we are charging our patients while doing investigative for the patients to whom we give big discounts or treat for free. The FDA actually allows doctors to charge (not gouge) reasonable fees for investigative work. During the silicone gel investigation (1992-2007), the breast implant manufacturers were still making on the order of $300 million USD each year. Also, citizens putting up their own money privately fund our work. In California, CIRM (California Institute for Regenerative Medicine) has spent nearly $2 billion USD funding a variety of research programs with public money. Imagine, the taxpayer has supported the building of large offices and laboratories on some campuses, where their endowments are in excess of $16 billion USD. How ethical is that? The PhDs are getting paid no matter whether they help someone or not. We would have stopped a long time ago if our work was fruitless or in any way harmful. While not everyone gets better from SVF deployment, so many do improve that we find ourselves in the midst of the most doing precisely what we dreamed of doing when, back in college, we answered the calling to become medical doctors. We doubt we could ever return to

cells to restore function and eliminate pain.

Disruptive

to help people. Our disruptive technology may very well lead to the use of routine autologous

SVF in every medical center in the world, as an adjunct to current standard medical therapies. This is all occurring years, even decades, before stem cell therapies provided by the pharmaceutical industry

no wonder that our work has stirred so much anxiety among many so-

stigative work

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So, while our critics continu

honestly surprised that anyone would be upset with us for actually trying to help patients. We

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them and forgo our procedure. We believe there will likely exist the desire to use your own DNA and freeze and store (cryo-preserve) your own cells for later use both to restore damaged tissues and regenerate naturally degrading tissues. This will not only restore function and

In recent months, we have answered several invitations to speak at medical meetings or help set

regulatory authorities in China, the European Union, and Australia to help create policies regarding the use of autol

our treatment results in peer-

that encompasses the safety and efficacy

e

be ethical to stop treating patients until after the article is published; we want to help patients as soon as possible.

Without courting the attention of the mainstream media, we have been contacted by reporters

Popular Science magazine had an excellent article on California Stem Cell Treatment Center and the Network.

Our affiliate in Ohio, cosmetic surgeon Dr. Mark Foglietti, was featured on his local news station for treating two high-profile patients. In February 2014, Fox8 Cleveland did an inspiring profile

, she decided to undergo investigational stem cell therapy with Dr. Foglietti. In April 2014, the Fox8 did a follow-

improvements to her breathing and range of motion.

replacement, but he chose autologous stem cell therapy instead. We were particularly impressed when the Fox8 reporter, Suzanne Stratford, referenced a pop-culture phenomenon to help

mpactful way to understand ASCs.

interview, Ms. Snyderman asked Dr. Gitt a well-known plastic surgeon with superlative credentials, practicing with our network in Arizona
work, since investigational stem cell work should be done in a university. Since then, her

Rand, Ms. Snyderman violated her own Ebola virus quarantine to sneak out for a meal with her camera crew. Ms. Snyderman has since resigned and it is notable that her interview of Dr. Gitt originally aired on the (who else but?) Brian Williams segment of NBC news.

We never know what direction a media story might take, or whether it will be positive or critical. But what we do know is that we had come to the end of the year, and our practice and network was still standing

Atlas Shrugged, the plot lines all intersect with a fictitious, New York-based railway enterprise called Taggart Transcontinental. We think of the Cell Surgical Network® as a bullet train to the future of medicine, transporting patients to an improved quality of life. CSN has grown to more than 85 affiliate physician groups in the United States

Addendum The newspaper critics

On September 9, 2013, *The New York Times*

tremendously powerful influencer of public opinion published an article by Laura Beil entitled

use of adult stem cells from fat. Although our practice was not mentioned, we promptly wrote a letter to the editor. Our letter was never published, and to date the *Times* has not approached us for input into an article about adult stem cell therapy.

What follows below is our response to the *Times* and what follows after that? The stories of how and why we started our practice, and the patients whose successes with stem cell therapy inspire us every day.

by LAURA BEIL
Published in *The New York Times* September 9, 2013

(Unpublished) Response by Mark Berman, MD and Elliot Lander, MD
California Stem Cell Treatment Center

Rancho Mirage, CA

September 12, 2013

To the Editor:

cience and

bioethics. Doctors have a responsibility to take care of their patients. Definitely, the promotion of

DOUBT that doctors can isolate cells from fat and other body tissues that are incredibly rich in regenerative cells (many of which are adult stem cells). Also, there is little doubt that these cells can provide an incredible resource to mend inflammatory or degenerative conditions. Such work has been demonstrated time and again with evidenced-based (i.e. scientific) studies in Europe and even in the United States, though predominantly in the veterinary industry. While

industry as thoroughly regulated as medicine with oversight at multiple levels, not the least of which is through the legal system.

The Cell Surgical Network® (www.stemcellrevolution.com) supports a number of affiliates throughout the United States and abroad that provide a simple closed surgical technique to provide deployment of adult regenerative cells from a mini-liposuction procedure under an IRB approved protocol. We are registered with Clinical Trials.gov through the National Institutes of Health (NIH).We house a huge online database and will likely publish findings of our initial safety studies within the next six months (trials of any kind take time). Transparency remains the foundation on which we base our efforts. Patients know from the start that they may not obtain positive results. Not infrequently, this is simply due to a poor harvest of regenerative cells and patients are offered repeat treatments at little or no cost under a variety of conditions.

