

Quantum Cellular Medicine “QCM”

Quantum Cellular Medicine “QCM” is the segment of medicine that focuses on cell function and cell communication in the diagnosis, treatment, and maintenance of health and wellness in the human body.

Quantum Cellular Medicine focuses on cell regeneration and preservation. Scientists and researchers examined the complex processes in the cell for more than two decades. Quantum Physics has given rise to Quantum Biology and Quantum Chemistry.

Our cells are under constant stress from pollutants, diet, too much or too little exercise, drugs, and other lifestyle factors. When our cells are weakened, we look and feel exhausted and we are more prone to illness. This is why we look at health from the cellular level.

QCM clinics utilize the most recent developments in Quantum Cellular Medicine in both diagnosis and treatment of disease and the maintenance of optimal health and wellness. Please browse through our website to learn more about the technologies and methods we utilize in our practices.

AMNIO MATRIX

Amniotic Fluid-derived EVs



General overview of Amnio Matrix

We are moving into the 3rd epoch of medical evolution. The first period of medicine relied upon limited anthropological and scientific knowledge. It was a brutal time. Our contemporary skills have advanced, but we still rely upon invasive, scholastic methods. However, we are currently in the process of opening up to a third epoch, self regeneration! The idea is that our bodies contain all of the “know-how” to build, repair and regenerate all of our tissues. When we’re developing in utero our body is endowed with literally unlimited regenerative capabilities. However, as we’ll see in these slides, we soon lose that ability after birth. Harnessing the power of perinatal products for the use in regenerative medicine. Here we will introduce Matrix which represents a breakthrough in Exosome Therapeutics.



Medieval

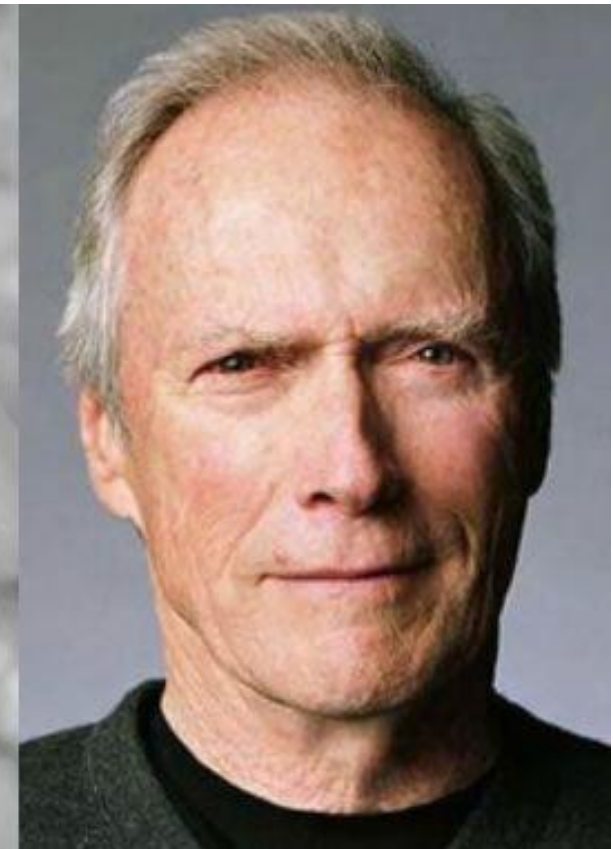
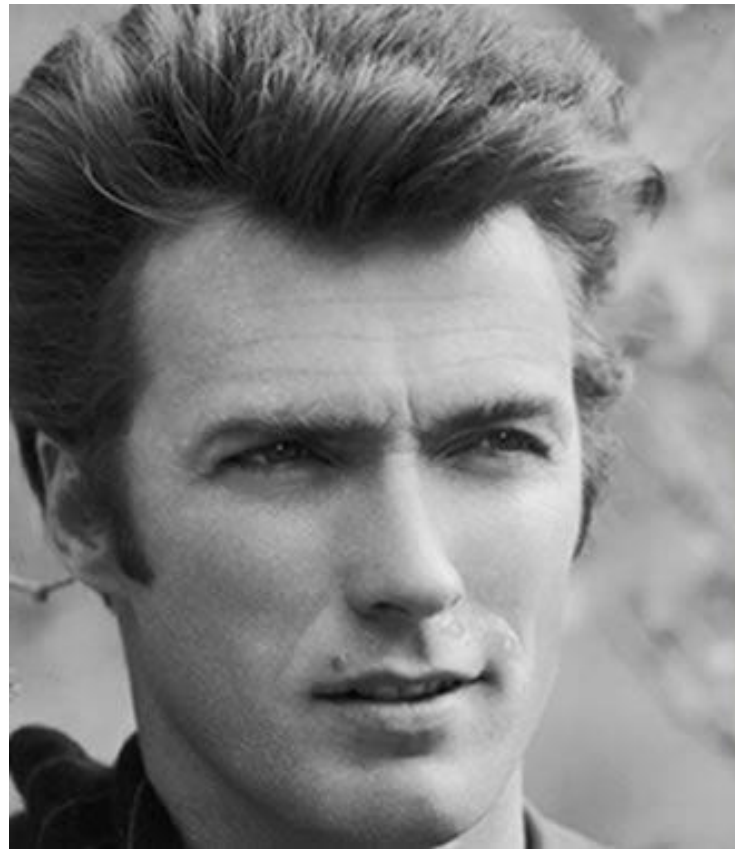


