

# STEM-KINE

STEM CELL SUPPORT



## PRODUCT INFORMATION 2015



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# AIDANPRODUCTS

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## FDA Disclaimer

Stem-Kine is a food supplement only. Statements in this document have not been evaluated by the FDA. This product is not intended to diagnose, treat, cure or prevent any disease.

## Stem-Kine Product Information

### Product Concept

Stem cells are the body's natural healing mechanism. If a person is injured bad enough, either internally or externally, the body recruits stem cells from the bone marrow into the bloodstream and they mobilize to the point of injury to begin the healing process. There is a body of knowledge that demonstrates a positive correlation between the number of these circulating stem cells and health and regenerative capabilities.

Dr. Neil Riordan, a leading stem cell researcher, hypothesized that certain food substances could trigger chemical signals in the body that would release stem cells from the bone marrow into circulation. Through his extensive knowledgebase and collaborative network of stem cell scientists, Dr. Riordan applied scientific methods to identify natural substances that would trigger such stem cell recruitment, leading to the development of Stem-Kine.

### Product Effectiveness

To date, there has been no nutritional supplement proven to be more effective than Stem-Kine at mobilizing stem cells. The following results are based on multiple 2-week in vivo clinical trials and were validated in peer-reviewed publications:

Stem Cell Type	Max increase over control	Day at which peak occurred	Increase over control at end of trial period
Endothelial Progenitor Cells	100%	14 days	100%
CD133+ Stem Cells	90%	7 days	20%
CD 34+ Stem Cells	53%	2 days	10%
Hematopoietic Colony Forming Stem Cells	45%	2 days	17%

- 100% increase in endothelial progenitor cells (EPC's), peaking at the end of the two week clinical trial period
- 90% increase in CD133+ stem cells, peaking at 7 days, with 20% increase over control at the end of the two week clinical trial period
- 53% increase in CD34+ stem cells, peaking at 2 days, with 10% increase over control at the end of the two week clinical trial period
- 40%-50% increase in hematopoietic colony forming stem cells, peaking at 2 days, with 15-20% increase over control at the end of the two week clinical trial period



### Validation by Stem Cell Experts

Results of Stem-Kine studies were validated in peer-reviewed publications co-authored by the following stem cell experts from independent universities including University of Utah - Salt Lake City, Indiana University, and University of California – San Diego.

### Proprietary Formula

Stem-Kine is a proprietary blend of natural extracts and fermented products including *Lactobacillus fermentum*, goji berry, green tea, astragalus root, beta 1,3 glucan, the antioxidant ellagic acid and vitamin D3. It is administered orally through capsule form.

### Availability

Stem-Kine is available for sale from healthcare practitioners and distributors. It is also available through online purchase at [www.stem-kine.com](http://www.stem-kine.com)

### Pricing

The retail price for a 60-capsule bottle of Stem-Kine is suggested at \$69.95. To avoid price competition with our distributors, the product is offered online at higher price points.

### Stem-Kine Name

“Kine” is a greek suffix meaning “to move, motion or division”.

### More Info

More information is available on our website at [www.stem-kine.com](http://www.stem-kine.com)

## Importance of Circulating Stem Cells

The following are examples of studies from leading journals that show a direct, positive correlation between the number of circulating stem cells and health and regenerative capabilities:

Subject	Finding	Source
Stroke	Following a stroke, individuals with a higher content of circulating stem cells recover better than individuals with fewer circulating stem cells.	Journal of Neurology, 2007
Smoking	Smokers have impaired circulating stem cells, which increase with cessation and decrease with resumption of smoking.	Arteriosclerosis, Thrombosis, and Vascular Biology, 2004
Vascular Health	Circulating stem cells correlate with vascular health and cardiac risk factors.	New England Journal of Medicine, 2003
Injury	Injured tissue mobilizes or “calls in” stem cells.	Circulation, 2001
Cardiac Regeneration	Increasing the number of circulating stem cells with G-CSF leads to a therapeutic effect in cardiac regeneration.	American Journal of Cardiology, 2007
Alzheimer’s Disease	Individuals with Alzheimer’s have reduced levels of circulating stem cells and a correlation exists between the decreased number of circulating stem cells and the severity of the disease.	Neurology, 2009
Migraine Headaches	Patients with migraine headaches have decreased circulating stem cells.	Neurology, 2008
Erectile Dysfunction	Erectile and endothelial function correlate with circulating endothelial progenitor cell levels.	Journal of Sexual Medicine, 2009

See Appendix A for more detailed information regarding these studies.

## Executive Summaries of Peer Reviewed Publications

### Circulating endothelial progenitor cells: a new approach to anti-aging medicine?

*Mikirova et al. Circulating endothelial progenitor cells: a new approach to anti-aging medicine? Journal of Translational Medicine 2009, 7:106.*

This paper discusses endothelial dysfunction as a potential cause for numerous age-related degenerative conditions. Endothelial precursor cells (EPCs) provide damaged or senescent blood vessels a constant source of replenishment. Evidence is provided regarding the biology of EPCs in a variety of pathologies, indicating that EPCs are an endogenous repair mechanism for the body.