We contend that if you read the AMA code of ethics, we meet every criterion for an ethical practice. Further, our primary team (the California Stem Cell Treatment Center) and all of our affiliates have been built upon a multidisciplinary team approach. Our Board Certified doctors cover multiple specialties including plastic surgery, orthopedic surgery, cardiology, urology, interventional radiology, neurosurgery, spine specialists, ophthalmologists, and others. All are highly respected and considered thought leaders in their respective fields. This is hardly an organization built on the backs of some nefarious underground community that wants to remain anonymous.

While we appreciate the need for evidence-based studies, please understand that empirical medicine is NOT USELESS. Our scientists have been housed in glorious laboratories for years now with little clinical data to show for their efforts. We know that we can help people now with their own cells, amazingly richly found in adipose tissue. Why not do it? It might not be safe,

re doing a study that studies safety as the primary objective. Barely three years and one thousand patients into the study, there are no signs of significant adverse events short of occasional complaints about soreness around the liposuction site (which is actually an expected sequelae).

Our secondary objective is to look at clinical outcomes and see if we can identify trends. Of

because patients may pay for treatment (and there are many that get their treatment for free) there may be a significant placebo effect and our results are valueless. Most of our patients, particularly with orthopedic conditions, have already had a multitude of treatments before they

course, every treatment, paid for or not, has a potential placebo effect. So, if after four or five failed treatments the patient actually gets better from cell deployment, why would the placebo effect be any greater from cell deployment than

Yet we see this assumption made frequently.

We also would argue that as we make headway with empirical successes, it will be easier for scientists to go back to the laboratory to understand why and how we can improve on the process. We have a Hippocratic duty to help our

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already works. When the

Unfortunately, the public is being bamboozled by big business, big pharma, big universities, and any organization that has a lot at stake in this multi-billion dollar industry of stem cells. Their rega

time and again with medical procedures and good medical discoveries. If it really works, doctors

unscrupulous characters ultimately get weeded out.

EPILOGUE

What does the future hold?

At this point we want to roll out our big crystal ball that predicts the future of stem cell therapies. We think that regenerative medicine will advance greatly but slowly over the next ten years and that cell therapy will continue to evolve into two main arenas. One will be the long term research and monetization of patents in parallel with the development of therapies that can be

other arena will contain cell based therapies using autologous cells isolated from the human body as the ultimate production laboratory in a point of care system of cell therapy. This second system has tremendous potential to influence the way medical care is delivered in the US and around the entire world obviating the need for multimillion dollar laboratories, patents, and delivery of care through big Pharma-based models. This is why we are calling this the Stem Cell Revolution® and it is a disruptive technology.

Our hope and vision is that cell therapy will be available to clinicians and every medical clinic based on simple, safe, sterile procedures and tissue transfer principles that we use every day in surgery. We hope and believe that these therapies will be affordable and reliable. Our early research has shown excellent safety but we find that many patients (especially those with neurodegenerative and auto-immune conditions) need repeat treatments requiring multiple

liposuctions adding to the expense and hassle of autologous treatments. However, we have been actively working from a scientific and regulatory perspective on finding methods of cryogenically freezing stromal vascular fraction so that multiple deployments can be provided economically and conveniently. Further, we believe that all adults should consider donating a small amount of their fat to a bio-bank that could preserve it for future needs i.e. as bio-insurance.

exciting, we can expand and grow them; effectively creating a nearly unlimited supply of a

healing stem cells that may be critical should one develop cancer, an illness, or suffer from trauma. Additionally, these expanded cells may be instrumental in prolonging vital longevity. To realize this potential, we have created

with American CryoStem.

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way. Indeed, fat may have even greater potential than umbilical tissue.

the distinct advantage of homing in on cancer tissues in an attempt to repair the damage caused by malignant growth. This feature may be exploited to carry cancer killing chemotherapy and

improve the delivery of such agents. We strongly believe that having a deposit of your own cells

, heart attack, stroke or sudden illness would provide you with a type of biologic health insurance superior in quality and at a fraction of the price to traditional health insurance.

All of the technology needed to cryogenically freeze and replicate your cells and then safely deliver them back to you already exists. See www.cellsonice.com

We predict that your own stem cells whether fresh or frozen or ultimately expanded will be routinely used for a variety of conditions not currently considered. For example, we believe that they could be used post-operatively for nearly every orthopedic operation, as they should help you mend much better and much quicker from injury or surgery. They will likely become a source of first intervention in heart attack, stroke and head trauma. Not only will they be used routinely to help athletes mend better and quicker, but may even be considered to help them maximize their potential. And lastly, for age mitigation strategies, one can continuously re-deploy expanded autologous cells to simply replace normally dying cells thus continually replenishing and restoring your vital organs and tissues. These cells could essentially be your ticket to a vital and functional increase in life-

these cells can be incredibly useful, but it may be necessary to see what kind of cells your own or those processed in a laboratory are going to be most functional. We believe that even if

benefit (unless you have a genetic defect) to receiving your own DNA.

many respects the future is here. There will be continued new discoveries and therefore the demand will likely increase with time.

