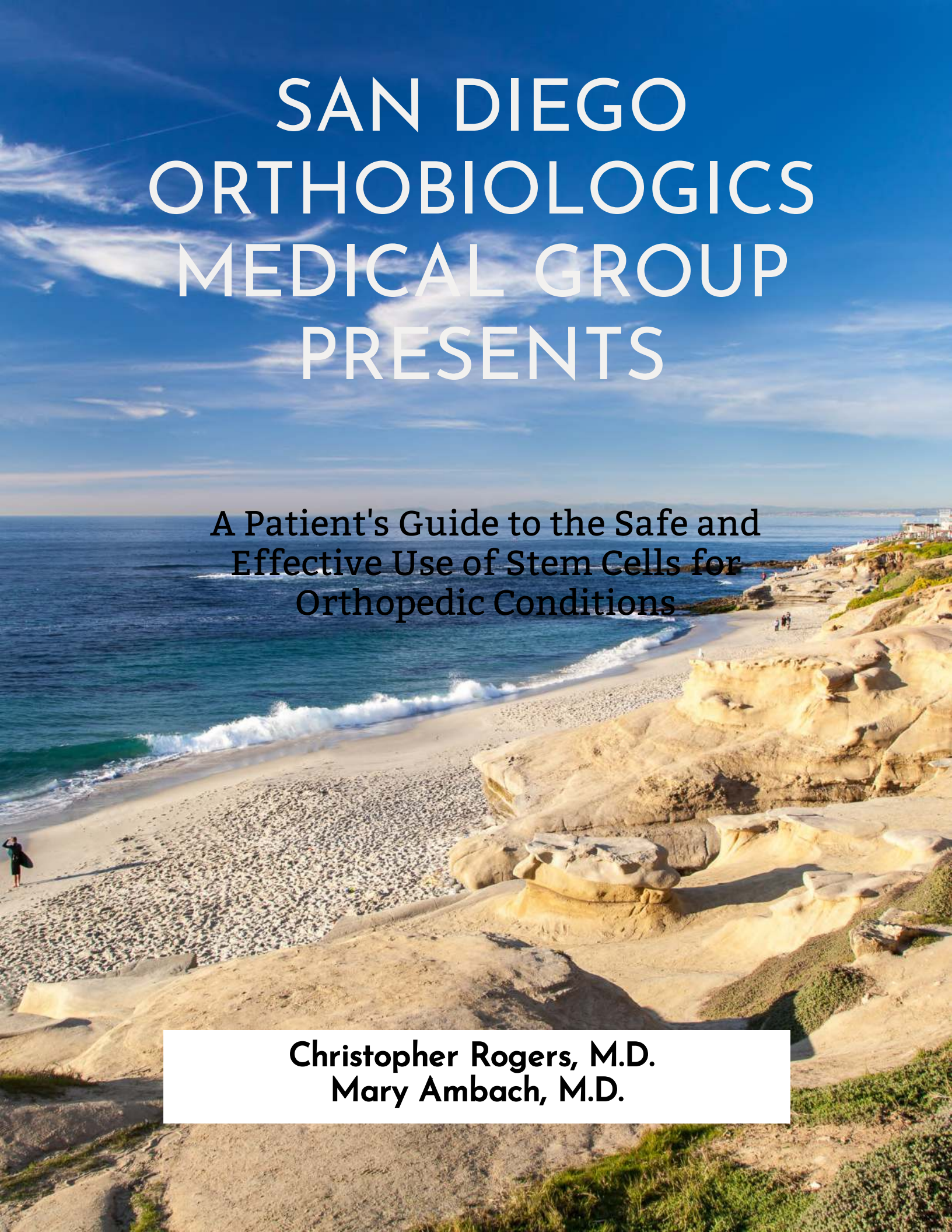

SAN DIEGO ORTHOBIOLOGICS MEDICAL GROUP PRESENTS

A Patient's Guide to the Safe and Effective Use of Stem Cells for Orthopedic Conditions

Christopher Rogers, M.D.
Mary Ambach, M.D.