Varying methods and controlling factors for EPC mobilization are discussed; including preliminary research on Stem-Kine, which provides a supplemental-based method for inducing stem cell mobilization. Co-authors of the publication include individuals from major universities and organizations, including Indiana University, University of California, San Diego, and University of Utah, Salt Lake City.

Through an independent clinical trial, it was shown that Stem-Kine supplementation administered over a 2 week period (2 pills a day, twice daily) resulted in a 100% increase from baseline of circulating endothelial progenitor cells by the end of the 2 week period.

### Nutraceutical Augmentation of Circulating Endothelial Progenitor Cells and Hematopoietic Stem Cells in Human Subjects

This research suggests that Stem-Kine, a commercially-available supplement, can increase the blood circulation of hematopoietic stem cells, which can give rise to all blood cells, and endothelial progenitor cells, which repair damage to blood vessels.

In this trial, Stem-Kine was administered twice daily to 18 healthy volunteers for a period of 14 days, where peripheral blood was assessed on days 0, 1, 2, 7, and 14 for cells expressing hematopoietic stem cell markers. Results indicated significant increases in cells expressing CD133 and CD34 stem cell markers. Additionally, Stem-Kine supplementation increased cells expressing the EPC phenotype. Furthermore, significant increases in colony formation were observed from blood extracted on days 1 and 2. This means that the cells expressing the EPC phenotype were not only increased, but also capable of forming CFU-E (colony forming unit endothelium) generating activity.

The investigation further discusses other nutritional supplements, noting either a lack of data or limited results over a short period of time. To the authors' knowledge, this was the first study showing data of potential clinical significance using a nutritional supplement-based approach.

## Background Information on Aidan Products and Dr. Neil Riordan

### History

Aidan Products was founded in 2001 by Neil Riordan, PhD, a renowned research scientist with an interest in alternative medicine. Dr. Riordan has held leadership positions at leading research institutes, including a ten year tenure at the Center for the Improvement of Human Functioning and the Bio-Communications Research Institute International in Wichita, Kansas, where he collaborated with his father, Hugh Riordan MD, a world renowned cancer researcher, and a group of other dedicated scientists to finding alternative therapies for cancer. In addition to his important cancer research surrounding the use of Vitamin C as a cancer therapy, Dr. Riordan made other significant discoveries including:

- Discovering a molecule from the bindweed plant that stops new blood vessels from growing, which are needed in order for abnormal tissue to grow and spread.
- Discovering a molecule from the cell walls of bacteria that both stimulates the immune system and encourages the immune system to produce a third molecule, which stops new blood vessels from growing. Both of these blood vessel inhibitor molecules were extensively tested and found to halt abnormal growth in multiple types of abnormal cell growth.

These discoveries formed the basis for several of Aidan's products including Imm-Kine, C-Staton and IVC-Max. Dr. Riordan continually researches and publishes new findings and now holds dozens of U.S. and International patents and pending patents on products and treatment methods and has authored 37 peer-reviewed publications.

### Dr. Riordan and Stem Cell Research

Dr. Riordan's research led him to an interest in stem cells and their regenerative capabilities. In 2005, Dr. Riordan founded the Institute for Cellular Medicine in Costa Rica, dedicated to the administration of stem cell therapies using safe, non-controversial adult stem cells on a fee-for-service basis and expanded these services in Panama in 2009 with the Stem Cell Institute. Since inception, thousands of patients have been treated using adult stem cells for conditions including autism, multiple sclerosis, heart disease and spinal cord injuries, and the Stem Cell Institute has become the largest and most reputable stem cell clinic in the Western Hemisphere.

Dr. Riordan is also the founder of Medistem Inc., a U.S. based biotech company that holds numerous patents and pending patents regarding the growth and application of adult stem cells. In 2007, Medistem discovered a new type of stem cell named the "endometrial regenerative cell". Dr. Riordan is the co-founder of the Riordan-McKenna Institute (RMI), which will be opening soon in Southlake, Texas. RMI will specialize in regenerative orthopedics including non-surgical stem cell therapy and stem cell-enhanced surgery using bone marrow aspirate concentrate (BMAC) and AlphaGEMS amniotic tissue product.

Dr. Riordan is founder and chief scientific officer of Amniotic Therapies Inc. (ATI). ATI specializes in amniotic tissue research and development. Its current product line includes AlphaGEMS and AlphaPATCH amniotic tissue-based products. Additionally, Dr. Riordan is the founder and chairman of Medistem Panama, Inc., (MPI) a leading stem cell laboratory and research facility located in the Technology Park at the prestigious City of Knowledge in Panama City, Panama. Founded in 2007, MPI stands at the forefront of applied research on adult stem cells for several chronic diseases. MPI's stem cell laboratory is ISO 9001 certified and fully licensed by the Panamanian Ministry of Health.





## Testimonials

Please visit our website at [www.stem-kine.com](http://www.stem-kine.com)

### Dr. Neil Riordan in the News

Dr. Riordan is the founder of Stem-Kine. His work with stem cell research and application has been the subject of many media articles, a few of which are set forth below.

#### Wichita man receives first umbilical cord stem cell treatment in US

<http://www.kwch.com/news/local-news/wichita-man-receives-first-umbilical-cord-stem-cell-treatment-in-us/28020960>

KWCH News, September 12<sup>th</sup>, 2014

Ryan Benton, 28, was diagnosed with Duchenne's muscular dystrophy (DMD) when he was three.