Contemporary

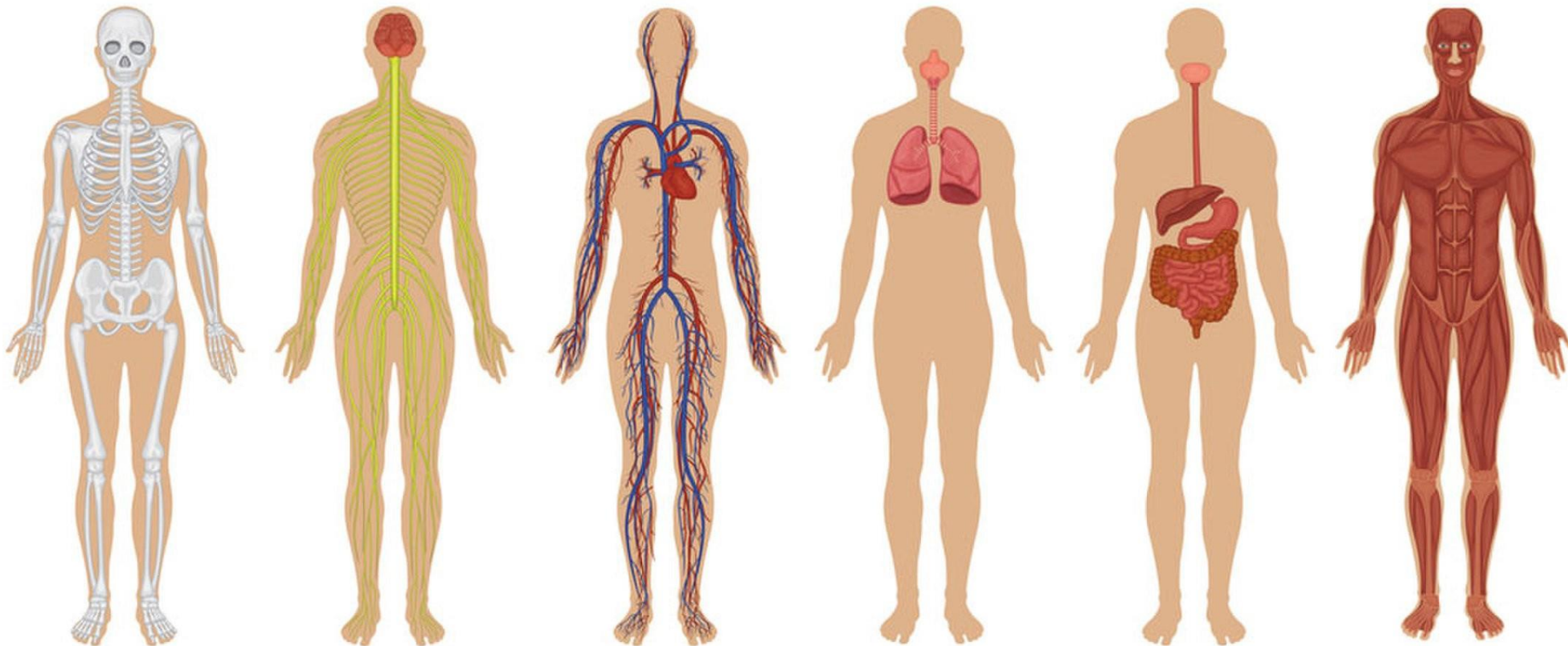


Self Regeneration

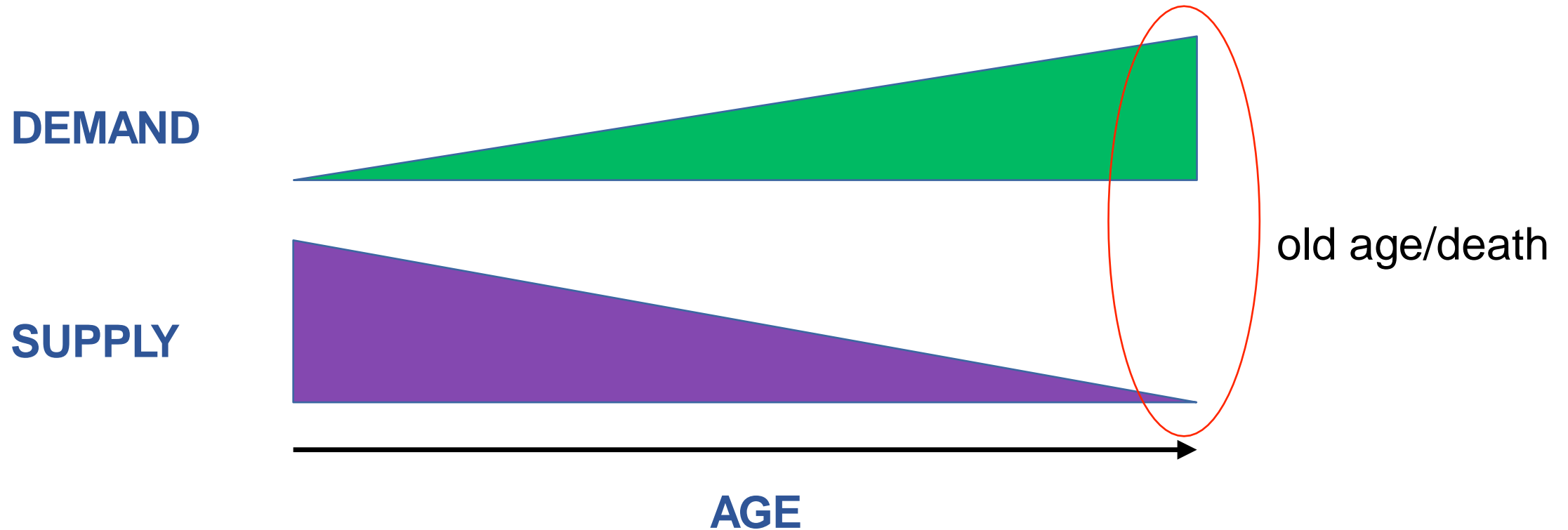
Aging in humans, and other species, is an evolutionally conserved mechanism. What does that mean? Well, as species evolved it was necessary to get rid of those individuals that had been around for a while in order to free up resources for a new generation that might be genetically better suited for changing environments, or to allow for exploration into new environments. There is a built-in mechanism to make individuals “expire”. That mechanism is what we call “aging”. Most of the ailments physicians see are related to inflammation and degeneration as we age. In the beginning (as newborns) we have a HUGE capacity to repair and replace tissues, but over time our cells become weaker creating degeneration. This is what we see and feel as aging.