END NOTE

that as the

do. Our physician colleagues in the Cell Surgical Network are now treating a wide range of

below is a list, in

alphabetical order. To locate the doctor nearest you, visit www.cellsurgicalnetwork.com

ALS

Alopecia Areata

Arrhythmia

Arthritis and degenerative Orthopedic conditions

Asthma

Autism

Autoimmune Hepatitis Diabetes Mellitus

Autoimmune Neuropathy

Cerebral Palsy

CIDP (Chronic Inflammatory Demyelinating Polyneuropathy)

Congestive Heart Failure

COPD/Emphysema

Critical Limb Ischemia

Dermatomyositis

Dry eyes

Erectile Dysfunction

Fibromyalgia

Glaucoma

Interstitial Cystitis

Lichen Sclerosus

Lung Disease

Lupus

Lymphedema

Macular Degeneration

Male Incontinence

Multiple Sclerosis

Muscular Dystrophy

Myasthenia Gravis

Myocardial Infarction

Optic Neuritis

Peyronie s

Polychondritis

Post Radical Prostatectomy

Rectal Fistula

Renal Failure

Retinopathy

Rheumatoid Arthritis

Scleroderma

Severe Peripheral Arterial Disease

Spasmodic Dysphonia

Stroke

Traumatic Brain Injury and Concussion

ACKNOWLEDGMENTS

This entire book represents an acknowledgment. Everyone mentioned in the book is the backbone for the story and we thank them all for their contributions. However, a few people not mentioned need to be and maybe a few of those mentioned should be further acknowledged.

The process of writing a book is laborious at best. We'd like to start by thanking Julia Szabo who co-wrote, organized, co-edited and conducted all of the interviews so that we could give our voice yet present our patients in an impartial manner without coaching them. Julia has written her own best-seller, *Medicine Dog: The Miraculous Cure That Healed My Best Friend and Saved My Life.* Perhaps too, we should thank her dog who ultimately brought her to us via Bob Harman, president of Vet-Stem. Vet-Stem has treated over 10,000 animals from poodles to thoroughbred horses using adipose derived cells. We established a wonderful relationship with Bob Harman whose efforts helped us advance our technique to its current status completely closed sterile surgical procedure with filtered cells.

The labor of writing this book reflects the somewhat divine intervention afforded to us through the special people we have met, worked with and ultimately became part of the CSCTC and CSN team. There would have been no book and no entry into SVF without the genius of Dr. Hee Young Lee. As mentioned in the book, Dr. Lee is medic
the Ironman movie. His most clever inventions are the foundation for our venture into therapeutic stem cell deployment. However, we would never have known of Dr. Lee had it not been for the tireless work of Peter Jung. Additionally, Steven Hwang, along with the rest of the Medikhan team has been invaluable with their efforts in helping us see this project into fruition.

We have been honored to have Jackie See MD, highly respected interventional cardiologist and stem cell pioneer, join our clinical research project when we first started out. He gave freely of his abundant knowledge and helped us shape our vision of regenerative medicine
to remain the ultimate patient advocate.

ns from our office staff. On the administrative side - Judi Meglio, Marlina Manchego, Annette Pinuelas, Chris Lindholm, Lauren Geddie, Nikki Mitchell and Raziq Noorali. In the surgical suite, Aylin Soleymanian, Jessica Valdez, Brittany Whitley, Shawntae Dowell, and Elideili Villicana have been instrumental in forwarding our techniques. Aylin, in particular, was there when we started and

ial patients the true pioneers that trusted us to try their own SVF to improve their conditions. In particular, Laurie Hanna our patient number one, gave us their trust, something for which there is no price.

ADDENDUM

History of Adipose Derived Stromal Vascular Fraction Stem Cells

The following information was gleaned from numerous reports, papers and journals prepared by colleagues of the authors Jackie See, MD and Dennis Ling. This is a chronological report of those findings.

2001

Zuk PhD, and her associates at the laboratory for regenerative bioengineering and repair, UCLA School of Medicine, Los Angeles, California, USA, determined that a population of stem cells could be isolated from human adipose tissue via processed lipoaspirate (PLA), suction-assisted lipectomy, better known as liposuction. These cells could be maintained in vitro for extended periods. PLA cells are of mesodermal or mesenchymal origin. These cells differentiate in vitro into adipogenic, chondrogenic, myogenic, and osteogenic cells in the presence of lineage-specific induction factors.

2002

Stafford, et al., examined whether murine and human adipose-derived adult stem (ADAS) cells can be induced to undergo neuronal differentiation. They isolated ADAS cells from the adipose tissue of adult BalbC mice or from human liposuction tissue and induced neuronal differentiation with valproic acid, butylated hydroxyanisole, insulin, and hydrocortisone. Again in 2002, Zuk, et al, Published another paper on their continuing research of isolating human adipose stem cells.