STEM CELLS FOR ORTHOPEDIC CONDITIONS

Everyone is excited about the promise that stem cell treatments offer for many untreatable medical conditions. However, most stem cell therapies are only in the early investigational stages. Significant advances have been made in the fields of cellular biology, genetics, immunology and tissue engineering. Yet, complete understanding of the safety and efficacy of stem cell therapies in orthopedics will take many more years.

In the meantime, several clinics offer cell-based therapies to their patients before important safety and efficacy studies have been completed. The level of physician training and the type of stem cell products they use varies widely from one clinic to another across the country.

> *We believe that it is important for physicians and their patients to understand the difference between evidence-based cell therapies and unproven "stem cell" therapies.*

WHAT IS A STEM CELL?

Stem cells are part of the body's repair kit and play an important role in healing. They have the unique ability to self renew and differentiate into other cell types such as bone, cartilage, tendon or muscle. In the body, stem cells have many additional abilities essential to healing including decreasing inflammation, improving blood flow and regenerating injured tissues.

WHERE ARE STEM CELLS FOUND?

Stem cells are found in every tissue in the body. Common sources of stem cells used for cell based therapies include bone marrow and minimally processed adipose (fat) tissue. These tissues are known to contain live stem cells, however since they contain a heterogenous mixture of cells, it is difficult to accurately determine the number of stem cells at the time of treatment without special cell counting equipment.

Adult stem cells are found among differentiated cells in tissues and can generate different cell types for the specific tissue in which they live. In 1988, a unique population of adult stem cells, the mesenchymal stem cell (MSC), was discovered to have an active role in connective tissue repair and possessed the capacity to differentiate into bone, cartilage and tendon cells.

WHAT ARE STEM CELLS USED FOR IN ORTHOPEDICS?

Stem cells can be used to treat chronic injuries that require assistance to heal completely. The use of cell based therapy for several orthopedic conditions has been described in the published medical literature. Bone marrow and adipose tissues have been used as a cell source in Regenerative Medicine for more than 20 years. The safety and efficacy for specific orthopedic conditions is well established. Several high quality clinical trials exist for bone marrow-derived cell therapies and adipose-derived cell therapies for knee and other joint osteoarthritis, non-healing fractures, tendinopathy, tendon tears, partial ligament tears, bone injuries and lumbar disc degeneration.

WHAT ARE ALLOGENEIC STEM CELL THERAPIES?

Allogeneic therapies use cells or cell products that are obtained from another person. Common examples of these donor tissues include birth waste tissues such as umbilical cord blood, umbilical cord tissue (e.g. Wharton's jelly), amniotic tissue, placenta and exosomes.

WHAT ARE EXOSOMES?

Exosomes are extracellular vesicles that facilitate cell to cell communication. They may contain proteins, messenger RNA, micro RNA and DNA. They are manufactured from stem cells that were grown in a lab. There is evidence that they may have therapeutic benefits, however evidence for their safety and efficacy in orthopedic conditions does not exist.

ARE ALLOGENEIC STEM CELL THERAPIES SAFE?

In January 2019, the Center for Disease Control and Prevention (CDC) identified more than a dozen patients who were treated for bacterial infections after receiving umbilical cord blood injections that were manufactured by Genetech and distributed by Liveyon. Read more about this risk.

There is some evidence that these products, obtained from donor tissues, may also induce changes in a patient's immune system. Whether or not these changes impact patient health has yet to been determined. Until proper scientific studies confirm the safety of umbilical cord blood, amniotic tissue, exosomes and other donor tissues, it's best to avoid them.

Helpful Links:

Stem Cell Treatment Side Effects: IV Umbilical Cord Risks

Immunoprivileged no more: measuring the immunogenicity of allogeneic adult mesenchymal stem cells

Mesenchymal stem cells: immune evasive, not immune privileged

Repeated intra-articular injection of allogeneic mesenchymal stem cells causes an adverse response compared to autologous cells in the equine model

ARE UMBILICAL CORD BLOOD, AMNIOTIC TISSUE CELLS AND EXOSOMES EFFECTIVE?