While we are alive our body is losing, on average, 300 million cells every minute – blood cells, skin cells, brain cells, etc. We'd soon be dead if those cells were not replaced. For the most part these cells are replaced from pools of tissue-specific stem cells that live inside our body. These adult stem cells reside within every tissue of the body and while we're young they are able to keep up with the demand for new cells.



The problem is we have this built in mechanism to “time us out” called “aging”. As we age we develop an issue with supply and demand. Our demand continues, while the whole time (right after birth) we are running out of stem cells. Our supply is dwindling due to telomere shortening and cellular senescence. Basically, each time a stem cell divides to either make a copy of itself or to make cells for new tissue, a part of the chromosomes, called telomeres, is shortened. Once it gets to a certain length the cell can no longer replicate. So we lose stem cells. This is why hair density is lost, skin thins, eyesight fades and tissues take longer and longer to repair.



Biological aging – is endogenous stem cell depletion

A wealth of scientific research has informed us that the fetus demonstrates a 100% capacity to repair injured tissue in utero. This capacity for repair is gradually lost as we age. When we're young our cells are robust and plentiful. We repair relatively fast and to a pretty high degree. If we scrape our knees as kids we typically recover well and with no scarring. Adults take longer to recover and most injuries result in fibrous scars. Our regenerative capacity declines with age, which is why Center for Regenerative Medicine Clinic and "CRM" Laboratory are focused on perinatal products. QCM Clinics provide components to prepare the terrain for pre and post Exosome Therapy. *Regeneration PEMF (resonance based personal daily use) *PDS Personal Detox System *Fermented Ginseng *Ionic Minerals *Structured Water systems