"It's a progressive disease where the body lacks protein called dystrophin and dystrophin helps build and maintain muscles," said Ryan Benton.

The disease is primarily found in boys and causes the muscles to weaken and lose function. It's the reason Ryan has spent most of this life in a wheelchair.

Ryan and his family searched for 19 years before they found their first glimpse of hope in fighting the effects of the disease.

"You know we crossed our fingers and always prayed for something like this," said Ryan.

That hope meant flying to South America, to visit Dr. Neil Riordan and his team at the Stem Cell Institute in Panama for treatments. There, Ryan was injected with mesenchymal stem cells that are found in umbilical cords.

"In Ryan's case, they secrete molecules that stimulate his muscles to grow," said Dr. Riordan. "He doesn't have the right molecules to stimulate his muscles to grow. These cells have the most potent regenerative capacity of any tool in our tool box right now. I really look forward to opening the door for other therapies like it."

Dr. Riordan says although this isn't a cure, this procedure has shown promise in reversing the course of many diseases like muscular dystrophy. Ryan made seven such trips to South America for treatments, but it wasn't enough to see the progress Dr. Riordan knew he was capable of. That's why he, along with Dr. Van Strickland, an allergy and immunology specialist in Wichita, worked to get the FDA's approval to bring Ryan's treatments to Wichita.

"To use this type of cell is absolutely a first for the US," said Dr. Riordan.

Tuesday, Ryan started a trial officially called "Allogeneic transplantation of human umbilical cord mesenchymal stem cells for a single male patient with Duchenne Muscular Dystrophy." Ryan is the only patient allowed to use this experimental treatment at this point. According to the FDA agreement, he'll receive 24 treatments in Wichita from Dr. Strickland over the next three years.

Ryan's family says he's living proof the treatments work.

"Seeing where he was before the treatments and seeing where he is now, you couldn't believe it," said his brother Blake. "With this treatment, if you continue at the rate that it'll allow, there's no reason that years down the road he shouldn't be able to start a rehab process that allows him to start walking again. I know that's a huge goal, but I'm not afraid to dream big."

Ryan wants others to benefit the way he has.

"I want so badly for every parent, once their kid is diagnosed with a disease like mine, to be able to just go get treated," he said. "It would be something that 20 years later the kid says to the parent, 'Didn't I have muscular dystrophy when I was younger?' The parent would say 'Ya, you did, but we got it treated.' That would be amazing to me."

## MD Breakthrough

<http://www.kake.com/home/headlines/69538137.html>

ABC News, November 8, 2009

I have co-hosted the MDA Labor Day Telethon for a decade. My goal has been to help raise awareness and funds to fight the disease so we can be one step closer to finding a treatment or a cure for people with muscular dystrophy. All of these years I have worked hoping someday we would find something that could help patients like my friend Ryan. Well, that someday may be here.

Let me introduce you to Ryan Benton. Ryan was diagnosed with duchenne muscular dystrophy when he was just a toddler. He has spent most of his life in a wheel chair while his muscles have slowly deteriorated. Most patients with Ryan's form of muscular dystrophy are confined to a wheel chair by their teenage years and do not live past their mid-twenties. Ryan is 23-years-old.

About a year and a half ago, Ryan went to see a physician in San Jose, Costa Rica who researches and works with adult stem cells. The physician's name is Dr. Neil Riordan and he is a native of Wichita. Dr. Riordan grew up with Ryan's parents and he is the founder of the ICM clinic.

The clinic researches stem cell rejuvenation, a process that is not yet legal in the United States. But, Dr. Riordan believes stem cell rejuvenation is the future of health care and Ryan's parents took him to Costa Rica to be treated.

Ryan is the first muscular dystrophy patient to be treated at the ICM clinic. Ryan received stem cells from his sister and donor umbilical cords. He received 46 shots over a week long period.

Muscular dystrophy patients don't produce enough dystrophin and this is what causes their muscles to deteriorate. Ryan has been treated at the clinic three separate times over the past year and half and he says the results have been amazing.

Dr. Riordan says an MD patient has a 0 to 5 dystrophin level which is what Ryan had before the treatments. A normal dystrophin level is 50 to 100. Ryan says his latest dystrophin tests show he is now at a normal level.

Ryan says he feels so much healthier and his neck and trunk muscles are stronger. He's gained 30 pounds and his balance and endurance are better.

Dr. Riordan says he had already seen people with multiple sclerosis and spinal cord injuries drastically improve with his adult stem cell treatments but now--he sees great hope for MD patients as well.

Since Ryan, three more MD patients have been treated at Dr. Riordan's clinic. They also report that they are seeing improvements. Dr. Riordan says he has not charged them or their families a dime because he says it is all about advancing the science to find a cure.

Dr. Riordan hopes to partner with an organization in the United States like the Muscular Dystrophy Association so more patients with muscular dystrophy can receive this treatment. I contacted a lead researcher at MDA and she wants to talk with Dr. Riordan about his research.

If you would like more information about the ICM clinic and Dr. Riordan's treatment for muscular dystrophy you can call toll free 1-800-980-STEM (7836) or click on related links.