Some clinics promote the use of these products for the treatment of many different medical conditions or make unproven claims about their safety and efficacy. At this time, there are no studies for the safety or efficacy for the products sold at these clinics. Recent evidence suggests that amniotic fluid and umbilical cord blood products do not even contain any living stem cells at all.

Helpful Links:

New Data on Amniotic and Cord Stem Cell Products: This Is a Scam By Chris Centeno, MD

Are Amniotic Fluid Products Stem Cell Therapies?

Proteomic analysis and cell viability of nine amnion-derived biologics

> *We advise patients and physicians to avoid the use of non-US FDA compliant birth tissue products, such as umbilical cord blood or exosomes, until adequate studies of safety and efficacy have been documented.*

ARE STEM CELL THERAPIES REGULATED BY THE FDA?

The U.S. Food and Drug Administration (FDA) is responsible for the evaluation of drug and biologic product safety. The FDA regulates the use of stem cells as Human Cells, Tissues, and Cellular and Tissue Based Products (HCT/Ps) under CFR Title 21 Part 1271. FDA Industry Regulation Guidance.

Therapies that use a patient's own bone marrow or minimally manipulated adipose tissue for homologous use are compliant with current FDA regulatory guidelines. FDA Industry Regulation Guidance.

Stem cell based products that do not satisfy specific FDA guidelines are regulated under Section 351 as a biological drug. These products require FDA approved clinical trials to confirm safety and efficacy. Products that contain umbilical cord blood, amniotic tissue cells or exosomes require FDA approval of a Biologics License Application (BLA) before they are allowed to be marketed to patients. At this time, such products are not FDA approved.

ARE SOME STEM CELL THERAPIES FDA APPROVED?

Yes, but only for blood related diseases such as leukemia. There are no FDA approved stem cell therapies for orthopedic conditions, autoimmune conditions, neurodegenerative conditions, anti-aging benefits and many other medical conditions.

The FDA will only approve a drug or biologic product after multiple clinical trials have been performed that demonstrate safety and efficacy. The FDA will give approval for a Biological License Application (BLA) that permits the manufacturer of the product to market to the public.

Marketing claims about a product's ability to treat, cure, alleviate symptoms or prevent diseases is simply not permitted by law without FDA approval.

> *Currently there are no FDA approved products that contain umbilical cord blood, amniotic fluid or exosomes. Patients may not use these products unless they are part of an FDA approved clinical trial.*

WHICH CELL BASED THERAPIES ARE ALLOWED BY THE FDA?

At this time, only platelet rich plasma (PRP), bone marrow derived cells and adipose tissue derived cells (that are not processed with enzymes) are compliant with FDA guidelines.

Below is a short list of clinical trials that have used bone marrow or adipose tissue for the treatment of orthopedic conditions.

Helpful Links:

Bone Marrow Aspirate Concentrate Clinical Studies:

A specifc protocol of autologous bone marrow concentrate and platelet products versus exercise therapy for symptomatic knee osteoarthritis

Increased knee cartilage volume in degenerative joint disease using percutaneously implanted, autologous mesenchymal stem cells

Clinical application of concentrated bone marrow aspirate in orthopaedics

A Prospective, Single-Blind, Placebo-Controlled Trial of Bone Marrow Aspirate Concentrate for Knee Osteoarthritis

Bone Marrow Cellular Therapies: Novel Therapy for Knee Osteoarthritis

The Role of Bone Marrow Aspirate Concentrate for the Treatment of Focal Chondral Lesions of the Knee

Minimally Processed Adipose Tissue Clinical Studies:

Early results of intra-articular micro-fragmented lipoaspirate treatment in patients with late stages knee osteoarthritis

Safety and Efficacy of Percutaneous Injection of Lipogems Micro-Fractured Adipose Tissue for Osteoarthritic Knees

Microfragmented adipose injections in the treatment of knee osteoarthritis

Autologous and micro-fragmented adipose tissue for the treatment of diffuse degenerative knee osteoarthritis

Micro-fragmented adipose tissue injection associated with arthroscopic procedures in patients with symptomatic knee osteoarthritis

Mesenchymal Stem Cells injection in hip osteoarthritis: preliminary results

More published scientific studies for orthopedic applications can be found at www.sdomg.com/fat and www.sdomg.com/bma.