Fetus

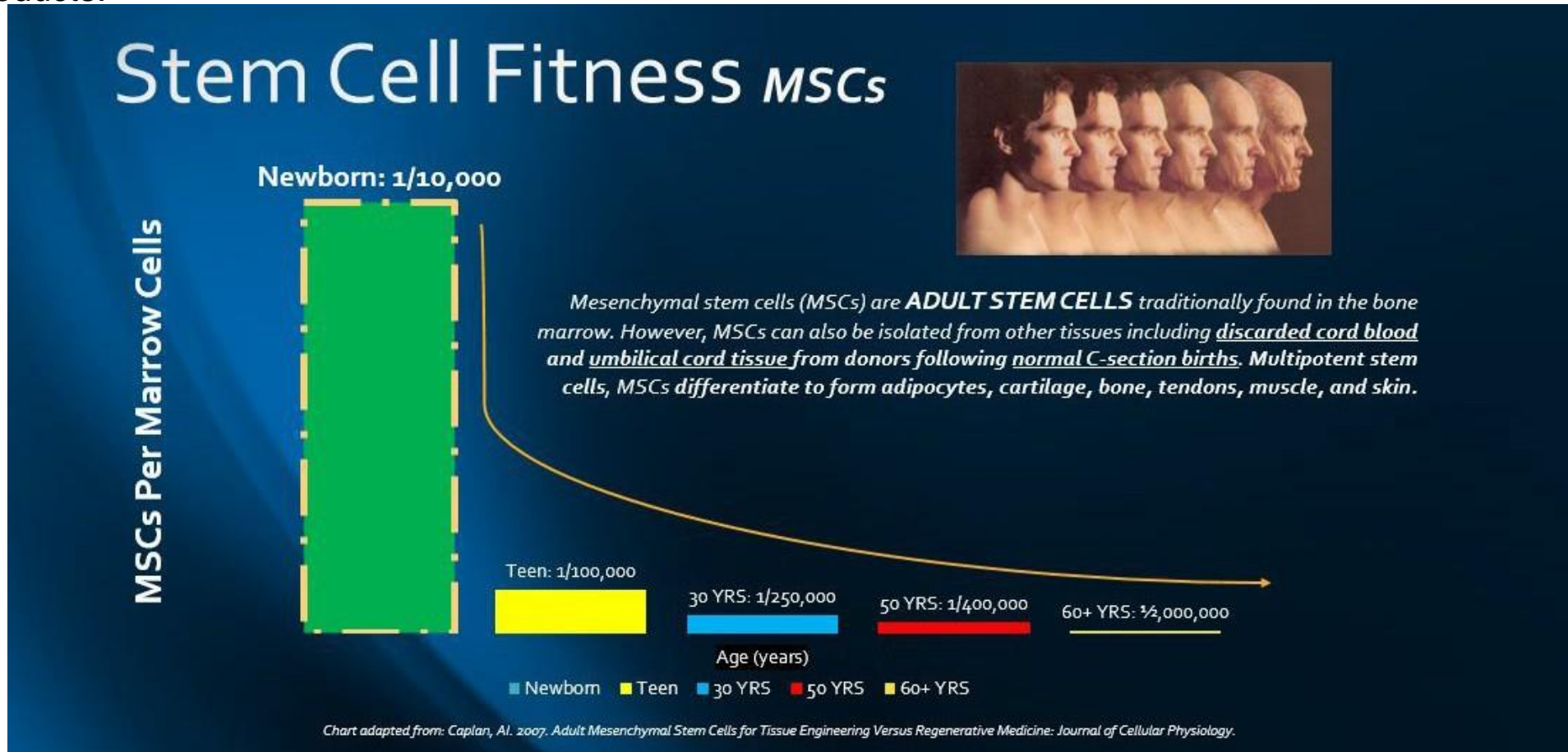
Complete Regeneration



Adult

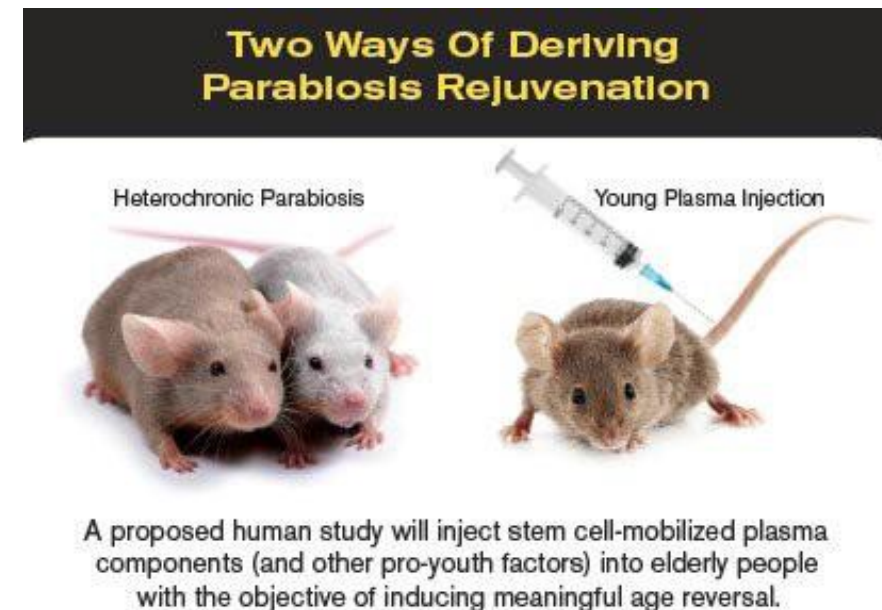
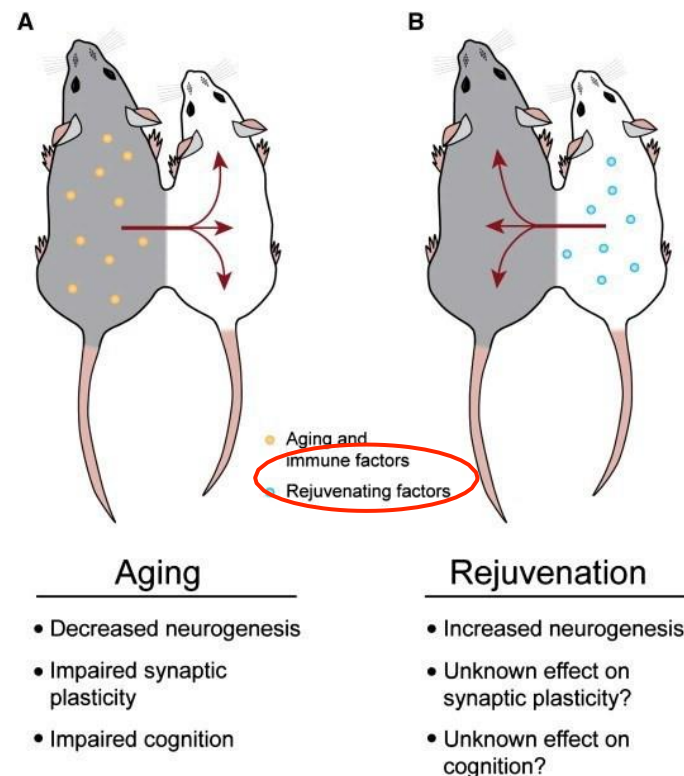
Incomplete Regeneration

This is a figure taken from a publication by Dr. Arnold Caplan (considered the “father of MSCs”). He nicely represents what we know about the regenerative capacity of cells in the body as we age. He is specifically talking about MSCs, but it holds true for all regenerative cells. Right after birth there is a precipitous drop in the “fitness” of MSCs. This means that even if we’re talking about teenage cells, there is a 90% decrease in regenerative capacity compared to newborn cells. Now imagine trying to use 50 yr old bone marrow cells or exosomes for regenerative medicine. Again, this is why CRM Laboratories is committed to producing the highest quality perinatal products.



Parabiosis –taking youth from the young to fix the old

Scientists at Harvard University worked on experiments where they connect the blood supply of an old mouse with that of a young mouse. This is called heterochronic parabiosis (“hetero” – different, “chronic” - time/age, “para” – together, “biosis” – living). They found that something in the blood of the young mouse literally reversed the symptoms of aging in the old mouse. In fact, they found that it was not even necessary to connect the two animals together to see this effect. Simply harvesting plasma from the young mouse and injecting it into the old mouse promoted tissue repair and anti-aging. They called them “rejuvenating factors”. We now know they were referring to extracellular vesicles “EV’s”. Indeed, these EVs are the mechanism by which the “paracrine effect” works when MSCs and other regenerative cytotherapy is given to patients. It’s not the cells of the young individual, it’s the EVs that are responsible for the effect.