### **Multiple Sclerosis Successfully Treated Yet Again With Adult Stem Cells**

<http://www.cellmedicine.com/nw-cbs-ms.asp>

CBS News, February 10, 2009

After participating in a small clinical trial at Northwestern University, Edwin McClure seems to have recovered from multiple sclerosis (MS). Conducted on 21 participants and led by Dr. Richard Burt, the clinical trial involved treating the MS patients with their own adult stem cells. The only drawback of the study, however, was the use of chemotherapy to destroy each patient's immune system prior to the adult stem cell therapy. Nevertheless, patients such as Mr. McClure have shown dramatic improvement.

Diagnosed with MS four years ago at the age of 18, Edwin McClure underwent a regimen of conventional MS medication but without any results. According to Mr. McClure, "I would get fatigued. I couldn't deal with the heat. I had really bad balance." Then he heard about the trial being conducted at Northwestern University in Chicago, and decided to participate. Now, he says, "I really don't feel like I have multiple sclerosis anymore." In regard to the chemotherapy, however, he adds, "It was rough."

Approximately 400,000 people in the U.S. and 2.5 million people globally are estimated to suffer from MS, which is a degenerative, autoimmune, demyelinating disease of the central nervous system, the precise causes of which remain unknown, and a precise cure for which has not previously existed. According to Dr. Burt, however, "Well now for the first time in battling MS, I think you can say there's a study that's shown we've turned the tide against the disease."

In actuality, other doctors have already had success in treating patients with multiple sclerosis, but without the brutal and deliberate destruction of the immune system with radiation. As previously reported on this website, prior to receiving the autologous stem cell transplantation in the clinical trial led by Dr. Burt, each patient also underwent immunological myeloablation, in which radiation is employed to destroy the patient's immune system. While such a procedure had previously been considered a necessary part of the therapy, even though it exposes the patient to potentially life-threatening risks, today an increasing number of doctors are questioning the logic and necessity of subjecting their patients to deliberate immune destruction, and with valid scientific reason. In a publication that appeared over two years ago, in the Journal of Translational Medicine in January of 2007, Dr. Neil H. Riordan et al. posed the following question: "...in patients who are not suffering from a disease that is associated with an aberrant bone marrow such as hematological malignancies or immunological dysfunctions, how is it justifiable to subject them to the high levels of morbidity and mortality associated with immune suppression?" Dr. Riordan and his team of scientists then examined compelling evidence which strongly indicates that pre-transplant immune suppression is unnecessary for many types of autologous hematopoietic cell therapies and even for some allogeneic therapies that utilize "universal donor" cells such as mesenchymal stem cells and the CD34+ stem cells that are found in umbilical cord blood, and for which immune rejection is not even a concern. As Dr. Riordan and his colleagues wrote in their 2007 paper in a section that is subtitled, "Mesenchymal stem cells do not need myeloablation for efficacy": "Currently there are several ongoing clinical trials in Phase I-III using 'universal donor' mesenchymal stem cells in non-conditioned recipients of Crohn's disease, GVHD (graft-versus-host disease) and myocardial infarction. Although these cells are bone marrow expanded mesenchymal cells, the superior proliferative potential of cord blood mesenchymal cells may allow them not only to escape immune destruction, but also to expand in vivo and mediate therapeutic effects superior to those derived from bone marrow. The fact that regulatory agencies have allowed advancement of 'off-the-shelf' universal donor mesenchymal stem cells supports the numerous reports of clinical efficacy in an allogeneic setting."

Nevertheless, for clinical trials such as those conducted by Dr. Burt at Northwestern University, the adult stem cell therapy offers tangible improvement - at least for those patients who survive the life-threatening destruction of their immune systems from radiation. One can only conclude, therefore, as has already been demonstrated by other doctors at other clinics, that patients would exhibit even greater and faster improvement if they did not have to recover from the deliberate destruction of their immune systems prior to receiving the stem cell therapy, and also if the stem cell therapy would utilize the "superior proliferative potential" of the "immune privileged" adult stem cells that are found in umbilical cord blood.

Edwin McClure and his mother, Bernice, were featured today on the Early Show with CBS television correspondent Debbye Turner Bell.

### **Breakthroughs on the Brink: Turning the Tide on MS**

<http://www.saturdayeveningpost.com/2009/06/29/wellness/general-health/research-front/breakthroughs-brink-turning-tide-ms.html>

Saturday Evening Post, June 29, 2009  
[excerpt from article]

#### **A Different Approach**

After undergoing conventional therapy for MS for several years, Fort Worth police sergeant Preston Walker learned about a new treatment for autoimmune disorders. Researchers were utilizing adult stem cells derived from cord blood at The Institute of Cellular Medicine in Costa Rica. Walker inquired about the potential of the treatment for multiple sclerosis.

"We knew that if the treatment worked, the potential benefits for multiple sclerosis patients could be limitless," says Walker.

Dr. Neil Riordan, CEO of the Institute, suggested a therapy under consideration — using stem cells derived from a patient's fat tissue. In May 2008, Walker flew to the clinic where doctors removed samples of his abdominal fat through a mini-liposuction, drawing out stem cells, which were later re-injected. According to Dr. Riordan, Walker and a colleague were the first to undergo this treatment protocol. "My quality of life has improved significantly," Walker told the Post. "The problems with depression, fatigue, and balance have been corrected. I feel really good."