Zuk et al., Adipose tissue, like bone marrow, is derived from the mesenchyme and contains a stroma that is easily isolated. Preliminary studies have recently identified a putative stem cell population within the adipose stromal compartment.

2003

Cousin, et al, published findings on the Reconstitution of lethally irradiated mice by cells isolated from adipose tissue. They determined that adipose tissue can expand throughout adult life and its expansion is not only due to mature adipocyte hypertrophy but also to the presence of precursor cells in stroma-vascular fraction (SVF).

Ashjian, et al, also from the UCLA Medical Center for Regenerative Bioengineering, reported in their findings that PLA cells can be induced to differentiate into early neural progenitors, which are of an ectodermal origin. Once again in 2003, **Dragoo, et al,** Published in the Journal of Bone and Joint Surgery, that tissue-Tissue-engineered cartilage and bone using stem cells from human infrapatellar fat pads. They extracted multipotential processed lipoaspirate (PLA) cells from five human infrapatellar fat pads and embedded into fibrin glue nodules]

Dragoo et al., To date, differentiation to nonmesodermal fates has not been reported. This study demonstrates that PLA cells can be induced to differentiate into early neural progenitors, which are of an ectodermal origin]

2004

Bacou, et al, published their findings that transplantation of adipose tissue-derived stromal cells increases mass and functional capacity of damaged skeletal muscle. Adipose tissue stromal cells labeled with Adv cyto LacZ from 3-day-old primary cultures (SVF1) were auto transplanted into damaged tibialis anterior muscles. Fifteen days later, beta-galactosidase staining of regenerated fibers was detected, showing participation of these cells in muscle regeneration.

Cowan, et al, of Stanford University of Medicine, published their findings that adipose-derived adult stromal cells heal critical-size mouse calvarial defects. Their study investigated the in vivo osteogenic capability of adipose-derived adult stromal (ADAS) cells, BMS cells, calvarial-derived osteoblasts and dura mater cells to heal critical-size mouse calvarial defects.

Safford et al, Duke University Medical Center, published their research results on the characterization of neuronal/glial differentiation of murine adipose-derived adult stromal cells. They extended these observations to test the hypothesis that murine (mu) ADAS cells can be induced to exhibit characteristics of neuronal and glial tissue by exposure to a cocktail of induction agents. Still in 2004, **Guilak, et al**, also

Adipose-derived Adult Stem Cells for

Cartilage Tissue engineering'. They deemed that ADAS cells show significant promise for the development of functional tissue replacements for various tissues of the musculoskeletal system.

Miranville, A, et al., Department of Cardiovascular Physiology, J-W Goethe University, Frankfurt, Germany, published their findings on the Improvement of postnatal neovascularization by human adipose

tissue-derived stem cells, to characterize the cell populations that compose the SVF of human AT originating from subcutaneous and visceral depots, fluorescence-activated cell sorter analysis was performed by use of fluorescent antibodies directed against the endothelial and stem cell markers CD31, CD34, CD133, and ABCG2.

Guilak, et al., ADAS cells show significant promise for the development of functional tissue replacements for various tissues of the musculoskeletal system.

Kang SK et al., of Tulane University Health Sciences Center, showed in their research on neurogenesis of rhesus adipose stromal cells, that they isolated and characterized a population **of non-human primate adipose tissue stromal** cells (pATSCs) containing multipotent progenitor cells. They showed that these pATSCs can differentiate into several mesodermal lineages, as well as neural lineage cells.

Lendeckel S, et al., Justus-Liebig-University Medical School, Giessen, Germany, published their findings on **autologous stem cells (adipose) and fibrin glue used to treat widespread traumatic calvarial defects.** This was a report of **a 7-year-old girl** suffering from widespread calvarial defects after severe head injury with multifragment calvarial fractures, decompressive craniectomy for refractory intracranial hypertension and replantation of cryopreserved skull fragments**.** Postoperative course was uneventful and CT-scans showed new bone formation and near complete calvarial continuity three months after the reconstruction.

2005

Seo MJ, et al., of the Pusan National University, Pusan 602-739, Republic of Korea, reported their findings on the differentiation of human adipose stromal cells into hepatic lineage in vitro and in vivo. They found that mesenchymal stem cells isolated from human adipose tissue are immunocompatible and are easily isolated. Therefore, hADSC may become an alternative source to hepatocyte regeneration or liver cell

transplantation. At the Department of Medicine/Nephrology, Johann Wolfgang Goethe-University, Frankfurt, Germany,

Brzoska M, et al., published findings on epithelial differentiation of human adipose tissue-derived adult stem cells. Their findings showed that ADAS-cells have epithelial potential. In 2005, from the UCLA Department of Urology,

Jack, et al., studied processed lipoaspirate cells for tissue engineering of the lower urinary tract and implications for the treatment of stress urinary incontinence and bladder reconstruction**.** PLA cells are an easily accessible source of pluripotent cells, them ideal for tissue regeneration. PLA cells may provide a feasible and cost-effective cell source for urinary tract reconstruction.