Heterochronic parabiosis –pregnancy

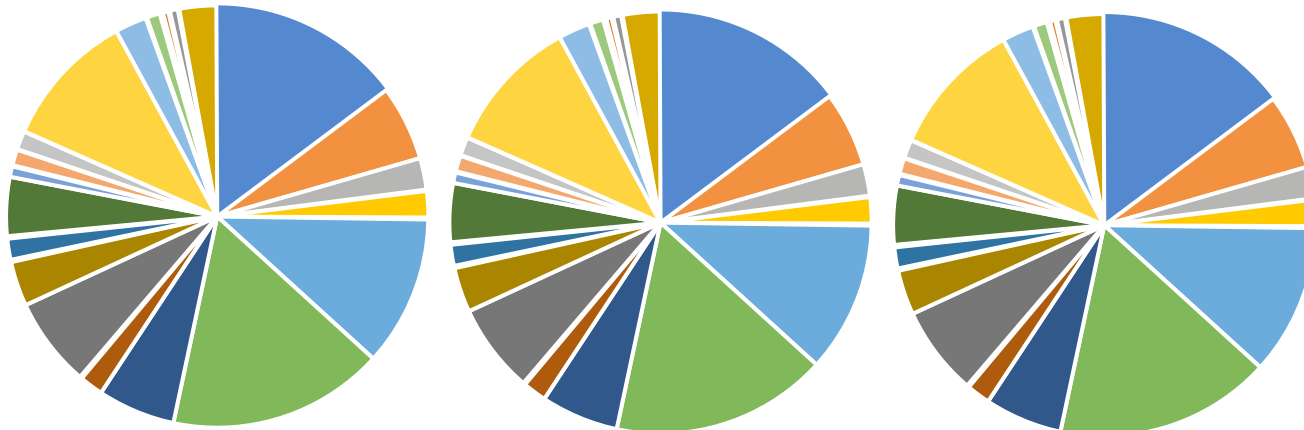
Pregnancy: A natural example of heterochronic parabiosis.

Matrix: Amniotic fluid EVs are the ultimate toolbox for tissue growth and repair and immune modulation.

All of the physiological changes the mother experiences, tissue growth, immune modulation, etc must come from communication with the fetus via Exosomes found in Matrix, .

All the material supplies needed for fetal growth must be delivered within an exquisitely refined inventory via Growth Factors, Chemokines, Hyaluric Acid combined with Exosomes in Matrix.

Unique and specific cargo ratios only seen in natural amniotic fluid filtered and concentrated and sterilized into Matrix



The heart of the third trimester mother is akin to that of an elite swimmer or runner, except, it is racing for three months instead of minutes for Olympians. If a male or non-pregnant woman tried to maintain this level of cardiac output they would die. Exosomes, shared by the fetus, placenta and mother, protect the mother from the stresses and rigors of pregnancy.

Matrix™ Breakthrough in Exosome Therapeutics

Matrix is derived from the amniotic fluid of healthy, full-term, c-section births carefully screened socially and physically tested. The miraculous synergy of Hyaluric Acid, 300+ Growth factors, Chemokines and Cytokines are included with the Exosomes which are the core regenerative Extra Cellular Vesicles "EV's" messengers. They are between 50 -150 nm in size, which is about 100 times smaller than a cell. As such they can pass through the placental barrier and the blood-brain barrier. Unlike exosomes derived from culture-expanded placental MSCs, Matrix is produced by a heterogeneous population of regenerative cells including epithelial cells, endothelial and hematopoietic progenitors and mature leucocytes (white blood cells), etc. However the main content of the Matrix come from the Mesenchymal Stem Cells "MSC" which create exosomes.

They accumulate in the amniotic fluid during pregnancy (a phase of pro-growth and anti-inflammation) creating a regenerative fluid which is advantageous over sole EVs created by culture-expanded cells. The CRM clinic has a foundation of 20 years of experience in regenerative therapy with unchanging passion to improve patient outcomes. This gave birth to the research and development in the last 3 years working with patients to develop Matrix and Alocyte. Matrix represents a breakthrough in Exosome therapeutics.

Far more powerful than any other Exosome product in the market. Matrix has several trillion exosomes per cc. This is far more exosomes per cc measured by third party testing.

Less Expensive per treatment Matrix is sterilized by CRM's own proprietary methodology prior to Cryo freezing. Because Matrix is sterilized, a time period is available after thawing allowing for reconstitution with saline or PRP for expanded use.

Matrix™ Breakthrough in Exosome Therapeutics

Far more powerful than any other Exosome product in the market. Matrix has more exosomes per cc measured by third party testing. Through a proprietary method of carefully putting pressure on the Mesenchymal Stem Cells in the Amniotic fluid Matrix achieves this high yield. When compared to main Exosome products it has **5 to 10 times more** Exosomes per cc.

A vial of Matrix is 1.5 cc. It is guaranteed to contain several trillion EVs in each vial. The laboratory retains full compliance to advanced cGMP guidelines and send batches out for 3rd party testing according to FDA guidelines. In the most recent 3rd party testing Matrix batches showed over 6 trillion exosomes in the 1.5cc vial. This is a concentration of 4 trillion Exosomes per cc represents 5 times more than the closest competitive Exosome product and over 10 times more exosomes than most of the market.