All other cell based therapies (umbilical cord blood, amniotic tissue, placenta and exosomes) are FDA non-compliant drugs. There is insufficient scientific evidence to support any unproven marketing claims and until studies are conducted physicians are not permitted to sell them. How to choose a legitimate stem cell clinic.

IS THERE A DIFFERENCE BETWEEN AN FDA REGISTERED PRODUCT AND AN FDA APPROVED PRODUCT?

Yes. A product is not **FDA approved** until it undergoes rigorous evaluation with multiple clinical trials. Phase I clinical trials evaluate the safety of the product, while Phase II and III studies evaluate efficacy. This process can take several years.

FDA registered products do not undergo this level of evaluation. The manufacturer is simply required to complete a short form stating that their product satisfies the exceptions to the FDA approval process. Several manufacturers make false claims about their FDA registered product. For example, they may report to the FDA that their product does not contain live stem cells, but then advertise them as a stem cell product to the public.

DOES THIS PRODUCT REALLY CONTAIN ANY STEM CELLS ?

> *Just because a product is registered with the FDA does not mean it contains stem cells or is FDA approved.*

To learn if a specific product contains live stem cells, visit the FDA's Public Query website.

Enter the registered product name (establishment) on the FDA website. If the "HCT/P described in 21 CFR1271.10" box is checked, it means the manufacturer has claimed to the FDA that their product does not contain any live stem cells.

QUESTIONS FOR YOUR PHYSICIAN WHEN CONSIDERING STEM CELL THERAPIES

We recommend that patients do their research before consenting to an investigational medical procedure that may not have sufficient scientific evidence to support its use. We recommend that you ask your physician these questions to determine if a treatment is right for you.

1. What medical training have you completed?

Ask your doctor if they are board certified in the medical specialty that treats your condition.

> *Patients with joint pain, spine pain, arthritis or tendon injuries require a doctor who has training in the diagnosis and treatment of orthopedic conditions.*

Typically, such physicians are board certified in Physical Medicine and Rehabilitation, Sports Medicine, Rheumatology, Anesthesiology, Radiology or Orthopedic Surgery. They may have advanced fellowship training in Regenerative Medicine, Sports Medicine or Pain Management.

Naturopathic doctors, physician assistants, chiropractors and nurse practitioners do not have the adequate training required to inject patients with cell based therapy. In most states, they are not allowed to perform any kind of injection, including stem cell or exosome injections.

Your doctor should also have advanced training in musculoskeletal ultrasound and x-ray guided injections. These are required to offer comfortable, effective and safe treatments. Finally, your physician should have the necessary training to manage any complications that may occur during your procedure.

2. What Regenerative Medicine training have you completed?

Medical schools and residency programs do not offer Regenerative Medicine training. Ask your doctor how they received their Regenerative Medicine education and skills. Well trained physicians will have completed a Regenerative Medicine fellowship or are board certified in Regenerative Medicine. They may train other physicians in fellowship programs or lecture at national medical conferences. Alternatively, they may obtain their comprehensive training with field experts and respectable institutions.

3. What "stem cell" source do you use?

The only cell based therapies that are allowed by the FDA at this time are platelet rich plasma (PRP), bone marrow derived cells and adipose tissue derived cells (that are not processed with enzymes). Avoid clinics that make unproven claims or use products that are not FDA compliant such as umbilical cord blood or exosomes.

4. Do you track clinical outcomes in a patient registry?

Responsible physicians track their patient outcomes in a registry and conduct follow-up care after treatment for up to one year or longer. There are several HIPAA compliant patient data registries, so there is no excuse to not use one.