In June 2009, Walker, who continues to take Avonex as a maintenance drug, plans a return trip to Costa Rica for a "tune-up," as he puts it. "I'm curious to see if they can further improve my cognitive abilities."

### **Glenburn Boy Returns from Costa Rica After Having Adult Stem Cell Therapy**

<http://www.wabi.tv/news/7451/glenburn-boy-returns-from-costa-rica-after-having-adult-stem-cell-therapy>

CBS News, September 4, 2009

A young boy from Glenburn recently returned from Costa Rica where he underwent a procedure that is not available in the United States.

Meghan Hayward tells what he had done and how he's coping.

Eight-Year-old Kenneth Kelley was diagnosed with autism at the age of two.



When we last talked with him and his family, they were preparing for a trip to Costa Rica where he would undergo adult stem cell therapy.

"Kenneth had stems cells from umbilical cord blood and he got about 24 million stem cells while we were there in Costa Rica. He had injections every day over a period of four days."

Marty Kelley is Kenneth's mother. She was told by the doctors in Costa Rica to not expect to see results for 8 weeks to 6 months.

It's only been 6 weeks since the procedure and she and her husband say they're already seeing changes.

"Immediately when we were in Costa Rica, he just started talking a lot more. His vocabulary is probably 20 percent more conversation. He started going up to strangers and talking to them."

Kenneth had no problem telling us what he did in Costa Rica.

"We went to the beach and rain forest."

The Kelley family had to go to Costa Rica for the procedure because it's not done in the United States.

Marty is happy they made the trip.

"We know this is going to work for him. And we are 100 percent confident we'll be going back to Costa Rica in January. This is what he needs and because done so well in hyperbaric oxygen chamber, we know this is going to be good for us."

The hyperbaric oxygen therapy puts oxygen into the areas of the brain that have never received it, and creates stem cells in the brain.

"We hope to have him fully recover from this."

Right now, they're just happy to see Kenneth make the small changes and enjoy being a kid.

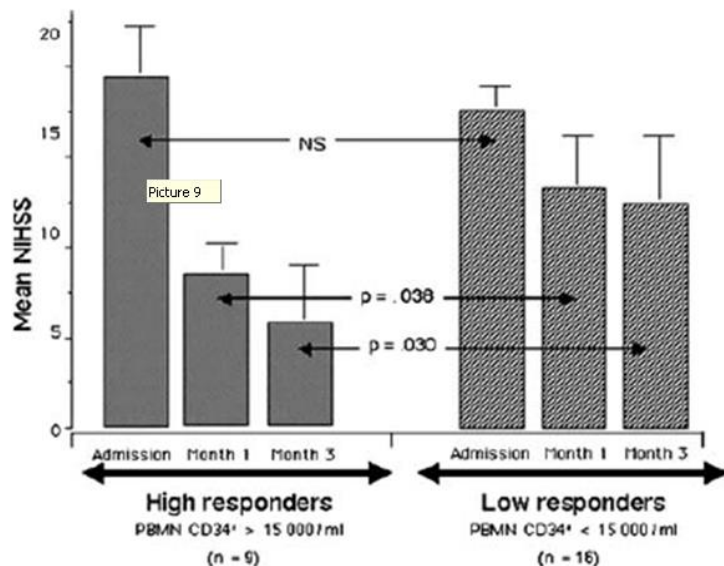
If you have questions about the procedure or want to follow Kenneth's journey, you can go to Marty's blog.

## Appendix A: Scientific Findings on Circulating Stem Cells

**Finding:** Following a stroke, individuals with a higher content of circulating stem cells recover better than individuals with fewer circulating stem cells.

In a study from the University Hospital Pasteur, 25 patients who incurred a stroke were divided into 2 groups. The first (left side in graph) had a higher number of circulating stem cells after the stroke, the second had a lower number (right side in graph). On the y-axis is severity of the stroke's effects. One and three months after the stroke, the patients with higher amounts of circulating stem cells had a more profound neurological recovery as compared to patients who had lower stem cell counts.

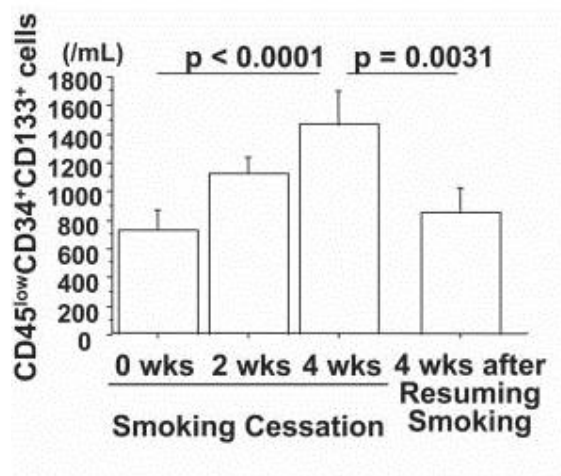
**Reference:** Dunac et al. Neurological and functional recovery in human stroke are associated with peripheral blood CD34+ cell mobilization. J Neurol. 2007 Mar;254(3):327-32.