2006

Conejero JA, et al., Division of Plastic and Reconstructive Surgery, New York Presbyterian Hospital, studies the repair of palatal bone defects using osteogenically differentiated fat-derived stem cells. Their study demonstrated the feasibility of reconstructing bony defects with fat-derived stem cells. In Switzerland, at the Department of Research, University Hospital in Basal,

Timper, et al., found that human adipose tissue-derived mesenchymal stem cells differentiate into insulin, somatostatin, and glucagon expressing cells. Using quantitative PCR a down-regulation of ABCG2 and up-regulation of pancreatic developmental transcription factors Isl-1, Ipf-1, and Ngn3 were observed together with induction of the islet hormones insulin, glucagon, and somatostatin.

Rodriguez LV, et al., also from the UCLA Department of Urology, found that adipose-derived cells have the potential to differentiate into functional smooth muscle cells and, thus, adipose tissue can be a useful source of cells for treatment of injured tissues where smooth muscle plays an important role. Their findings

showed that clonogenic multipotent stem cells in human adipose tissue differentiate into functional smooth muscle cells.

2007

Fang B, et al., from the Department of Hematology, Henan Institute of Hematology, 127 Dongming Road, hengzhou, Henan, China, reported in their findings that using human adipose tissue-derived mesenchymal stem cells as salvage therapy for hepatic graft-versus-host disease resembling acute hepatitis concluded that it is worthwhile to administer AMSC as a treatment for common hepatic GVHD, particularly for atypical cases presenting as acute hepatitis. A 43-year-old woman with chronic hepatic graft-versus-host disease (GVHD) who failed previous immunosuppressive therapy with cyclosporine and prednisone was treated with tacrolimus starting on day 165 after allogeneic hematopoietic stem cell transplantation.

Banas A, et al., at the National Cancer Center Research Institute, Tokyo, Japan, found recent observations indicate that several stem cells can differentiate into hepatocytes; thus, cell-based therapy is a potential alternative to liver transplantation. They used AT-MSCs from different age patients and found that, after incubation with specific growth factors (hepatocyte growth factor [HGF], fibroblast growth factor [FGF1], FGF4) the CD105(+) fraction of AT-MSCs exhibited high hepatic differentiation ability in an adherent monoculture condition.

Kim, et al., studied the systemic transplantation of human adipose stem cells attenuated cerebral inflammation and degeneration in a hemorrhagic str -derived stem cells, are readily accessible multipotent mesenchymal stem cells and are known to secrete multiple growth factors. They found that ASCs transplantation in the ICH model reduced both acute cerebral inflammation and chronic brain degeneration, and promoted long-term functional recovery.

Mauney JR, et al., Department of Biomedical Engineering, Tufts University, 4 Colby Street, Medford, MA 02155, USA, studied engineering adipose-like tissue in vitro and in vivo utilizing human bone marrow and adipose-derived mesenchymal stem cells with silk fibroin 3D scaffolds. Their results suggested that macro porous 3D AB and HEIP silk fibroin scaffolds offer an important platform for cell-based adipose tissue engineering applications.

Heydarkhan-Hagvall S, et al., at the Regenerative Bioengineering and Repair Laboratory, at UCLA, Los

Human adipose stem cells: a potential cell source for cardiovascular tissue engineering. Their results indicate that hASCs are a potential cell source for cardiovascular tissue engineering; however, the differentiation capacity of hASCs into SMCs and ECs is passage number- and culture condition-dependent. As it was in 2004, 2008 was a very productive year for ADSC research. Hsu et al., at the University of Wisconsin, studied the efficacy of bone morphogenetic protein (BMP)-2-producing adipose-derived stem cells in inducing a posterolateral spine fusion in an athymic rat model. In one group of eight rats, spinal fusion was demonstrated to be successful.

Hsu, et al., Adipose-derived stem cells show promise as gene transduction targets for inducing bone formation to enhance spinal fusion in biologically stringent environments.

Park BS, et al., at the Division of Stem Cell Research, Prostemics Research Institute, Seoul, Korea, published their findings concerning adipose-derived stem cells.. ADSCs and their secretory factors show promise for application in cosmetic dermatology, especially in the treatment of skin aging.

Trottier V, et al., Laboratoire d'Organogénèse Expérimentale Quebec, Canada, reported using human adipose-derived stem/stromal cells for the production of new skin substitutes. By exploiting the adipogenic potential of ASCs, they produced a more complete trilayered skin substitute consisting of the epidermis, the dermis, and the adipocyte-containing hypodermis, the skin's deepest layer.

Xu Y, et al., at the Department of Neurology, Zhejiang University, PR China, in studying the myelin-forming ability of Schwann cell-like cells induced from rat adipose-derived stem cells in vitro, determined that SC-like cells induced from adipose-derived stem cells (ADSC) may be one of the ideal alternative cell systems for SC. Their data demonstrated that SC-like cells from ADSC were able to form myelins and these cells may benefit the treatment of peripheral and central nerve injuries.