Less Expensive per treatment. Matrix is sterilized by CRM's own proprietary methodology. With other Exosome products, you must take care to retain sterility by flash cryo freezing in processing. Therefore, upon thawing they must be extracted into a syringe and injected immediately. If there is a delay then the product must be discarded. Because Matrix is sterilized prior to Cryo freezing, there is a time period available after thawing. This allows for reconstitution with saline or PRP for expanded use allowing for multiple injections. This allows the clinic to perform multiple treatments (2 to 5) per vial which brings the cost way below other products in the market.

Manufactured at the quality standards

All manufacturing is performed by qualified, trained scientists under GMP conditions, within pristine clean rooms. Sterility is tested by independent third party labs.



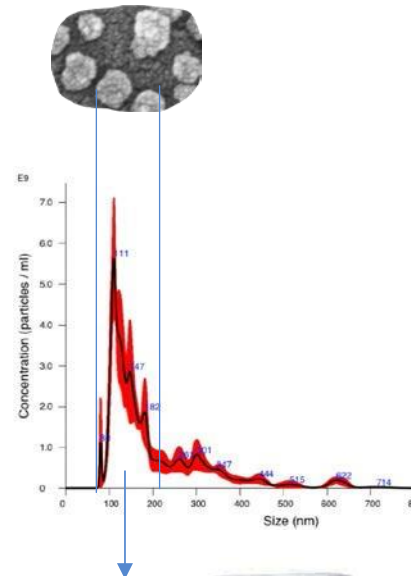
The raw amniotic fluid is collected by FDA-approved and AABB accredited cord-blood banks within the USA and shipped overnight to our labs. Mothers are consented and tested for infectious diseases and other exclusion criteria at the time of normal full term pregnancy in situation of planned delivery by C-section.



Centrifuged



Filtered

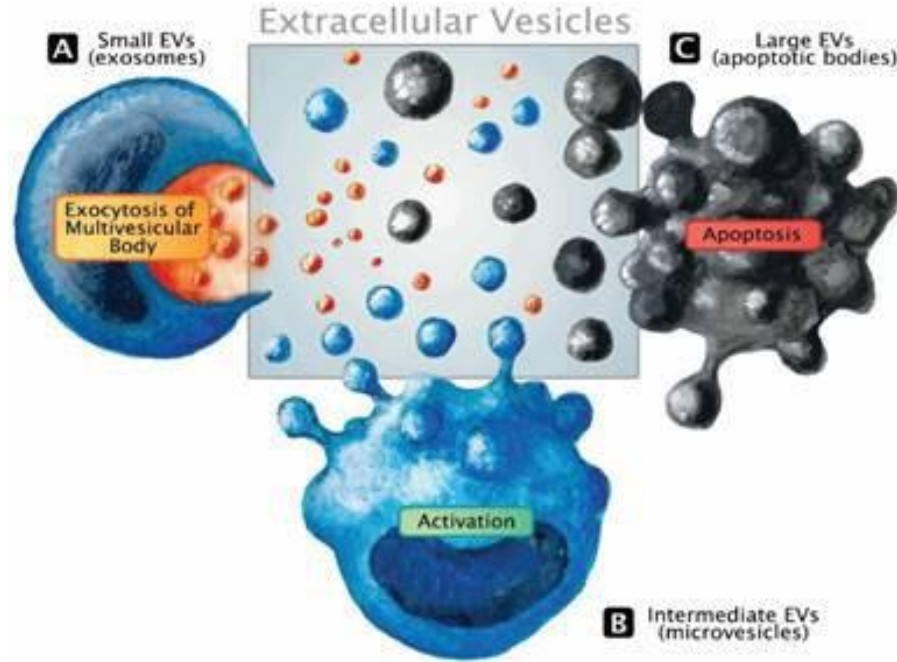


Using proprietary techniques, requiring minimal manipulation of the material, raw amniotic fluid is transformed into Matrix™. The vials are quarantined for 14 days while lots are tested by independent labs for sterility and endotoxin. We have a 100% clean record over the 3 years that our scientists have been producing Matrix™.

Vials are shipped on dry ice within tamper-proof insulated shippers, together with product details and a certificate of analysis, which includes EV count, size and testing results. Upon delivery the vials should be stored between -20 and -80 degrees. The cryovials should never be submerged in the liquid phase of liquid nitrogen.



The difference between Matrix™ and alternative



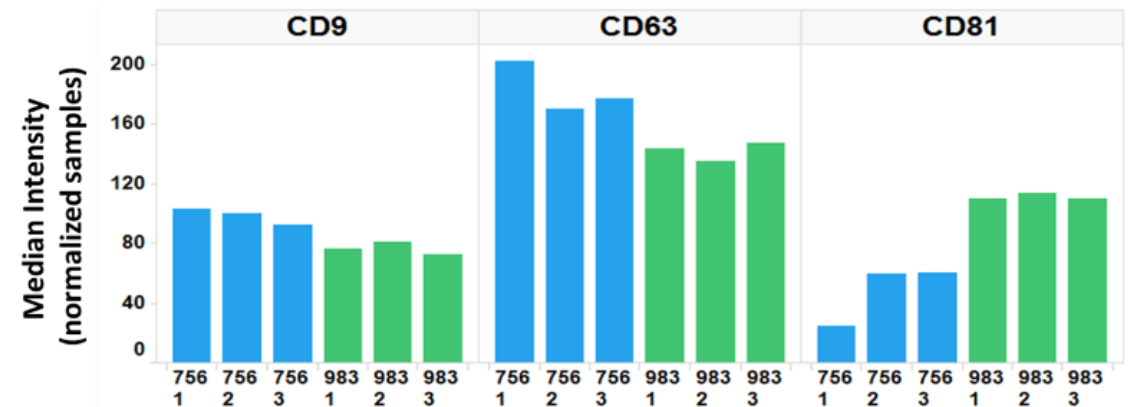
Not all extracellular vesicles are exosomes

Exosomes are between 50-150 nm and require a specific profile. Larger EVs are non-regenerative microvesicles and “apoptotic bodies” produced by dying cells. We use a propriety method for removing micronized material. Then we apply our proprietary sterilization process which no other laboratory has. The retain EVs need to have a balanced profile of surface proteins CD9, CD63 and CD81.