**Finding:** Smokers have impaired circulating stem cells, which increase with cessation and decrease with resumption of smoking.

The effects of chronic smoking and subsequent termination were examined on circulating EPC levels. Participants included 14 nonsmokers and 15 smokers; all of the smokers quit smoking. It was found that circulating PCs and EPCs increased promptly after cessation and decreased again following resumption of smoking (resembling a level similar to pre-termination). Recovery of EPCs was found to be greater in light smokers than in heavy smokers. The graph on the left illustrates the levels of circulating progenitor cells corresponding to various time frames following smoking cessation and resumption.

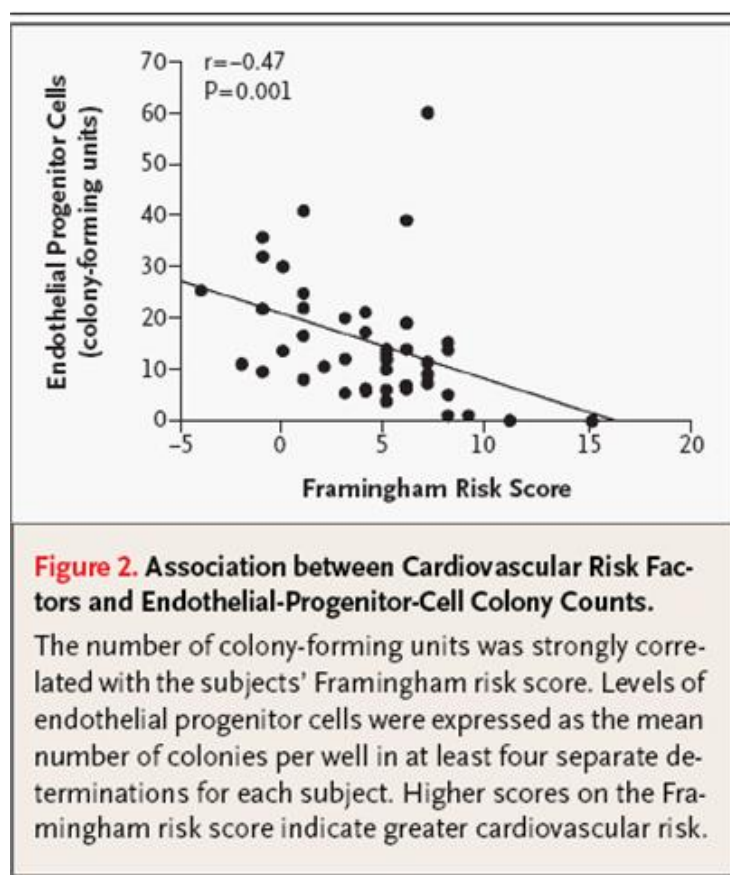
**Reference:** Kondo et al. Smoking cessation rapidly increases circulating progenitor cells in peripheral blood in chronic smokers. *Arterioscler Thromb Vasc Biol.* 2004 Aug;24(8):1442-7.



**Finding:** Circulating stem cells correlate with vascular health and cardiac risk factors.

In a study published in the New England Journal of Medicine, it was hypothesized that EPCs had a significant role in continuing endothelial repair, where decreased or damaged mobilization would contribute to endothelial dysfunction and cardiovascular disease progression. They measured the amount of circulating EPCs that were able to form colonies (colony-forming units) in blood samples of 45 men who had differing degrees of cardiac risk factors but had never suffered cardiovascular disease. It was shown that a strong correlation existed between the number of circulating EPCs and the subject's Framingham Risk Score — a measure of risk for cardiovascular disease (see graph to the right). Significant correlations also existed between the amount of progenitor cells and the participant's endothelial function; levels of circulating EPCs were actually a better predictor of vascular reactivity than the existence or nonexistence of cardiac risk factors.

**Reference:** Hill et al. Circulating endothelial progenitor cells, vascular function, and cardiovascular risk. N Engl J Med. 2003 Feb 13;348(7):593-600.

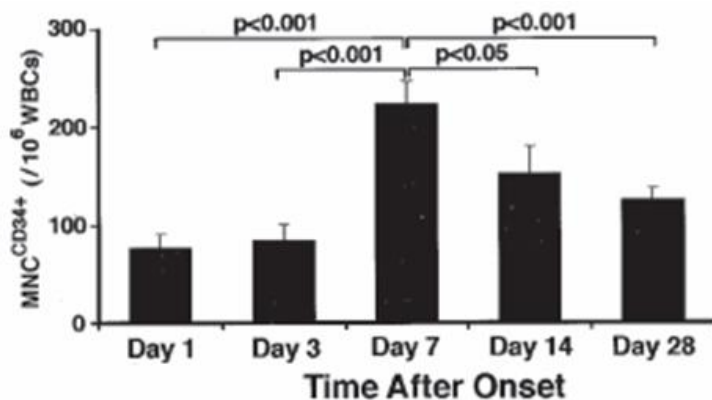




**Finding:** Injured tissue mobilizes or “calls in” stem cells.

Authors of this study sought to see if EPCs and CD34+ cells were mobilized in peripheral blood (PB) following acute myocardial infarction. Participants included 16 people who had just suffered an acute myocardial infarction and 8 control subjects who had no evidence of any cardiac ischemia (but suffered from abnormal chest pain). Flow cytometry analysis demonstrated that circulating CD34+ counts significantly increased following onset of myocardial infarction, reaching a peak at day 7 (see graph on the left), where control groups had no change. Furthermore, induced culture of a sample of these cells from the patients with acute myocardial infarction developed higher levels of cell clusters and EPCs from PB obtained from day 7 than day 1. This shows not only that levels of EPCs and CD34+ increase in response to an injury, but their capabilities to mobilize and colonize also increase (demonstrating their importance in response to injury).