2009

Okura et al., published their findings on transdifferentiation of human adipose-derived stromal cells into insulin-producing clusters, in The Japanese Society for Artificial Organs Journal, 2009. They reported that the autoimmune destruction of insulin-producing beta cells is the cause of type 1 Diabetes mellitus. They feel that their insulin-producing cells derived from ADSCs could potentially be used for cell therapy of type 1 diabetes mellitus.

Nakada A, et al., at the Department of Bioartificial Organs, Institute for Frontier Medical Sciences, Kyoto University, Japan, published their findings on the regeneration of central nervous tissue using a collagen scaffold and adipose-derived stromal cells. Their data suggests that ASCs seeded into a collagen scaffold may have the potential to promote regeneration of nervous tissue after cerebral cortex injury.

Kondo et al., at the Department of Cardiology, Nagoya University Graduate School of Medicine, Nagoya, Japan, reported on their study of the implantation of adipose-derived regenerative cells enhancing ischemia-induced angiogenesis. They concluded Adipose tissue would be a valuable source for cell-based therapeutic angiogenesis. Moreover, chemokine SDF-1 may play a pivotal role in the ADRCs-mediated angiogenesis at least in part by facilitating mobilization of EPCs.

Garcia-Olmo D, et al., Department of Surgery and Cell Therapy, La Paz University Hospital, Madrid, Spain reported their findings on the **a**dministration of expanded ASCs (20 to 60 million cells) in combination with fibrin glue is an effective and safe treatment for complex perianal fistula and appears to achieve higher rates of healing than fibrin glue alone. Patients with complex perianal fistulas associated with Crohn's were randomly assigned to intralesional treatment with fibrin glue or fibrin glue plus 20 million ASCs. Fistula healing and quality of life were evaluated at eight weeks and one year. If healing was not seen at eight weeks, a second dose of fibrin glue or fibrin glue plus 40 million ASCs was administered. They reported that the administration of expanded ASCs (20 to 60 million cells) in combination with fibrin glue is an effective and safe treatment for complex perianal fistula and appears to achieve higher rates of healing than fibrin glue alone.

Lin et al., school of Medicine, Department of Urology, University of California-Knuppe Molecular Urology Laboratory, San Francisco, studied the potential of adipose-derived stem cells for treatment of erectile dysfunction. The adipose derived stem cells are paravascularly localized in the adipose tissue, and under specific induction medium conditions, these cells differentiated into neuron-like cells, smooth muscle cells and endothelium in vitro. The ADSCs are a potential source for stem cell-based therapies, which imply the possibility of an effective clinical therapy for ED in the near future.

Puissant et al., Laboratoire d'Immunologie, Toulouse France, reported their findings on the **Immunomodulatory effect of human adipose tissue-derived adult stem cells: comparison with bone marrow mesenchymal stem cells. L**ike mesenchymal stem cells from bone marrow (BM-MSCs), adipose tissue-derived adult stem cells (ADAS cells) can differentiate into several lineages and present therapeutical potential for repairing damaged tissues. The use of allogenic stem cells can enlarge their therapeutical interest, provided that the grafted cells could be tolerated. We investigate here, for the first time, the immunosuppressive properties of ADAS cells compared with the well-characterized immunosuppressive properties of BM-MSCs. ADAS cells did not provoke in vitro alloreactivity of incompatible lymphocytes

and, moreover, suppressed mixed lymphocyte reaction (MLR) and lymphocyte proliferative response to mitogens. The impairment of inhibition when ADAS cells and BM-MSCs were separated from lymphocytes by a permeable membrane suggests that cell contact is required for a full inhibitory effect. Hepatocyte growth factor is secreted by both stem cells but, similar to interleukin-10 and transforming growth factor-beta (TGF-beta), the levels of which were undetectable in supernatants of MLR inhibited by ADAS cells or BM-MSCs, it did not seem implicated in the stem cell suppressive effect. These findings support that ADAS cells share immunosuppressive properties with BM-MSCs. Therefore, ADAS cell-based reconstructive therapy could employ allogenic cells and because of their immunosuppressive properties, ADAS cells could be an alternative source to BM-MSCs to treat allogenic conflict.

Riordan et al., Medistem Inc, San Diego, CA, USA, published their findings in the Journal of Translational **Non-expanded adipose stromal vascular fraction cell therapy for multiple sclerosis.'** In this paper, they discussed the rationale for use of autologous SVF in treatment of multiple sclerosis and described their experiences with three patients. Based on this rationale and initial experiences, we propose controlled trials of autologous SVF in various inflammatory conditions. They treated three patients with varying levels of MS. The patients treated were part of a compassionate-use evaluation of stem cell therapeutic protocols in a physician-initiated manner. Previous experiences in MS patients using allogeneic CD34+ cord blood cells together with MSC did not routinely result in substantial improvements observed in the three cases described above. While obviously no conclusions in terms of therapeutic efficacy can be drawn from the above reports, we believe that further clinical evaluation of autologous SVF cells is warranted in autoimmune conditions.