5. Do you publish your outcomes or present data at national medical conferences?

Responsible physicians participate in physician education and conduct clinical research to advance the field of Regenerative Medicine. They publish their results in peer-reviewed medical journals or medical textbooks.

6. How do you justify the cost of your treatment?

Physicians should not overcharge patients for cell based treatments.

Well trained physicians who harvest bone marrow or adipose tissues for their regenerative medicine treatments can assure patient comfort, safety and efficacy. If they can support these claims with peer-reviewed published data or an IRB approved patient registry, then the cost of treatment may be warranted. Here's how to choose a legitimate stem cell clinic.

7. Do you offer informed consent?

Physicians must discuss the risks and benefits of all treatment options prior to performing any medical procedure. The patient will sign a consent form to acknowledge their understanding of these risks and benefits.

8. Do you use products that are not permitted by the FDA?

At this time, umbilical cord blood, amniotic tissue, placenta and exosomes are not permitted for use by the FDA (unless part of an FDA approved clinical trial). Adipose tissue that has been processed with enzymes is also not permitted (again, unless part of an FDA approved clinical trial).

The FDA has posted public safety warnings and filed injunctions against clinics that use these products outside of an FDA approved clinical trial.

Helpful Links:

FDA Warns About Stem Cell Therapies

Public Safety Notification on Exosome Products

FDA sends warning to companies for offering unapproved umbilical cord blood products that may put patients at risk

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WHERE CAN I FILE A COMPLAINT ABOUT A HEALTHCARE PROVIDER OR PRODUCT MANUFACTURER WHO IS NOT IN COMPLIANCE WITH THE LAW?

Reporting a doctor for unprofessional conduct

Contact a state medical board.

In California:

Medical Board of California Complaint Form

REPORT CHIROPRACTORS TO THE BOARD OF CHIROPRACTIC EXAMINERS

Contact the Board of Chiropractic Examiners in your state.

In California:

Board of Chiropractic Examiners Complaint Form

REPORT NATUROPATHIC DOCTORS TO THE MEDICAL BOARD

In California:

Naturopathic Medicine Committee Complaint Form

REPORT MANUFACTURERS TO THE FOOD AND DRUG ADMINISTRATION (FDA)

MedWatch Online Voluntary Reporting Form

REPORT AN ADVERSE EVENT FROM A STEM CELL TREATMENT TO THE FDA

FDA Adverse Event Reporting System

MedWatch Consumer Voluntary Reporting

REPORT FRAUD TO THE FEDERAL TRADE COMMISSION

In California:

Submit a Consumer Complaint to the FTC

Or mail to:

Federal Trade Commission / CRC
600 Pennsylvania Avenue NW
Washington DC 20580

THE BEST WAY TO PROTECT YOURSELF IS TO STAY INFORMED

Helpful Links:

Regulatory Considerations for Human Cells, Tissues, and Cellular and TissueBased Products: FDA Guidance

Nine Things To Know About Stem Cell Treatments

Avoid the Stem Cell Scam: A Patient Speaks Out

The Niche: Patients guide to treatments

Stem Cell Basics: Cells in the human body

WE HOPE THIS INFORMATION IS HELPFUL TO YOU!

THE AUTHORS

Christopher J. Rogers M.D.

Board certified, American Board of Physical Medicine and Rehabilitation

Mary A. Ambach M.D.

Board certified, American Board of Physical Medicine and Rehabilitation
Board certified, American Board of Pain Medicine

San Diego Orthobiologics Medical Group, Inc.

6125 Paseo Del Norte, Suite 100
Carlsbad, CA 92011
760-909-2355

If you have any questions, please contact us at:

Email: admin@SDOMG.com
Website: https://sdomg.com
YouTube: https://www.youtube.com/channel/UC2EZ1dbU-WZQM-Dk24fpA_A
Facebook: https://www.facebook.com/SanDiegoOrthobiologics/