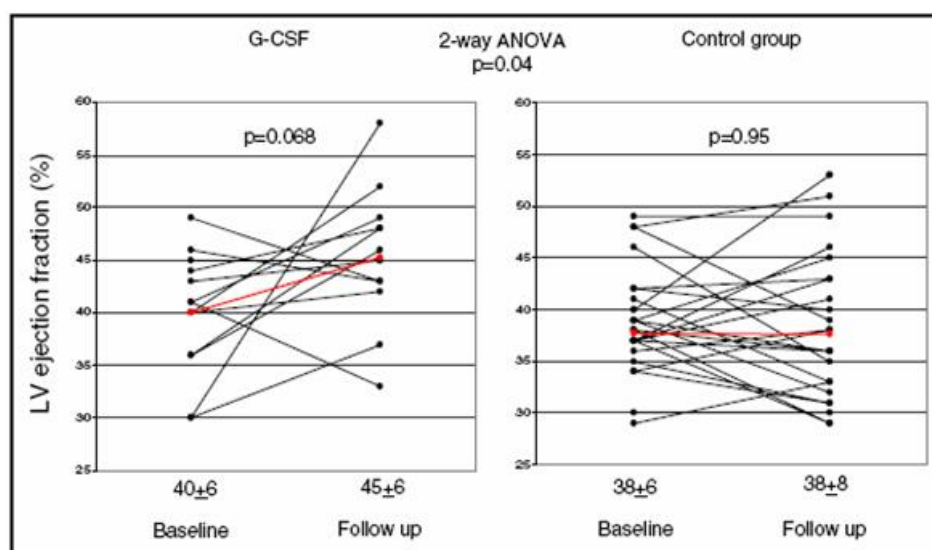
**Reference:** Shintani et al. Mobilization of endothelial progenitor cells in patients with acute myocardial infarction. Circulation 2001; 103:2776-2779.



**Finding:** Increasing the number of circulating stem cells with G-CSF leads to a therapeutic effect in cardiac regeneration.

Granulocyte colony-stimulating factor (G-CSF) is a drug that mobilizes EPCs, a type of circulating stem cell. This study shows the effectiveness of having increased circulating stem cells in regards to cardiac regeneration (following acute myocardial infarction). The current study took 41 patients with large anterior wall acute myocardial infarction who were at increased risk of unfavorable cardiac remodeling, randomizing them into a control group and a treatment group. After a follow-up of 5 months, patients treated with G-CSF showed a substantially higher LV ejection fraction (left ventricular ejection fraction — the heart's pumping ability) than those treated by conventional methods. Using G-CSF (a means of increasing circulating EPCs) prevented unfavorable cardiac remodeling and improved LV function significantly (see graph to the right).

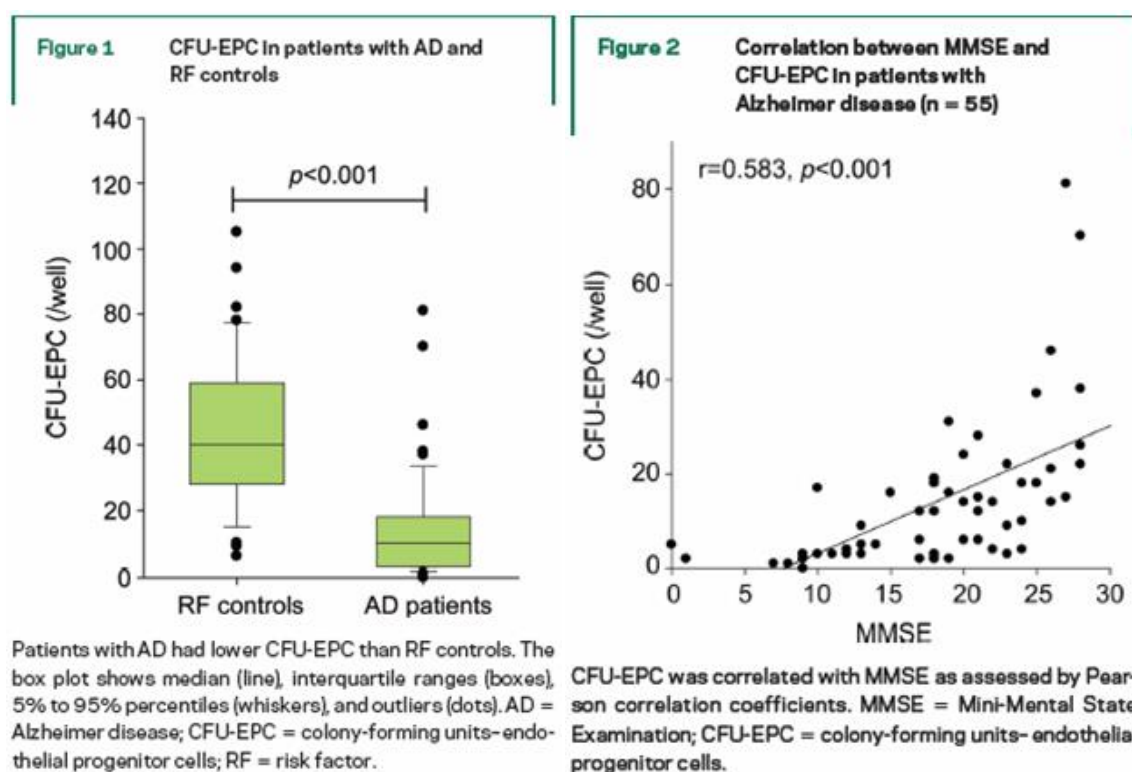
**Reference:** Leone et al. Usefulness of granulocyte colony-stimulating factor in patients with a large anterior wall acute myocardial infarction to prevent left ventricular remodeling (the rigenera study). Am J Cardiol 2007, 100:397-403.