Gonzales et al., Tres Cantos, and Fundación Centro Nacional de Investigaciones Cardiovasculares Madrid, **Treatment of experimental arthritis by inducing immune tolerance with human adipose-derived mesenchymal stem cells.'** Mice with collagen-induced arthritis were treated with human AD-MSCs after disease onset, and clinical scores were

determined. Inflammatory response was determined by measuring the levels of different mediators of inflammation in the joints and serum. Systemic infusion of human AD-MSCs significantly reduced the incidence and severity of experimental arthritis. Human AD-MSCs emerge as key regulators of immune tolerance by inducing the generation/activation of Treg cells and are thus attractive candidates for a cell-based therapy for RA.

Froelich et al., Division of Cardiovascular Diseases, Mayo Clinic, Rochester, MN 55905, USA, reported in their findings that Adipose tissue is an abundant source of endothelial cells as well as stem and progenitor cells which can develop an endothelial phenotype. It has been demonstrated that these cells have distinct angiogenic properties in vitro and in vivo. These data suggest that ADECs represent an autologous source of proliferative endothelial cells, which demonstrate the capacity to rapidly improve reendothelialization, improve vascular reactivity, and decrease intimal formation in a carotid artery injury model.

Gonzalez-Reyetal., School of Medicine, University of Seville, Seville, Spain, reported in their paper on **Human adult stem cells derived from adipose tissue protect against experimental colitis and sepsis',** that acute and chronic colitis was induced in mice with dextran sulfate sodium, and sepsis was induced by caecal ligation and puncture or by endotoxin injection. Colitic and septic mice were treated intraperitoneally with hASCs or murine ASCs, and diverse disease clinical signs and mortality was determined. Their conclusion was hASCs emerge as key regulators of immune/inflammatory responses in vivo and as attractive candidates for cell-based treatments for IBD and sepsis.

Lee et al., at the Department of Neurology, Clinical Research Institute, Seoul National University Hospital, Seoul, South Korea, slowed progression in models of Huntington disease by adipose stem cell transplantation. In a quinolinic acid (QA)-induced rat model of striatal degeneration, human ASCs (1 million cells) were transplanted into the ipsilateral striatal border immediately after the QA injection. human ASCs reduced apomorphine-induced rotation behavior, lesion volume, and striatal

apoptosis. Adipose-derived stem cells (ASCs) are readily accessible and secrete multiple growth factors. Here, we show that ASC transplantation rescues the striatal pathology of Huntington disease (HD) models.

Ryu HH, et al., published their findings on **Functional recovery and neural differentiation after transplantation of allogenic adipose-derived stem cells in a canine model of acute spinal cord injury,** in the Journal of Veterinary Science. In their study, they evaluated if the implantation of allogenic adipose-derived stem cells (ASCs) improved neurological function in a canine spinal cord injury model. Results suggest that improvements of neurological function after transplantation of ASCs to dogs with spinal cord injuries might be partially due to neural differentiation of implanted stem cells.

Lin G, et al., at the University of California, San Francisco, California, USA, reported the derivation of insulin-producing cells from human or rat ADSC by transduction with the pancreatic duodenal homeobox 1 (Pdx1) gene. RT-PCR analyses showed that native ADSC expressed insulin, glucagon, and NeuroD genes that were up-regulated following Pdx1 transduction. ELISA analyses showed that the transduced cells secreted increasing amount of insulin in response to increasing concentration of glucose.

2010

Kajiyama et al., published their findings in The International Journal of Developmental Biology, that the human Pdx1 gene was transduced and expressed in murine adipose tissue-derived stem cells (ASCs). To evaluate pancreatic repair, they used a **mouse model** of pancreatic damage resulting in hyperglycemia, which involves injection of mice with streptozotocin (STZ**). STZ-treated mice** transplanted with Pdx1-transduced ASCs. The ease and safety associated with extirpating high numbers of cells from adipose tissues support the applicability of this system to developing a new cell therapy for IDDM. Results suggested that dx1-ASCs are stably engrafted in the pancreas and that high numbers of cells from adipose tissue support the development of a new cell therapy for IDDM.

Long et al., published their in The American Laryngological, Rhinological and Otological Society, on the potential treatment option for severe vocal fold scarring is to replace the vocal fold cover layer with a tissue-engineered structure containing autologous cells. As a first step toward that goal, we sought to develop a three-dimensional cell-populated matrix resembling the vocal fold layers of lamina propria and epithelium. A three-dimensional structure of fibrin and adipose-derived stem cells was created as a prototype vocal fold replacement. Two segregated cell phenotypes occurred, producing a bilayered structure resembling epithelium over lamina propria. This preliminary work demonstrates the feasibility of tissue engineering to produce structures for vocal fold replacement.

Gonzalez-Rey et al., at the **S**chool of Medicine, University of Seville, Seville, Spain, found that human adipose-derived mesenchymal stem cells reduce inflammatory and T cell responses and induce regulatory T cells in vitro in rheumatoid arthritis. Adult mesenchymal stem cells were recently found to suppress effector T cell and inflammatory responses and have emerged as attractive therapeutic candidates for immune disorders. In rheumatoid arthritis (RA), a loss in the immunological self-tolerance causes the activation of autoreactive T cells against joint components and subsequent chronic inflammation. In conclusion, their work identified hASCs as key regulators of immune tolerance, with the capacity to suppress T cell and inflammatory responses and to induce the generation/activation of antigen-specific regulatory T cells.