In the most recent 3rd Party testing Matrix showed over 6 trillion exosomes per 1.5ml.

Center for Regenerative Medicine Laboratories ZetaView Analysis

Sample	Particle Diameter (nm)		Concentration (particles/mL)
	Mean	Mode	
ALOCYTE_Vial1_ab2040756_062520B	112.8	72.5	6.30E+12
ALOCYTE_Vial2_ab2040756_062520B	104.2	77.5	5.40E+12
ALOCYTE_Vial3_ab2040756_062520B	112.9	87.5	4.40E+12
MATRIX_Vial1_ab2040983_06302020	134.2	92.5	6.30E+12
MATRIX_Vial2_ab2040983_06302020	133.9	92.5	6.10E+12
MATRIX_Vial3_ab2040983_06302020	137.1	87.5	7.00E+12



Amnio Matrix is derived from human amniotic fluid donated from consenting adults during routine, planned cesarean sections under IRB approved donor screening. Donor qualification was performed under FDA CFR 1271. Donor qualification was certified following the review of the mother's medical history, social history, physical examination, and raw product recovery information.

Relevant communicable disease testing was completed, and the mother was reported to have negative/non-reactive results for:

- CMV total Ab,
- Hepatitis B core total Ab,
- Hepatitis B surface Ag,
- Hepatitis C virus Ab,
- HIV-1/HIV-2 Plus O,
- HTLV I/II Ab,
- Syphilis screening—non-treponemal
- Treponema pallidum.
- Ultrio Elite HBV,
- Ultrio Elite HCV,
- Ultrio Eliter HIV-1/2,
- WNV

The collected amniotic fluid is subjected to centrifugation and proprietary filtration to remove large particle debris and preserve the natural protein, nanoparticle, and exosome composition of amniotic fluid. The final product is after meeting the release criteria requirements. The specific release criteria parameters for the product administered in these treatments are:

- sterility (14-day cultures: no growth for aerobic, anaerobic, and fungal contamination),
- Proprietary flash ultra violet sterilization
- endotoxin (<0.05 EU/mL)
- nanoparticle composition size,
- protein concentration,
- hyaluronic acid concentration.

The product is stored frozen and shipped on dry ice to the treatment location following validated storage and shipping methods.



CERTIFICATE OF ANALYSIS

PRODUCT: Exosomes
CATALOG NUMBER: CA-09
STORAGE: -80°C
LOT NUMBER: see tables below
LOT COMPOSITION: Number of donor(s) : NA
Passage number : NA

Copy of Third Party Certificate of Analysis

Zen-Bio Inc,
Research Triangle Park, North Carolina
(919) 547-0692
information@zen-bio.com

DESCRIPTION

Exosomes arrived frozen in 1mL aliquots

QUALITY CONTROL

- Exosome quality was be assessed using a Thermo NanoDrop spectrophotometer for protein determination and approximate RNA concentration by direct absorbance; **exosomes were not be lysed, stained, or RNA extracted prior to taking these measurements.**
- Particle diameter and concentration was be assessed by Nanoparticle Tracking Analysis (NTA) using a Particle Metrix ZetaView®.

Sample	Protein mg/mL	RNA ng/uL	A260/280	A260/230
ALOCYTE_Vial1_ab2040756_062520B	19.6	612	0.79	0.19
ALOCYTE_Vial2_ab2040756_062520B	19.38	621.1	0.79	0.2
ALOCYTE_Vial3_ab2040756_062520B	19.83	608.8	0.78	0.19
MATRIX_Vial1_ab2040983_06302020	6.31	183.5	0.79	0.3
MATRIX_Vial2_ab2040983_06302020	6.26	182.1	0.78	0.39
MATRIX_Vial3_ab2040983_06302020	6.61	192.1	0.8	0.38

Sample	Diameter Mean (nM)	Diameter Mode (nM)	Concentration (particles/mL)
ALOCYTE_Vial1_ab2040756_062520B	112.8	72.5	6.30E+12
ALOCYTE_Vial2_ab2040756_062520B	104.2	77.5	5.40E+12
ALOCYTE_Vial3_ab2040756_062520B	112.9	87.5	4.40E+12
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MATRIX_Vial2_ab2040983_06302020	133.9	92.5	6.10E+12
MATRIX_Vial3_ab2040983_06302020	137.1	87.5	7.00E+12

Precautionary Notes: This product is for research only. It is not intended for human, veterinary or in vitro diagnostic use.
Limited Product Warranty This warranty limits our liability to replacement of this product. No other warranties of any kind, express or implied, including without limitation, warranties of merchantability or fitness for a particular purpose, are provided by Zen-Bio, Inc. Zen-Bio shall have no liability for any direct, indirect, consequential or incidental damages arising out of the use, the results of use, or the inability to use this product.