**Finding:** Individuals with Alzheimer's have reduced levels of circulating stem cells and a correlation exists between the decreased number of circulating stem cells and the severity of the disease.

In a recent study, the authors sought to investigate the levels of various circulating stem cells involved in angiogenesis (such as EPCs) in patients with Alzheimer's disease. Study participants included 55 who were newly diagnosed with Alzheimer's (AD), 37 who had non-AD neurodegenerative diseases, and nondemented risk factor control subjects for both groups after matching for sex, age, and Framingham risk factor score. Results demonstrated that patients with AD had significantly lower amounts of CFU-EPC (colony-forming units) than the risk factor (RF) controls (see Figure 1). Furthermore, lower amounts of CFU-EPC in patients with AD were independently associated with either a higher Clinical Dementia Rating scale score or a lower Mini-Mental State Examination score (see Figure 2).

**Reference:** Lee et al. Reduced circulating angiogenic cells in Alzheimer's disease. *Neurology*. 2009 May 26;72(21):1858-63.

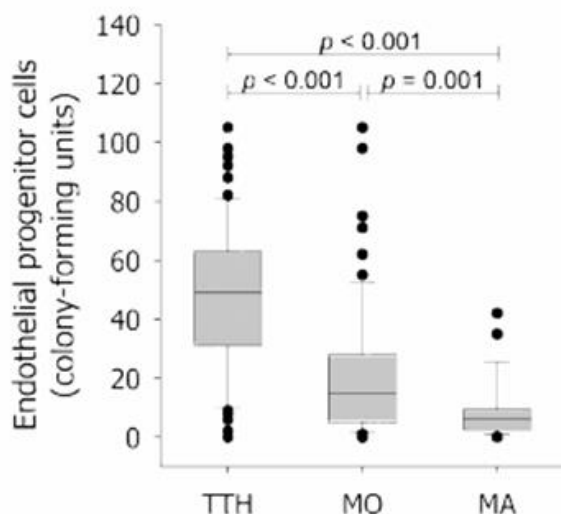


**Finding: Patients with migraine headaches have decreased circulating stem cells.**

Study authors investigated patients with migraines to see if irregularities in EPC amounts or abilities existed. A large sample was enlisted, including 166 total consecutive headache patients with varying degrees of severity (severity determined separation into three more groups). Peripheral blood samples were taken to determine CFU-EPCs in the patients; results indicated that those with migraines had significantly lower EPC levels (migraine with aura being lower than migraine without aura). EPCs from migraine patients demonstrated a decreased migratory capacity and increased cellular senescence compared to EPCs from normal subjects or those with tension-type headaches. These findings suggest that EPC numbers and functions may represent a link between migraines and cardiovascular risk factors.

**Reference:** Lee et al. Decreased number and function of endothelial progenitor cells in patients with migraine. *Neurology*. 2008 Apr 22;70(17):1510-7.

**Figure 1** Endothelial progenitor cell counts in headache patients



Migraine without aura (MO) patients had lower numbers of circulating endothelial progenitor cells than tension-type headache (TTH) patients, and migraine with aura (MA) patients had lower levels than MO or TTH patients. The box plot shows the median (line), interquartile ranges (boxes), 5% to 95% percentiles (whiskers), and outliers (dots). *P* values were calculated using a two-tailed Student *t* test.



**Finding: Erectile and endothelial function correlate with circulating endothelial progenitor cell levels.**

Endothelial dysfunction has been identified as a necessary connection with erectile dysfunction (ED). The objective of this study was to discover any potential trends in EPC levels of overweight men with and without ED. 30 overweight, yet healthy individuals with symptomatic ED for a period of at least 6 months were matched with 30 control subjects of same age and weight without ED. Erectile function was assessed and multiple subpopulations of circulating EPCs were measured through flow cytometry. It was found that certain EPCs were significantly reduced in overweight subjects with ED and were related to the severity of the disease.

**Reference:** Esposito et al. Circulating CD34+ KDR+ endothelial progenitor cells correlate with erectile function and endothelial function in overweight men. J Sex Med 2009; 6(1):107-114.