Josiah et al., Brain Tumor Center of Excellence, Department of Neurosurgery, Wake Forest University School of Medicine, Winston-Salem, North Carolina, published their findings on **Adipose-derived stem cells as therapeutic delivery vehicles of an oncolytic virus for Glioblastoma,** in Molecular Therapy, the official journal of the American Society for Gene & Cell Therapy. They found that glioblastoma multiform (GBM) accounts for the majority of primary malignant brain tumors and remains virtually incurable despite extensive surgical resection, radiotherapy, and chemotherapy. They hypothesized that adipose-derived stem cells (ADSCs) possess the ability to home and deliver myxoma virus to glioma cells and experimental

gliomas. They infected ADSCs with vMyxgfp and found them to be permissive for myxoma virus replication. Their data suggests that ADSCs are promising new carriers of oncolytic viruses, specifically myxoma virus, to brain tumors.

Okura et al., Department of Somatic Stem Cell Therapy, Foundation for Biomedical Research and Innovation , Kobe, Japan, published their findings on **Cardiomyoblast-like cells differentiated from human adipose tissue-derived mesenchymal stem cells improve left ventricular dysfunction and survival in a rat myocardial infarction model.** They examined whether human ADMSCs (hADMSCs) could differentiate into cardiomyoblast-like cells (CLCs) by induction with dimethylsulfoxide and whether the cells would be utilized to treat cardiac dysfunction. Dimethylsulfoxide induced the expression of various cardiac markers in hADMSCs, such as alpha-cardiac actin, cardiac myosin light chain, and myosin heavy chain; none of which were detected in noncommitted hADMSCs. The induced cells were thus designated as hADMSC-derived CLCs (hCLCs). To confirm their beneficial effect on cardiac function, hCLC patches were transplanted onto the Nude rat myocardial infarction model, and compared with noncommitted hADMSC patch transplants and sham operations. Echocardiography demonstrated significant short-term improvement of cardiac function in both the patch-transplanted groups. However, long-term follow-up showed rescue and maintenance of cardiac function in the hCLC patch-transplanted group only, but not in the noncommitted hADMSC patch-transplanted animals. The hCLCs, but not the hADMSCs, engrafted into the scarred myocardium and differentiated into human cardiac troponin I-positive cells, and thus regarded as cardiomyocytes. Transplantation of the hCLC patches also resulted in recovery of cardiac function and improvement of long-term survival rate.

Uysal AC, et al., studied tendon regeneration and repair with adipose derived stem cells, at the Department of Plastic and Reconstructive Surgery, Baskent University, Faculty of Medicine, Bahcelievler, Ankara, Turkey. Tendon, the crucial element of the musculoskeletal system, when damaged, never restores the biological and biomechanical properties completely. Recently, tissue engineering and regenerative

medicine have enabled the differentiation of postnatal somatic stem cells or mesenchymal stem cells (MSCs) to different cell lineages and tissues including tendon. In addition, the MSCs, mainly bone marrow derived stem cells (BSCs) were proven to enhance tendon healing. Adipose derived stem cells (ASCs) were shown to be as effective as the other MSCs by their multipotency and proliferative efficiency. However, neither the differentiation of ASCs to tenocytes nor the tendon regeneration using ASCs have been described in literature. Advances in biomaterial technology will improve the methodology in tendon regeneration however, up to date ASCs present an ideal cell source for experimental and clinical research on tendon engineering.

Li K, et al., at the Institute of Basic Medical Sciences and School of Basic Medicine, People's Republic of China, investigated the differentiation characteristics and the role of MSCs in renal tubular injury, human adipose-derived MSCs (hAD-MSCs) were transplanted into ischemia-reperfusion (I/R) kidneys in C57BL/6 mouse model. Results showed that hAD-MSCs were able to differentiate toward renal tubular epithelium at an early stage of injuries. The differentiated donor cells replaced the vacant space left over by the dead cells, contributed to maintenance of structural integrity and preceded to a subsequent tissue repair process. Furthermore, MSCs as supportive cells may promote repair via secreting cytokines. The differentiation and replacement of MSCs at an extremely early stage play important roles for the subsequent self-repair and -renewal of functional cells. Direct differentiation of MSCs, as an important mechanism of injured kidney repair, warrants further investigation.

di Summa et al., Chirurgie Plastique et Reconstructive CHUV, Université de Lausanne, Rue de Bugnon 46, 1005 Lausanne, CH, Switzerland, decided to test new fibrin nerve conduits seeded with various cell types (primary Schwann cells and adult stem cells differentiated to a Schwann cell-like phenotype) for repair of sciatic nerve injury. Two weeks after implantation, the conduits were removed and examined by immunohistochemistry for axonal regeneration (evaluated by PGP 9.5 expression) and Schwann cell presence (detected by S100 expression). The results show a significant increase in axonal regeneration in

the group of fibrin seeded with Schwann cells compared with the empty fibrin conduit. They published their findings in an International Journal of Surgical Reconstruction.

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