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<http://www.zen-bio.com> • e-mail: information@zen-bio.com

	Particle Diameter (nm)		Concentration
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Copy of Third Party Certificate of Analysis

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**Size and surface proteins analysis are critical
to verify Exosomes are being measured.**

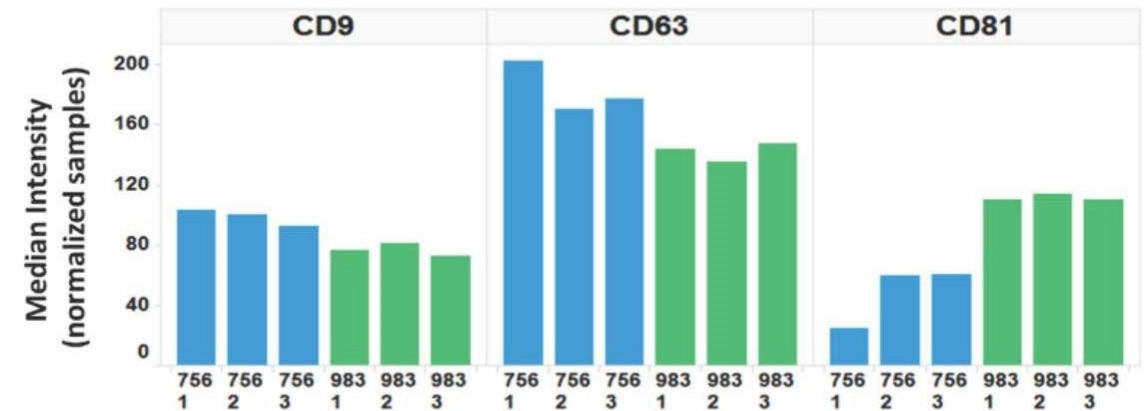
Zen-Bio Inc Conclusion:
“These are Exosomes”

Results:

- Two lots (ALOCYTE and MATRIX) were analyzed for surface proteins (Vial 1, Vial 2, Vial 3)
- While the mean and mode sizes of the particles between the two lots show variation, there is consistency within each lot for the triplicate samples
- Particle size for all samples is the size expected for exosomes
- Similar, particle concentration within each lot is consistent

Conclusion:

- Manufacturing process is robust
- Large quantities of particles are obtained (trillions)



Results:

- Two lots (ALOCYTE 756 and MATRIX 983) were analyzed for surface proteins CD9, CD63 and CD81, in triplicate (Vial 1, Vial 2, Vial 3)
- While the relative amounts of CD39, CD53, and CD81 between the two lots show variation, there is consistency within each lot for the triplicate samples

Conclusion:

- Particles obtained from the two lots are indeed exosomes.

Representative sample of Published Papers by CRM Director of Operations Darcy DiFede DL.

Allogeneic Mesenchymal Stem Cells Ameliorate Aging Frailty: A Phase II Randomized, Double-Blind, Placebo-Controlled Clinical Trial.

J.Gerontol A Biol Sci Med Sci. 72(11):1513-1522. Tompkins BA, **DiFede DL**, ... Goldschmidt-Clermont PJ, et al. (2017)

Allogeneic Human Mesenchymal Stem Cell Infusions for Aging Frailty. Golpanian S, **DiFede DL**, ... Goldschmidt-Clermont PJ, et al. (2017) *J Gerontol A Biol Sci Med Sci. Placebo-Controlled Clinical Trial. J Gerontol A Biol Sci Med Sci.* 72(11):1513-1522.

Transendocardial Mesenchymal Stem Cells and Mononuclear Bone Marrow Cells for Ischemic Cardiomyopathy: The TAC-HFT Randomized Trial. Heldman AW, **DiFede DL**, Fishman JE, et al. *JAMA.* 2014;311(1):62-73. doi:10.1001/jama.2013.282909.

Amniotic Exosomes and Pregnancy” Goldschmidt-Clermont PJ, **DiFede DL**, White IA. (2019) e-Letter:“. *Science Translational Medicine.* <https://stm.sciencemag.org/content>.

Clinical and Neurophysiological Changes after Targeted Intrathecal Injections of Bone Marrow Stem Cells in C3 Te.traplegic Subject Santamaria**DiFede DL**, Khan A, Pujol MV, Dietrich WD, Marttos A, Green BA, Hare JM, Guest JD. *J Neurotrauma.* 2019 Feb 1;36(3):500-516. Doi:10.1089/neu.2018.5716.Epub 2018 Jul 23.

Effects of Transendocardial Stem Cell Injection on Ventricular Proarrhythmia in Patients with Ischemic Cardiomyopathy: Results from the POSEIDON and TAC-HFT Trials Ramireddy A, Brodt CR, Mendizabal AM, **DiFede DL**, Healy C, Goyal V, Alansari Y, Coffey JO, Viles-Gonzalez JF, Heldman AW, Goldberger JJ, Myerburg RJ, Hare JM, Mitrani RD. Effects of Transendocardial Stem Cell Injection on Ventricular Proarrhythmia in Patients with Ischemic Cardiomyopathy: Results from the POSEIDON and TAC-HFT Trials. *Stem Cells Transl Med.* 2017 Mar 2. doi: 10.1002/sctm.16-0328. [Epub ahead of print]

Advancing the Field of Regenerative Medicine. **Darcy L. DiFede** (2013) Advancing the Field of Regenerative Medicine. *J Cardio Vasc Med* 1:1.

Use of stem cells for ischemic cardiomyopathy--reply Hare JM, **Difede D**, Heldman AW. . *JAMA.* 2013 Apr 10;309(14):1458-9. doi: 10.1001/jama.2013.2893. PubMed PMID: 23571573

Question and Answers

Go to www.calendly.com/QCM

Make an appointment to discuss your questions and receive advice on optimizing your wellness and vibrant life extension.

Go to www.QCMedicine.com

for videos and technology available at QCM Clinics